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“Excuse me, what does it mean?”

A socio-linguistic analysis of patient information
leaflets in doctor-patient interactions.

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Table of Contents

Introduction.....	3
Chapter one: medical language throughout history.....	7
1.1 Historical overview.....	7
1.1.1 Greek-Latin terminological core	9
1.1.2 National medical languages	10
1.1.2.1 English influence on Italian medical language	14
1.2 "Remedia curant morbum non verba"	17
Chapter two: linguistic features of English for Medical Purposes (EMP)	23
2.1 Lexical Features	23
2.1.1 Metaphors.....	26
2.2 Syntactic Features	39
Chapter three: patients and the language of medicine	45
3.1 Doctor-patient interactions.....	46
3.2 Changing dynamics in doctor-patient relationship	55
3.3 Survey: doctor-patient relationship in Lusiana	63
Chapter four: analysis of Patient Information Leaflets (PILs).....	69
4.1 Legal framework.....	69
4.2 Patient Information Leaflets	73
4.3 Quantitative investigation into the complexity of patient information leaflets. 76	
4.3.1 The type/token ratio	76
4.3.2 Lexical density.....	80
4.3.3 Lexical variation.....	85
4.3.4 Specialized terms and LSP collocations.....	91
4.3.5 Readability of patient information leaflets.....	95
4.3.6 Keyness	98
Conclusions.....	103
References.....	107
Appendices:	115
APPENDIX 1: Articles for Italian general practioners	117
APPENDIX 2: Articles taken from <i>Scientific American</i> and <i>Le Scienze</i>	122

APPENDIX 3: Articles taken from the magazines National Geographic and National Geographic Italia	137
APPENDIX 4: Doctor Shmerling's answers.....	143
APPENDIX 6: Questionnaire for general practitioners.....	144
APPENDIX 8: Corpus of English patient information leaflets	163
APPENDIX 9: Concordance results.....	176

Introduction

Medici obbligati a "parlare facile". Stop allo sfoggio di tecnicismi.

«Dottore, parla come mangi». È la rivoluzione nell'informazione al paziente dell'azienda ospedaliera. La decisione è contenuta in una disposizione al personale per porre fine alla situazione tragicomica che si ripete da anni al letto del malato.

*Il medico che dice: «Parliamo del fastidio postprandiale che avverte in sede epigastrica». Ed il paziente che risponde: «Oddio, ma io ero venuto qui solo perché ho mal di pancia dopo aver mangiato». Ed il camice bianco che ribatte: «È quello che ho appena detto». (Fabiana Pesci, *Il Mattino di Padova*, 8 Luglio 2010, p.3)*

These are the title and the first lines of the newspaper article published in *Il Mattino di Padova*, which focuses on the language used by doctors and on the patients' inability to understand it. When I read this article I thought 'finally someone is aware that, at times, doctors' language is incomprehensible', and I remembered when, few years before, my family doctor told me that I had a hiatus hernia. At first, I thought he would explain to me what he was talking about; he only talked about treatments instead. Therefore, I had to ask him what the meaning of hiatus hernia was and, then, he explained it to me through an anatomical sketch. That was the first time I thought about the language used by doctors in everyday medical encounters.

As is well known, medicine has always occupied a prominent place in all cultures and times, because it is a common concern of all human beings: their health and healthcare are at the top of the political agenda in most parts of the world. However, the language through which medical knowledge and concepts are conveyed has often been criticized for being difficult to understand. In order to provide an historical overview, the present study, in Chapter one, shows how medical language and its terminology evolved over time, and how much the language of medicine has been criticized over the centuries. Moreover, in Chapter two, the linguistic and syntactic features which characterize the language used by physicians are presented, thus providing a way to become closer to the language of the medical community.

Since the language of medicine generally causes problems of understanding to laypeople, in Chapter three and four, two different situations in which patients may come in contact with medical terms have been investigated: doctor-patient interactions and patient information leaflets.

In Chapter three, the attention focuses on medical practice and on the communication between health professionals and non-expert people. Central to medical practice are doctor-patient relationships and interactions which have recently been identified as the key factors for successful treatment. Physicians need to adapt the language they use according to their patients' age, educational level and comprehension skills in order to communicate in an effective way with their patients, thus avoiding misunderstandings.

Another relevant aspect of modern medical practice is patients' need to be informed about their health conditions and to be involved in shared decision-making about treatments and medications. In this respect, in the last decade, there has been a major change in the amount of information made available to people other than the traditional experts in the medical field – the doctors, pharmacists and other medical practitioners. Many countries have adopted policies which mandate that adequate information be made available about treatments, medications and surgical procedures, thus allowing people to participate in an informed way in the management of their own health. However, in more recent times, a technological innovation, the Internet, has assumed considerable importance among the sources which provide health-related information, thus challenging doctors' essential role. The technological revolution which is underway reshapes the way that health care is organized and delivered, and traditional resources - such as consultations with physicians - are being supplemented and replaced in increasing numbers. In order to see whether doctors succeed in maintaining their central role in small towns – where doctors have always been seen as an important guide for the social community – in section 3.3, the results of a survey in the town of Lusiana are presented.

In Chapter four the attention shifts to another kind of communicative context: patient information leaflets. Though in our society, there is an enormous amount of information about health and medications which is available from many different sources, it is not always easy for patients to access medical information. For many people, the primary source of information about drugs remains the statutory patient information leaflet (PIL) which has to provide all the essential information patients need to use medications safely. Since patient information leaflets should be 'informative texts' for all types of patients, the present study aims at verifying to

what extent patient information leaflets of over-the-counter drugs are informative texts for laypeople. In this respect, a corpus-based quantitative analysis into the complexity of these texts (Italian and English PILs) was carried out by investigating the phenomena of lexical density, lexical variation, readability and keyness. In addition, a linguistic analysis of lexis, specialized terms and LSP collocations found in the corpora under investigation is provided.

Chapter one: medical language throughout history

The importance that has always been attached to the suffering of body and soul suggests that medical texts, together with religious writings, are amongst the most ancient domains of translation. Due to the development of medical sciences and the need to term new concepts, medical language evolved over the centuries and medical vocabulary has continuously been expanded. To understand how medical language has changed and how new terms have been coined, the following paragraphs will try to sketch a time line that will highlight what have been the most significant facts in the evolution of medical language.

1.1 Historical overview

The scientific methods that characterize modern western medicine are traceable to Classic and Hellenistic Greece, when the Greek physician Hippocrates first attributed illness to physical causes. The importance of Hippocrates' thought derives from the fact that he distinguished medical practice from priestly ministrations and pioneered the belief that poor health should be examined through logical reasoning and actual observation. Hippocrates and his successors produced a large body of medical texts in Greek and many of the anatomic, pathologic and therapeutic terms found in those texts remain in use today – some of them with little or no change in meaning (Dirckx 2005:9). During the classical era, Greek medical writing was the most important medium for medical scholars to communicate their ideas. At the time of the Roman Empire and later in medieval Europe medical language changed considerably.

At the time Greece was absorbed by the Roman Empire, the centres of learning moved from Greece to Egypt. Despite of this change, Greek physicians succeeded in maintaining their importance: Greek medical texts began to be translated into Arabic and only marginally into Latin.

After the demise of the Roman Empire in the 5th century, most works of the Greek physicians remained unknown in Western Europe until the 11th and 13th centuries. At the time, Western society began to rediscover ancient Greek scientific texts thanks to the discovery of Arab repositories of learning in Spain and elsewhere during the Crusades, and ancient works were translated from Arabic into Latin (Berghammer 2006:40). Although the translation of texts had been made from their Arabic versions, Arabic had contributed relatively little to western medical terminology. Therefore, it can be said that Arabic represented a bridge that provided access to the Hellenic system of science.¹

Later on, after the Ottoman conquest of Constantinople in the 15th century, Greek scholars migrated to Italy bringing with them their ancient works. During the Renaissance, when Greek was no longer so widely understood, Greek texts were directly translated into Latin, which absorbed Greek and Arabic medical terminology through transliteration or overlay with Latin prefixes and suffixes (Berghammer 2006:40).

Between 1000-1800AD, Latin served as a universal language for scholarly communication and, being the language of the Roman Empire, which included most of Europe, part of Asia and Africa, Latin assumed the role of *lingua franca* of medicine. Until the early modern era, the language of medicine consisted largely of Latin terms and still today it remains the official language of anatomic terminology and taxonomic nomenclature (Dirckx 2005:9). However, because of the increasing need to communicate with non-university-trained physicians, students and patients, Latin as the language of medicine was almost entirely replaced by local languages – even though all of them retained the Greco-Latin terminological core (Berghammer 2006:40).

Undoubtedly, throughout history, dominance in knowledge has implied repercussions on the language used in medical discourse, as is the case with the

¹ A basic change in European medicine occurred following the translation into Latin of Arabic scientific treatises. Through their Latin versions, three of the early Arabic medical encyclopedias soon came to dominate European medical theory. Two of them were massive attempts at synthesizing all available medical knowledge and the first Arabic medical treatise to be translated into Latin was the comprehensive medical compendium *Pantegni* (Loudon 1997:15).

English language. From the second half of the 20th century, English has become the shared medium of the medical community and English terms have been imported into many other national languages. This may be clearly seen as a direct consequence of United States leadership in many fields.

The advantages of a common, shared language for scientific research are obvious. However, the predominance of English gives English native speakers a competitive edge over those who first have to acquire the necessary linguistic skills in order to be able to read English materials and to communicate their ideas and findings in a foreign language.

1.1.1 Greek-Latin terminological core

As has been said above, much of the medical terminology of western European languages consists of roots and affixes drawn from Greek and Latin. The advantages of this terminological core are the following: it serves as an artificial language; it no longer changes because Latin and Greek are dead languages; and it is precise and internationally comprehensible and accepted (Berghammer 2006:40).

The oldest written sources of western medicine are the Hippocratic texts from the 5th and 4th century BC, which cover all aspects of medicine known at that time; in fact, many medical terms had been coined in that period. Then, Romans, who had no similar medical tradition, imported Greek medicine as well as Greek terminology, for instance, the words *catarrh* (downflow), *diarrhoea* (throughflow), *dyspnoea* (bad breathing) (Wulff 2004:187-188).

At the beginning of the first century AD, when Greek was still the language of medicine in the Roman world, a relevant development took place. A Roman aristocrat from Narbonne, Aulus Cornelius Celsus, wrote *De Medicina*, an encyclopaedic overview of medical knowledge based on Greek sources. Celsus was very important for western medical language because he was the first to face a testing terminological problem: the majority of Greek medical terms had no Latin equivalents (Wulff 2004:187-188).

As Wulff (2004:187-188) states, from a linguistic point of view, the manner in which Celsus succeeded to solving this problem is of considerable interest. Firstly, he imported a few Greek terms directly, even preserving their Greek grammatical endings, and wrote them with Greek letters; he included, for instance, the Greek word *pyloros* (now pylorus). Secondly, he transliterated Greek words, writing them with Latin letters and replacing Greek inflectional endings with Latin ones, for example the word *stomachus*. Thirdly, he retained the imagery of the Greek anatomical terminology by translating Greek terms into Latin, such as *dentes canini* from the Greek *Kynodontes* (dog teeth). It is for the same reason that we can still enjoy the old Greek tradition of likening the shape of anatomical structures to musical instruments, as in the words *tuba-trumpet*, *tibia-flute*.

Celsus' *De Medicina* appeared in print in 1478 and, in the following centuries, almost all important medical works were published into Latin. Therefore, medical vocabulary expanded but, basically, the language did not change: it was a compound of ordinary Latin and numerous Greek and Latin medical terms (Wulff 2004:187-188). The era of Latin gradually came to an end during the 19th century. In Britain, William Heberden's *Commentarii* was probably the last notable medical text to be written in Latin. It appeared in 1802 and it is also referred to as *ultimus Romanorum* (the last text of the Romans). In other countries medical Latin survived a little longer.

1.1.2 National medical languages

Though national medical languages had much in common, since most of the medical terms derived from medical Latin, there were some differences in the translation process that still persist. Germanic languages often adopt anatomic terms and disease names with their correct Latin endings, whereas Romance languages tend to adapt the terms according to the norms of each particular language while Slavic languages tend to translate the terms (Wulff 2004:187-188).

For example², the Latin terms *nervus musculocutaneus* and *ulcus ventriculi* are considered below:

- Germanic languages: *nervus musculocutaneus / ulcus ventriculi*

- Romance languages:

French: *le nerf musculo-cutané / ulcère gastrique*

Italian: *il nervo musculocutaneo / ulcera gastrica*

English: *the musculocutaneous nerve / gastric ulcer*

- Slav languages:

Russian : *kozhno-myzhechny nerv* ('skin-muscle nerve') / *jasva zheludka* ('ulcer of stomach').

Furthermore, national medical languages did not limit themselves to importing terms already found in medical Latin. Scientists continued to develop new concepts that needed to be named, coining for this reason a multitude of new terms. However, since Latin does not permit the formation of composite words to the same extent as Greek, these neologisms were usually composed of Greek rather than Latin roots (Wulff 2004:187-188), as it can be seen in the following examples:

Erythrocyte-Etymology: Gk, erythros + kytos, cell;

Nephrectomy-Etymology: Gk, nephros, kidney + ektomē, excision. (M'sMM 2009)

The huge neoclassical wordstock with Greek roots, which is still being used, presents other characteristics of linguistic importance, such as:

- the special meaning attached to certain Greek suffixes (-itis, -oma),

Arthritis [ärthri'tis]

Etymology: Gk, arthron, joint + Gk, itis, inflammation

any inflammatory condition of the joints, characterized by pain, swelling, heat, redness, and limitation of movement. (M'sMM 2009)

Lymphoma [limfō'mə] pl. lymphomas, lymphomata

Etymology: L, lymphā + Gk, oma, tumor

a type of neoplasm of lymphoid tissue that originates in the reticuloendothelial and lymphatic systems. It is usually malignant but in rare cases may be benign. It usually responds to treatment. Two main kinds of lymphomas are Hodgkin's disease and non-Hodgkin's lymphoma (NHL). (M'sMM 2009)

² The examples are taken from the article "The language of medicine" by Wulff, 2004.

- and the fact that some prefixes and suffixes are more productive than others.

For instance, focusing on the coining process of a new word within medical discourse, it is clear that the Greek prefix *hyper-* is more productive than its Latin equivalent *super-* (Wulff 2012:187-188). Therefore, we say *hypertension* rather than *supertension*. The productiveness of the Greek prefix *hyper-* can be demonstrated by the analysis of the online corpus *WebCorp LSE* and focusing on the sub-corpus "health". In fact, the results show that the number of words with the prefix *hyper-* is much higher than the one presenting the prefix *super-*. Some of the occurrences taken from *WebCorp* are reported in Table 1.1 below:

Hyper*[N*] 1490 occurrences	Hyper*[Adj*] 238 occurrences
Hypertension Hypersensitivity Hypercalcemia Hyperphosphatemia Hypervitaminosis Hyperkalemia Hyperactivity Hyperplasia Hyperglycemia Hypertriglyceridemia Hyperthyroidism Hyperparathyroidism Hypeuricemia Hypertrophy Hyperlipidemia Hypercholesterolemia Hyperthermia Hyperventilation Hyperaldosteronism hyper-reninism hyperalgesia hyperreflexia hyperammonemia hypercalciuria hypernatremia hyperpigmentation	Hyperplastic Hypertensive Hyperactive Hypersensitive Hypercapnic Hyperkalemic Hypermetabolic Hypertrophic Hyperendemic Hyperchloremic Hypertonic Hyperbaric Hyperechoic Hyperglycemic Hyperacute Hypercoagulable Hypercellular Hyperextended Hyperfractionated Hyperinsulinemic Hyperintense Hyperthermic Hypercalcemic Hyperserotonergic hyperpigmented
Super*[N*]	Super*[Adj*]
Supervision Supervisor Superoxide Superoxol Superbug Supernatant superinfection	Superior Supervised Superficial Supernatant Super-oxidized superacid

Table 1.1. Occurrences of nouns and adjectives with the prefixes *hyper-* and *super-* taken from the online corpus *WebCorp LSE- health*.

Focusing now on recent times, all the most influential medical journals are written in English and English has become the language for international medical communication. However, while in the past new medical terminology consisted of classical roots, today words are often borrowed from general English. As an example, we can consider the following definitions of the word *bypass* (Oxford 2013):

1. (*general En.*) A road that passes around a town or city rather than through the centre.
2. (*med.*) A medical operation in which blood is directed along a different route.

As can be seen, both definitions refer to a different direction that is being taken. Therefore, the meaning of the ordinary noun is assigned to the medical term.

For what concerns other national languages, doctors from non-English-speaking countries can choose between importing these English neologisms directly into their mother language as loan words, translating them into their own language or coining new terms. The term *bypass*, for instance, is accepted in Italian, whereas in French it is translated into *pontage* (Wulff 2004:187-188). The different attitude towards borrowing can probably be explained by the resistance of French language towards English loan words that can be seen not only in the medical field, but also in the language of technology, as is the case with computer science:

Computer - ordinateur

mouse – souris

mailing list - liste de distribution

home page – page d'accueil

browser – navigateur

Web – Toile/ réseau

1.1.2.1 English influence on Italian medical language

The increasing and rapid expansion of English in medical journals is demonstrated in a recent article "*Le lingue della comunicazione scientifica*" (Carli and Calaresu 2003:27-74), where the authors analysed the editorial policies of five medical Italian journals from 1990 to 2000. The research shows that two of the five medical Italian journals started to publish articles in English already in 1990. From 2001, they only accept contributions in English and they even translated the name of the journals - *Italian Health Journal* (since 2000) and *Italian Journal of Pediatrics* (since 2001). However, the *Italian Health Journal* continues to publish articles in Italian, but it attaches different functions to the two languages: while Italian is seen as the medium to broaden international scientific knowledge and its implications in clinical practice, English is seen as the language for experimental researches, shared by scientists from all over the world.

Despite this difference of purpose of the two languages in the journals, it can be seen that loan words from English are used even in journal articles that have been written in Italian and that are intended for Italian doctors. According to Serianni (2005:186), in Italian medical discourse we can distinguish five different types of loans from English:

- a. general loan words, that are terms which can also be found outside medical discourse and can be substituted by Italian words, such as 'ipertensione *borderline* (ai limiti della norma)'; 'core lipidico (nucleo)'; 'l'inserzione di un *patch* (innesto)'; 'sensazione di *handicap* (disagio)'; 'turnover cellulare (ricambio)'.
- b. Loan words which refer to the pathology, some of them well consolidated in their use, such as 'shock emorragico (sindrome a insorgenza acuta caratterizzata da complessi disturbi della dinamica circolatoria)'; '*bulky-disease* (massa tumorale rilevante)'.
- c. Loan words which refer to surgery, introduced in recent times but generally used, such as 'posizionamento di uno *stent* coronarico (tipo di protesi)'.
- d. Loans that refer to diagnosis, such as '*breath-test* (test del respiro)', '*follow-up* (controllo periodico)'.
- e. Loans that belong to the biological field, such as 'incremento degli *spike* (picchi)', 'teoria dell'*underfilling* and teoria dell'*overfilling*' (respectively 'scarso ed eccessivo riempimento').

In order to see how frequently these loans from English are used in articles addressed to the Italian audience, seven on-line articles (Appendix 1) have been taken into account. In a corpus of almost 2.700 words, 13 English loan words have been found. Most of them are general loans (*step, test, database, checklist, team, target, counselling, borderline, handicap*) while the others are loan words that refer to diagnosis (*follow-up, Framingham risk score, Cac score*). Only one loan word (*reuptake*) belongs to the biological field. The word *reuptake* is part of the complex medical term *selective serotonin reuptake inhibitors*, and in Italian the complex term can be found in two variants: *inibitori selettivi della ricaptazione delle serotonina* or *inibitori selettivi del reuptake della serotonina*.

As shown above, the presence of English terms in journal articles addressed to Italian general practitioners is limited to words that are widely recognized by the medical community and to those that can also be found outside the medical field.

To this end, the success in maintaining the use of Italian in journals for general practitioners can be explained by the fact that Italian is the language through which Italian doctors express themselves better and through which they can have a better understanding (Serianni 2005:184).

In addition to loans from English, the influence of English language can also be observed in the coining process of Italian medical terms. Coining models derived from the Anglophone society - which are unusual in Italian - are recently expanding in their use. For instance, we can observe Italian adjectives formed of a subordinate sequence Noun + Adj., as in the term *calcio-antagonista*, or the form that follows the English suffix *-like*, as in the terms *aspirino-simile*, *antibiotico-simile*. This last sequence can also occur in the inverse sequence Adj. + Noun, as in *simil-virale*, *simil-neoplastico*. Moreover, we can find the juxtaposition of two nouns in the sequence Determiner + determined, as in the following examples *coronavirus* and *papillomavirus* (Bellina 2011:2).

Another relevant aspect that is worth considering is that English language is influencing not only Italian medical lexis but also the word order within the sentence (Serianni, 2005:185). As is recognized, the topological rule of Italian language imposes the postposition of the rhematic subject to the predicate, as in the examples that follow:

___ = predicate

[...] = rhematic subject

Chi vuol giocare? Gioco [io] .

Come con gli altri FANS, sono stati riportati [rari casi d'insufficienza renale]. (Borocilina)

In caso di sovradosaggio, possono essere utili [la lavanda gastrica e l'impiego di carbone attivo]. (Peridon)

Despite this accepted rule, in medical Italian, some sequences rheme-theme patterned after the English structure can be found. Some examples taken from over-the-counter drug leaflets are reported below:

[Una stretta sorveglianza medica e una terapia di supporto] sono raccomandate...
(Peridon)

[Eritema e moderata secchezza e desquamazione della pelle] sono stati osservati in una piccola percentuale di casi. (Zovirax)

[Gravi reazioni cutanee alcune delle quali fatali, includenti dermatite esfoliativa, sindrome di Stevens-Johnson e necrolisi tossica epidermica,] sono state riportate molto raramente in associazione con l'uso dei Fans. (Moment)

At this point, one question comes to mind. If medical language causes many problems of understanding when medical concepts are expressed in people's mother tongue, how can the presence of English words facilitate comprehension?

1.2 "Remedia curant morbum non verba"³

The criticism against medical language is not unusual and neither recent. The language used by physicians has always caused problems of understanding and literary traditions give us various, intense satirical statements against doctors. At times, the criticism hits just one particular aspect, that is the doctors' lack of technical preparation: paradoxically, doctors that are supposed to nurse patients cause the death of sick people because of their inability in health care. Other times, critics focalize on the intangible linguistic code exhibited by clinicians. Indeed, the favourite target is represented by specialized terms which are apparently unfathomable in their meaning. In the following text, several examples of satire will help us to understand how prolific the criticism against doctors has been over the centuries.

At the very beginning, we find Petrarch's *Invective contra medicum*. Through this piece of writing against a doctor of the Papal Court at the time of Clemente VI, Petrarch blames doctors to provide only useless words to their patients,

³ Alexander Knipps Macoppe (1662-1748), he practiced and taught medicine in Padua. He built up a great reputation for treating venereal disease and for spa therapy applied to various conditions. Aphorism : "sono le medicine, non le parole, a curare le malattie" (Macoppe 1984:26).

"*intempestivos flosculos inutilium verborum*" (Serianni 2005:14). Later on, Petrarch's criticism becomes more intense in the work *Seniles*. Some parts of the letter to Giovanni Boccaccio are quoted below:

[...]nulla aver potuto fare ne fatto il medico, da quello in fuori di cui è capace un ciarliero dialettico fecondo di noie, e sterile di rimedi. Ora mi scrivi che ricaduto nella malattia non chiamasti alcun medico: onde io non mi meraviglio che tu sia presto guarito. Non v'è strada più corta a risanare del tenersi lontano il medico.

[...]per l' uso delle continue menzogne artificiosamente adoperate.[...]

In questo si convengono gli uni cogli altri, che come fra i guerrieri quegli è stimato più grande che più numerose e più larghe mena le stragi; così fra i medici chi a furia di esperimenti e di prove mette più vite in pericolo, questi mostrato a dito è più celebrato, e dagli altri tenuto a

duce e maestro. Gran pratica, dicono, grande esperienza è la sua: il che significa aver egli contratta l'abitudine di ammazzare con securtà.[...]

Ma qualunque sproposito a que'dottoroni esca di bocca intorno alle cose naturali, dal volgo non solo come dogma sicuro, ma come divino oracolo è ricevuto or ti so dire che tutti sono uomini dotti, cortesi, egregi parlatori, acuti nel disputare, efficaci nel persuadere, tali in somma che dolcissimamente, e quasi a ragion veduta ammazzano altrui, e sanno sempre abbastanza scusare e difendere il fatto loro.

[...] disprezzo ed abborro que' ciurmatori, che sotto una vernice di superficiale dialettica cianciano a vuoto invece di medicare, e non solamente immensa noia a chi è sano, ma a chi è malato procaccian la morte[...]

[...] Pure a tornare in pace anche con essi, e per non avere più a parlare contro questa genia, vorrei, che come credono di farsi grandi con nomi di malattie e di rimedi presi dal greco, come alla greca si ammalano, così alla greca si lasciassero curare.[...]

Greca la improntitudine di quegli impostori, e la nomenclatura dell' erbe, delle piante, delle radici, balausto, rabarbaro, calaminto, tutta è dal greco, anzi pur dall'arabico, perchè quanto più estranio, tanto più costoso sia il bugiardo medicamento. Non aprono la bocca a dichiarare la malattia che non lo facciano con greca voce: e se non l' hanno già pronta, se la compongono: e questa dicono apoplessia, quella epilessia, questa risipola. Bei nomi invero, bei paroloni che a chi li ascolta danno diletto, e invogliano di sapere come in greco si chiami quello per cui soffre un latino, quantunque poi non si trovino rimedii ne latini, né greci.
(Fracassetti 1892:285-300)

As can be seen, Petrarch thinks that doctors are unable to cure illnesses and that they display their linguistic knowledge without providing any real medical care. Physicians are conceived as skillful orators who use dialectic and unknown terms only to exhibit their linguistic eloquence. They use terms that come from Greek and Latin, terms that only men of learning can understand, and if they do not know any word to express a concept, they coin a new term without the interference of an educated

audience that could criticize them. Similarly, criticism is found in the letter to Donato Albanzani, where doctors' inability and ignorance in medical care are emphasized:

*[...]molti ne conobbi ed ebbi amicissimi, eloquenti, letterati, in molte scienze dottissimi, ma solo nella medicina dappoco. Cosa veramente mirabile: saper di tutto da quello in fuori che si vuole e che si deve.
[...]noi la Dio mercé pieni di buona salute ridiamoci della credulità degl' infermi e dell' ignoranza de' medici.* (Fracassetti 1982:301-305)

In France as well, criticism against doctors was widespread. Montaigne, for instance, is ironical about the obscure way in which doctors express themselves. Doctors' linguistic skills are seen as a source of prestige to be displayed in front of a naïve audience. Similarly, in Molière's work *Le malade imaginaire* (*The Imaginary Invalid*, 1673), we find both criticism of the patients' confidence on healthcare and of the physicians' inexperience. Doctors are grotesque figures with ridiculous names and strange behaviour, like Mr. Purgon, Mr. Diafoirus, and in the comedy every physician is portrayed as selfish and hypocrite. Moreover, Mr. Diafoirus' son is exactly the type of physician that Molière wants to criticize sharply: a young doctor who has just finished his studies, who talks about things learnt by heart and who is unable to understand what he is supposed to do in real situations. Every doctor in the comedy displays his knowledge of ancient languages, and the author's criticism is clear in what follows:

*Béralde : Ils savent la plupart de fort belles humanités; savent parler en beau latin, savent nommer en grec toutes les maladies, les définir, et les diviser; mais pour ce qui est de les guérir, c'est ce qu'ils ne savent point du tout.
Argan: Mais toujours faut-il demeurer d'accord, que sur cette matière les médecins en savent plus que les autres.
Béralde: Ils savent, mon frère, ce que je vous ai dit, qui ne guérit pas de grand-chose ; et toute l'excellence de leur art consiste en un pompeux galimatias, en un spécieux babil, qui vous donne des mots pour des raisons, et des promesses pour des effets.* (Marcou 1995 : 131-134)

Affirming that physicians speak Latin and Greek very well and stating that they are able to use these languages to name and define every kind of illness, Molière highlights the fact that their linguistic ability consists just of a sublime set of words and promises instead of concrete answers and real medical treatments.

In another part of the text, the author shows the doctors' superiority compared to their patients: doctors are educated people who use sophisticated words, which have Greek and Latin origins, while patients are ignorant and unable to understand what doctors say. Therefore, doctors can even insult their patients, as is the case in the following lines:

Et je veux qu'avant qu'il soit quatre jours vous deveniez dans un état incurable, que vous tombiez dans la bradypepsie, de la bradypepsie dans la dyspepsie, de la dyspepsie dans l'aepsie, de l'aepsie dans la lientérie [...] (Marcou 1995: 139).

Following the same common theme, in the 20th century, in Italy, we find Totò and his satire against medical language in the comedy of Tramonti (1993):

Sig.ra: Io ho un dolore qui ed al mattino viene piano piano, al pomeriggio diventa forte forte, la sera ritorna piano, e la notte ridiventa forte forte. Che sarà dottore?

Mardocheo: Un piano forte

Sig.ra: Ma come? Ho un pianoforte in petto?

Mardocheo: Noialtri medici sintetiziamo i termini. La vostra malattia la chiamiamo malattia del piano forte.

Sig.ra: E cosa sarebbe?

Mardocheo: E' il cuore che trovandosi a contatto col velopendolo asciatico, gonfia i variosceli e la moscia.

Sig.ra: Ma io non capisco nulla.

Maedocheo: Nemmeno io.

Nik: Vede, Signora, è la vera scienza. Non bisogna mai capire nulla.

Mardocheo: Guai se l'ammalato capisse qualche cosa! Allora i medici che ci starebbero a fare? (Serianni 2005:20)

As in Molière's criticism, the comedy quoted above shows that the patients' inability to understand the language of medicine allows doctors to load their talk with any kind of technicalities. Physicians can use invented terms, such as *moscia* and *asciatico* and they can even talk about pathologies that cannot affect certain types of patients, as is demonstrated in the explanation of the "piano forte" disease. In this case, the doctor says that the heart stretches the varicoceles. However, being varicocele *an abnormal distension of the veins of the spermatic cord in the scrotum*⁴, it is obvious that this pathology only affects male human bodies. Therefore, it cannot be a proper diagnosis for a female patient, as is the case in the comedy above. Moreover, when doctor Mardocheo finally says that without their patients' ignorance

⁴ Definition taken from: <http://medical-dictionary.thefreedictionary.com/varicocele>

doctors would be useless, we find a strong criticism against medicine as a profession which emphasizes doctors' need of having naïve patients.

Again, in Spain, the playwright Enrique Jardiel Poncela defines medicine as « *el arte de acompañar con parablas griegas al sepulcro* » (the art that, using Greek words, lead ill people to their grave) (Serianni 2005:21).

Over and above its criticism by men of letters, medical language was a relevant theme among doctors themselves. In the 5th century, very well known were the positions taken by the Italian physician Francesco Redi. In the letter to a sick lady, Redi uses a language that is very different from that of his colleagues:

non aspetti da me che io voglia farle, come sogliono i medici, un lungo discorso nel produrre in campo quelle abstruse cagioni produttrici delle sue indisposizioni perchè, siccome non le indenderei forse io, che pur le scrivo, così parimente mi do a credere che per avventura non le sprej fare intendere a V.S. Illustrissima e particolarmente se io volessi servirmi de' termini reconditi e misteriosi che usa l'arte medicinale e ancora de' suoi greci e arabi e barbari nomi da far spirare i cani. (Serianni 2005:22)

Redi criticizes the use of ancient words while explaining to patients the diagnosis and treatment for their illnesses. He highlights the fact that physicians usually use complex terms even though they may not know the real meaning of the words they use. Therefore, they just display their rhetorical skills without allowing patients to understand the content of the speech. As can be seen, the main problem is represented by the use of specialized terms which have Greek and Latin origins, and by the fact that patients are unable to understand the meaning of such terms.

In the 20th century, we can remember the severe judgment of Whitehead (1956:390), who affirms that the medical curriculum is a "long and systematic exercise to verbosity", and in the same period, we find the irony of Crichton who states that medical writing is a "highly skilled attempt to confuse the reader" (Williams 1990:10).

However, as any other specialized language, medical language is characterized by the presence of highly informative terms the use of which cannot be avoided. Certainly, the use of highly specialized terms should be adapted according to the interlocutors (experts or non-experts) engaged in the communicative act. According

to Baldini (1989:94), this is exactly what doctors are unable to understand: doctors use complex specialized terms even though the communicative context does not require them.

Beyond doctors' misuse of specialized terms, another aspect has to be considered. According to Vitali (1983:196), the language of medicine is characterized by a high number of abbreviations, acronyms and synonyms which refer to the same medical concept. For instance, if we consider the Salk vaccine, we can see that it has been abbreviated in many different ways (Baldini 1989:94): *Salk V.*, *Salk vacc.*, *Salk vac.*, *Polio v.*, *Polio vac.*, *Salk Polio vac.*, *S. Polio vac.*, and *Polio Vac.* The tendency to use different denominations to refer to the same medical concept can lead to misunderstandings and confusion even in expert-to-expert communication. Therefore, Vitali (1983:196) suggests that medical language needs a terminological standardization in order to increase its degree of clarity and reduce confusion. In Vitali's words (1983:196):

Il linguaggio medico ha bisogno di una rigida serie di norme di standardizzazione della terminologia al fine di eliminare quella torre di Babele di abbreviazioni, sigle e sinonimi che affollano le opere e le produzioni verbali dei medici.

Undoubtedly, criticism evolved over time. Differently from the past, when it was thought that doctors' use of abstruse and incomprehensible words would have increased their social prestige⁵, in more recent times, it seems necessary to consider transparency and patients' awareness about diagnoses and medical treatments as the fundamental pillars over which the doctor-patient relationship should be created. Therefore, nowadays, the need to communicate in an effective way, using 'comprehensible' terms or explaining complex terms through the use of plain words, seems to acquire more and more importance.

⁵ This idea derives from Galeotto Marzio da Narni (a physician of the 15th century) who stated that doctors should vary their language depending on the patient's cultural level: "con gli uomini dotti, a quali è nota la verità, [il medico] dee usare parole comuni e chiare, ma col volgo ignorante e con le vecchierelle e cotali persone, anche quelle cose si potranno dire comodamente in latino [...] o con parlare più oscuro e con parole o greche o arabesche: perciocché gli uomini plebei e volgari alcune fiata stimano quello essere ottimo e salutifero che non intendono" (Serdonati, in Serianni 2005:24).

Chapter two: linguistic features of English for Medical Purposes (EMP)

Since a highly specialized language, as is medical language, is often criticized for its cryptic and obscure nature, the following section will focus on the linguistic characteristics of medical English in order to provide a way to become closer to the language of the medical community.

2.1 Lexical Features

According to Romich (2001:23), "studying medical terminology is like learning a new language". In fact, at first sight, words look different and complicated. However, by understanding some important guidelines that govern medical language, people may become interested in and aware of how medical terminology works.

Beyond the origins of its terms, medical terminology shows some relevant characteristics that distinguish it from ordinary English:

a. Monoreferentiality

Medical English vocabulary is characterized by what Maglie (2009:24) calls *semantic univocity*. This feature implies that, in medical language, there is only one term that designates a specific meaning or concept. Consequently, medical terms cannot be appropriately replaced by synonyms but, rather, by periphrasis. As an example, the term *hepatitis* can be explained through the periphrasis *an inflammation of the liver, caused by infectious or toxic agents*. Although monoreferentiality is the ideal characteristic for specialized languages, occurrences of synonyms can always be found. For instance, several technical expressions refer to *megacolon*, which is known as *Hirschsprung's disease*⁶ by the Danes, whereas by the Dutch it is called *Ruysch's disease* (Maglie, 2009:24). Another example of synonymy among technical terms can be seen in the three specialized terms which refer to *a tumor that is*

⁶ Descriptions of children with Hirschsprung's Disease date back to the 17th century, when Ruysch (1691), a Dutch anatomist, described a 5-year-old girl who died of intestinal obstruction (O'Neil et al. 2003:46).

*malignant and tends to spread to other parts of the body*⁷: *malignant tumor, malignant neoplasm and metastatic tumor.*

A different example of synonymy is shown by the terms *varicella* and *chickenpox*. In this case, *varicella* is the technical name for chickenpox, thus synonymy is obtained by relating two terms which belong to different registers.

b. Denotation

The medical term denotes one precise meaning. To provide an example, when the word *brain* is used in the medical domain, it refers to the part of the central nervous system contained within the cranium⁸ (*her sister died of a brain tumour/ Her brain was damaged in the accident*), whereas in standard English it can acquire a connotative value (e.g. *use your brain to find a solution!*).

Despite the presence of technical terms, medical language contains a wide range of words and phrases that belong to general English. Below, some figures of speech are taken as an example (Maglie, 2009:25):

- **Catachresis**: it expands a word beyond the limits of its own meaning. The medical term *neck of uterus* means the corpus/body of uterus: the meaning of the general English word *neck* has been expanded.

- **Eponym**: it is a person, whether real or fictitious, after whom a particular place, era, discovery, disease, or other item is named, for instance, the expressions Parkinson's disease and Alzheimer's disease.

- **Toponym**: it is a name of a physical or mental disorder derived from a place or a region, e.g. Rio Bravo fever.

c. Conciseness

In medical language, several concepts are expressed in the most concise lexical and syntactic form. To provide an example, we can consider the term *urinalysis* -

⁷ Definition taken from <http://medical-dictionary.thefreedictionary.com/malignant+tumor>.

⁸ Definition taken from <http://medical-dictionary.thefreedictionary.com/brain>

*the physical, chemical, and microscopic examination of urine*⁹ - which derives from the fusion of the two words *urino* and *analysis*; and the term *contraception*, which is the result of the union of the two words *contra* and *conception* (Etymology: Latin, *contra* + *concipere*, to take in).

Another linguistic device physicians use to express a concept in a concise manner is represented by acronyms, such as *HIV* (human immunodeficiency virus), *AIDS* (acquired immunodeficiency syndrome), *HCV* (hepatitis C virus), and many others. In addition, other concepts are expressed through abbreviations, such as *CV* (cardiovascular), *Fld* (fluid), and stacked noun phrases, such as *body mass index* (BMI) (Maglie 2009:29).

Physicians use a variety of abbreviated forms and acronyms in order to quickly record and refer to patients' information. Moreover, these expressions are comprehensible, 'economical' and accepted within the medical community, thus allowing physicians to communicate effectively. However, since these shortened forms are also used for prescriptions, understanding these terms may help patients to decipher their medical records.

d. Precision

Since each term can be directly referred to its meaning, monoreferentiality leads to the phenomena of precision and transparency of medial language. Words can be structurally analyzed dividing them into their basic components: prefix, root and suffix. For instance, the term *hyperglycaemia* can be divided as follows: the prefix *hyper-*, the root *-glyc-* and the suffix *-aemia*. After dividing the word into its components, the meaning can be gleaned by examining the suffix, followed by the prefix and then the root. In *hyperglycaemia*, the suffix *-aemia* means blood condition, the prefix *hyper-* means excessive and the root *-glyc-* means sugar. By assembling the components' meanings, we obtain the final meaning: a blood condition of excessive sugar (Maglie 2009:28). The same process can be showed using the term *choledocholithotomy* which is a surgical operation to remove (-otomy)

⁹ Definition taken from <http://www.nlm.nih.gov/medlineplus/ency/article/003579.htm>

a stone (-litho-) that originated in the gall bladder (chole-) but is currently located in the common bile duct (-docho-) (Fallon 2002:1).

However, even in medical language there are cases of imprecision, as is demonstrated by the suffix *-oma* in the terms *carcinoma*, *lymphoma* and *glaucoma*. In fact, while in the formers, the suffix *-oma* designates a very life-threatening tumor (Etymology: Gk, *karkinos* + *oma*, tumor¹⁰ and L, *lymph*a + Gk, *oma*, tumor¹¹), in the term *glaucoma*, the suffix *-oma* does not denote an eye cancer but "*an abnormal condition of elevated pressure within the eye because of obstruction of the outflow of aqueous humor*"¹².

2.1.1 Metaphors

Throughout the history of rhetoric, metaphors have always been understood as a matter of language, a sort of creative linguistic ornament that is mainly used in poetry and rhetoric. In this view, metaphors have always been considered as paraphrasable in terms of literal language without the loss of cognitive content (Richards 1936:49).

The important claim that metaphor is not just a linguistic embellishment was firstly made by Richards in 1936. According to Richards (1936:51), metaphor is pervasive in everyday life, not just in language but also in thought and action. Thought is in itself metaphoric and proceeds by comparison; thus, metaphor of language can be defined as the explicit medium through which the metaphoric nature of our conceptual system is expressed. In Richards' words:

In asking how language works, we ask about how thought and feeling and all the other modes of the mind's activity proceed. (Richards 1936:52)

Following this idea, Richards states that when we use a metaphor, two thoughts simultaneously interact in our minds. By comparing the different relations which these two thoughts hold to one another, we can understand the meaning of a metaphor (Richards 1936:52). He calls these two thoughts *tenor*, that is the principal subject, and *vehicle*, that is the thought connected with the principal subject - in the

¹⁰ <http://medical-dictionary.thefreedictionary.com/carcinoma>

¹¹ <http://medical-dictionary.thefreedictionary.com/lymphoma>

¹² <http://medical-dictionary.thefreedictionary.com/glaucoma>

example *John is a lion*, John is the *tenor* and lion is the *vehicle*. The meaning of a metaphor results from the interactions between *tenor* and *vehicle*; such interactions may work through resemblances as well as through disparities between the two thoughts (Richards 1936:60). Following Richards' reasoning, the linguistic metaphors are just mere representations of the way in which we see the world. Therefore, since language reflects our thinking, by looking at language, we may understand how our concepts are formed and how our conceptual system works.

Largely influenced by Richards' view and on the basis of linguistic evidence, in the book *Metaphors we live by* (1980), Lakoff and Johnson state that our conceptual system is fundamentally metaphorical in nature and, although we are not aware of the fact that our everyday thoughts and actions are structured by metaphors, we constantly understand one thing in terms of another (Lakoff and Johnson 1980:3). In addition, they claim that our conceptual system is grounded in our experience and that it is culturally conditioned by the constant interactions we hold with our environments. Therefore, our knowledge and our understanding are based on such interactions (Ortony 1993:209). In line with Richards, they suggest that metaphorical expressions should be seen as the superficial representations of an underlying metaphorical conceptual system:

metaphors as linguistic expressions are possible precisely because there are metaphors in a person's conceptual system. (Lakoff and Johnson 1980:6)

Metaphors are defined as metaphorical concepts that structure our everyday activity and, by using several examples of conceptual metaphors, the authors show that they are reflected in our everyday language by a variety of metaphorical expressions. A conceptual metaphor consists of two conceptual domains, in which one domain is understood in terms of another. Therefore, there is a *source domain*, from which we draw metaphorical expressions to understand another conceptual domain, and a *target domain*, that is the domain we try to understand through the use of the source domain. Between source and target domains there is a set of systematic correspondences, in the sense that the constituent conceptual elements of the target domain correspond to the constituent conceptual elements of the source domain (Kövecses 2010:5-13).

These conceptual correspondences are usually referred to as *mapping* and according to Lakoff (1993:202):

everyday metaphor is characterized by a huge system of thousands of cross-domain mappings [...] between source and target conceptual elements the mapping is tightly structured.

After this brief account on the evolution of the definition of metaphor, in what follows we shall see how metaphors work in the field of medicine. According to Periyakoil (2008:842-843), medical language is built around sets of conceptual metaphors including:

- sports metaphors, which project the idea that a patient and his/her illness are playing on opposite teams. Every competitor has to play until the end as quitting the game would be associated with loss of 'face' (humiliation);
- machine metaphors, which are derived from Descartes' theory by which the human body is seen as a machine with defective parts which can be removed and replaced;
- war metaphors, which encourage the fight against illnesses. The patient/soldier has to fight to the end to avoid a retreat that could be perceived as a shameful and coward act.

As regards metaphors created upon the concept of war, it can be seen that military metaphorical expressions appear in every aspect of medical language and jargon. Phrases such as "*She's got an infiltrating carcinoma*", "*the body defences*", "*he's having a heart attack*", "*killer T cells*", "*the war on cancer*", "*we must treat him aggressively and use everything in therapeutic armamentarium*" (Hodgkin 1985:1820) show that the language used, while coping with an illness, is cast almost entirely by the metaphor 'medicine is a war'. The reason for the introduction of military images in the language of medicine lies in the full institutionalization of the germ theory of disease by Pasteur (Montgomery 1996:142). This does not mean that the association between war and disease was not present before. However, military

expressions did not enter medical discourse before the XVIII century because of the predominance of other images for referring to disease¹³.

The medical use of war metaphors is not limited to physicians and patients; also pharmaceutical companies use them in marketing their products, as can be seen in the following slogan through which Novartis Pharmaceuticals promoted the aromatase inhibitor Fermara-letrozole: "*Fight hard and fight back in your battle against advanced breast cancer*" (Reisfield and Wilson 2004:4024-4027). However, since the conceptual metaphor 'medicine is a war' is predominant in oncology, what follows presents the strengths and limitations of military language in this area, considering the patient-physician relationship and the patient's experience of his/her illness.

According to Reisfield and Wilson (2004: 4024-4025), the use of war metaphors in oncology has several reasons:

- this metaphor is highly present in our society: it is applied to express several different concepts, like the 'wars' on drugs, on poverty, on teen pregnancy;

¹³ In the Middle Age, disease was seen as a punishment for sin and disobedience. In the Seventeenth and in Eighteenth centuries, disease became "a vision of discord and anarchy, these being the central aspects of deviance from nature" (Montgomery 1996:157). In the Nineteenth century, disease was seen as the result of the contact with the external environment or some external forces. At this time, ideas of struggle and conflict had a central importance. In particular, as Montgomery (1996:158) shows, the military metaphor was strictly connected with the concept of organicism of the century, when the nation-state was considered as a living body.

- it is easily adaptable to cancer because there is a perfect set of correspondences among its elements:

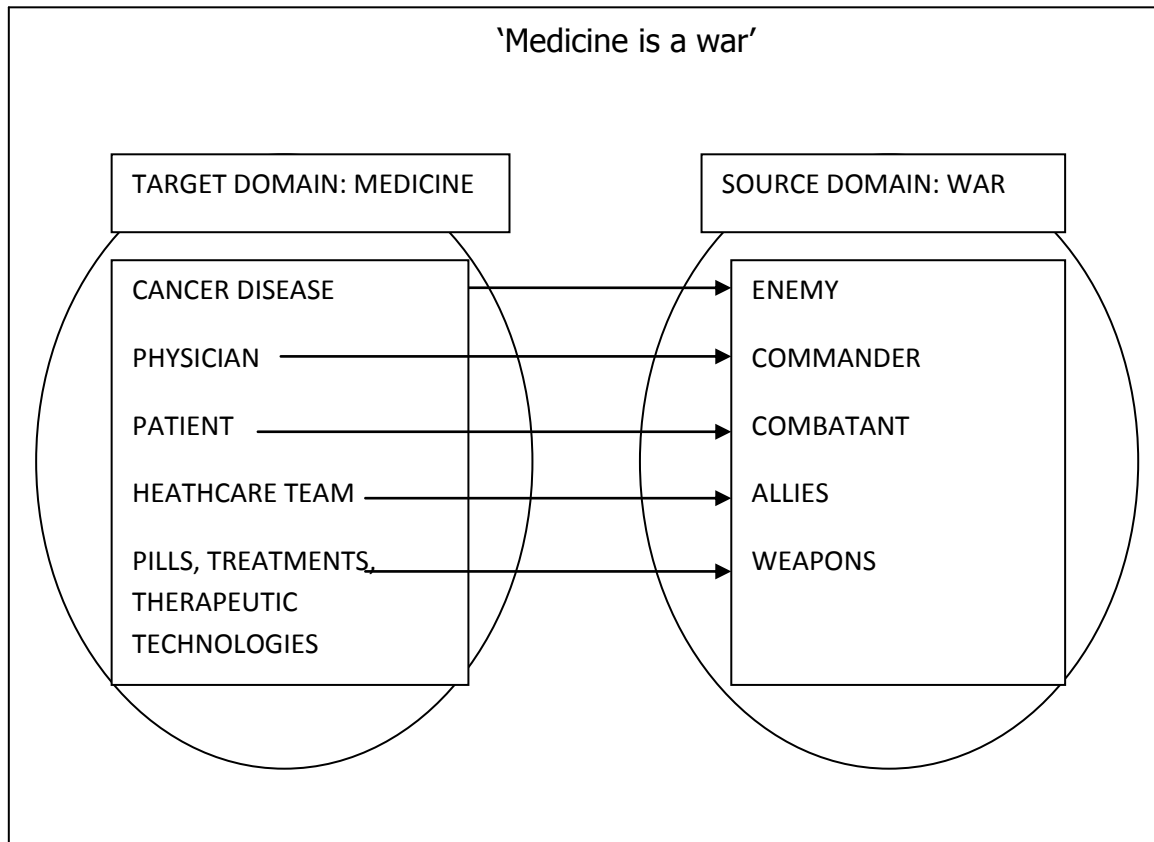


Figure 2.1. Set of correspondences between the source and target domain in the conceptual metaphor '*Medicine is a war*'.

- it has a serious purpose that matches perfectly the aim to cope with the illness;
- war, its images of power and aggression, serve as strong ideas in patients' mind which limit the feelings of powerless and passivity often associated to patients affected by serious illness.

Although the conceptual metaphor '*medicine is a war*' could be thought to fit perfectly the concept of cancer disease, there are some relevant limitations. The '*war*' metaphor is inherently masculine, power-based and violent; it emphasises that taking action is in itself a virtue; and it suggests that the defeat of cancer is only a matter of fighting hard enough (Reisfield and Wilson 2004:4026-4027). However, patients often cannot find the strength to fight this battle and, for some patients, conflict, fighting and war are not the preferred modes of coping with their illness. Moreover, the vast majority of malignant diseases cannot be eradicated because of

limited knowledge of the illness in medicine, which leads to inevitable treatment failures. Undoubtedly, *keep fighting* and *be courageous* - as concepts conveyed through the metaphor of war - may encourage physicians and patients to resist as much as possible, embarking on additional therapies with little or no expected medical benefit. However, the underlying idea that opting out of therapy would mean to lose the fight could affect patients' decisions about their lives. Patients might feel guilty or inadequate because of their inability to keep combating, accepting for this reason other treatments that would not provide any benefit. The rest of patient's life is often disregarded because all resources must be used in the battle.

According to Creaturo (2004:4025), the metaphor of war in oncology has conceptual weaknesses too. The battle against cancer is paradoxical: there are no real enemy invaders because the enemy consists of affected cells which are part of the patient's body. Therefore, therapeutic treatments indiscriminately destroy cancer cells (the enemy) and the immune system (the defender). Hence, the patient's battle could be described as a fight against him/herself. In Creaturo's words, "the weapons being brought to bear are real and powerful, and they can turn quite treacherously against the very individual they are intended to protect" (Creaturo 2004:4025).

In Lakoff and Johnson's view (1980:156), metaphors can emphasize some aspects and hide some others. Thus, different set of correspondences generate different metaphorical entailments. If we consider contemporary uses of the 'medicine is a war' metaphor, we can notice that the disease is always treated as the enemy, but two subtypes of fights should be distinguished: one in which there is a correspondence between the patient and the fighter, and the other in which the patient comes to be the battlefield and the role of soldiers is conferred to physicians (Fuks 2012:4). The latter seems to be the more common of the two and brings in itself relevant implications: the disease becomes the focus of physician's attention supplanting the patient's interlocutor role in the doctor-patient relationship. This shift of attention may lead patients to feel abandoned, as they may think that physicians are not able to understand and listen to their needs, concerns and feelings any longer. In Fuks's opinion (2012:2), the dialogic construction of the narrative of illness, created through the patient's voice and the doctor's talk, is supplanted by the

physician's desire for diagnostic clarity which overlooks the patient's need for relief of suffering.

In medical communication, the emotional sphere is very important and has a relevant influence on the patients' decision-making processes. However, at times, people's thoughts and feelings cannot be expressed by literal language. Therefore, people use metaphorical expressions.

Metaphor is one of the most important tools for trying to comprehend partially what cannot be comprehended totally: our feelings, aesthetic experiences, moral practices, and spiritual awareness. (Lakoff and Johnson 1980:193)

Metaphorical language may also be used by physicians to explain unknown medical concepts. On the one hand, by drawing on patients' past experiences¹⁴ and present knowledge to introduce unfamiliar concepts, physicians can help patients to understand and connect new information - about an illness and its treatment - with something they already know. On the other hand, using metaphorical language, clinicians can help patients to break down pre-existing ideas and mind-sets in order to discover something new about the illness. Moreover, in medical settings, metaphors are often used euphemistically to discuss and relate to complex and risky situations in a non-threatening and indirect manner. Metaphors may facilitate crucial conversations and difficult decisions: it is much simpler, for instance, to talk about fatal illnesses in terms of something else. In addition, in scientific discourse, metaphors may also be considered as a preferred method to coin new terms which, once they become part of the specialized language of the scientific community, could eventually be accepted as standard terms.

Nevertheless, metaphorical language has to be used carefully because it could lead to misperceptions and misunderstandings. For instance, when patients use metaphors that do not fit the illness concept, clinicians have to identify and explain the possible discrepancies, correcting in this way misperceptions and redirecting the patient to the real situation. Certainly, for physicians, metaphors can be time-efficient

¹⁴ *The primary function of a metaphor is to provide a partial understanding of one kind of experience in terms of another kind of experience. This may involve preexisting isolated similarities, the creation of new similarities, and more. The only similarities relevant to metaphor are similarities as experienced by people. Experiences may differ from culture to culture, and may depend on our understanding. (Lakoff and Johnson 1980:154)*

tools to help the patient understand complex biological processes; for patients, metaphors can facilitate the understanding process, helping them to be aware of their illness and allowing them to achieve an efficient communication.

To sum up, patients devise their own metaphors based on things they know and value, and are thus able to arrange their experiences in personally meaningful ways. Metaphors facilitate communication, serving as powerful tools to establish a consensual understanding of the therapeutic treatment; they allow patients to comprehend distinctive moments of the illness and can have profound effects on the illness experience. However, metaphorical language does not have to be used in an inappropriate way. Physicians have to be aware of the use of metaphors in clinical discourse; they should consider the fact that some patients may find the use of certain metaphors inappropriate; and they should pay attention to patients' metaphorical expressions. By listening to the language used by sick people, physician may understand how patients are living their illness experience, how they feel and which their attitude is towards further treatments (Reisfield and Wilson 2004:4024-4027).

As has been explained above, metaphorical expressions are used to facilitate patients' understanding. However, metaphors, metonymy, and similar kinds of transferred meanings always pose potential problems for non-specialists and non-native-language people (Salager-Meyer 1990:146).

Although metaphorical expressions do not hamper overall comprehension, they limit comprehension and can foster misunderstandings. While native speakers, by living in a given society, can easily understand metaphorical terms, simply by widening the application of known semantic concepts, terms based on metaphors are difficult to understand by foreign people for two principal reasons (Salager-Meyer 1990:147):

- foreign people may not know the concept's meaning in their mother tongue, thus they are unable to make the appropriate transfer;

- non-native speakers may know the concepts in their mother tongue but their knowledge of the target language is not sufficient to allow this transfer of meaning from one term to another.

An interesting comparative study was carried on by Salager-Meyer in 1990. Aiming at identifying and analysing metaphorical medical terms, she constituted a corpus of 30 texts in medical English, 30 texts in medical French and 30 in medical Spanish. Though the percentage of metaphorical expressions that was found is rather low, her analysis shows that scientific writers make use of a variety of source domains to express a concept or idea through metaphorical language. For example, considering the architectural domain, in medicine we find terms such as 'aortic *arch*'; 'fibrillation *threshold*'; while within the phytomorphical domain, we have 'coronary *tree*' and 'nerve *roots*' (Salager-Meyer 1990:151).

According to Salager-Meyer (1990:150), medical metaphors have a precise and definite terminological meaning and the semantic transfer of meaning takes place, in the three languages, within the same grammatical categories: the majority of metaphorical words belong to the nominal group and to a lesser extent to the adjectival and verbal groups:

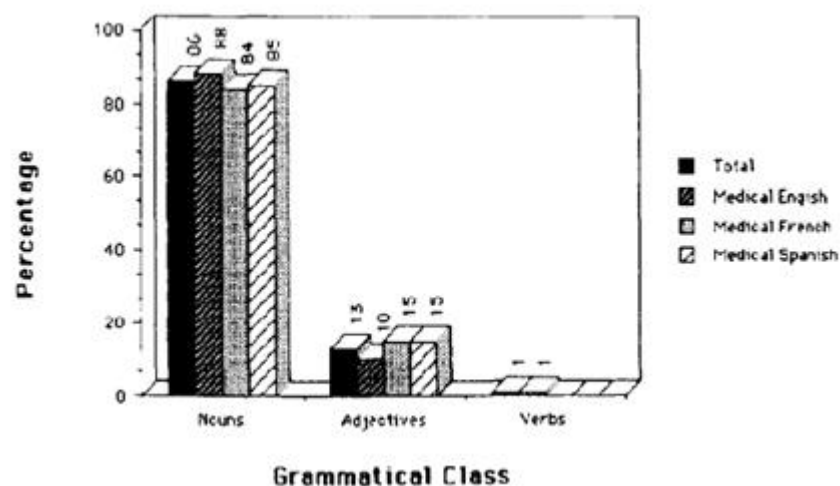


Figure 2.2 Grammatical classes of metaphorical terms in the three corpora. (Salager-Meyer 1990:152)

Furthermore, according to Salager-Meyer, the analogical way in which the transfer of meaning takes place in the three languages considered, could suggest

that medical metaphorical expressions are not linked to culture-specific idiosyncrasies. A number of other previous contrastive analyses confirm that similarities exist in the type, amount and manner in which information is conveyed in scientific discourse, thus supporting the hypothesis that scientific discourse is universal (Salager-Meyer 1990:153).

In order to see how metaphorical language is used in English and in Italian articles which talk about medicine, I have analysed seven articles taken from the section 'health' in the magazines *Scientific American* and *Le Scienze* (Appendix 2). The analysis shows that both Italian and English articles present several linguistic metaphorical expressions which are originated from the same conceptual metaphor, thus referring to the same *source domain*. Four frequent conceptual metaphors, which structure the way of talking in medical discourse, have been identified:

Conceptual metaphors	Italian	English
Medicine is a war	<ul style="list-style-type: none"> - Tumori <i>aggressivi</i> - La medicina sembra avere poche <i>armi</i> - La <i>battaglia</i> quotidiana con la malattia - <i>Proteggere</i> - <i>catturare</i> - <i>Attacco</i> di cuore - Funzione <i>difensiva</i> - <i>Bersaglio</i> - <i>Armati e all'erta</i> - <i>The ancient war</i> 	<ul style="list-style-type: none"> - <i>Aggressive</i> tumors - <i>Heart</i> attack - <i>Invasion</i> - Virus that <i>killed</i> - <i>Protect</i> - <i>capture</i> - <i>Body's defences</i> - <i>Counterattack</i> - <i>A fusilade of antibodies</i> - <i>Target</i> - <i>Armed and vigilant</i> - <i>L'antica lotta</i>
The human body is a machine	<ul style="list-style-type: none"> - <i>Meccanismo</i> - <i>Riparare</i> - <i>Danno/danneggiato</i> - Funzione di <i>pompa</i> 	<ul style="list-style-type: none"> - <i>Mechanism</i> - <i>restore/repair</i> - <i>Damage/damaged</i> - <i>To pump</i> blood
The genome is a text	<ul style="list-style-type: none"> - RNA <i>messaggero</i> - <i>Elaborare</i> l'informazione - <i>Decodificare</i> - <i>Risposta</i> 	<ul style="list-style-type: none"> - <i>Messenger</i> RNA - <i>Elaborate</i> - <i>decoding</i> - <i>answer/ response</i>
Cells are human beings	<ul style="list-style-type: none"> - <i>vita e morte delle cellule</i> - ciclo di vita: <i>generare-proliferare-degenerare-rigenerare/replicare-coltivare- alimentare</i> - <i>Popolazione</i> 	<ul style="list-style-type: none"> - The <i>birth</i> and <i>fate</i> of heart muscle cells - Life cycle: <i>generate-proliferate-degenerate-regenerate/renew/mak e copies- culture-nourish</i> - <i>population</i>

Table 2.3. Linguistic metaphorical expressions created upon the concepts of war, machine, communication and biology. The examples above are taken from articles in *Le Scienze* and *Scientific American* (Appendix 2).

By comparing the English articles with their Italian versions, it can be observed that metaphorical expressions do not change in the two languages. The *'war'* and *'machine'* metaphors are widely recognized by the scientific community and they are also widely understood by both Italian and English speakers. The metaphors referring to the domain of *'communication'* are quite widespread in genetics, where people talk about information written in the DNA, messages that are sent, and signals which have to be decoded. In this case, the underlying idea is that the flow of information from DNA to RNA is called *'transcription'*. According to Rijn-van Tongeren (1997:73), this conceptual metaphor could be formulated as "A genome is a text". Similarly to the metaphoric expressions which refer to war and machines, the metaphor of *'text'* can be understood without any difficulties by both the Italian and the English community. The same reasoning can be applied to the biological metaphors which depict cells as living bodies having a life cycle and living within a *population of cells*.

Yet, every time we discuss about science, considering text type is essential. The use of metaphorical language may largely differ depending on the type of text and on the level of assumed shared information between the target reader and the writer. For example, in articles found in *Scientific American* and *Le Scienze* (medium-level interspecialist popular science magazines), a familiarity with some of the basic concepts of medicine is taken for granted, whereas in articles published by popular science magazines, such as *National Geographic*, the writer needs to explain the scientific concept in a more direct and thus comprehensible way. Therefore, in Italian and English popular-level-science articles, concepts may be expressed through different semantic structures, such as culture-specific metaphors, and they may also be influenced by the author's writing style.

In order to see the differences that may exist between the English source text and its Italian translation, some metaphorical expressions taken from two articles published in *National Geographic* and *National Geographic Italia* (Appendix 3) are considered in the following table.

Italian version	English version
<p>“Influenza, la caccia ai nuovi vaccini”</p> <p>(computer metaphor)</p> <ul style="list-style-type: none"> - Occorre <u>aggiornare</u> il vaccino <p>(war metaphor)</p> <p>Virus- nemico:</p> <ul style="list-style-type: none"> - <u>Contrastare</u> le proteine del virus - un vaccino che <u>combatta</u> il virus - un vaccino universale che <u>protegga</u> dall’influenza stagionale - <u>combattere</u> ceppi particolarmente aggressivi del virus <p>Natura “sfuggente” del virus dell’influenza</p> <ul style="list-style-type: none"> - Geneticamente flessibile - “E come dover mettere un capotto nuovo ogni inverno” <p>“Avremmo anche noi l’udito di superman?”</p> <ul style="list-style-type: none"> - Udito di <u>Superman</u> <p>Suono a 20 Hz:</p> <ul style="list-style-type: none"> - ciò che sentiremmo “a un <u>concerto rock</u> se ci trovassimo vicino al bassista” <p>Coclea:</p> <ul style="list-style-type: none"> - A forma di chiocciola 	<p>“How far off is a better flu shot?”</p> <p>(computer metaphor)</p> <ul style="list-style-type: none"> - The vaccine has to be <u>updated</u> <p>(war metaphor)</p> <p>Virus-enemy:</p> <ul style="list-style-type: none"> - <u>Target</u> proteins in the influenza virus - A vaccine <u>against</u> the virus - a universal vaccine that <u>protects</u> against seasonal flu - <u>fend off</u> a major new flu virus - A dangerous <u>threat</u> <p>Influenza virus is a <u>slippery character</u></p> <ul style="list-style-type: none"> - “genetically plastic” - “It’s like putting on a new sport coat every winter” <p>“Superhuman hearing possible, experiments suggest”</p> <ul style="list-style-type: none"> - Superhuman hearing <p>20Hz sound:</p> <ul style="list-style-type: none"> - what you'd hear if "you were at an <u>R&B concert</u> and you just stood next to the bass” <p>Cochlea:</p> <ul style="list-style-type: none"> - Resembling a tiny snail

Table 2.4. Figurative expressions in two English articles and their Italian versions (taken from *National Geographic* and *National Geographic Italia*).

In the articles, we see the underlying presence of two conceptual metaphors (the one which refers to *war* and the other which refers to *communication* in computer science¹⁵). The metaphorical expressions which are created on these two concepts are used in the same way in English and in Italian. However, by observing other examples quoted above, we see that in the two languages, metaphorical concepts may be expressed by different linguistic forms.

¹⁵ Information theory entered medical discourse only in the last five decades, precisely in 1953, when Watson and Crick discovered the structure of DNA. The language introduced with the information theory is called by Montgomery (1996:150) *bioinformationism*, and it is more likely to be found when talking about genes or about how viruses and cells work.

For example, if we consider the English metaphor '*Influenza virus is a slippery character*', we can see that, throughout the paragraph, there is a sort of 'development' in the explanation of this metaphor:

- the idea of '*Influence is a slippery character*' is firstly simply outlined as a metaphor;
- later in the paragraph, the explanation of its slippery nature is slightly extended with the sentence stating that the influence virus is '*genetically plastic*';
- finally, the meaning of 'genetically plastic' is depicted through the simile '*It's like putting on a new sport coat every winter*'.

The Italian translation follows the same 'development', yet the initial metaphor has been changed: the Italian version presents the '*slippery character*' as an attribute of the influenza virus.

Furthermore, we can observe that, in *National Geographic* articles, concepts are expressed in a more direct manner that is easily comprehensible by a wider variety of non-specialist readers. Therefore, the writer may also choose to explain a concept through the use of suggestive images, as can be seen in the example where '*Superman*' is used in the Italian text to express the idea of a super hearing. Similarly, according to the purpose of clarity and accessibility of the content, the writer may also refer to popular-culture, which provides - in this case - the necessary background knowledge for understanding such images. For instance, if we consider the image of the concert, we can see that the idea of the bass sound during an R&B concert is conveyed in Italian with the idea of a bass sound in a rock concert. In this case, since Rhythm and Blues music is a popular African-American genre, which has no corresponding consolidated tradition in Italy, the Italian author refers to the idea of rock music because it is more effective for the target readers. Therefore, we can notice that concepts may be expressed in different ways depending on the cultural and social backgrounds of the readers.

2.2 Syntactic Features

Medical English shows not only morphological peculiarities but also particular syntactic characteristics. The main phenomena are introduced and explained in the following text through several examples taken from medical journal articles and patient information leaflets.

a. Noun phrases (NPs)

Scientific medical writing is characterized by a high presence of long and complex noun phrases. This phenomenon can be explained by the fact that medical formal writing needs a syntactic device¹⁶ which allows the expert to convey the meaning of a complex medical concept in a highly precise and concise manner. Medical concepts are usually complicated to express and the expert need to include a various number of information in the explanation. Additional elements which define a given concept could seem unnecessary for non-experts, but in medical contexts, the specialist has to be as precise as possible to avoid ambiguities and misunderstandings. Therefore, the use of compound noun phrases helps the writer to avoid long and detailed descriptions which would create difficult syntactical constructions. In fact, according to Varantola (1984:209), noun phrases are a powerful syntactical tool which allows users to incorporate a great deal of information in a compact and synthesized form. Obviously, their structure can vary from very simple forms to extremely complicated constructions according to the genre of the text, its assumed addressees and the author's communicative aims.

Considering two different genres of written medical discourse, patient information leaflets and specialized journal articles¹⁷, it has been observed that noun phrases are usually created through the elimination of post-modifier clauses.

¹⁶ According to Beneventiste (1971, in De Mauro 1994:9), the expert creates an utterance which is impersonal and extemporal. The meaning of the utterance is conveyed through terms which are reduced to their semantic content.

¹⁷ "Aortic pulse wave velocity measurement in systemic sclerosis patients" (Colaci et al. 2012:360-367). "Rheumatoid arthritis, anti-tumour necrosis factor therapy, and risk of malignant melanoma: nationwide population based prospective cohort study from Sweden" (Raaschou et al. 2013:1939).

For instance, prepositional phrases with *of*, *in*, *for* are generally replaced by pre-modifier elements of the head noun. Some examples are quoted below:

Root nodule bacteria (bacteria to be found in root nodules)

The operating room (the room for carrying out operation)

Fibroblasts activation (activation of fibroblasts)

Aortic pulse wave velocity measurement (measurement of the velocity of the wave of the aortic pulse)

In this way, different elements are put together without the use of grammatical words which would just complicate the syntax and increase the length of the sentence. In specialized discourse, the omission of all those words which do not carry any lexical meaning allow experts to communicate most rapidly. Therefore, highly specialized texts are generally lexically dense: the number of content words is higher than that of grammatical words. The so-called function words, such as articles, prepositions, conjunctions, auxiliary verbs and pronouns, do not convey the meaning of an utterance; they just show the syntactic and grammatical relationships which link the different elements of a sentence. In fact, according to Maglie (2009:35), the omission of phrasal elements does not prejudice the understanding of the text, because they do not convey any lexical meaning and their grammatical value can be easily re-established by the specialist.

Nevertheless, in my opinion, complex noun phrases expressing detailed and precise information about the head noun may cause some problems of decoding for non-specialist people, who may not be able to establish the exact semantic relationship which links all the lexical elements of the nominal group. To provide an example of this problem, we can consider the nominal clause "*a cumarinic anticoagulant-based therapy (warfarin, dicumarol,...)* (Moment medication's leaflet)". In this nominal clause, we can immediately understand that the therapy is based on treatment with anticoagulants. However, if the reader does not know what *cumarinic* is, s/he would find it difficult to understand the connection between the word *cumarinic* and the other elements in the nominal group. One may think that cumarine is a kind of anticoagulant drugs, instead of understanding that cumarine is actually an enzyme that is present in anticoagulant drugs. Therefore, the reader would not be able to decode the exact meaning which is being conveyed.

To support this statement, we can notice that the patient information leaflet of Moment tends to clarify and give an idea of what cumarinic anticoagulants are, by providing some examples within parenthesis, i.e. *warfarin, dicumarol*.

Similarly to prepositional phrases, in specialized medical texts relative clauses are often avoided for the sake of economy and simplicity. They are often replaced by other elements within the nominal clause or shortened by omitting some elements. We find, for instance:

- relative clauses replaced by nouns

Patients who are affected by scleroderma -> *scleroderma patients*

Patients who have systemic sclerosis -> systemic sclerosis patients -> *SSc patients*

- relative clauses replaced by adjectives

Non-invasive tools (tools which are not invasive)

Abnormal pulmonary function (pulmonary function which is abnormal)

- relative clauses replaced by gerunds

May cause allergic reactions, *including asthma* (Strepsils)

There have been rare reports of blood disorders in people *taking products containing paracetamol*,..(Benylin)

Moreover, when the verb in the relative clauses is in the passive form and does not take a complement, it may become a past participle used in adjectival position, as in the following examples:

The registered waves (the waves which have been registered);

All recruited female patients (all female patients who have been recruited).

Or, if it takes a complement, subject and auxiliary are often omitted:

Thirty-five patients [...] followed at the Rheumatology centre and [...] affected by SSc...

[that have been]

[who were]

For the same reason of concision and shortness, negative relative clauses are usually expressed by the prefix *un-* before a past participle in adjectival position, as in the following examples:

Unwanted/ unexpected/ undesirable effects;

Unselected SSc patients.

To sum up, there are several ways to simplify the syntax of a text and several functional elements can be omitted without prejudice the sentence's meaning. However, syntactic simplification does not make a text easier to understand; on the contrary, at times, it may be a source of ambiguities and incomprehension.

a. Sentence complexity

Despite this search for concision in medical terminology and in the structure of clauses, medical texts present a high degree of sentence complexity. In fact, both kinds of text - patient information leaflets and specialized journal articles - show that medical sentences are longer than those of everyday language. Although the length of the sentence is another factor which complicates the comprehension of medical texts, it is very difficult to reduce sentences' length because the omission of certain necessary elements could create information gaps or ambiguities. In addition, according to Maglie (2009:36), the complexity of medical sentences derives from the use of a great number of non-finite verb forms, which occur with double the frequency in medical specialized texts in comparison with standard English.

Considering an example taken from the patient information leaflet of Moment medication, we can observe how and why medical sentences are long and complicated:

"In some patients with impaired renal function (such as dehydrated patients or elderly patients with impaired renal function), the co-administration of an ACE-inibitor or an Angiotensin II Antagonist and agents inhibiting the cyclo-oxigenenase system can lead to further impairment of the renal function, including a possible, usually reversible, acute kidney insufficiency." (Moment)

Patients: dehydrated patients, elderly patients with impaired renal function

Kinds of inhibitors: ACE-inhibitors, Angiotensin II Antagonist, inhibitors of the process cyclo-oxygenase

Effects: further impairment of the renal function, possible acute kidney insufficiency.

In the sentence quoted above, it can be seen that the writer has to explain within parenthesis which are the types of patients he/she is referring to. He/she has to list all kinds of inhibitors which should not be co-administrated with *Moment* in patients with impaired renal function; and he/she has to specify that further impairment of the renal function may also means a possible kidney insufficiency. Therefore, although specialist writers tend to be as concise as possible, we may state that exhaustiveness and precision are the key terms of medical English and assume a more relevant role in comparison with concision.

b. Impersonal structures

As many other specialized languages, medical English shows the tendency to give more importance to nouns instead of verbs. This tendency can be demonstrated by three different devices: the creation of long nominal phrases without the presence of a verb in the finite form (as has been explained in the previous paragraph); the use of nouns - which express lexical meanings - while verbs are conceived as mere syntactical connectors (Serianni 2005:255); the reduction of inflected forms of verbs, the use of which is usually limited to the 3rd and 6th person of the indicative form. All these phenomena provide not only a formal tone to the text, but also an impersonal style.

Another characteristic that is worth highlighting is the use of passive voice. The frequent use of passive forms satisfies the need for depersonalization of medical discourse: specialists are more interested in focusing on the effects, conditions and results of an action than in stressing who the author of an action is. In fact, in medical writing the agent is seldom expressed. The elimination of the agent can be explained by the fact that, usually, medical articles are not written by doctors themselves or because the articles are co-authored; the writer's primary aim is to describe something that has been done, focusing in methods and results. In addition,

it is quite obvious that implicit agents are physicians and researchers; therefore, it would be useless and redundant to explicit the agent.

Authors, editors, and publishers have a choice about the role of the passive voice in their publications, and there is considerable debate about what that role should be. On the one hand, there is the argument that medical writers should minimize the use of passive voice because it is less clear, less forceful, and more verbose than active voice alternatives. Of this opinion is Sheen (2010:98), who defines passive voice as:

the bane of medical writing; it pervades medical literature with the haze and heaviness of stagnant air. Writers sometimes use passive voice in an attempt to make their work sound scholarly and scientific, when actually they are perpetuating a writing tradition that is fraught with ponderous and obscure language.

The opposing argument asserts that passive structure should be the predominant style of most types of medical writing because it reflects the objectivity of the scientific method, it avoids using a first-person pronoun in a way that would be impolite, and it conforms to the style with which medical peers are most familiar. This idea is supported by Scarpa (2008:46), who states that the major function of passivization is to "spersonalizzare e oggettivizzare ciò che viene scritto". Therefore, the use of passive voice confers not only an impersonal style to the text but also a higher degree of formality, which, together with objectiveness, is one of the major aims of medical texts.

Chapter three: patients and the language of medicine

Considering several theories through which language has been analysed, the contextualised approach appears to be the most effective. A large number of linguists define discourse as a process of social interaction, considering the linguistic act just a part of it (Graddol et al.1994:16). According to Hyland (2009:20), "discourse analysis is a way of studying language in action, looking at spoken and written interactions in relation to the social context in which they are used".

An understanding of how language functions in context is central to comprehend the relationship between what is said and what is understood in spoken and written discourse. The *context of situation* (Halliday 2006:53) of what someone says is, therefore, crucial to interpret and decode the meaning that is being conveyed. The *context of situation* includes the physical context, the social context and the roles of people involved in the interaction. As Thomas (1995:22) puts it:

meaning is not something that is inherent in the words alone, nor is it produced by the speaker alone or the hearer alone. Making meaning is a dynamic process, involving the negotiation of meaning between speaker and hearer, the context of utterance (physical, social and linguistic), and the meaning potential of an utterance.

Therefore, meaning is produced during interactions: it is jointly accomplished by both the speaker/writer and the hearer/reader who collaborate in the production of meanings as they communicate with each other.

Following this approach, medical language cannot simply be defined as the medium through which physicians, nurses and doctors communicate among themselves within the specialized medical community. Since health care is a fundamental aspect of everybody's life, we need to be aware of the fact that knowledge of various medical concepts and terms is quite common even among ordinary people. Medical language is used in a variety of contexts in which participants are non-expert health professionals. By watching, for instance, television programmes which talk about particular diseases, advertisements of pharmaceutical products, information leaflets for patients, and promotions of prevention campaigns against particular diseases, we can see that this specialized information are

addressed to a non-specialized audience. Therefore, even though people do not come into direct contact with an expert in the field, the doctor, they may collect a number of specific concepts and specialist medical notions in various alternative ways.

For this reason, what follows will focus on two different situations in which common people may come in contact with the language of medicine: doctor-patient interactions and patient information leaflets. The former (spoken interaction) implies a contact with a health professional, while the latter (written discourse) does not necessarily need the mediation of an expert, such as a doctor or a pharmacist.

3.1 Doctor-patient interactions

The fundamental interaction in health care is the one which occurs between patient and physician. Its importance in medical practice is well established and it has become the focus of increasing interest through several different routes. Doctor-patient relationships are fundamental to providing and receiving excellent care, to the healing process and to improved outcomes. Therefore, it is important to understand their underlying elements and to identify which elements allow us to define it a *good relationship*.

The doctor-patient relationship is a socially sanctioned, institutionalized encounter governed by mini-rituals of opening and closing, by a logic of information exchange, by time, place and task constraints, and by setting specific diagnostic aims. (Manning 1987:20)

Clinical practice is centered on the patient¹⁸; its main active agent is the physician or the therapeutic team; their main activities deal with patient history, diagnosis, prognosis, therapy and prevention. The relationship between doctor and patient is usually created through the clinical encounter: by expecting the physician to be an expert, the patient decides to consult a doctor to have medical care and advice. The clinical encounter serves many purposes and among the most important

¹⁸ A widespread misconception about medicine is that medicine is just concerned with illness and disease. However, the subject of medicine is the patient and all the activities have to be directed towards the prevention and relief of human suffering (Sadegh-Zadeh, 2012:110).

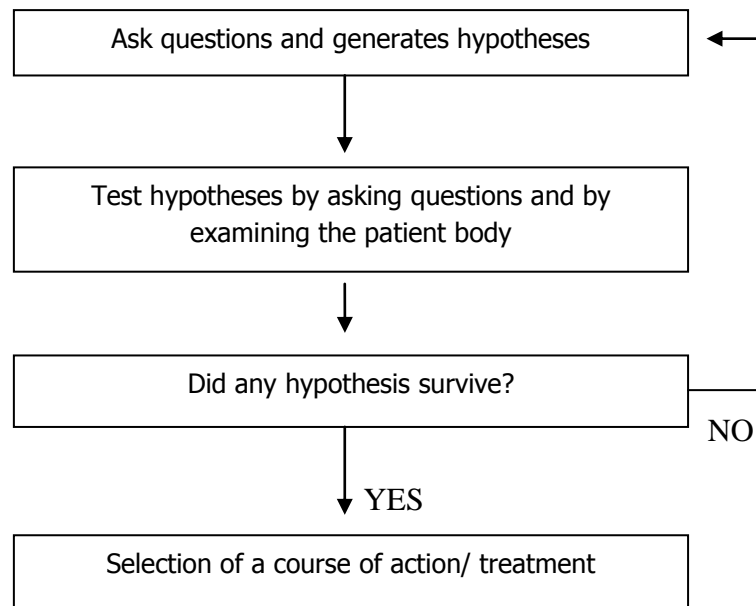
of them, we can find the task of establishing a relationship of mutual trust between the physician and the patient.

The clinical interview of the patient, the so-called *history taking* or *anamnesis* (Sadegh-Zadeh, 2012:275), is the verbal component of the inquiry through which the physician elicits information to understand what affects the patient and what should be done for him/her. Diagnoses are usually made from the *medical history*, and a good history almost always means that communication between doctor and patient has to be effective. Therefore, patient-doctor communication¹⁹ is the building block upon which the physician's relationship with the patient is made.

a. The physician's role

Generally, from the very beginning of the clinical interview, the physician generates and tests diagnostic hypotheses. Starting only from a few elements, such as the patient's initial problem, gender, age, voice and appearance, the doctor automatically forms an initial idea of what the patient might have. However, since the data initially provided by the patient are not sufficient to form a clinical judgment, throughout the interaction, the doctor asks specific questions to acquire more data which would be useful to evaluate and test his/her initial hypothesis. During the interview, the physician continues to adapt the dialogue, asking questions which are considered relevant to obtain a final and unique diagnosis. As Sadegh-Zadeh (2012:278) suggests, the entire interview, including the physical examination which follows, can be defined as a cyclical process of hypothesis-testing actions. The clinical reasoning of doctors is schematized below:

¹⁹ Doctor-patient communication consists of both the verbal and non-verbal processes through which doctors obtain and share information with patients (Sadegh-Zadeh 2012:285).



Clinical reasoning is generally referred to as *differential diagnostics* (Sadegh-Zadeh, 2012:277). This term reflects the common belief that in clinical practice, the physician initially considers all diseases that may be apt to explain the current problem the patient presents; secondly, the physician selects the potential diseases according to their probability and plausibility; and finally, the doctor differentiates between true and false diagnoses by testing them. Nevertheless, according to several claims this logical process does not occur in real medical practice because no method of clinical reasoning is taught to medical students (Sadegh-Zadeh 2012:278). As a result, physicians usually lack methodological knowledge about how to generate meaningful diagnostic hypotheses, how to use patient data correctly and effectively, and how to evaluate the hypotheses during the medical encounter. Moreover, despite the recent development of high-technology diagnostic procedures, it is claimed that the majority of patients' problems could still be solved during the first few minutes of the patient interview (Cutler in Sadegh-Zadeh, 2012:278).

As regards all the activities that a physician is supposed to do during a medical encounter, we recognize that it is quite a hard job. Doctors not only have to establish a good and purposeful relationship with the patient, organize and adapt the conversation, and make hypotheses about diseases and treatments, but they also

have to listen carefully to the patient, to give him/her the attention needed, to solicit the patient to present his/her concerns and to interpret all the information – whether useful or not - the patient provides. Physicians have to “ask a variety of detailed questions, evaluate patients’ accounts, comment on their general state of health, and suggest reasons for their problem and possible courses of action” (Mishler 1984:5).

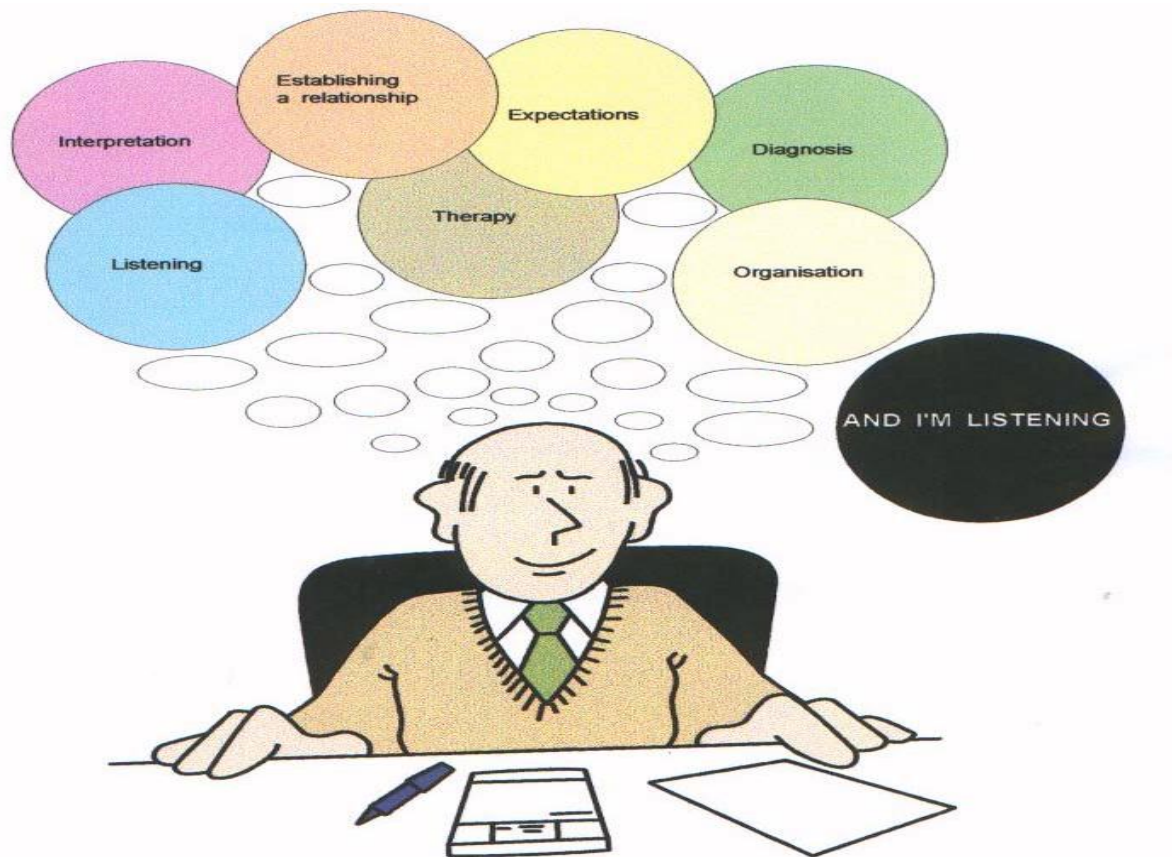


Figure 3.1. Physicians’ activities during medical encounters. This image was taken from Welsby (2003:3).

In May 1999, at a conference sponsored by the Bayer Institute for Health Communication and the Fetzer Institute, seven components were identified as fundamental to all encounters between clinician and patient. These points could enhance efficiency in doctor-patient communication, improve quality of care and time management (Nelson in Bakić 2008:75):

- Build the relationship
- Open the discussion
- Gather information
- Understand the patient's perspective

- Share information
- Reach agreement on problems and plans
- Provide closure

However, despite the application of these guidelines, the situation of the medical interview is complex, dynamic and often unpredictable: all doctor-patient interactions are usually influenced by the expectations of both parties (Haftel, 2008:1); there are no standard doctors and patients; and what may be useful or accepted by a patient may not be suitable for another.

According to Simpson et al. (1991:1385), most complaints about physicians do not deal with clinical competency problems, but with communication problems; and the majority of malpractice allegations arise from communication errors. Among the deficiencies in doctor-patient communication, a substantial problem seems to be the high number of patients who do not understand or remember what their doctors tell them about diagnoses and treatments. Moreover, patients' dissatisfaction has been shown to be mainly related to uncertainty and lack of information, explanation, and feedback from the doctor. Doctors are often blamed for not listening to their patients' concerns and they are often criticized for not having enough time for their patients. As a result, many patients leave the consultation without asking questions concerning doubts that are troubling them and feel unsatisfied for the health service provided (Simpson et al. 1991:1387).

Another important element which contributes to the patients' dissatisfaction is the language used by doctors. It is often unclear and contains medical jargon that is not fully comprehensible by patients who do not possess the same medical knowledge as their physicians. The use of medical jargon may cause misunderstandings and it can also encourage patients to use medical terms improperly. As highlighted by Welsby (2003:7), words may have different meanings in different contexts and this is exactly the case when general words are used in medical discourse. Patients may think they understood the terms. Instead, they may have attributed non-medical meanings to them.

The examples in Table 3.2 below show different meanings which may be attached to different terms by medical professionals and by patients:

TERMS	MEDICAL MEANING	NON-MEDICAL MEANING
acute	Rapid onset	severe
numb	Lack of cutaneous sensation	Any abnormal sensation
chronic	Long term, long-lasting	severe
migraine	A specific headache syndrome	Any severe headache
cancer	Histologically malignant	Universally fatal

Table 3.2. How terms can be differently perceived from patients and physicians. The examples are taken from Welsby (2003:7).

Therefore, while passing from doctors’ mouths to patients’ ears, terms may take on different connotations, because they may be understood in inappropriate ways. Therefore, physicians’ explanations and check about what patients understand is fundamental in order to avoid misinterpretations. Doctors should monitor the level of jargon they use, they should provide explanation in a totally comprehensible language, and they should avoid the use of potentially frightening words - such as cancer - because they could result in patients’ negative reactions (Welsby 2003:8).

b. The patient

A living human body is not a mere assemblage of things such as arms, legs, stomach, brain, cells, and other elements. A patient is a living being consisting of body and mind, a member of a family, of a community and of a larger cultural society. When patients seek the advice and care of a doctor, they go to the physician’s clinic and, with the help of questions doctors ask to gather information, they start describing their symptoms. During their explanations, patients may load their narratives with unnecessary information and personal concerns, which are, for patients, of primary interest. The importance that patients give to some additional information may not be appropriate for doctors, who have the ‘power’ to shift the conversation towards the most medically-relevant aspects. However, a great influence on the success of medical treatments has to be attributed to patients’ illness framework in terms of their subjective experience and meaning of illness,

psychological impacts on the patient's self concept and everyday life, patients' beliefs, priorities and preferences for treatment (Myfanwy 2008:55). According to Waitzkin (1991:3), illness affects the whole of people's lives and a patient's experience of physical problems is inseparable from the wider social context in which these problems occur. Effective diagnoses depend not only on the identification of physical symptoms, but also on the identification of those symptoms that may have psychological or social origins, thus requiring different treatment plans (Bird et al. 1993:1). Therefore, doctors who attentively listen to their patients facilitate and encourage the patient's active involvement during the healing process.

In Mishler's opinion (1984:95-96), physicians always control the contents of their consultations. The relevance and appropriateness of information can be defined in terms of what physicians choose to attend to and to ask about. Occasionally, the flow of the interview can be interrupted by the *voice of patients* (Mishler 1984:95) when they refer to the personal and social contexts of their problems. But, generally, such disruptions are always reasserted by physicians. Despite the leading role of physicians during the consultations, patients can always assume a more participative attitude by interrupting the doctor with questions or requests for explanations.

In this respect, according to Myfanwy (2008:56), younger people seem more likely to expect a relationship of mutual participation than elderly people do. Similarly, patients with higher educational level tend to participate more during the consultation compared with patients from lower socio-cultural background. However, despite these differences of attitudes, patients' participative approach during the communicative exchange generally increases over the course of an illness as patients gain more knowledge and understanding of their health condition (Myfanwy 2008:57). It can also be pointed out that because in general practice there is the opportunity for continuity of care, with doctors and patients often knowing each other over a long period, patients may feel more at ease to express their own concerns, doubts and worries than in other settings, such as hospitals (Myfanwy 2008:58).

The asymmetry which characterizes doctor-patient relationships may also be explained by looking at participants' different priorities. On the one hand, doctors

need information to establish the right diagnosis and treatment plan; whereas, on the other hand, patients need to know and understand what is going on and they need to feel listened to and understood. According to the *European Task Force on Patient Evaluations of General Practice* (1998:175-186), the most highly rated priorities of patients are: humanness, competency, patients' involvement, doctors' listening skills and provision of information.

Another fundamental element which has to be considered while talking about medical consultations is the underlying concept of informed consent. The patients' right to make decisions about medical treatments has been enshrined in legal and ethical statements throughout the world. The *Declaration of Lisbon on the Rights of the Patient* (WMA 2005, Art.7) reads:

The patient has the right to self-determination, to make free decisions regarding himself/herself. The physician will inform the patient of the consequences of his/her decisions. The patient has the right to the information necessary to make his/her decisions. The patient should understand clearly what is the purpose of any test or treatment, what the results would imply, and what would be the implications of withholding consent. Information should be given in a way appropriate to the patient's culture and in such a way that the patient can understand.

Therefore, a necessary condition for informed consent is effective communication between physicians and patients. Physicians have to provide patients with all the information they need to make their decisions. They have to explain complex medical diagnoses, prognoses and treatment regimes in simple language, ensuring that patients understand what they say. They should present all treatment options, advantages and disadvantages of each treatment. Physicians' successful communication will provide all necessary information to patients, thus allowing them to make an informed decision about how to proceed.

Similarly, the *European Charter of Patients' Rights* (2002) reads:

Art.3. Right to Information: Every individual has the right to access to all kind of information regarding their state of health, the health services and how to use them, and all that scientific research and technological innovation makes available.

Art 4. Right to consent: Every individual has the right of access to all information that might enable him or her to actively participate in the decisions regarding his or her health; this information is a prerequisite for any procedure and treatment, including the participation in scientific research. Health care providers and professionals must use a language known to the patient and communicate in a way that is comprehensible to persons without a technical background.

Art.5. Right to free choice: Each individual has the right to freely choose from among different treatment procedures and providers on the basis of adequate information.

As can be seen, both documents emphasize the need to use a language that patients know and they highlight the fact that medical information should be provided in a way that is coherent with the linguistic and technical background knowledge of patients.

However, despite all misunderstandings which may occur during medical encounters, spoken discourse can be regarded as taking place in real time and being generally interactive: people speak in turns and have a direct feedback from the real audience they are addressed to. Therefore, during consultations, both doctors and patients have a direct feedback. On the one hand, doctors may always modify their talk when they realize that their message is not passing and they can always check whether the message is clear enough for their patients or not. On the other hand, patients always have a chance to interrupt their doctors to ask for further explanations.

To sum up, according to doctor Shmerling (Appendix 4):

[...] the main difficulty is that physicians spend so much time immersed in the language doctors use that they forget that patients cannot understand them. And patients are often hesitant to ask for clarification. Much like translating a foreign language, doctors have to remember to slow down and communicate in terms their patients will understand. Conversely, patients need to understand that it is okay to ask their doctors to explain things more clearly.

2.3 Changing dynamics in doctor-patient relationship

Before the information era, knowledge of medicine belonged only to the physician. In early 1980s, doctors were seen as “intractable holders of power, collectors and analyzers of technical information elicited from patients” (Mishler 1984:10). Patients were perceived as passive objects whose only task was to answer physicians’ queries, listen to doctors’ indications and comply. Because of widespread ignorance and illiteracy among people, and the consequent difficulties in accessing medical information, patients could not form their personal opinions. Therefore, for any health problem, patients used to go visit the doctor, who was the only channel for them to acquire information on their health status.

Parson (1951), who was one of the earliest sociologists to examine the role of doctors and patients, portrayed doctor-patient relationship as an asymmetrical relationship: by virtue of his or her specialist knowledge, the doctor occupied the dominant position and the patient merely cooperated (Myfanwy 2008:54). This paternalistic view about the role of doctors traditionally characterized medical consultations. Patients relied on the doctor and were relieved of worries and responsibilities of decision-making, while doctors directed care and made decisions about treatments on their own, thus maintaining an authoritarian behavior and a high control over their uninformed patients. However, this asymmetry of power resulted in inevitable inequalities between doctor and patient in terms of status, knowledge and access to other health related services (Todd and Fisher 1993:ix).

In more recent years, medical consultations began to change. Patients became increasingly involved during the consultation, thus creating a relationship of mutual exchange of ideas and opinions between doctors and patients. In this way, the doctor brings his/her clinical skills and knowledge to the consultation in terms of diagnostic techniques, knowledge of the diseases’ causes, prognoses, treatment options and preventive strategies, while patients bring their own experiences, explanations of their illnesses, their social circumstances and their treatment preferences (Myfanwy 2008:54). Consequently, in the communicative act, patients are seen as partners whose knowledge gaps should be filled by educating them.

But still, according to Andersons et al. (2003:75), the doctor plays the role of the active interlocutor and medical information is provided at the physician's discretion.

The doctor-patient relationship continued to evolve and nowadays it is rather complex to explain. People's educational level and health awareness have increased. In the past 30 years, medical care in the Western world has increasingly emphasized patient autonomy in decision making (Gotti and Salager-Meyer 2006:11) and the trend toward preventive medicine contributed to the patients' desire to acquire as much medical knowledge as possible. As a result, patients assume more responsibility for their own health and they actively participate in health-related decisions that affect them.

Health information has become more accessible: the doctor is no longer the only channel to acquire medical information and physicians are increasingly confronted with patients who empower and educate themselves using different sources. In recent time, the media, such as the television, the radio, newspapers and magazines, provide a constant and readily accessible supply of health care information and advice. The media cover advances in medical treatments and new drugs; they alert their audiences to health risks; they promote the value of taking care of the self; and they may also provide detailed insights on socio-political issues like medical funding and health service delivery. The provision of health information is widely distributed across the media occurring, for instance, in news stories, documentaries, medical and science programs, and health promotion campaigns²⁰ (McKay 2006:311). In this way, the information gap between doctors and patients is reversed and physicians feel threatened by the fact that many patients seem to have more information than doctors (Anderson et al. 2003:77).

However, nothing has influenced doctor-patient relationship more fundamentally than one technological innovation: the Internet.

²⁰ Nowadays, health and illness are major themes in entertainment media forms too, like television dramas and TV series, lifestyle shows and soap operas (McKay 2006:311).

In the article *La rivoluzione del paziente informato nel "villaggio globale"*, Miglino (2012:14) states:

Sono lontani i tempi in cui il medico era un vero e proprio oracolo e il sapere discendeva da lui verso un paziente in forte soggezione e timore reverenziale. Oggi chiunque abbia un problema di salute accende un computer, digita una parola chiave su Google, entra in un sito, legge, stampa e corre dal medico con la frase che lo indispette più di ogni altra cosa: Dottore ho letto su Internet... .

According to Akerkar and Bichile (2004:120), we are now assisting to the *e-patient revolution*:

they are arriving at your clinic armed with information they have found on the web, with a preconceived idea about their diagnosis and treatment options, more demanding regarding convenience and ease of access. They want to actively participate in therapeutic decisions and want all the decisions to be informed and intelligent. Meet the new empowered patient!-empowered by the information technology and its benefits.

The Web has upended the past scenario. It has become a source of health information and it offers virtually unlimited amounts of information: health and medical websites provide an enormous range of health-related material, while chat rooms and newsgroups facilitate patient-to-patient interactions and discussions (McKay 2006:312). Generally, greater access to high-quality medical information on the Internet increases the number of informed patients who bring detailed and often complex questions to their doctors and desire to participate in decisions concerning their care (Myfanwy 2008:63). The Internet changed the exclusive focus of health care from curing diseases to preventing diseases and enhancing health status (Anderson et al. 2003:68). The first health contact traditionally represented by the *family physician* is slowly being replaced by the Internet in many cases. Everyone can now visit many of the sites that inform and educate doctors. Besides, popular search engines, such as Google and Yahoo, provide portals with several kinds of data (primary data, criticism and different opinions). As a result, patients surf the Net and consult their physician armed with information or, after the medical visit, they may check the efficiency of treatments suggested by their doctor (Akerkar and Bichille 2004:120).

A driving force behind the demand for online health information seems to be patients' dissatisfaction with traditional health-related services (Anderson et al. 2003:72). Nowadays, doctors have less and less time to spend with their patients;

the health systems of industrialized countries are coming under increased cost-saving pressure; the cost of medical care has risen and patients increasingly have to pay out of their own pockets for medications and other health products and services; insurance companies and government agencies often demand a share in decision-making power, thus reducing the freedom of choice of both the patient and the doctor in many ways (Gotti and Salager-Meyer 2006:11). Therefore, patients have to think more about the quality and costs of their medical treatment choices.

Particularly via the Internet, patients can find accessible and inexpensive sources of information about health and medicine, health insurance, physicians, hospitals, and other health-related topics. By surfing the Net, patients may even obtain information about the rarest health conditions and experimental or alternative treatments, which often physicians do not know anything about. The Internet offers the possibility to communicate with health experts, even anonymously, thus avoiding the embarrassment that may occur in face-to-face communication. Moreover, because of the immediacy of feedback and information availability 24 hours a day, it simply appears more convenient to look for information online rather than getting an appointment with a doctor (Anderson et al. 2003:73).

The widespread use of the Net for health information has been proved by various research projects in America and in Italy. According to the study *Health Online 2013* carried out by the Pew Research Center's Internet & American Life Project (2013:3-18), seventy-two percent of internet users say they looked online for health information in 2012. On the one hand, for one-third of U.S. adults, the Internet is a diagnostic tool. Therefore, they use it in order to figure out what medical condition they or someone else have and to look for specific medical problems. On the other hand, one in four U.S. adults sees the Internet as a useful tool to have peer-to peer healthcare information. Women, younger people, white people and those with higher educational level were found to be the most active among online health information seekers.

In Italy, in 2012, the Censis and the Forum per la Ricerca Biomedica carried out a similar research: *Quale futuro per il rapporto medico-paziente nella nuova sanità*. According to the study (2012:18-20), thirty-two percent of the interviewees

said they use the Internet to look for health information. Although the use of the Web as a health-informative tool greatly varies according to people's age and education, the data show that the use of the Web among people aged between 40 and 60-years-old is increasing. As regards information type, the majority of online health information seekers (90.4 %) look for information about particular medical conditions and about physicians and health services (58.6%), whereas only 13.9% of Internet users look for peer-to peer health information.

As shown above by a summary of the most relevant data, the Internet has a relevant position among the channels which offer information about health and its use is quite widespread among the American and Italian people. According to Anderson et al. (2003:68), this technological innovation is reshaping the way in which health care is organized and delivered and, since 'it is here to stay', in few years more and more people will use it.

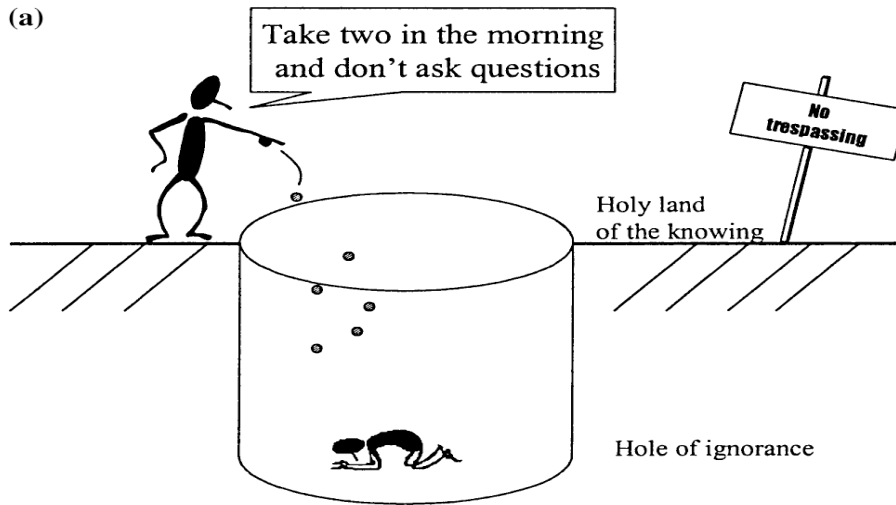
However, despite noteworthy effects of the Internet as a valuable informative tool, some physicians remain skeptical about the advantages of using the Internet more actively in their practices, while, some others worry that patients who consult web sites for information (*e-patients*) may not consult actual doctors when serious problems arise (Anderson et al. 2003:68). Other relevant factors determining the resistance from health care professionals is the variable and unreliable nature of medical information on the Net, the loss of human touch and also the perception of the informed patient as the 'problematic patient' (Akerkar and Bachile 2004:121).

As shown by the Censis and Pew Project researches, only one-third of e-patients later talked to doctors or other health professionals about the information they found online, whereas two-thirds did not (Pew Internet & American Life Project 2006:6; Censis 2012:24). The problem is that the Internet is a double-edged sword. On the one hand, it offers an enormous quantity of information about almost anything, even giving the possibility to enter into contact with highly specialist notions. On the other hand, specialist information for non-experts can lead to potentially dangerous misperceptions and misunderstandings (Censis 2012:16). Therefore, e-patients should discuss with their doctor the information they found online in order to relate these information to their personal health condition. In this

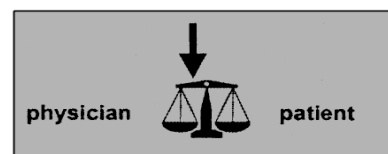
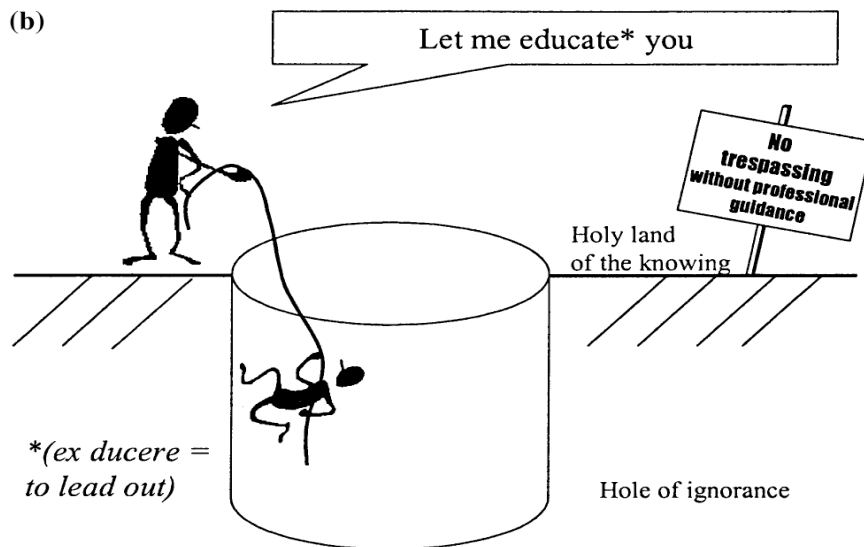
way, they could effectively understand such information. However, the majority of e-patients do not consistently check the source and date of the information they find online (Pew Internet & American Life Project 2006:11), and when they bring the printed information to the doctor, the latter cannot verify their reliability. Furthermore, it has been shown that most e-patients began their search at a search engine such as Google, Bing, or Yahoo; while the percentage of those who began at a site that specializes in health information is rather low (Pew Internet & American Life Project 2013:8). The central role of search engines is undoubtedly due to the fact that they allow people to find various kinds of information in a limited amount of time. However, the risk to find inappropriate and imprecise information (at times related to business interests) increases when starting at a search engine. Generally, the first results provided by search engines consist of links to Wikipedia's pages or other websites that are not specialized in health information. Links to institutional web sites, such as the NIH (National Institute of Health) and the NHS (National Health Service), usually appears later on the following pages (Laurent and Vickers 2009:471-479).

Certainly, patients need to be informed about their health, but they also need to pay attention to the quality and reliability of information they find. It is just through the use of reliable information that patients can create a relationship of mutual exchange of information, thus an effective communication with their doctors.

(a)



(b)



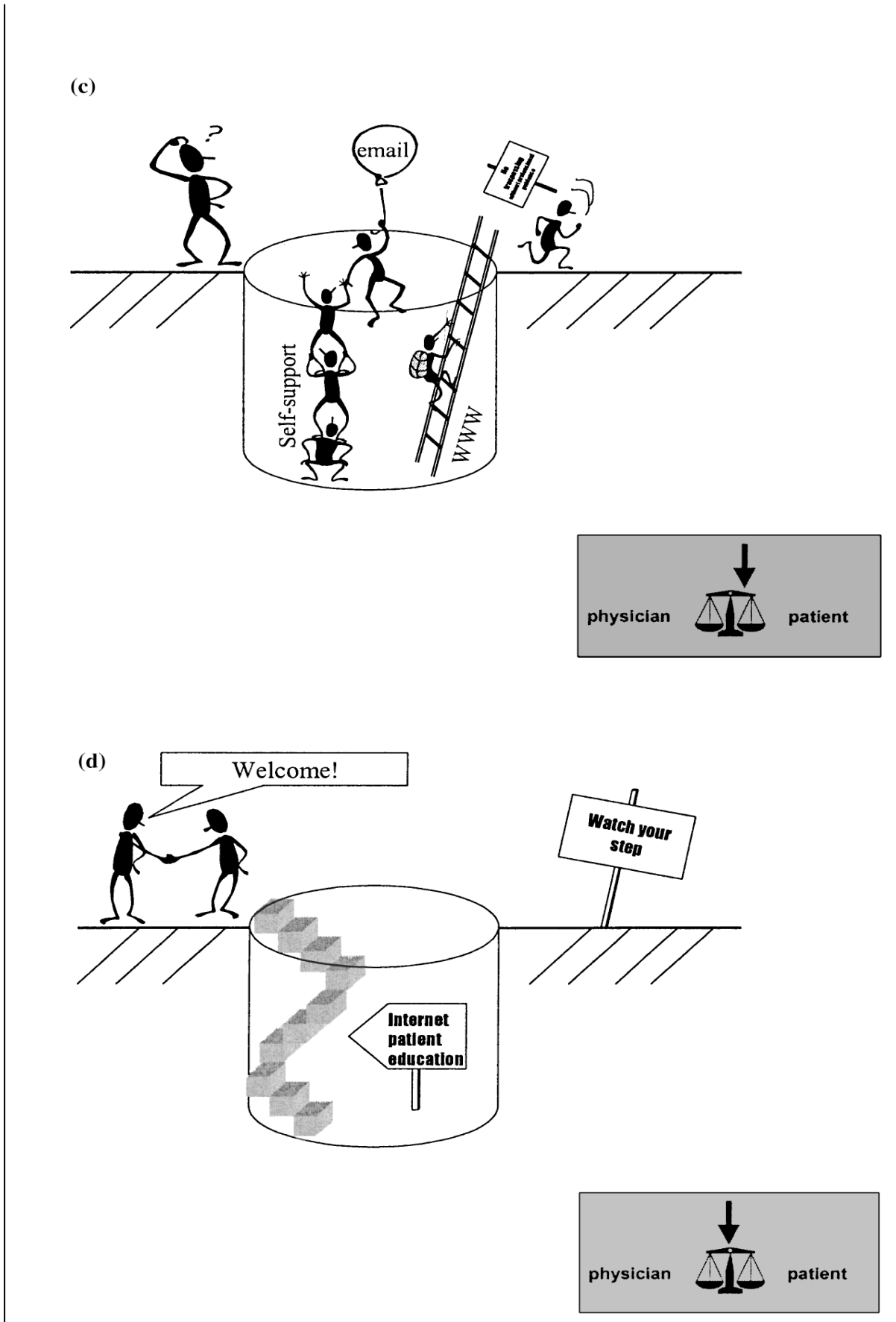


Figure 3.3. Evolution of the patient-physician relationship in terms of 'information gap' (Anderson et al. 2003:76-78).

3.3 Survey: doctor-patient relationship in Lusiana

In small towns, the role of doctors has always had a great importance. Together with mayors and priests, doctors have always been an important guide for the social community. In small contexts, doctors usually know all inhabitants and, generally, they create close relationships with their patients. Physicians meet their patients not only in their clinics, but also outside the medical context. Therefore, they know almost everything about their patients' everyday activities and lives. Similarly, patients know everything about their physicians. Hence, doctors need to act in the most appropriate way in order to maintain their good reputation.

Within this social context, physicians often succeed in creating a relationship of mutual trust with their patients, and patients show a confident attitude towards their medical practitioners. The *family doctor* is seen as a fundamental figure: once a patient has a health problem, he/she just goes to the doctor asking for advices and cures.

Another aspect that seems worth highlighting is the fact that these close relationships between doctors and patients often result in activities doctors are not paid for. For instance, doctors often go visit elderly people at home just to see if they feel well (even though patients did not call them), or, if they know that one of their patients has been sent to the hospital, they go there to visit him/her. Differently from a city context, doctors in small towns have more time to spend with their patients and they know them better. Moreover, this social context allows patients to have a greater degree of confidentiality with their doctors, thus patients assume an active attitude.

As has been previously shown in section 3.2, the relationship between doctor and patient has changed considerably over time. Especially with the information era, new technological devices, in particular the Internet, seem to acquire more and more importance even within the context of health.

In order to see whether the Internet affects doctor-patient relationships even in small towns, patients were asked to answer some questions. All of the considered patients live in the town of Lusiana, where four male doctors provide healthcare

services. The questionnaire was addressed to patients aged between twenty and forty years old (henceforth referred to as younger patients), and to patients aged between fifty and sixty-five years old (henceforth referred to as older patients). The same questions (Appendix 5) were asked to both groups of people. People who answered the questionnaire were 21 in each group.

According to their answers, doctors still succeed in maintaining a relevant role within the community under investigation. Both younger patients and older patients still see their doctor as a fundamental figure to obtain health-related information. Certainly, since younger people make use of the Internet to a higher extent compared to older people, they also look for health-related information on the Web (18 younger people out of 21 look for health-related information online). Nevertheless, even among those people, the doctor maintains an important role. Differently from what I expected, just 2 out of 21 younger patients see their physician as *'one of the various sources which provide health-related information'* and only 7 out of 18 younger patients, who uses the Internet to find information about their health conditions, do not discuss with their physician about the information they found on the Web. Moreover, 13 out of 21 younger patients *always* search for doctor's advice before starting a new treatment; 7 of them *often* or *at times* look for medical advice; just one does not search for physician's advice.

As far as older patients are concerned, just 8 out of 21 patients, at least once, looked for health-related information online. Among them, just two patients did not discuss with their doctor about the information they found, and just two patients see the doctor as one of the available sources to obtain medical information. Moreover, 17 out of 21 younger patients *always* search for doctor's advice before starting a new treatment; 3 of them *often* look for medical advice; just one does not search for physician's advice.

As regards physicians' attitude towards information found online, the answers show that physicians are always keen to provide further explanations, though, at times, they criticize the kind of information patients found. Moreover, the answers of both groups of patients highlight the fact that physicians never recommended useful websites which provide reliable and useful information about health. This datum

shows that physicians in Lusiana are reluctant to suggest the use of the Internet for health information researches. According to doctors, it is much better to talk directly with patients about health problems because highly specialized medical information written on the Internet may be difficult to understand for lay people. Moreover, doctors state that even though patients can find reliable information on the Web, they may not be able to elicit information that is useful for their own health conditions. According to doctor Rasotto (Appendix 6):

sul Web [i pazienti] acquisiscono varie conoscenze non sempre corrette e, comunque, anche quando sono corrette [i pazienti] non sanno contestualizzarle. La conoscenza che spesso le persone acquisiscono per tale via è magari abbondante, ma frequentemente fuorviante e talora non incentrata sull'essenza del problema.

As regards the quality of online information, one out of 18 younger patients thinks that the information found on the Web is exhaustive and just 5 of them think that online information is totally comprehensible. Moreover, the majority of younger patients think that *at times*, or *often*, online information creates confusion. On the other hand, among the 8 older patients who look online for health-related information, just four patients think that online information is exhaustive, and only one patient thinks that online information is totally comprehensible. In addition, except for one patient, all the others think that the Web creates confusion.

Considering now the language used by doctors, 25 out of 42 patients who answered the questionnaire said that *at times* they find doctors' language difficult to understand and 38 out of 42 patients said that they *at times* ask the doctor for further explanations about terms' meanings.

Below, Figure 3.1 shows the comparison between younger and older patients' answers concerning four different topics.

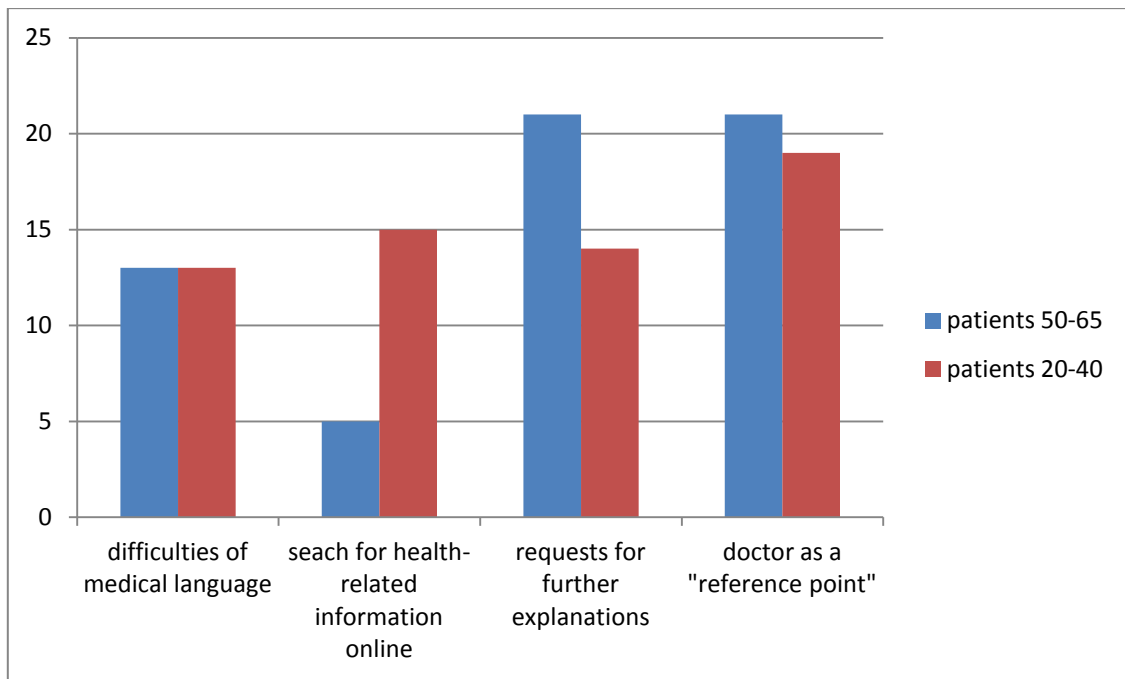


Figure 3.4. Comparison between younger and older patients' answers to four different questions.

In order to understand the doctors' point of view, a different questionnaire was prepared (Appendix 6). The physicians' answers show that every time doctors speak, they adjust their talk according to their patients. The language changes according to several aspects, such as patients' age, patients' educational level and comprehension skills. For instance, since the majority of people in Lusiana are elderly people, who only know dialect, physicians often need to recur to the use of dialect during medical visits.

In addition, doctors highlight the fact that they always try to use *simple language* to convey medical concepts: they tend to use simple words that belong to general language. Moreover, some doctors often synthesize at the end what they have said throughout the visit, and all doctors under investigation continuously check patients' feedback in order to see whether the patient understands him or not.

All physicians state that they use a language that is very different from the so-called 'language of medicine' with all kinds of patients. However, three out of four doctors still make use of medical terms providing all the explanations patients need in order to comprehend the terms' meaning. When patients ask for clarifications,

doctors make use of different kinds of devices. Those indicated by physicians are listed below:

- common language or dialect,
- examples taken from everyday life,
- similes and metaphors,
- anatomical sketches or figures taken from journals or other written papers,
- sketches or diagrams downloaded in real time from the Internet,
- scholarly citations (when patients are able to understand them).

As far as mass media are concerned, doctors think that the Web does not have a relevant role for patients living in Lusiana. Most patients are elderly people who do not use the Internet. Instead, some patients may watch TV health-related programs. Therefore, all data show that doctors in Lusiana still succeed in maintaining their central role and are not replaced by technological innovations yet.

Chapter four: analysis of Patient Information Leaflets (PILs)

Patients increasingly expect to access information which enables them to make informed decisions about their health. Good information helps patients to participate in shared decision-making with their healthcare professionals. Similarly, patients need to have sufficient and high-quality information about drugs, in particular over-the-counter drugs which are not prescribed by physicians.

As regards prescription medications, a significant part of information, in terms of usage and effects, derives from the consultation with a healthcare provider. However, even in this case, the physician's advice cannot be relied on as the only source of information for all patients. For medications purchased over the counter, the interactions between the patient and a healthcare expert may be limited or unavailable. As a result, written information has a great importance for safe use of medicinal products.

In our society, there is an enormous amount of information about health and drugs which is available from many different sources. However, it is not always easy for patients to access information. For many people, the primary or only source of information about their medicinal treatment remains the statutory patient information leaflet (PIL), which has had to be supplied with all drugs since 1999. This text provides the essential information patients need to use medications safely and gain the most benefit. Unlike other sources of information, the patient information leaflet is a highly regulated text. All PILs are required to be reviewed and approved by the Medicines and Healthcare products Regulatory Agency before being supplied with the medicinal product.

4.1 Legal framework

All medicinal products placed on the European market are required by European Community law to be accompanied by labelling and package leaflets which provide a set of comprehensible information which enables patients to use drugs appropriately.

In 1992, the European Commission issued *Directive 92/27/EEC on the labelling of medicinal products for human use and on package leaflets*. The Directive brought together requirements for detailed information that must accompany medicines to ensure their safe and effective use. The directive was fully implemented into UK legislation with the *Medicines Labelling and Medicines Leaflets Amendment Regulations* which enter into force in January 1993. UK legislation on labeling and patient information leaflets had to comply with European law by the 31st December 1998. As a result, since the 1st January 1999, it has been a legal requirement that all licensed medicinal products in the UK would be supplied with a patient information leaflet (PIL). Similarly, Italian law implemented the European Directive with the D.L.vo 540: *Attuazione della direttiva 92/27/CEE concernente l'etichettatura ed il foglietto illustrativo dei medicinali per uso umano* (30 December 1992).

According to the law, the PIL must provide comprehensive information that reflects information detailed in the *Summary of Product Characteristics* (SmPC). Information has to be accessible to and understandable by patients who receive it, thus allowing them to properly and safely use medicinal products. Article 8 of the European Directive 92/27/EEC reads:

the package leaflet must be written in clear and understandable terms for the patient and be clearly legible in the official language or languages of the Member State where the medicinal product is placed on the market.

Subsequently, other European Directives (2001/83/EC; 2004/27/EC) have come into force in order to amend the previous legislation.

Finally, in January 2009, aiming at providing guidance on how to ensure accessibility of the information contained in the labeling and package leaflets, the European Commission issued the *Guideline on the Readability of the Labeling and Package Leaflet of Medical Products for Human Use*²¹. In the document, attention is focused not only on the quality of information provided, but also on the quantity and type of information that is necessarily required by the law. As a result, the guidance gives advice on the presentation of the content, on the design and on the layout of

²¹ This guideline is published in accordance with Article 65(c) of Directive 2001/83/EC, which provides for the development of guidelines concerning the legibility of particulars on the labelling and package leaflet.

the labelling and package leaflet in order to optimize their usability. According to the guideline, the package leaflet, that is primarily intended for patients, has to be well designed and clearly worded, thus allowing a wider range of people to use that information. In what follows, I will try to summarize the most relevant recommendations provided by the guideline in section A: *Readability of the package leaflet and the labeling* (ENTR/F/2/SF/jr(2009)D/869:7-11):

1. Type size and font

An easily readable font should be chosen and the type size should be as large as possible to aid readers. Different text sizes could be appropriate to enable key information to stand out and to facilitate navigation in the text, as is the case with headings.

2. Design and layout of the information

As the space between lines is an important factor influencing the clarity of the text, line spaces should be kept clear. Contrast between the text and the background is important in order to avoid interferences with the written text which would make it harder to read. When a multilingual leaflet is proposed there should be a clear demarcation between the different languages used.

3. Headings

Headings are an important navigation tool and can help patients to find the information looked for. Where complex information has to be communicated, multiple levels of headings may be needed. All main section headings covered by Article 59 (1) of Directive 2001/83/EC has to be included within the leaflet:

- the name of the medicinal product and pharmaco-therapeutic group;
- therapeutic indications;
- the information which is necessary before the use of the medicinal product (contraindications; precautions for use; interactions with other medicinal products; special warnings);
- the instructions for proper use (the dosage; the method, the route and the frequency of administration; etc.);

- a description of adverse reactions which may occur under normal use of the medicinal;
- a reference to the expiry date with special storage precautions, the full qualitative and quantitative composition (active substance and excipients), the pharmaceutical form and content in weight, volume or units of dosage;
- the name and address of the marketing authorization holder and of the manufacturer;
- The date on which the package leaflet was last revised.

Sub-headings and associated text should only be included if these are relevant for the particular medicine. For example, in the patient information leaflet of Lempisip medication, in the section *Before you take this medicine*, there is a sub-heading *Important information about some of the ingredients in your medicine*. This further section was added because some of the ingredients in Lempisip lozenges can be harmful for people affected by phenylketonuria (an inherited genetic disorder).

4. Syntax

As some people may have poor reading skills and poor health literacy, simple words of few syllables should be used. Long sentences should be avoided because long paragraphs can confuse the readers, particularly where the list of side effects are included. The use of bullet points (preferably no more than 6) for such lists is considered more appropriate. Particularly important is the order in which side effects are set out; generally, they should be listed progressively basing on their frequency of occurrence (starting with the most frequent side effect). For instance:

- *Occasionally X can cause a temporary reddening of the skin;*
- *very rarely people report blood disorders.*

5. Style

An active style is recommended instead of the use of passive voice.

Instructions should be followed by reasons, for example *'do not take X if you have asthma- it may bring on an attack'*.

Abbreviations and acronyms should not be used unless these are appropriate. When first used in the text, the meaning should be spelled out in full.

As scientific symbols (e.g. >) are not well understood, their use should be avoided.

As regards the language used:

Medical terms should be translated into language which patients can understand. Consistency should be assured in how translations are explained by giving the lay term with a description first and the detailed medical term immediately after. On a case by case basis the most appropriate term (lay or medical) may then be used thereafter throughout the package leaflet in order to achieve a readable text. Make sure that the language used alerts the reader to all the information relevant to him/her, and gives sufficient detail on how to recognize possible side effects and understand any action which may be necessary. (ENTR/F/2/SF/jr (2009) D/869:9-10)

6. Use of symbols and pictograms

The use of images, pictograms and other graphics is permitted in order to aid the comprehension of the information, but any element of a promotional nature is excluded. Images and pictograms may be used as a supplement to the text and should not replace it. Some examples are shown below.

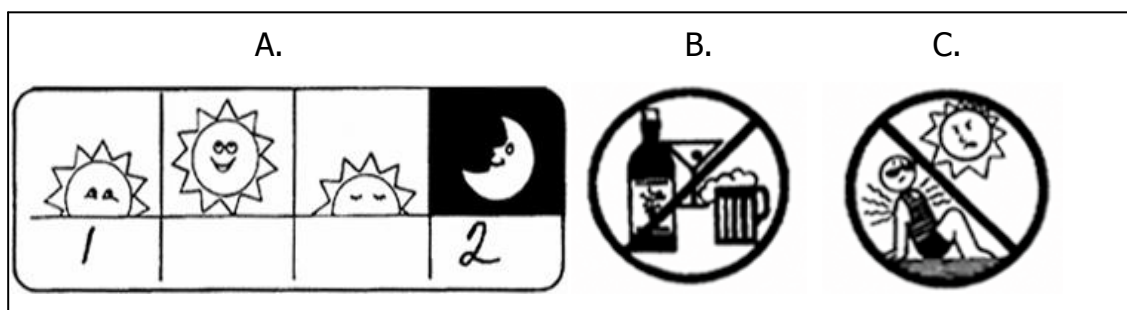


Figure 4.1. Examples of pictorials indicating to take one tablet in the morning and two at bedtime (A); not to drink alcoholic beverages when taking the medication (B); to avoid excessive sun exposure (C). (Katz et al. 2006:2394)

4.2 Patient Information Leaflets

Language varies as its function varies. It differs in different situations. (Bhatia 1993:5)

According to Bhatia's definition (1993:13), genre is a recognizable communicative act primarily characterized by a set of communicative purposes that it is intended to fulfil. The set of communicative purposes shapes the genre and gives it an internal structure. Most often, it is a highly structured and conventionalized

communicative event and it displays constraints in terms of its intent, positioning, form and functional value.

Following this definition, patient information leaflets can be seen as a sub-genre which belongs to the more general genre of 'instructions for use' texts. Its main aim is to provide useful and clear information on the use of medicinal products in order to allow patients to use medicines in a way that is appropriate for their own health problems. Therefore, patient information leaflets are a communication medium between experts and non-experts, in particular between doctors and patients.

As all specialized texts, patient information leaflets share some proprieties with highly specialized medical texts - the most evident shared characteristic is represented by the use of technical lexis. However, according to Cortellazzo (1994:21), when a specialized language is used in expert-layperson communication, it loses some of its characteristics and becomes '*closer*' to natural language. This changing may be observed when technical terms are substituted by words which belong to the general lexis; when technical terms appears together with glosses or periphrases written in general language; or when technical terms are explained through definitions, metaphors, analogies or examples (Cortellazzo 1994:21). Some examples taken from the English corpus of patient information leaflets (Appendix 8) are quoted below:

- Medications such as Moment can be associated to a slightly risk of heart attack ("myocardical infarction") or stroke;
- Headache (or cefalea);
- Menstrual pain (or dysmenorrhea)
- Antiplatelet drugs like aspirin;
- Moment is included in the analgesic anti-inflammatory group, that is inflammation and pain relieving medications;
- Hemicrania, so called because the pulsating pain only affects one side of the head;
- Glaucoma (increased pressure in the eye)
- Oral contraceptives ("the pill")
- Anti-coagulants (to thin the blood e.g. warfarin)
- Lesions without wounds (contusions) characterized by pain in the area of the trauma
- Small superficial haemorrhages (bruises)

- Jaundice (yellowing of the skin or whites of the eyes)
- Rarely, agranulocytosis, a disease of the blood, may occur...

Despite this 'simplification/explanation' of specialized terms, patient information leaflets have often been criticized for being difficult to understand. The question of comprehensibility of patient information leaflets started to be discussed long time ago and concerns patient information leaflets as a particular text-genre in itself independently from the language in which they are written (Puato 2012:89).

However, by considering two different languages (Italian and English), we can see whether some differences in terms of readability and comprehensibility exist. Italian patient information leaflets generally have a lower degree of accessibility for laypeople compared with their English equivalents. This difference is primarily determined by the fact that Italian language is more inclined than English to use a formal and 'bureaucratic' register in written texts. Moreover, in Italy, patient information leaflets are used by doctors too. In fact, Summaries of Product Characteristics (SmPC), which are prepared by pharmaceutical companies and are intended for health professionals, are often difficult to find and they are less practical to use. Therefore, doctors often look for information in the *Prontuario farmaceutico* wherein they can find the same information as those described in patient information leaflets.

As a consequence, poor comprehensibility of Italian patient information leaflets may be explained by the same nature of these texts. On the one hand, they are supposed to be informative tools for patients (laypeople/non-experts) and, at the same time, for doctors (experts); while, on the other hand, they are pharmaceutical documents which have to adapt to precise national and international legal norms. Hence, patient information leaflet writers have to find a sort of compromise between information completeness and information clarity.

As far as non-expert addressees of patient information leaflets are concerned, another relevant aspect needs to be considered. These informative texts are intended for a highly heterogeneous public of non-experts, which differs in terms of sex, age, and cultural-educational background knowledge. Therefore, the texts' degree of comprehensibility also varies according to the patient who makes use of it.

Furthermore, differently from oral consultations, if patients cannot understand the information written in the leaflet and have some doubts, they have to ask for explanation to a third interlocutor, who generally is the pharmacist or the physician. This is emphasized through many phrases within patient information leaflets, like the following examples:

“if any....ask the doctor or pharmacist”;

“ask your doctor or pharmacist for further information” .

4.3 Quantitative investigation into the complexity of patient information leaflets.

The aim of this study is to investigate texts' readability and the phenomena of lexical density, lexical variation, and keyness in patient information leaflets in order to understand how these leaflets are written and to highlight possible differences between Italian and English texts.

Consequently, fourteen patient information leaflets were collected in two different corpora. One consists of Italian texts (Appendix 7) and the other collects English texts (Appendix 8). Each corpus contains seven patient information leaflets of self-treatment drugs which relieve the symptoms associated with colds and flu. The considered leaflets were chosen in relation to their active ingredients and excipients in order to compare English and Italian texts which provide information about equivalent drugs.

4.3.1 The type/token ratio

The type/token ratio is the ratio of the number of different words (types) to the number of running words (tokens) in a given text or corpus. According to McEnery and Wilson (1996:158), this index indicates, on average, the frequency of new *word-forms* in a text. Therefore, it can be seen as a method of measuring vocabulary and lexical diversity in a given text or corpus.

However, three important factors need to be taken into account. Firstly, the index varies widely according to the length of the text (Biber et al. 1999:53).

Secondly, this index does not distinguish between lexical and grammatical words. Therefore, function/grammatical words contribute to lexical diversity to the same extent as lexical words (Castello 2008:42). Thirdly, this index does not consider *word families*. Therefore, words which belong to the same family are counted as different words (e.g. medicine, medicines, medicinal). In Sinclair’s words, this index is based on the occurrence of “any unique string of characters bounded by spaces” (Sinclair 1991:176).

The texts of the English corpus (Appendix 8) under investigation vary considerably in terms of length: as can be seen from Table 4.1, their lengths range between 355 tokens (text 03) and 1226 tokens (text 04). As far as the size of patient information leaflets is concerned, we need to take into account that these texts are usually written basing on pre-defined templates indicating all the necessary information which needs to be included in the texts. However, additional information may be added at the discretion of pharmaceutical companies.

In Table 4.1, the number of words (tokens), of different words (types) and the value of the type/token ratio (TTR) are listed.

English texts	Tokens	Types	TTR
Text 01 (Anadin)	813	408	50.18
Text02 (Vicks)	449	252	56.12
Text 03 (Sinex)	355	205	57.74
Text 04 (Lempisip)	1226	540	44.04
Text 05 (Benylin)	1039	418	40.23
Text 06 (Actifed)	666	313	46.99
Text 07 (Strepsils)	900	379	42.11

Table 4.1. Data comprising the number of tokens, types and the value of TTR in the English texts under investigation.

Furthermore, in Figure 4.2, the number of tokens, of types and the values of TTR are plotted on the diagram for comparison.

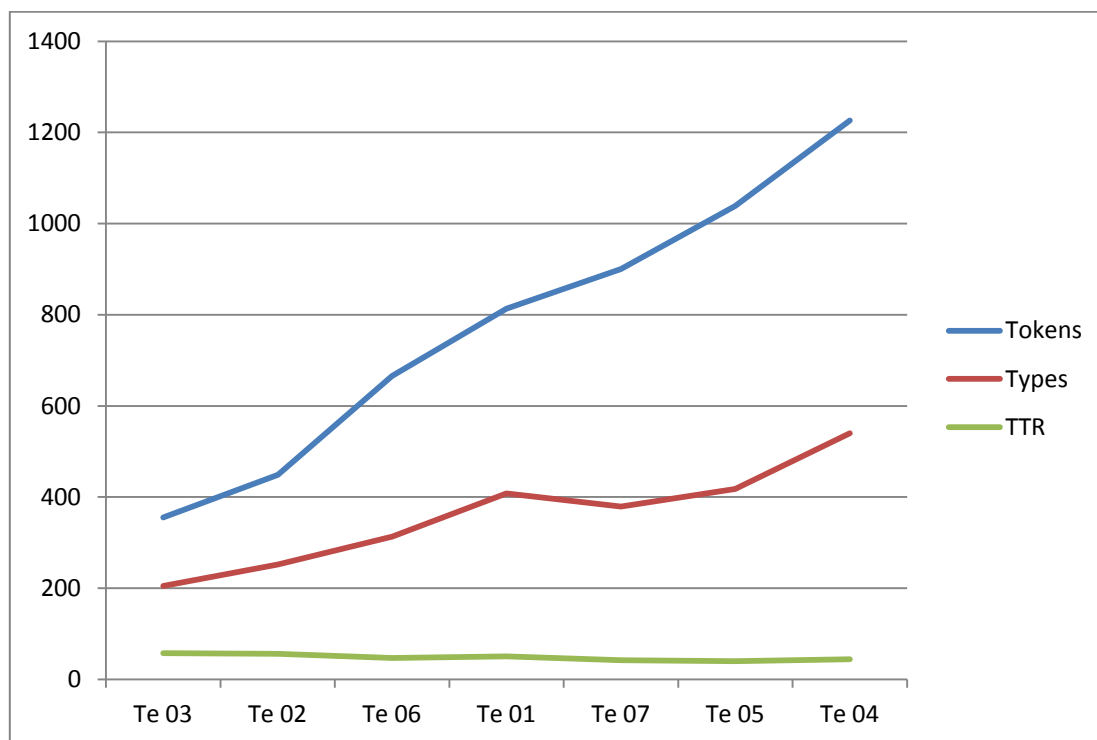


Figure 4.2. The number of tokens and types in the texts and the value of the TTR.

As can be noticed from the graph in Figure 4.2, as the number of tokens increases from Text 03 to Text 04, the value of the TTR tends to decrease. In other words, the longer the text, the smaller the index tends to become²².

At this regard, Biber et al. (1999:53) state that in longer texts, there is a greater probability that words will be repeated. This seems to be true both for the most frequent words which recur in all kind of texts (i.e. function words: the, and, of, etc.) and of the words which are connected with the topic of a particular text (i.e., in patient information leaflets: doctor, medicine, pharmacist, product, effects, etc.)

The same investigation has been carried out considering Italian patient information leaflets. As their English equivalents, Italian texts under investigation

²² The same tendency was observed by Castello (2008:44) in the investigation of texts used for testing purposes.

(Appendix 7) vary considerably in terms of length: as can be seen from Table 4.3, their lengths range between 860 tokens (text 07) and 1666 tokens (text 01).

Italian texts	Tokens	Types	TTR
Text 01 (Cibalgina)	1666	714	42.85
Text02 (Vicks)	1038	515	49.61
Text 03 (Sinex)	985	573	58.17
Text 04 (Tachifludec)	1295	616	47.56
Text 05 (Actidue)	1340	667	49.77
Text 06 (Actifed)	1281	661	51.60
Text 07 (Benagol)	860	407	47.32

Table 4.3. Data comprising the number of tokens, types and the value of TTR in the English texts under investigation.

The number of tokens, of types and the value of TTR are showed in Figure 4.4 below.

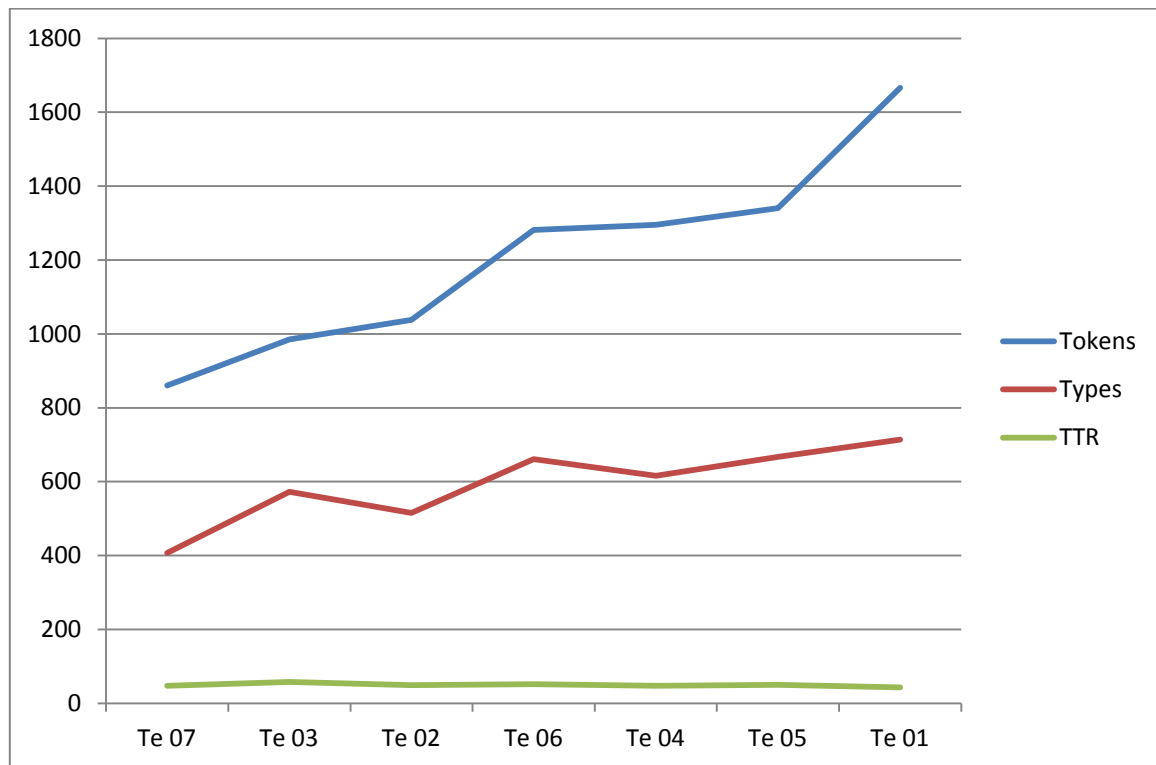


Figure 4.4. The number of tokens and types in the texts and the value of the TTR.

As is apparent from both Figure 4.2 and Figure 4.4 above, the value of TTR tends to decrease in both languages as the number of running words increases. This could mean that longer texts are characterized by a higher degree of repetitions. However, as has been said before, this index accounts for grammatical words too, which are obviously the most repeated words within a text. If we consider the list of words of both English and Italian texts, we can see that grammatical words are the most repeated.

Rank	Freq	Word	Rank	Freq	Word
1	147	the	1	322	di
2	135	or	2	201	e
3	119	to	3	184	il
4	117	and	4	95	o
5	104	of	5	94	medico
6	103	you	6	93	la
7	74	not	7	93	per
8	71	in	8	92	in
9	68	your	9	83	del
10	67	a	10	76	a
11	63	this	11	76	con
12	62	are	12	76	l
13	53	any	13	70	non

Table 4.5. The most recurrent words in the English and Italian corpora.

4.3.2 Lexical density

As previously suggested in section 4.3.1, one of the limits of the type/token ratio is the fact that it does not discriminate between grammatical/function and lexical words. Therefore, this index cannot provide precise information about the lexical density of a given text. In addition, because this index does not consider word-families, it can neither provide information about the frequency of lexical repetition nor about the degree of lexical variation. In order to obtain these kinds of information, we will make use of two methods which have been used by a large number of scholars to measure lexical density and lexical variation for different purposes.

Lexical density can be measured in various ways. According to Halliday (1987:60):

lexical density is the proportion of lexical items (content words) to the total discourse. It can be measured in various ways: the ratio of lexical items either to the total running words or to some higher grammatical unit, most obviously the clause; with or without waiting for relative frequency (in the language) of the lexical items themselves.

As Castello (2008:49) points out, in text- and corpus-based linguistics both types of lexical density measurement have been used in studies of different kinds of corpora. In particular, in 1971, Ure measured the lexical density of a 42,000-word corpus, calculating the index as a proportion of running words.

However, one of the main problems to carry out lexical density analysis consists on the distinction between grammatical and lexical words. The problem is that there is not a definite distinction between these two categories (Castello 2008:53). In Halliday's words, "grammar and lexis form a unified lexicogrammar system" (Halliday 1989:63). At this regard, Halliday (1989:63) suggests that prepositions and certain classes of adverbs are on the borderline, and defines grammatical/function words as the words which function in *closed systems* in the language. He states:

In English, [function words are] determiners [including articles], pronouns, most prepositions, conjunctions, some classes of adverbs, and finite verbs.

On the other hand, lexical words are defined as content words which function in lexical sets, which are *open systems* (Halliday 1999:63). Moreover, he specifies that, differently from words in the usual sense, lexical words are *items* because they may consist of more than one word (Halliday 1999:63) (i.e., in patient information leaflets the terms *beta blockers, non-steroidal anti-inflammatory drugs (NSAIDs), etc.*).

For the present study, in order to calculate the number of lexical words, two lists of grammatical words, one for English and one for Italian, were used. These lists were used as stop-lists with the software *AntConc*. Later, the following formula was used to calculate lexical density values:

$$LD = \frac{\text{number of lexical words}}{\text{total number of words}} \times 100$$

English texts	Tokens	Lexical words	LD
Text 01	813	478	58.79
Text 02	449	256	57.01
Text 03	355	211	59.43
Text 04	1226	718	58.56
Text 05	1039	611	58.80
Text 06	666	357	53.60
Text 07	900	471	52.33

Table 4.6. The number of tokens, lexical words and the values of LD in the English texts of the corpus.

Italian texts	Tokens	Lexical words	LD
Text 01	1666	943	56.60
Text 02	1038	576	55.49
Text 03	985	608	61.17
Text 04	1295	738	56.98
Text 05	1340	793	59.17
Text 06	1281	740	57.76
Text 07	860	450	52.32

Table 4.7. The number of tokens, lexical words and the values of LD in the Italian texts of the corpus.

	LD (English texts)	LD (Italian texts)
Text 01	58.79	56.60
Text 02	57.01	55.49
Text 03	59.43	61.17
Text 04	58.56	56.98
Text 05	58.80	59.17
Text 06	53.60	57.76
Text 07	52.33	52.32

Table 4.8. The values of LD in both English and Italian texts of the two corpora.

The lexical density values of Italian and English texts were plotted on the following diagram for comparison.



Figure 4.9. The values of LD in both English and Italian texts of the considered corpora.

As is apparent from Figure 4.9, texts 03 clearly stand out as the densest ones in both corpora, while texts 07 as the sparsest ones. Lexical density values of English texts vary between 52.33 and 59.43, while lexical density scores of Italian texts vary between 52.32 and 61.17. In addition, while text length may be seen as a possible element which influences lexical density values in the English texts under consideration (Te 07: 900 tokens; Te 03: 355 tokens), it does not seem to be the case for Italian texts (Te 07: 860 tokens; Te 03: 985 tokens).

A linguistic feature that is bound to contribute to the high lexical density of these texts is the frequent use of complex noun groups containing pre- and post-modifying elements - such elements convey information that necessarily need to be expressed in patient information leaflets. Moreover, according to Halliday (2004:654), written language is characterized by being lexically dense, since "it packs a large number of lexical items into each clause". The concentration of information within a nominal group makes the latter longer and more informative (Ventola 1995:181). In specialized discourse, this information packaging is usually

realized through the phenomenon of nominalization, when verbs are changed into nouns. According to Scarpa (2008:41):

la trasformazione di un sintagma verbale in uno nominale è un meccanismo molto produttivo, che avviene per ragioni stilistiche, ma anche funzionali in quanto serve a impostare il discorso all'insegna della concisione e permette sia una ricchezza concettuale sia una sintassi sintetica e compatta.

As far as English is concerned, the great use of nominalization can also be explained by the fact that it allows authors introducing the new information at the beginning of the sentence, thus providing greater objectivity. As regards Italian, Balboni (2000:42) highlights the translators' tendency to maintain the nominal style of English language. Some examples of nominal groups and nominalizations taken from the two corpora under investigation are quoted below:

- disturbi cronici o ricorrenti dello stomaco o dell'intestino
- insufficienza renale epatica
(examples of post-modification of the head noun);
- La somministrazione di inibitori della sintesi di prostaglandine ha mostrato...
(example where the verb *somministrare* has been turned into the noun *somministrazione*);
- ...assunzione di altri farmaci attivi sul fegato (example of nominalization of the verb *assumere*);
- ...a previous history of asthma (pre- and post-modification of the head noun);
- ...a temporary reddening of the skin (pre- and post-modification of the head noun);
- reduction in white blood cells (example of nominalization of the verb *to reduce*);
- stimulation of the nervous system (example of nominalization of the verb *to stimulate*).

According to patient information leaflets' need to provide all of the necessary information, noun phrases seem to be a valid space-saving linguistic tool. Nevertheless, detailed information packed within noun phrases are not always simple to decode for non-expert people. As Scarpa (2008:43) suggests:

dal momento che al sintagma nominale viene delegata la responsabilità di trasmettere gran parte dei contenuti, una conseguenza negativa alla densità lessicale è una complessità semantica che può nuocere alla chiarezza e alla facilità di comprensione del testo.

4.3.3 Lexical variation

Lexical variation measurement aims at quantifying the amount of lexical repetition or lexical diversity in a given text (Castello 2008:64). In lexical variation, the count is limited to lexical words, thus leaving out grammatical words which tend to be more frequent in occurrence.

As far as lexical items are concerned, Halliday (1989:64) states that “their repetition reduce the effect of density – since even if a word is intrinsically rare, its occurrence sets up the expectation that it will occur again”.

In the present study, the formula that was used to quantify lexical variation (LV) is the following:

$$LV = \frac{\text{number of different words (types)}}{\text{total number of lexical words}} \times 100$$

According to the formula above, a low value of lexical variation means that the text is characterized by a high number of repeated lexical items. On the contrary, if a given text shows a high value of this index, it means that the same lexical words were not often repeated (Castello 2008:64).

English texts	Lexical words	Types	LV
Text 01	478	317	66.31
Text 02	256	187	73.04
Text 03	211	157	74.40
Text 04	718	424	59.05
Text 05	611	332	54.33
Text 06	357	237	66.38
Text 07	471	269	57.11

Table 4.10. The number of lexical words, types and the value of LD in the English texts of the corpus.

Italian texts	Lexical words	Types	LV
Text 01	943	582	61.71
Text 02	576	380	65.97
Text 03	608	448	73.68
Text 04	738	466	63.14
Text 05	793	499	62.92
Text 06	740	508	68.64
Text 07	450	231	51.33

Table 4.11. The number of lexical words, types and the value of LD in the Italian texts of the corpus.

Furthermore, as pointed out by Linnarud (1975:50) and Gibson (1993:164), the length of a text plays an important role in determining the value of lexical variation. High values of LV are more likely to characterize a short rather than a long text. In order to see if LV's values change according to the length of the texts under investigation, below, Table 4.12 and Table 4.13 show the number of tokens and the values of LV for each text.

English texts	Tokens	LV
Text 01	813	66.31
Text 02	449	73.04
Text 03	355	74.40
Text 04	1226	59.05
Text 05	1039	54.33
Text 06	666	66.38
Text 07	900	57.11

Table 4.12. The number of tokens and the values of LV of the English texts under investigation.

Italian texts	Tokens	LV
Text 01	1666	61.71
Text 02	1038	65.97
Text 03	985	73.68
Text 04	1295	63.14
Text 05	1340	62.92
Text 06	1281	68.64
Text 07	860	51.33

Table 4.13 The number of tokens and the values of LV of the Italian texts under investigation.

Below, the values of LV are plotted on the following diagrams for comparison.

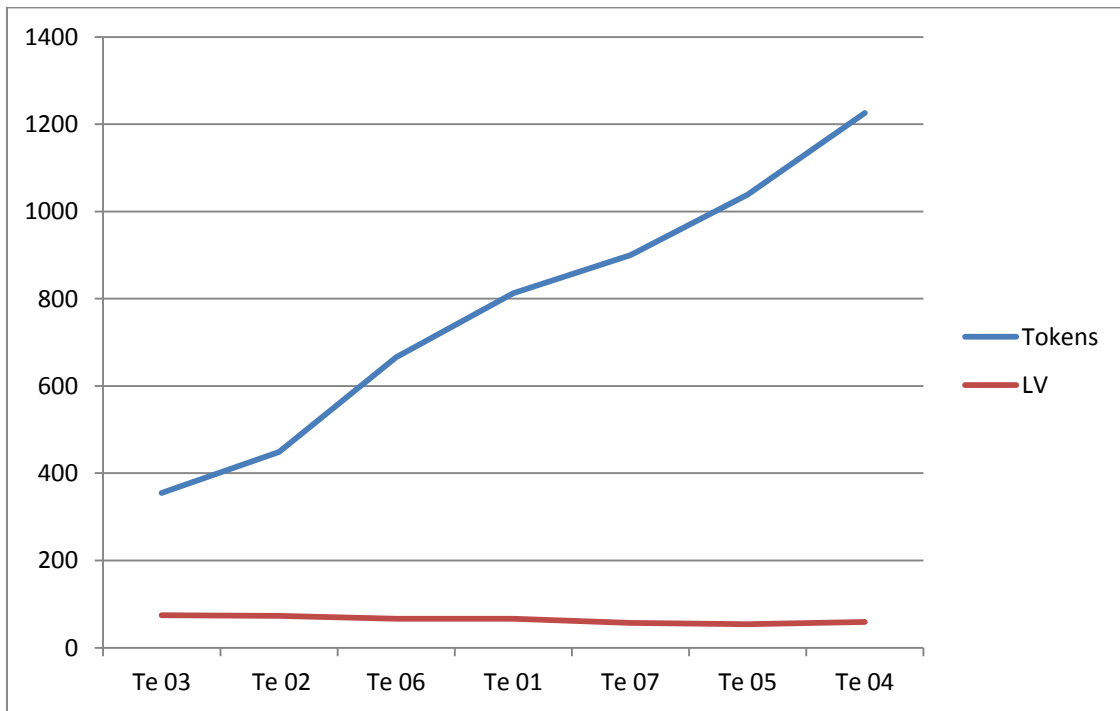


Figure 4.14. The number of token and the values of LV of the English texts.

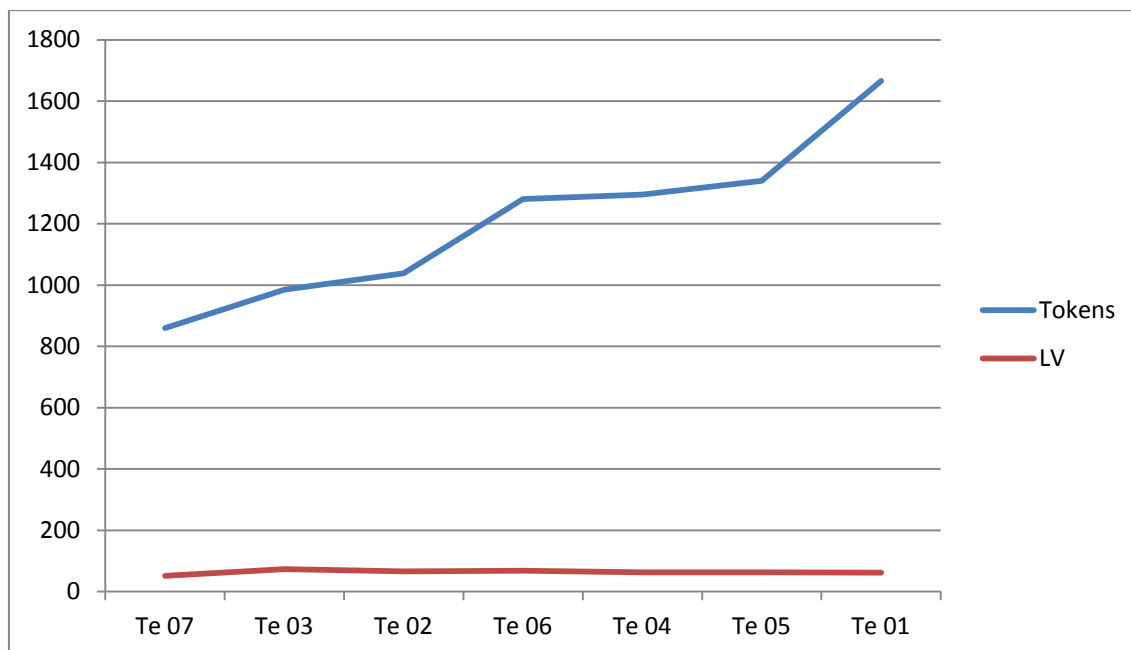


Figure 4.15. The number of token and the values of LV of the Italian texts.

As can be seen from Figure 4.14 and Figure 4.15, in English patient information leaflets the values of lexical variation tend to decrease as the number of tokens increases (Te 03: 355 tokens, 74,40 LV; Te 04:1226 tokens, 59,05 LV). On the contrary, in the Italian texts under investigation, the values of lexical variation do not seem to decrease as texts become longer (Te 07: 860 tokens, 51,33 LV; Te 01: 1666 tokens, 61,71 LV).

Nevertheless, the analysis shows that all patient information leaflets score quite high values of lexical variation. These values may be explained by the fact that the language of pharmacology uses different specialized terms to refer to diseases, cures, medications' effects and ingredients. In effect, the lexis which is used in this kind of texts consists of various words, which belong to general language, other terms which belong to the language of pharmacology, and other terms which belong to different specialized languages, such as the language of chemistry, biochemistry, and medicine.

As far as terms deriving from chemistry are concerned, we can see that, in patient information leaflets, the majority of these terms are found in the section *What it is*, wherein the medicinal product's active ingredients and other substances are listed. As can be seen from the table below (Table 4.16), while enzymes are

named in the same way in both bio-chemical and pharmaceutical languages, the name of substances differs according to the field of use. Table 4.16 shows that, in chemistry, the IUPAC nomenclature is usually used to refer to substances; while, in pharmaceutical language, the names of active ingredients are the international non-proprietary names (INN) recommended by the World Health Organisation.

Lexical items which derive from chemistry	
CHEMICAL LANGUAGE	PHARMACEUTICAL LANGUAGE
-IUPAC nomenclature ²³	-Active Pharmaceutical Ingredients' generic, non-proprietary name ²⁴ .
(R)-3-[-1hydroxy-2-(methylamino)ethyl]phenol	Phenylephrine
2-acetoxybenzoic acid	Aspirin/Acetylsalicylic acid
N-(4-hydroxyphenyl)acetamine	Paracetamol
(S,S)-2-methylamino-1-phenylpropan-1-ol	Pseudoephedrine
2-[(E)-1-(4-methylphenyl)-3-pyrrolidin-1-yl-prop-1-enyl]pyridine	Triprolidine
2-(diphenylmethoxy)-N,N-dimethylethanamine	Diphenhydramine
Biochemical terminology:	
Glucose-6-phosphate dehydrogenase L-Monoamine oxidases Prostaglandin-endoperoxide synthase/Cyclooxygenase (COX) Fructose-bisphosphate aldolase	

Table 4.16. Non-proprietary names of active ingredients found in the corpora, their chemical denomination, and other terms found in the corpora which belong to the language of biochemistry.

²³ The most used chemical nomenclature is the one created by the International Union of Pure and Applied Chemistry (IUPAC). The primary function of chemical nomenclature is to ensure that a spoken or written chemical name leaves no ambiguity concerning to what chemical compound the name refers. Each chemical name should refer to a single substance and its structure.

²⁴ For the past fifty years, it has been the task of the World Health Organization to assign International Non-proprietary Names (INN) to pharmaceutical substances. Over this period, various policies have been adopted by the INN Programme. According to the European Medicines Agency (EMA), the name of the medicinal product "may be either an invented name not liable to confusion with the common name, or a common name or scientific name accompanied by a trade mark or the name of the marketing authorisation holder" (Article 1(20) of Directive 2001/83/EC). A common name is "the international non-proprietary name (INN) recommended by the World Health Organisation" (Article 1(21) of Directive 2001/83/EC).

As said above, the lexis of patient information leaflets also consists of medical terms which refer to diseases or illnesses. In this respect, an important aspect has to be taken into account. While some terms - those underlined in Table 4.17 below - can be easily understood by most of patients (though people may not know the terms' exact meaning), other terms sound awkward to most of people (even to highly educated people which are not experts in the field of medicine). According to Serianni (2005:122), this fact can be explained by the terms' frequency of occurrence. For example, terms such as *hypersensitivity*, *diabetes*, *sinusitis*, *asthma*, *diarrhea*, *lumbago* are usually known by a greater number of ordinary people because these terms are also used by general practioners while talking to their patients about diagnoses, symptoms, etc. Similarly, ordinary people may also understand specialized terms which designate diagnostic tests, such as CAT, even though they may know neither the acronym's expansion (in this case *computerized axial tomography*) nor the proper definition of the specialized term. Table 4.17 shows some examples of medical terms found in the corpus used for this study.

Lexical terms which belong to the language of medicine	
MEDICAL LANGUAGE	————→ PHARMACEUTICAL LANGUAGE
Haemofilia; peptic ulcer; <u>diarrhoea</u> ; Reye's syndrome; <u>history of asthma</u> ; agranulocytosis; <u>sinusitis</u> ; <u>hypertension</u> ; Raynaud's syndrome; <u>diabetes mellitus</u> ; history of pre-eclampsia; glaucoma; phenylketonuria; thrombocytopenia; <u>hypersensitivity/hypersensitive</u> ; <u>lumbago</u> ; <u>neuralgia</u> ; <u>epilepsy</u> .	

Table 4.17 Medical terms found in the English corpus.

Considering now the 'language of pharmacy', in the corpora, we find terms which belong to pharmacology - that is the study of the preparation, properties, uses, and actions of drugs - and terms which belong to pharmacokinetics - that is a branch of pharmacology that describes how the body affects a specific drug after administration and the chemical changes of the substance in the body).

Pharmacological terms
<p>-Pharmaceutical terms which classify medicinal products according to their therapeutic effects (in both corpora):</p> <p>Analgesics; Antidepressants (anti-MAO); Anti-coagulants; Anti-inflammatory drugs (i.e. NSAIDs); Antipyretics; Antistamines; Appetite suppressants; Barbiturates; Contraceptives; Corticosteroids; Decongestants; Sedatives; Stimulants.</p>
<p>-Other terms which belong to pharmacology (in both corpora):</p> <p>Excipients, active ingredients, decongestionants, vasodilators, vasoconstrictors, sympathomimetics, inhibitors (i.e. monoamine oxidase inhibitor (MAOI), beta-blockers.</p>
<p>-One term which belong to pharmacokinetics (in the Italian corpus):</p> <p>Emivita (half-life): The period of time required for the concentration or amount of drug in the body to be reduced to exactly one-half of a given concentration or amount.</p>

Table 4.18. Terms which belong to the language of pharmacology and pharmacokinetics.

4.3.4 Specialized terms and LSP collocations

According to Serianni (2005:127), specialized languages do not only consist of specialized terms (what he calls *tecnicismi specifici*), but also of other particular words (names, adjectives, verbs and phrases) which are used to maintain a high register.

The language of medicine, he says (2005:128), cannot only use specialized terms such as *deltoid* or *granuloma*. In order to connect the various parts of medical discourse, other words are needed. Although these particular words have a lower rate of technicalness in comparison with specialized terms, they characterize medical language to the same extent as specialized terms do. In addition, they generally sound unusual to ordinary people. These words are called by Serianni (2005:128) *tecnicismi collaterali*.

An important aspect of these 'specialized words' (LSP collocations) is that they can be substituted by other words which belong to general language without affecting the exactitude of the scientific information that is being conveyed. For instance, a doctor can convey the same message by saying *the disease began with a*

rise in body temperature, or, by using general language, *the disease began with high body temperature*. Similarly, when a patient says that *he feels a bad headache*, the doctor may translate it into *the patient complained of acute headache*.

Furthermore, Serianni (2005:129) suggests that, while specialized terms may also be known or used by laypeople, the use of LSP collocations is limited to experts in the field. In addition, differently from specialized terms which refer to one determined specialized language, these *tecnicismi collaterali* can be used in different specialist fields. For instance, in Italian, the prepositional phrase '*a carico di*' can be found in both medical and judicial languages (i.e. *danni a carico dell'apparato respiratorio; processo a carico di qualcuno*). According to Serianni (2005:128):

Una lingua speciale è fatta anche di vocaboli altrettanto caratteristici di un certo ambito settoriale, che però sono legati non a effettive necessità comunicative bensì all'opportunità di adoperare un registro elevato, distinto dal linguaggio comune.

In the corpora under investigation, several occurrences of LSP collocations have been found:

- in the Italian corpus, it is frequent to find the noun *assunzione* or the verb *assumere* followed by *medicinal product/medicine* instead of the verb *prendere*, while, in English, we always find the verb *to take* (appendix 9-concordance results 1);

- in the English corpus, we find the verb *to treat* followed by symptoms and diseases, while, in Italian, we find the nominalized form *trattamento* followed by symptoms (appendix 9-concordance results 2);

- in the Italian corpus, we find the noun *insufficienza* followed by relational adjectives like *renale* or *epatica*. No occurrences of the noun *insufficiency* have been found in the English corpus (appendix 9-concordance results 3);

- in Italian we find the nominalized form of the verb *comparire* (*comparsa*) followed by side effects or symptoms; while, in English, we find the verb *to experience* followed by symptoms or side effects (appendix 9-concordance results 4);

- in English, we find some occurrences of the noun *inhibitor*, while, in Italian, we find both the noun *inibitore* and the nominalized form of the verb *inibire* (*inibizione*) (appendix 9-concordance results 5);

- in English, we find the verb *to develop* followed by symptoms, while, in Italian, we have just one occurrence of the verb *evolvere* followed by the symptom (appendix 9-concordance results 6).

The comparison between English and Italian texts also shows that the language used in English patient information leaflets under investigation is much more direct and simpler to understand than Italian language. This fact can firstly be explained by the tendency of Italian language to recur to medical terms, while English uses more familiar terms which belong to general language, for example:

- You are allergic to paracetamol;
- Ipersensibilità verso i componenti;
- You have high blood pressure;
- In caso di ipertensione;
- Irregular or fast heartbeats;
- Tachicardia.

Secondly, English tends to use more common hypernyms to refer to diseases, like the words *problem*, *constraint*, *disorder*, while Italian uses more specific hyponyms, as in the examples below:

- Kidney disorders/problems (all types of problem which may affect kidneys);
- Insufficienza renale (renal failure: a medical condition in which the kidneys fail to adequately remove waste products and fluids from the blood).

Thirdly, Italian texts show a higher degree of nominalization, as is demonstrated by the following examples:

- If you have taken more tablets than you should;
In caso di ingestione/assunzione;
- Vicks VapoRub is used to relieve nasal catarrh and congestion, sore throat and coughs due to colds;
Vicks VapRub si usa per il trattamento balsamico nelle affezioni delle prime vie respiratorie;
- If you experience any hypersensitivity to this product stop taking this medicine;

In caso di comparsa di fenomeni di sensibilizzazione o irritativi occorre interrompere l'assunzione del farmaco.

Beyond the lexical level, some differences can also be found by looking at syntactic structures. Italian texts tend to use a number of prepositional phrases that do not occur in the English texts under investigation. Some examples are provided below:

- 'A carico di/del' followed by the name of the affected anatomic zone (i.e. *malattie a carico dello stomaco*);
- 'A livello di' followed by the name of the affected anatomic zone or by an equivalent relational adjective (i.e. *a livello dello stomaco, a livello oculare*);
- 'In presenza di' meaning 'with' (i.e. *in presenza di terapie concomitanti*);
- 'In assenza di' meaning 'without' (i.e. *in assenza di risposta terapeutica*).

As can be seen from the examples above, Italian language often recurs to specialized terms, nominalizations and prepositional phrases. Therefore, Italian language tends to use a more formal register than English, using lexical and syntactic devices which increase sentences' length and texts' degree of complexity.

This tendency collides with the need for simplicity and concision of patient information leaflets. Specialized medical terms are difficult to understand, and if they are not followed by an explanation written in general language, they may lead to misunderstandings. However, the presence of both the specialized term and its explanation will result in an increase of sentence length. This problem may be solved with the use of more general words as is done in English texts. Moreover, since simple prepositions can convey the same meaning as prepositional phrases, the latter could be avoided for the sake of concision.

4.3.5 Readability of patient information leaflets

Readability is what makes some texts easier to read than others. (DuBay 2004:2)

The problem of readability is under investigation since 1920s, when educators discovered a way to use vocabulary difficulty and sentence length to predict the difficulty level of a text. They embedded this method in several readability formulas, and they deeply investigate the concept of readability. Writers like Rudolf Flesh, George Klare, Edgar Dale, and Jeanne Chall brought the formulas and the research supporting them to the marketplace (DuBay 2004:2). The formulas were widely used in journalism, research, health care and other fields. By the 1980s, there were 200 formulas and over a thousand studies published on the readability formulas attesting to their strong theoretical and statistical validity (DuBay 2004:2).

The primary aim of such formulae is to measure the grade level a person must have to read and comprehend a given text. Readability formulas work by measuring certain features of a text based on mathematical calculations.

For the present study, three readability indexes were made used of: the *Flesh Reading Ease (FRE)* and the *Flesch-Kinkaid Grade Level (FKGL)* were used to measure readability of the English texts under investigation, while the *Gulpease index* was used to measure readability of the Italian texts considered for this study.

The *Flesch Reading Ease (FRE)* index was devised by Rudolf Flesh and is the most widely used formula outside of educational circles. It measures reading from 100 (extremely easy) to 0 (very difficult to read). Flesh has identified 60 as the minimum score for Plain English. The formula for the *Flesch Reading Ease (FRE)* test is:

$$206.835 - 1.015 \left(\frac{\text{total words}}{\text{total sentences}} \right) - 84.6 \left(\frac{\text{total syllables}}{\text{total words}} \right)$$

The *Flesch-kinkaid Grade Level (FKGL)* formula converts the 0-100 score into a U.S. grade level. The grade level is calculated with the following formula:

$$0.39 \left(\frac{\text{total words}}{\text{total sentences}} \right) + 11.8 \left(\frac{\text{total syllables}}{\text{total words}} \right) - 15.59$$

For the present study, the *Flesch Reading Ease* readability scores and the *Flesch-kinkaid Grade Level* for each text of the English corpus were obtained automatically from Microsoft Word. Below, Table 4.19 shows the results:

English texts	FRE	FKGL	School levels
Text 01	44.8	10.2	13 th and 14 th grade
Text 02	55.6	8.4	10 th and 12 th grade
Text 03	53.7	8.6	10 th and 12 th grade
Text 04	49.1	9.5	13 th and 14 th grade
Text 05	43.2	10.6	13 th and 14 th grade
Text 06	45.4	10.5	13 th and 14 th grade
Text 07	48.2	9.8	13 th and 14 th grade
All texts	47.5	9.9	13 th and 14 th grade

Table 4.19 *FRE* scores, *FKGLs* and U.S. grade levels (as specified by Flesch 1948:149).

As can be seen, the *Flesch Reading Ease* readability scores gave an average score of 48.45 (minimum value = 43.2; maximum value = 53.7). The *Flesch-kinkaid Grade Levels* reveal an average score of 9.5 (minimum value = 8.4; maximum value = 10.6). According to these data, the English patient information leaflets under investigation are expected to be understandable by high school students (13th and 14th grade, which correspond to 4th-year-students in European high schools). Therefore, as specified by Flesch (1948:149), they style is *fairly difficult*.

In order to measure readability of the Italian texts under investigation, the *Gulpease* index was used.

The *Gulpease* index was devised by the *GULP* (Gruppo Universitario Linguistico Pedagogico) of the University of Rome. It is a widely used readability formula for the Italian language. Differently from the *FRE* index, that calculates word length in number of syllables, the *Gulpease* index measures word length in number of letters. The *Gulpease* index is calculated with the following formula:

$$89 + \frac{300 * (\text{number of sentences}) - 10 * (\text{number of letters})}{\text{number of words}}$$

The value of such index may vary from 0 (hardest to read) to 100 (easiest to read). The score may be translated into school grades: a minimum value of 80, for example, indicates that the text proves to be comprehensible for users with an elementary school level of education, 60 for Italian secondary school students (aged from 10 to 13), and 40 for Italian high school students (Lucisano and Piemontese 1988:110-124).

For the present study, the *Gulpease* readability index scores for each text of the Italian corpus were obtained automatically from Microsoft Word. Below, Table 4.20 shows the results:

Italian texts	Gulpease scores
Text 01	48
Text 02	57
Text 03	49
Text 04	49
Text 05	47
Text 06	49
Text 07	53
All texts	50

Table 4.20. Gulpease scores for each text.

As can be seen, the *Gulpease* readability scores gave an average score of 52 (minimum value = 47; maximum value = 57). Therefore, Italian patient information leaflets have a medium difficulty level.

In order to compare English and Italian texts' readability values, another corpus was created. The latter consists of the mostly read sections of the texts under investigation. These sections are: *what the medicine is for; before taking the medicine; how to take the medicine; possible side effects*. The *Flesch Reading Ease* and the *Gulpease* readability scores (respectively 50.6 and 49) indicate that both

Italian and English texts are expected to be comprehensible for users with a high school educational level.

These data reveal a problem. Patient information leaflets should be informative texts intended for all types of patients. Instead, they are not accessible to patients with poor literary skills and with low educational level. This can be a relevant problem, for example, for elderly people. Usually, they do not have a high educational level, and they are not able to use technological tools. Therefore, their only available sources to gain information about treatments and drugs are: doctors, pharmacists and patient information leaflets.

4.3.6 Keyness

Lexical items enjoy equal status in the lexicon of a given language, but their importance varies from the point of view of text (Bondi 2010:1).

Each particular word form contributes to the construction of meaning in text. However, only some words, the so-called keywords, play a relevant role in identifying important elements of the texts. Thus, keywords are often defined as markers of the 'aboutness' and style of a text (Scott and Tribble 2006:59-60).

The study of keywords has become central in corpus linguistics, especially through the development of techniques for the analysis of the meaning of words in context (Bondi 2010:3). In a quantitative perspective, according to Scott and Tribble (2006:62):

keywords are those whose frequency in a text is statistically significant, when compared to the standards set by a reference corpus.

In order to measure *keyness* of words in a given text or corpus, the absolute frequency of words (tokens) and their relative frequency in the source text(s) are calculated and, then, compared with those of a reference corpus by means of log likelihood statistics using *AntConc* software. These tests allow us to compare the frequencies we found with those of a reference corpus considered as standard in the domain, i.e. sources of health-related information.

Words that are more frequent than in the reference corpus have positive keyness values, while words that are less frequent have negative keyness values.

According to Musacchio and Palumbo (2009:225), the words that usually turn out to be key are proper nouns, words suggesting what the text is about, and high frequency words that are more indicative of style.

For the present study, two reference corpora were created, one consisting of English newspaper articles (articles taken from *The Guardian*), and the other consisting of Italian newspaper articles (articles taken from *La Stampa*). All the articles taken from the two newspapers talk about illnesses, treatments and drugs. Consequently, the analysis of keyness was carried out by using *AntConc* software.

Firstly, a wordlist of lexical words - for both Italian and English texts - was made by using two stop-lists of Italian and English function words.

Concordance				Concordance Plot				File View				Clusters				Collocates				Word List			
Hits				Total No. of Word Types: 1386				Total No. of Word Tokens: 4807				Hits				Total No. of Word Types: 929				Total No. of Word Tokens: 2946			
Rank	Freq	Word	Lemma Word Form(s)	Rank	Freq	Word	Lemma Word Form(s)																
1	101	medico		1	61	tablets																	
2	64	medicinale		2	57	take																	
3	55	effetti		3	56	medicine																	
4	49	indesiderati		4	52	doctor																	
5	41	caso		5	38	pharmacist																	
6	41	uso		6	37	taking																	
7	39	trattamento		7	32	product																	
8	37	pastiglie		8	31	effects																	
9	36	gravidanza		9	29	use																	
10	36	prodotto		10	28	side																	
11	35	mg		11	27	medicines																	
12	35	usato		12	25	blood																	
13	34	bambini		13	25	leaflet																	
14	34	consultare		14	24	children																	
15	33	foglio		15	20	time																	
16	33	illustrativo		16	20	used																	
17	33	usare		17	19	contains																	
18	30	limone		18	19	information																	
19	30	possono		19	19	ingredients																	
20	29	paracetamolo		20	19	paracetamol																	
21	27	dosi		21	19	please																	
22	27	farmacista		22	19	tablet																	

Table 4.21. The Italian and English lexical word lists in the patient information leaflets corpora under investigation.

Then, the keyword lists of lexical words were obtained by means of log likelihood statistics for Italian:

Concordance		Concordance Plot	File View	Clusters	Collocates	Word List	Keyword List
Hits		Keyword Types Before Cut: 1386		Keyword Types After Cut: 360			
Rank	Freq	Keyness	Keyword				
1	101	259.560	medico				
2	64	214.786	medicinale				
3	49	142.746	indesiderati				
4	37	124.173	pastiglie				
5	35	117.461	mg				
6	33	110.749	foglio				
7	33	110.749	illustrativo				
8	35	108.735	usato				
9	36	105.973	gravidanza				
10	55	105.862	effetti				
11	34	105.436	consultare				
12	29	97.325	paracetamolo				
13	41	94.178	uso				
14	33	91.337	usare				
15	27	90.613	farmacista				
16	30	86.545	limone				
17	36	85.504	prodotto				
18	26	79.116	gusto				
19	27	76.884	dosi				
20	21	70.476	allattamento				
21	39	69.161	trattamento				
22	20	67.120	eccessiva				

Table 4.22. List of keywords in the Italian corpus.

and then for English. As shown by the data in Table 4.22 above and Table 4.23 below, most keywords are also the most frequent lexical words in the corpora. We can see that words such as *uso*, *medicinale*, *effetti indesiderati*, *pastiglie*, *foglio illustrativo*, *uso*, *usare*, *prodotto*, *dosi*, *trattamento*, suggest the topic of the texts. Similarly, in English, words such as *tablets*, *medicine*, *product*, *leaflets*, *side effects*, *symptoms*, *use*, *ingredients*, give an idea of what the texts are about. Among these keywords, we can see that, in Italian, the adjective *indesiderati* has a higher value of keyness in comparison with the keyness value of its noun head *effetti*. The opposite case is shown in English, where the head noun *effects* has a higher value of keyness in comparison with its pre-modifier adjective *side*.

Moreover, in both corpora, words like *doctor*, *pharmacist*, *ask/consultare* appear to be keywords. This is probably due to the fact that all patient information leaflets contain numerous phrases which invite patients to see a doctor or a pharmacist in case of doubt or of side effects. In this respect, we also find in the

English corpus the keyword *please*, which generally precedes these recommendations.

Concordance				Concordance Plot				File View				Clusters				Collocates				Word List				Keyword List			
Hits		Keyword Types Before Cut: 929								Keyword Types After Cut: 194																	
Rank	Freq	Keyness	Keyword																								
1	61	206.451	tablets																								
2	52	148.053	doctor																								
3	38	134.755	pharmacist																								
4	57	123.729	take																								
5	56	105.821	medicine																								
6	32	94.119	product																								
7	25	88.654	leaflet																								
8	37	70.263	taking																								
9	19	67.377	paracetamol																								
10	19	67.377	please																								
11	19	67.377	tablet																								
12	31	63.479	effects																								
13	25	57.639	blood																								
14	19	54.913	contains																								
15	19	54.913	ingredients																								
16	28	54.890	side																								
17	18	51.572	ask																								
18	27	50.139	medicines																								
19	16	49.505	symptoms																								
20	13	46.100	date																								
21	29	44.017	use																								
22	12	42.554	hydrochloride																								

Table 4.23. List of keywords in the English corpus.

Another element which is worth highlighting is the presence of the ingredient *paracetamol* in both keyword lists. This word is certainly a keyword in these texts because almost all of the drugs under investigation contain paracetamol as active ingredient, which acts by relieving from the symptoms of flu and colds. Therefore, it gives an idea about the kind of drugs we are talking about.

Furthermore, we can see that, in the Italian texts, the unit of weight *mg* is a keyword, while in English it does not appear in the keyword list. This can be explained by the fact that in English patient information leaflets different units of weight are used. We find *mg*, *w/w*, *ml* and *w/v* according to the kind of drugs we are referring to: *mg* unit is used with tablets; *weight/weight* unit is used with creams and *weight/volume* or *ml* units are used with sprays. In Italian, the quantity of ingredients is generally measured in *mg* (at least in the patient information leaflets considered for the present study).

As has been shown above, an analysis of keyword lists can provide useful insights to understand to what extent and why some words function as keywords within a carefully selected group of texts.

Conclusions

This study has investigated communication between experts and non-experts in medical settings. In Chapter three, doctor-patient interactions were taken into account in order to see the difficulties patients may encounter while talking with general practitioners about their health conditions. Despite the asymmetry - in terms of different educational background knowledge - which characterizes doctor-patient relationships, their interactions can be defined as successful communicative events. Since spoken discourse takes place in real time, both patients and doctors can have a direct feedback from their interlocutors. Therefore, in case of misunderstanding or doubt, patients always have the chance to interrupt their doctors to ask for further explanations. Conversely, doctors can always adjust their talk according to their patients' answers. Nevertheless, physicians need to keep in mind that patients may not comprehend all the medical terms they use, thus they should always check their patients' understanding. On the other hand, patients should not feel embarrassed to ask questions or explanations to their physicians – after all, they are talking about their own health.

The advantages of real-time interactions help me to raise another important point concerning the use of the Internet. Beyond providing broader, speedier access to information, the Web is profoundly changing communication between doctors and patients. However, though many patients - especially young people - use the Internet to find health-related information, they generally are not equipped to access and understand high-quality medical information without the mediation of an expert in the field. Moreover, since most *e-patients* start their search with a general search engine and they do not usually verify the validity of the sources, the use of online information may reveal itself dangerous and may be the cause of additional misunderstandings. In addition, as far as Internet-based services - such as *Ask the Doctor Services* - are concerned, we can state that exchanging e-mails with patients is quite different from speaking with a patient face-to-face: replies may be delayed, sentences may be more stilted and the tone of voice is absent. Therefore, both doctors and patients must consider carefully what they say, how they say it and how to interpret information. Furthermore, it is impossible to judge the effect on patients

of information transmitted through cyberspace: doctors who do not have a direct feedback from their patients cannot check their patients' understanding and cannot adjust their talk according to their patients' non-verbal expressions. As a result, in my opinion, the Internet has to be used in a careful manner and patients should see their general practitioners as *consultants* even in case of online health-related information. Physicians are in the best position to weight information and advise patients, drawing on their understanding of available evidence as well as their training and experience. On the other hand, since the Web is not going to disappear, physicians should figure out the best use of this technology in the interests of their patients and themselves, for example, by providing useful online references in accordance with their patients' needs.

As far as written discourse is concerned, this study has investigated the text-inherent complexity and the receiver-oriented difficulty of two corpora of fourteen patient information leaflets of over-the-counter drugs. To this end, quantitative and qualitative research was carried out on the texts. In Chapter 4, seven formulas allowed for an objective measurement of various aspects of the complexity of the texts under investigation. Although each measurement captured a specific aspect of the texts' complexity, all scores – namely, the number of lexical words in the texts, the high values of lexical variation and the readability scores - demonstrate that the language used in patient information leaflets is quite difficult to understand. These results collide with the purpose of these texts which are thought to be informative texts for all types of patients. The language used in these texts seems not to be accessible for patients with poor literacy skills and low educational levels, thus increasing the need to recur to a third interlocutor such as a doctor or a pharmacist. In this respect, even though in the websites of many pharmaceutical companies it is possible to find a section where the language used in patient information leaflets is explained, we should remember that not all patients can access online information, and that for some patients, especially the elderly, patient information leaflets remain the primary available source of information.

For what concerns differences between Italian and English texts, I tried to demonstrate that the Italian texts are less accessible than their English equivalents.

The Italian tendency to use a formal register results in a higher use of specialized terms, nominalizations and prepositional phrases which increase the difficulty of the texts under investigation. Probably, the use of a more direct and simpler language could facilitate patients' understanding. Therefore, patient information leaflets can be defined as informative texts for all types of readers.

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Appendices:

- Appendix 1: Articles for Italian general practitioners.
- Appendix 2: Articles taken from the magazines *Scientific American* and *Le Scienze*.
- Appendix 3: Articles taken from the magazines *National Geographic* and *National Geografic Italia*.
- Appendix 4: Doctor Shmerling's answers.
- Appendix 5: Patients' answers.
- Appendix 6: Questionnaire for general practitioners in Lusiana.
- Appendix 7: Corpus of Italian patient information leaflets.
- Appendix 8: Corpus of English patient information leaflets.
- Appendix 9: Concordance results.

APPENDIX 1: Articles for Italian general practitioners

Allergia all'uovo non impedisce vaccino antinfluenzale

Il vaccino trivalente contro l'influenza stagionale può essere somministrato con sicurezza anche nei bambini con una grave allergia alle proteine dell'uovo

Il vaccino trivalente contro l'influenza stagionale può essere somministrato con sicurezza anche nei bambini con una grave allergia alle proteine dell'uovo. Ogni anno l'influenza stagionale è causa, negli Stati Uniti, di circa 300mila ricoveri di cui 21mila riguardano bambini sotto i 5 anni. La vaccinazione potrebbe azzerare il ricorso all'ospedale per complicanze, la maggior parte delle quali interessa bambini con asma, patologia che frequentemente si associa all'allergia grave all'uovo (diffusa a sua volta nell'1,5% della popolazione infantile). Lo studio multicentrico pubblicato da *Annals of allergy, asthma and immunology*, è stato condotto da Matthew Greenhawt, dell'Università del Michigan, e si è svolto in due fasi tra ottobre 2010 e marzo 2012. Sono stati inclusi i bambini che avevano avuto una grave reazione allergica, comprese le crisi anafilattiche, a seguito dell'ingestione di uova, con test cutaneo positivo o ancora con titolo anticorpale IgE specifico per l'uovo elevato. La prima fase è consistita in uno studio randomizzato, prospettico, in doppio cieco, in cui a un gruppo di bambini (gruppo A) è stata somministrata una prima dose di 0,1 mL di vaccino antinfluenzale, seguito 30 minuti dopo, in assenza di reazione, dal resto della dose. Il secondo gruppo di bambini (gruppo B) ha ricevuto una prima dose iniziale di salina e 30 minuti dopo il 100% della dose stabilita in base all'età. A questo protocollo si sommava uno studio retrospettivo su bambini eleggibili che avevano ricevuto una dose intera o frazionata di vaccino ma che avevano rifiutato di partecipare allo studio randomizzato e controllato. Su 31 partecipanti allo studio controllato della fase 1 (14 appartenenti al gruppo A e 17 al gruppo B), e i 112 della fase 2, valutati retrospettivamente (87 con la dose singola e 25 con la dose split), nessuno ha sviluppato una reazione allergica in seguito alla somministrazione del vaccino trivalente, sebbene il 45,1% dei bambini arruolati nella fase 1, e il 77,6% dei bambini della fase 2, avessero avuto una storia di anafilassi dopo ingestione di uova. «Questo studio dimostra che il vaccino è ben tollerato anche nei bambini con grave allergia all'uovo e precedenti reazioni anafilattiche» spiegano gli autori. «Inoltre è ben tollerata anche la somministrazione con singola. Non è quindi necessaria né la somministrazione in due step né il test cutaneo». La sola precauzione necessaria, conclude lo studio, è che i bambini con questo tipo di allergia vengano monitorati per 30 minuti da un medico, dopo aver ricevuto la dose, in modo da poter intervenire tempestivamente nel caso si manifestasse una reazione allergica, una pratica che in Italia viene attuata di prassi in tutti i bambini.

Rianimare per più di 20 minuti può salvare un bambino

L'inutilità della rianimazione cardiopolmonare (Rcp) protratta per più di venti minuti nei pazienti pediatrici è stata recentemente confutata da uno studio condotto da Renee I. Matos dell'Università di Pittsburgh. La ricerca, pubblicata su *Circulation*, ha stabilito la relazione tra durata delle manovre di Rcp in caso di arresto verificatosi in ospedale e gli effetti sia sulla sopravvivenza dei pazienti sia sugli eventuali esiti neurologici. Lo studio ha preso in considerazione i casi di arresto cardiaco in ambiente ospedaliero censiti dal registro multicentrico *Get With The Guidelines—Resuscitation*, l'unico database esistente che segnala tutti gli arresti cardiaci e gli esiti delle rianimazioni. Nell'analisi sono stati inclusi 3.419 bambini con arresto cardiaco avvenuto in ospedale tra gennaio 2000 e

dicembre 2009, selezionati da 328 strutture ospedaliere di Stati Uniti e Canada. I pazienti sono stati suddivisi per reparto di ricovero: chirurgia cardiaca, cardiologia, medicina generale, chirurgia generale e traumatologia. Le comorbidità più frequenti sono state insufficienza respiratoria per il 59,1% dei pazienti e ipotensione per il 39,9%. Tra i pazienti ricoverati in cardiologia e chirurgia cardiaca, il 29,6% ha avuto un'aritmia. Gli arresti si sono verificati per il 66,8% nelle unità di terapia intensiva, seguite dal pronto soccorso per il 14,4%, dal reparto ospedaliero (10%) e infine dalla sala operatoria (6,2%). In 2.178 pazienti, pari al 64% del campione, si è avuto un ritorno spontaneo del circolo dopo più di 20 minuti di massaggio cardiaco. Erano vivi a 24 ore dall'evento 1.373 pazienti (40%); 954 (27,9%) sono sopravvissuti fino alle dimissioni e infine 651, pari al 68,2 per cento dei sopravvissuti (19% rispetto al totale), hanno dimostrato una buona ripresa neurologica. In caso di Rcp praticata per un tempo compreso tra 1 e 15 minuti, la sopravvivenza diminuisce linearmente del 2,1% ogni minuto, e il tasso di esiti neurologici favorevoli diminuisce dell'1,2% al minuto. La probabilità di sopravvivenza in caso di Rcp da 1 a 15 minuti è pari al 41%, mentre per tempi superiori ai 35 minuti si attesta sul 12%. Tra i sopravvissuti, l'esito neurologico favorevole è presente nel 70% dei pazienti che hanno subito una Rcp inferiore a 15 minuti, e nel 60% in caso di Rcp superiore ai 35 minuti. La durata della rianimazione cardiopolmonare è quindi indipendentemente associata alla probabilità di sopravvivenza e all'esito neurologico favorevole. Protrarre le manovre di rianimazione per un periodo superiore ai 20 minuti non è quindi inutile nei bambini. Non va dimenticato che durate più brevi, pari a 10 minuti, sono comunque associate a migliori tassi di sopravvivenza globali: le probabilità di sopravvivenza e i recuperi neurologici diminuiscono con il trascorrere del tempo, e per questo rimane salda la necessità di intervenire tempestivamente. «Questo studio sfata i preconcetti secondo i quali la Rcp è inutile oltre i 20 minuti. Il tasso di danni neurologici è sufficientemente contenuto da permettere di prendere in considerazione anche una manovra di durata prolungata» afferma lo studio. «Gli operatori sanitari dovranno prendere in considerazione questi dati in caso di arresto nei bambini, al fine di salvare più vite».

Gli antidepressivi hanno un effetto modesto sul Qt

Alcuni antidepressivi appartenenti alla classe degli inibitori selettivi del reuptake della serotonina (Ssri) possono dare luogo a un modesto prolungamento all'Ecg dell'intervallo Qt

Alcuni antidepressivi appartenenti alla classe degli inibitori selettivi del reuptake della serotonina (Ssri) possono dare luogo a un modesto prolungamento all'Ecg dell'intervallo Qt, fattore di rischio per l'aritmia ventricolare, secondo quanto è emerso da uno studio americano teso a esplorare questo legame. In particolare l'analisi riguarda il citalopram e altri antidepressivi dal profilo farmacologico simile. Lo studio osservazionale trasversale, condotto da Victor M Castro e pubblicato su *British medical journal*, ha utilizzato i dati registrati nelle cartelle cliniche elettroniche, le prescrizioni mediche e i risultati dell'elettrocardiogramma, per analizzare la relazione tra uso di antidepressivi, la loro dose e l'intervallo QT. Il metadone, noto per la sua capacità di aumentare il Qt, è stato utilizzato come controllo per dimostrare la sensibilità della valutazione. I 38.397 partecipanti sono stati seguiti con elettrocardiogrammi effettuati dopo la prescrizione di antidepressivi o metadone, in un periodo compreso tra febbraio 1990 e agosto 2011. Sono state prese in considerazione anche le caratteristiche cliniche e sociodemografiche note per influenzare l'intervallo Qt, come età, sesso, etnia, storia clinica della depressione, eventuali episodi pregressi di infarto del miocardio o di aritmia ventricolare, ipertensione, iperlipidemia e comorbidità. L'associazione tra un prolungamento del Qt e l'assunzione di antidepressivi in funzione della dose è stata osservata per citalopram, escitalopram e amitriptilina, ma non per altri antidepressivi esaminati. Un'associazione tra farmaco e riduzione del

QT è stata identificata con l'assunzione di bupropione. Questo studio conferma quindi un modesto prolungamento dell'intervallo Qt. «Tuttavia» sottolineano i ricercatori «per la maggior parte dei pazienti i benefici ottenuti dal trattamento di ansia e depressione superano i rischi incorsi con l'aumento modesto del QT, che può essere tenuto sotto controllo grazie agli esami e alle cartelle cliniche elettroniche». Studi di farmacovigilanza che sfruttino le cartelle cliniche elettroniche potrebbero fornire, infatti, un valido strumento per identificare potenziali rischi associati a trattamenti con antidepressivi.

Una checklist migliora l'efficacia in sala operatoria

Le equipe mediche che lavorano con una checklist a portata di mano aderiscono in modo più fedele ai protocolli di emergenza in caso di eventi avversi, come arresto cardiaco ed emorragie, durante un intervento

Le equipe mediche che lavorano con una checklist a portata di mano aderiscono in modo più fedele ai protocolli di emergenza in caso di eventi avversi, come arresto cardiaco ed emorragie, durante un intervento. A dimostrarlo uno studio, pubblicato sul New England journal of medicine da Alexander Arriaga dell'Harvard school of public health, che ha analizzato il comportamento di 17 equipe mediche durante l'esecuzione di 106 scenari di crisi. I partecipanti sono stati reclutati da tre istituzioni ospedaliere, un centro medico accademico e due ospedali nella zona di Boston, per un periodo di 17 mesi (da agosto 2010 fino a dicembre 2011). Le equipe comprendevano medici e infermieri specializzati, tecnici di sala operatoria e un chirurgo (un attore, a eccezione di pochi casi nei quali alcuni chirurghi volontari si sono prestati allo scenario). Ciascun team ha trascorso sei ore in una sala operatoria ricostruita in modo fedele dove i partecipanti sono stati sottoposti a scenari di crisi, e il loro comportamento analizzato in relazione all'aderenza ai protocolli di emergenza. In metà di questi scenari, scelti in modo casuale, il team ha avuto accesso a una checklist di passaggi chiave da eseguire in caso di evento avverso, nell'altra metà invece la memoria era l'unico strumento a disposizione dell'equipe, come avviene nella pratica clinica abituale. Oltre a valutare l'adesione ai protocolli con e senza checklist, i ricercatori hanno chiesto ai partecipanti di esternare le loro percezioni sull'utilità clinica dell'uso di un promemoria. L'utilizzo della checklist ha ridotto del 75% i casi di mancata adesione a uno o più passaggi descritti dalle linee-guida. In particolare con l'uso della checklist la percentuale di gestioni approssimative è scesa dal 23% ad appena il 6%. Quanto alla percezione soggettiva, ben il 97% dei professionisti ha espresso il desiderio di avere a disposizione una checklist per gestire le situazioni di emergenza durante la pratica chirurgica quotidiana. «I risultati ottenuti nelle simulazioni dimostrano che l'utilizzo di una checklist è associato a un significativo miglioramento della gestione degli eventi avversi che si sono presentati in sala operatoria» conclude Arriaga. «La chirurgia può essere quindi migliorata grazie all'utilizzo di questo strumento».

Colesterolo: raccomandazioni in attesa di nuove linee guida

Le ultime linee guida Atp III del Nccp per il trattamento e la prevenzione dell'ipercolesterolemia risalgono a 10 anni fa. In attesa delle Atp IV, un gruppo di clinici del Johns Hopkins Center di Baltimora suggerisce alcune importanti raccomandazioni

Le ultime linee guida Atp III (Adult treatment panel) del Nccp (National cholesterol education program) per il trattamento e la prevenzione dell'ipercolesterolemia risalgono a 10 anni fa, con un

solo breve update nel 2004. Con lo scopo dichiarato di aiutare nel difficile compito gli estensori delle Atp IV, un gruppo di clinici - guidati da Seth S. Martindel Johns Hopkins Ciccarone center for the prevention of heart disease di Baltimora (Usa) – ha fornito 9 raccomandazioni attraverso le quali si possono traslare tutte le evidenze disponibili in nuove linee guida ampliate di prevenzione cardiovascolare, ma redatte in modo semplice, e quindi con maggiori probabilità di essere implementate nella pratica clinica.

Dalla semplificazione degli algoritmi all'elasticità dei follow-up

La prima raccomandazione è quella di “definire in modo più accurato il rischio”: non si può più ricorrere solo al Framingham risk score, perché tale metodo limita gli input ai soli fattori di rischio tradizionali, mentre occorre incorporare altri dati, come i livelli di proteina C-reattiva, il Bmi, lo spessore intima-media carotideo, lo score Cac: tutti valori più correlati all'attività delle statine. “Semplificare l'algoritmo iniziale” è la raccomandazione n.2: vanno abolite le attuali complesse procedure per stabilire il valore target, e va legato direttamente il grado di rischio alla terapia. In pratica se il soggetto, sulla base dei parametri citati, è a basso rischio, ci si deve limitare a un counselling cardiovascolare generale, mentre se il rischio è elevato si deve incidere sugli stili di vita e valutare il ricorso alle statine. Il terzo punto, “dare priorità alla terapia con statine”, è in linea con l'attuale visione e non con quella dell'Atp III che mette al primo posto acido nicotinico e sequestranti degli acidi biliari. La quarta raccomandazione è: “essere elastici sulla durata del follow-up per la ripetizione degli esami di laboratorio”; dunque non applicare meccanicamente la regola della visita 6 settimane dopo l'inizio della farmacoterapia per controllarne gli esiti, ma personalizzare l'arco di tempo e gli interventi svolti in esso.

Criteri innovativi per la definizione del valore target

Al 5° punto c'è: “stabilire <70 mg/dl come target ideale di colesterolemia-Ldl”; tale valore è considerato adatto per i soggetti ad alto rischio i quali in realtà, essendo riportato nell'Atp III come valore normale <100 mg/dL, potrebbero essere disincentivati al trattamento ipolipemizzante. “Approvare ulteriori obiettivi al di là della colesterolemia-Ldl” è la raccomandazione n.6: nessuno si focalizza più solo sulle Ldl, ed è ormai chiara l'importanza di altri parametri, quali la colesterolemia totale, i trigliceridi, il colesterolo-Hdl, l'apolipoproteina A-I, l'apolipoproteina B, e il colesterolo non-Hdl. Segue la settima norma: “definire i livelli terapeutici target sulla base del percentile equivalente di popolazione”; “soddisfacente” e “ideale” corrispondono nell'ordine al 40° e al 10° percentile. Gli ultimi due punti, di taglio più pratico che clinico, sono: “eliminare l'uso di descrittori fuorvianti, del tipo borderline alto” e “rendere più semplici i messaggi sullo stile di vita”.

Aiutare il cuore dei bambini: un sms solidale per contribuire

Ogni anno nel mondo nascono circa 1 milione di bambini affetti da cardiopatie e malformazioni cardiache congenite e i dati dicono che circa l'80% non ha la possibilità di essere curato ed operato nel proprio Paese, a causa dell'assenza di strutture ospedaliere o professionalità mediche adeguate e per l'alto costo delle operazioni. Questo significa che nel mondo quasi 800.000 bambini cardiopatici ogni anno rischiano la vita e in mancanza di cure mediche e chirurgiche tempestive, la metà di loro è destinata a non raggiungere il primo anno di vita. Gli altri vanno incontro a gravi problemi di crescita e di sviluppo psicosomatico, perché affetti da handicap respiratori e/o circolatori.

In questo contesto si inserisce l'attività di organizzazioni come la Fondazione "Aiutare i bambini" che dal 2005, attraverso la campagna "Cuore di bimbi", raccoglie fondi per salvare i bambini cardiopatici che nascono nei Paesi più poveri, attraverso tre differenti modalità: operare i bambini in Italia presso alcune strutture convenzionate, nei casi in cui non sia possibile operarli nei loro Paesi di origine, operarli nel loro Paese grazie a missioni periodiche di équipe mediche costituite da volontari italiani, oppure operarli direttamente nel loro Paese, sostenendo le strutture locali dove esistono medici e ospedali in grado di realizzare le operazioni ai bambini, ma mancano attrezzature, macchinari o la copertura dei costi degli interventi. Per il 2013 l'obiettivo è operare nel complesso 310 bambini, e verranno realizzate 10 missioni di medici italiani volontari nei seguenti Paesi: Kazakistan (con il team degli Ospedali Riuniti di Bergamo), Cambogia (con il team dell'Ospedale Niguarda di Milano), Uzbekistan (con un team misto degli Ospedali Riuniti e dell'Ospedale Niguarda), Eritrea (con il team dell'Ospedale G. Pasquinucci di Massa) e Kurdistan (con il team del Policlinico di San Donato Milanese). Cambogia e Cameroun sono invece i due Paesi nei quali la Fondazione sosterrà i costi delle operazioni per le famiglie dei bambini più poveri. Infine, altri bambini arriveranno in Italia da Albania, Kosovo e Zimbabwe per essere sottoposti a intervento qui da noi, perché nei loro Paesi mancano oltre che i medici anche le strutture ospedaliere adeguate.

Tutti possono contribuire a sostenere la campagna con un sms o una telefonata da rete fissa al numero 45501: il valore della donazione è di 2 euro oppure 5 euro a seconda della modalità scelta e dell'operatore telefonico. L'iniziativa è valida dal 4 al 24 febbraio 2013.

APPENDIX 2: Articles taken from *Scientific American* and *Le Scienze*.

A Change of Heart.

Authors: Jabr, Ferris. Source: *Scientific American*; Apr 2013, Vol. 308 Issue 4, p50-52, 3p.

Stem cells may transform the way doctors treat heart failure .

IN EARLY 2009 Mike Jones bought a newspaper at a convenience store in Louisville, Ky., and read about a local doctor who wanted to try something unprecedented: healing an ailing heart by harvesting and multiplying its native stem cells -- immature cells with regenerative powers. Jones, then 65, had congestive heart failure: his heart was no longer pumping blood efficiently. He contacted the doctor, Roberto Bolli of the University of Louisville, and in July of that year Jones became the first person in the world to receive an infusion of his own cardiac stem cells.

Before treatment, Jones could barely climb stairs. Today he feels well enough to chop his own firewood and clear fallen tree limbs from his nine-acre property. His "ejection fraction," a measure of how much blood the heart pumps from one chamber to another, increased from 20 to 40 percent in the two years following the experimental treatment -- lower than a typical level (in the 55 to 70 percent range) but still a dramatic improvement.

Since then, hundreds of other patients with heart damage have similarly improved after doctors injected them with stem cells extracted from their own heart or bone marrow, as well as stem cells from unrelated donors. Researchers think the stem cells turn into new tissue and stimulate other cells to divide. Many important questions remain unanswered, however. Scientists still do not know which of the different kinds of stem cells work best and how exactly to prepare the cells before treatment -- but they are quickly gaining insights. "I think we are at the dawn of one of the biggest revolutions in medicine in our lifetime," Bolli says. "We still need to learn how to use these cells properly -- but this is real. In the future, we will collect our own stem cells, grow them and keep them in freezers until we need them."

PRIMING THE PUMP

FOR THE PAST FOUR DECADES scientists thought of the human heart as a powerful but vulnerable living pump. Because the adult heart appeared incapable of regenerating its cells, any cell death would irrevocably weaken the organ, researchers reasoned. Now and then, however, a scientist glimpsed adult heart cells dividing under the microscope. Carbon dating of preserved heart tissue has since confirmed that the adult heart replaces its cells throughout life, although this turnover is modest compared with that in the gut and skin. Biologists now estimate that the heart replaces 1 percent or more of its four to five billion muscle cells each year. Researchers have also learned that the new cells arise from duplication of mature heart cells as well as from stem cells embedded in the heart.

These native stem cells allow the heart to repair itself in small ways. After a heart attack, for example, resident stem cells mature into new heart cells and encourage existing cells to divide. This self-repair lasts only a week or two, however, which is not nearly enough time to replace the more than one billion cells lost in a typical heart attack. The result is a large area of inflexible scar tissue. Just as a car tire bulges where it has been damaged, the human heart swells where it has been scarred; the once efficient football-shaped organ becomes a flabby, ineffectual pump.

Stem cell therapy works by giving the heart a mega dose of its own repair cells. Animal studies indicate that some injected stem cells mature into adult cells, but most die within a few days. Before the cells expire, however, they secrete a cocktail of proteins that encourage healthy heart cells to

proliferate, as well as enzymes that break down the collagen fibers in scar tissue, making way for new heart muscle.

So far researchers have completed only a few small trials with patients. Bolli and his colleagues harvested a small piece of heart tissue from each of 23 patients with heart damage or failure, including Jones. The researchers nurtured tiny gardens of the heart cells in petri dishes, altering out stem cells by searching for a stem cell-specific protein marker known as c-kit. They then allowed the stem cells to make millions of copies of themselves.

Sixteen patients received one million cardiac stem cells each via a catheter fed into the coronary artery, and seven patients received standard care (which consisted mainly of beta blockers and diuretics). Four months later the ejection fraction had increased from a starting average of 30.3 percent to an average of 38.5 percent in patients who received stem cells, but it had barely budged in standard care patients (inching from 30.1 to 30.2 percent). One year after treatment the average weight of scar tissue in stem cell patients had decreased by 30 percent.

In a similar trial, Eduardo Marbán of the Cedars-Sinai Heart Institute in Los Angeles and his colleagues treated 17 patients with their own stem cells and another eight patients with standard care. Marbán and his team used remotely controlled forceps to pinch off peppercorn-size specks of heart tissue to grow in the lab. Whereas Bolli had extracted mainly "true" stem cells displaying c-kit from his lab cultures, Marbán extracted a more diverse mixture of cells -- some of which may have a more limited repertoire. Patients who received standard care showed no statistically significant change in scar mass or healthy heart tissue. Stem cell patients showed a 42 percent decrease in scar mass and a 13-gram increase in healthy tissue over one year, although their ejection fraction hardly improved.

Other researchers have attempted to treat heart failure with so-called mesenchymal stem cells derived from bone marrow, which are appealing because they are less likely to become cancerous compared with other stem cells. Mesenchymal stem cells secrete growth factors that prompt nearby cells to multiply and can turn into heart muscle in the right environment. Trial results have been inconsistent so far -- some patients clearly improve, whereas others show few or no positive changes.

Joshua Hare of the University of Miami wondered if heart patients would tolerate bone marrow stem cells donated by a stranger or reject them as foreign. Hare gave 15 patients injections of their own bone marrow stem cells, and another 15 people donated cells. Thirteen months later none of the patients in either group had rejected the stem cells, and scar tissue had diminished by more than one third in both groups. Elderly patients may benefit more from the stem cells of young donors than from their own because younger cells have not endured as much wear and tear.

"Up until now, we had no way to remove the scar that follows a heart attack," Hare says. "Showing you can reduce scarring and replace it with new tissue is the home run we have been looking for. I think we will transform the treatment of heart failure."

HEART REPAIR

Harvesting semispecialized stem cells from an ailing heart, helping them to make millions of copies of themselves and injecting those cells into the heart enable the organ to break down scar tissue and grow new muscle.

The Myth of Antioxidants.

Authors: Moyer, Melinda Wenner. Source: Scientific American; Feb 2013, Vol. 308 Issue 2, p62-67, 6p.

The hallowed notion that oxidative damage causes aging and that vitamins might preserve our youth is now in doubt.

DAVID GEMS'S LIFE WAS TURNED UPSIDE DOWN IN 2006 BY A GROUP OF WORMS THAT kept on living when they were supposed to die. As assistant director of the Institute of Healthy Aging at University College London, Gems regularly runs experiments on *Caenorhabditis elegans*, a roundworm that is often used to study the biology of aging. In this case, he was testing the idea that a buildup of cellular damage caused by oxidation-technically, the chemical removal of electrons from a molecule by highly reactive compounds, such as free radicals-is the main mechanism behind aging. According to this theory, rampant oxidation mangles more and more lipids, proteins, snippets of DNA and other key components of cells over time, eventually compromising tissues and organs and thus the functioning of the body as a whole.

Gems genetically engineered the roundworms so they no longer produced certain enzymes that act as naturally occurring antioxidants by deactivating free radicals. Sure enough, in the absence of the antioxidants, levels of free radicals in the worms skyrocketed and triggered potentially damaging oxidative reactions throughout the worms' bodies.

Contrary to Gems's expectations, however, the mutant worms did not die prematurely. Instead they lived just as long as normal worms did. The researcher was mystified. "I said, 'Come on, this can't be right,' " he recalls. " 'Obviously something's gone wrong here.' " He asked another investigator in his laboratory to check the results and do the experiment again. Nothing changed. The experimental worms did not produce these particular antioxidants; they accumulated free radicals as predicted, and yet they did not die young-despite suffering extreme oxidative damage.

Other scientists were finding similarly confounding results in different lab animals. In the U.S., Arlan Richardson, director of the Barshop Institute for Longevity and Aging Studies at the University of Texas Health Science Center in San Antonio, genetically engineered 18 different strains of mice, some of which produced more of certain antioxidant enzymes than normal and some of which produced fewer of them than normal. If the damage caused by free radical production and subsequent oxidation was responsible for aging, then the mice with extra antioxidants in their bodies should have lived longer than the mice missing their antioxidant enzymes. Yet "I watched those goddamn life span curves, and there was not an inch of difference between them," Richardson says. He published his increasingly bewildering results in a series of papers between 2001 and 2009.

Meanwhile, a few doors down the hall from Richardson, physiologist Rochelle Buffenstein has spent the past 11 years trying to understand why the longest-living rodent, the naked mole rat, is able to survive up to 25 to 30 years-around eight times longer than a similarly sized mouse. Buffenstein's experiments have shown that naked mole rats possess lower levels of natural antioxidants than mice and accumulate more oxidative damage to their tissues at an earlier age than other rodents. Yet paradoxically, they live virtually disease-free until they die at a very old age.

To proponents of the long-standing oxidative damage theory of aging, these findings are nothing short of heretical. They are, however, becoming less the exception and more the rule. Over the course of the past decade, many experiments designed to further support the idea that free radicals and other reactive molecules drive aging have instead directly challenged it. What is more, it seems that in certain amounts and situations, these high-energy molecules may not be dangerous but useful and healthy, igniting intrinsic defense mechanisms that keep our bodies in tip-top shape. These ideas not only have drastic implications for future antiaging interventions, but they also raise questions about the common wisdom of popping high doses of antioxidant vitamins. If the oxidative-damage theory is wrong, then aging is even more complicated than researchers thought-and they may ultimately need to revise their understanding of what healthy aging looks like on the molecular level.

"The field of aging has been gliding along on this set of paradigms, ideas about what aging is, that to some extent were kind of plucked out of the air," Gems says. "We should probably be looking at

other theories as well and considering, fundamentally, that we might have to look completely differently at biology."

THE BIRTH OF A RADICAL THEORY

THE OXIDATIVE DAMAGE, or free radical, theory of aging can be traced back to Denham Harman, who found his true calling in December 1945, thanks to the Ladies' Home Journal. His wife, Helen, brought a copy of the magazine home and pointed out an article on the potential causes of aging, which he read. It fascinated him.

Back then, the 29-year-old chemist was working at Shell Development, the research arm of Shell Oil, and he did not have much time to ponder the issue. Yet nine years later, after graduating from medical school and completing his training, he took a job as a research associate at the University of California, Berkeley, and began contemplating the science of aging more seriously. One morning while sitting in his office, he had an epiphany—"you know just 'out the blue,' " he recalled in a 2003 interview: aging must be driven by free radicals.

Although free radicals had never before been linked to aging, it made sense to Harman that they might be the culprit. For one thing, he knew that ionizing radiation from x-rays and radioactive bombs, which can be deadly, sparks the production of free radicals in the body. Studies at the time suggested that diets rich in food-based antioxidants muted radiation's ill effects, suggesting—correctly, as it turned out—that the radicals were a cause of those effects. Moreover, free radicals were normal by-products of breathing and metabolism and built up in the body over time. Because both cellular damage and free radical levels increased with age, free radicals probably caused the damage that was responsible for aging, Harman thought—and antioxidants probably slowed it.

Harman started testing his hypothesis. In one of his first experiments, he fed mice antioxidants and showed that they lived longer. (At high concentrations, however, the antioxidants had deleterious effects.) Other scientists soon began testing it, too. In 1969 researchers at Duke University discovered the first antioxidant enzyme produced inside the body—superoxide dismutase—and speculated that it evolved to counter the deleterious effects of free radical accumulation. With these new data, most biologists began accepting the idea. "If you work in aging, it's like the air you breathe is the free radical theory," Gems says. "It's ubiquitous, it's in every textbook. Every paper seems to refer to it either indirectly or directly."

Still, over time scientists had trouble replicating some of Harman's experimental findings. By the 1970s "there wasn't a robust demonstration that feeding animals antioxidants really had an effect on life span," Richardson says. He assumed that the conflicting experiments—which had been done by other scientists—simply had not been controlled very well. Perhaps the animals could not absorb the antioxidants that they had been fed, and thus the overall level of free radicals in their blood had not changed. By the 1990s, however, genetic advances allowed scientists to test the effects of antioxidants in a more precise way—by directly manipulating genomes to change the amount of antioxidant enzymes animals were capable of producing. Time and again, Richardson's experiments with genetically modified mice showed that the levels of free radical molecules circulating in the animals' bodies—and subsequently the amount of oxidative damage they endured—had no bearing on how long they lived.

More recently, Siegfried Hekimi, a biologist at McGill University, has bred roundworms that overproduce a specific free radical known as superoxide. "I thought they were going to help us prove the theory that oxidative stress causes aging," says Hekimi, who had predicted that the worms would die young. Instead he reported in a 2010 paper in *PLoS Biology* that the engineered worms did not develop high levels of oxidative damage and that they lived, on average, 32 percent longer than normal worms. Indeed, treating these genetically modified worms with the antioxidant vitamin C prevented this increase in life span. Hekimi speculates that superoxide acts not as a destructive

molecule but as a protective signal in the worms' bodies, turning up the expression of genes that help to repair cellular damage.

In a follow-up experiment, Hekimi exposed normal worms, from birth, to low levels of a common weed-controlling herbicide that initiates free radical production in animals as well as plants. In the same 2010 paper he reported the counterintuitive result: the toxin-bathed worms lived 58 percent longer than untreated worms. Again, feeding the worms antioxidants quenched the toxin's beneficial effects. Finally, in April 2012, he and his colleagues showed that knocking out, or deactivating, all five of the genes that code for superoxide dismutase enzymes in worms has virtually no effect on worm life span.

Do these discoveries mean that the free radical theory is flat-out wrong? Simon Melov, a biochemist at the Buck Institute for Research on Aging in Novato, Calif., believes that the issue is unlikely to be so simple; free radicals may be beneficial in some contexts and dangerous in others. Large amounts of oxidative damage have indisputably been shown to cause cancer and organ damage, and plenty of evidence indicates that oxidative damage plays a role in the development of some chronic conditions, such as heart disease. In addition, researchers at the University of Washington have demonstrated that mice live longer when they are genetically engineered to produce high levels of an antioxidant known as catalase. Saying that something, like oxidative damage, contributes to aging in certain instances, however, is "a very different thing than saying that it drives the pathology," Melov notes. Aging probably is not a monolithic entity with a single cause and a single cure, he argues, and it was wishful thinking to ever suppose it was one.

SHIFTING PERSPECTIVE

ASSUMING FREE RADICALS accumulate during aging but do not necessarily cause it, what effects do they have? So far that question has led to more speculation than definitive data.

"They're actually part of the defense mechanism," Hekimi asserts. Free radicals might, in some cases, be produced in response to cellular damage—as a way to signal the body's own repair mechanisms, for example. In this scenario, free radicals are a consequence of age-related damage, not a cause of it. In large amounts, however, Hekimi says, free radicals may create damage as well.

The general idea that minor insults might help the body withstand bigger ones is not new. Indeed, that is how muscles grow stronger in response to a steady increase in the amount of strain that is placed on them. Many occasional athletes, on the other hand, have learned from painful firsthand experience that an abrupt increase in the physical demands they place on their body after a long week of sitting at an office desk is instead almost guaranteed to lead to pulled calves and hamstrings, among other significant injuries.

In 2002 researchers at the University of Colorado at Boulder briefly exposed worms to heat or to chemicals that induced the production of free radicals, showing that the environmental stressors each boosted the worms' ability to survive larger insults later. The interventions also increased the worms' life expectancy by 20 percent. It is unclear how these interventions affected overall levels of oxidative damage, however, because the investigators did not assess these changes. In 2010 researchers at the University of California, San Francisco, and Pohang University of Science and Technology in South Korea reported in *Current Biology* that some free radicals turn on a gene called HIF-1 that is itself responsible for activating a number of genes involved in cellular repair, including one that helps to repair mutated DNA.

Free radicals may also explain in part why exercise is beneficial. For years researchers assumed that exercise was good in spite of the fact that it produces free radicals, not because of it. Yet in a 2009 study published in the *Proceedings of the National Academy of Sciences USA*, Michael Ristow, a nutrition professor at the Friedrich Schiller University of Jena in Germany, and his colleagues

compared the physiological profiles of exercisers who took antioxidants with exercisers who did not. Echoing Richardson's results in mice, Ristow found that the exercisers who did not pop vitamins were healthier than those who did; among other things, the unsupplemented athletes showed fewer signs that they might develop type 2 diabetes. Research by Beth Levine, a microbiologist at the University of Texas Southwestern Medical Center, has shown that exercise also ramps up a biological process called autophagy, in which cells recycle worn-out bits of proteins and other subcellular pieces. The tool used to digest and disassemble the old molecules: free radicals. Just to complicate matters a bit, however, Levine's research indicates that autophagy also reduces the overall level of free radicals, suggesting that the types and amounts of free radicals in different parts of the cell may play various roles, depending on the circumstances.

THE ANTIOXIDANT MYTH

IF FREE RADICALS are not always bad, then their antidotes, antioxidants, may not always be good—a worrisome possibility given that 52 percent of Americans take considerable doses of antioxidants daily, such as vitamin E and beta-carotene, in the form of multivitamin supplements. In 2007 the Journal of the American Medical Association published a systematic review of 68 clinical trials, which concluded that antioxidant supplements do not reduce risk of death. When the authors limited their review to the trials that were least likely to be affected by bias—those in which assignment of participants to their research arms was clearly random and neither investigators nor participants knew who was getting what pill, for instance—they found that certain antioxidants were linked to an increased risk of death, in some cases by up to 16 percent.

Several U.S. organizations, including the American Heart Association and the American Diabetes Association, now advise that people should not take antioxidant supplements except to treat a diagnosed vitamin deficiency. "The literature is providing growing evidence that these supplements—in particular, at high doses—do not necessarily have the beneficial effects that they have been thought to," says Demetrius Albanes, a senior investigator at the Nutritional Epidemiology Branch of the National Cancer Institute. Instead, he says, "we've become acutely aware of potential downsides."

It is hard to imagine, however, that antioxidants will ever fall out of favor completely—or that most researchers who study aging will become truly comfortable with the idea of beneficial free radicals without a lot more proof. Yet slowly, it seems, the evidence is beginning to suggest that aging is far more intricate and complex than Harman imagined it to be nearly 60 years ago. Gems, for one, believes the evidence points to a new theory in which aging stems from the overactivity of certain biological processes involved in growth and reproduction. But no matter what idea (or ideas) scientists settle on, moving forward, "the constant drilling away of scientists at the facts is shifting the field into a slightly stranger, but a bit more real, place," Gems says. "It's an amazing breath of fresh air."

New threat from poxviruses.

Authors:Shah, Sonia. Source:Scientific American; Mar2013, Vol. 308 Issue 3, p66-71, 6p.

Smallpox may be gone, but its viral cousins -- monkeypox and cowpox -- are staging a comeback

TEN THOUSAND YEARS AGO, WHEN SMALLPOX FIRST EMERGED, HUMANKIND COULD do little more than pray to the gods for succor. Later known as variola, the virus that caused the disease first attacked the linings of the nose or throat, spreading throughout the body until a characteristic rash followed by virus-filled blisters developed on the skin. Over the course of recorded history, the "speckled monster" killed up to a third of the people it infected. During the 20th century alone, it felled more than 300 million men, women and children.

By the late 1970s, however, the deadly scourge had been eliminated from the face of the earth thanks to mass vaccination campaigns that protected millions and left them with a small scar on their upper arm. With nowhere to hide in the natural world -- humans are the virus's only host -- variola was beaten into extinction. Today the only known viral samples are locked in two specialized government laboratories, one in the U.S. and the other in Russia. Absent a catastrophic lab accident, deliberate release or the genetic re-engineering of the virus, smallpox will never again spread death and misery across the globe.

The World Health Organization, which had organized the eradication campaign, sounded the official all clear in 1979, two years after the last sporadic case was recorded, in a Somali hospital worker. Since then, no country has routinely vaccinated its citizens against smallpox, although the U.S. began inoculating certain health personnel and selected members of its armed forces after the terror attacks on September 11, 2001. Thus, an entire generation has reached adulthood without any exposure to either the disease or the vaccine, which sometimes caused serious side effects.

And therein lies the rub. The smallpox vaccine did not protect just against the variola virus. Anyone who was vaccinated against smallpox also developed immunity to infection with variola's viral cousins -- including monkeypox and cowpox. Given the much larger scale of smallpox infections at the time, this secondary protection was seen as a minor benefit.

Now that the smallpox vaccine is no longer widely given, the question becomes: Could these obscure pathogens, which, like smallpox, belong to the Orthopoxvirus genus, pose a new danger to humans? There are reasons to worry. Unlike smallpox, cowpox and monkeypox naturally lurk in rodents and other creatures, so they can never be fully eliminated. The number of cases of monkeypox and cowpox in humans has steadily risen in recent years. And both viruses have begun to infect different creatures beyond their normal hosts, raising the possibility that they might spread through new paths around the planet.

No one knows how monkeypox and cowpox will change over time, but virologists worry that if they mutate to jump more easily from one person to the next, they could devastate large parts of the globe. That grim possibility drives a small band of virologists to learn more about these -- or any other -- potential pox plagues in the making, so as to sound the alarm if they show signs of developing into more threatening forms.

VARYING SEVERITY

THE HISTORY AND BIOLOGY of poxviruses offer some clues as to what to expect from smallpox's kin in the future. Historically, 60 percent of the pathogens that plague humankind, including the orthopoxviruses, have originated in the bodies of other vertebrates. Variola's closest living relative, taterapox, was isolated from a wild gerbil in Africa in 1968. Molecular analyses suggest that smallpox's evolutionary ancestor probably got its start in an African rodent species, possibly now extinct. Similarly, cowpox and monkeypox, despite their names, live in voles, squirrels or other wild rodents.

When variola's ancestor first jumped into humans, it probably was not very contagious, says microbiologist Mark Buller of Saint Louis University. Then, somewhere along the line, he and other researchers surmise, a variant emerged that was much more transmissible. The critical change allowed the virus to broadcast itself via the coughs, exhalations or sneezes of an infected person. Meanwhile human beings started living in much closer quarters, making it that much more likely for one person to pass the infection on to another. The combination of the biological change and the altered environment gave the emerging virus the edge it needed to become a global scourge.

Just because a virus is easily transmitted, however, does not necessarily make it lethal. Indeed, scientists still cannot explain why poxviruses vary so greatly in their severity. In most people, cowpox,

camelpox and raccoonpox infections trigger little more than a skin rash, with virus-filled pustules that harmlessly clear up on their own. Monkeypox infections, on the other hand, can be quite deadly in humans. Even at that, not all monkeypox viruses are equally dangerous. The worst subtype, found in the Congo Basin, kills about 10 percent of people who are infected, whereas another version, from West Africa, rarely if ever ends in death. As it happens, the West African strain in 2003 caused the first-ever recorded cases of monkeypox in the Western Hemisphere. The outbreak, which occurred in six states in the U.S., led to the hospitalization of 19 people, including a child who suffered encephalitis and a woman who was blinded, necessitating a corneal transplant. Investigators traced the infection to rodents imported from Ghana that passed the virus to pet prairie dogs, which in turn infected their owners. Such intermediary animals allow a virus that normally lives in animals with little human contact to reach potentially large numbers of people.

Subtle genetic differences may help explain the shifting severity of pox infections. For example, some poxviruses possess genes for proteins that interfere with the ability of the immune system to respond effectively to the infection. When researchers compared the genes from different poxviruses, they zeroed in on one that was found in several different kinds of poxviruses. In the most deadly strains of variola, this gene triggered the production of a protein that evidence suggests prevents some immune cells from efficiently coordinating their counterattack against the virus. But the equivalent gene in the Congo Basin strains of monkeypox (which are less deadly than smallpox) provided the hereditary instructions for a much shorter protein. When researchers looked at the milder West African version of monkeypox, the gene was missing altogether and the protein in question could not be manufactured. Thus, the evidence suggested that the shorter protein in the Congo Basin strains of monkeypox somehow made them less deadly than smallpox.

Speculation among researchers about how different species of poxvirus acquired this and other genes indicates why monkeypox and its cousins could potentially become more dangerous threats than they are now. The genes, which are not essential for poxvirus replication, appear to be faithful copies of genes the viruses acquired at some point in the evolutionary past from organisms they infected. Yet, curiously, the viruses do not in the normal course of an infective cycle come anywhere near the genetic material stored in the nucleus of the host cells.

One possible explanation, popular among pox virologists, posits the simultaneous infection of a human or other vertebrate host with a poxvirus and a retrovirus. Such co-infections are probably pretty common, researchers say. Retroviruses are known for incorporating their own genes into their host's DNA. (About 8 percent of the human genome consists of DNA that originated in retroviruses.) It is possible that the unusual biochemical activity of the retrovirus inside the cell could allow the poxvirus to capture its host's genes.

If true, this hypothesis could prove portentous. Poxviruses are genetically stable and do not usually mutate quickly. If they can steal genes from their hosts that make them more virulent, then there is no predicting what a relatively harmless, not to mention an already deadly, poxvirus might do under the right circumstances. The change from mild to dangerous threat could occur more quickly and unpredictably than anyone might have previously suspected.

MONKEYPOX IS BETTER poised than any of its viral cousins at present to emerge as a global threat. Virologists refer to it as smallpox's "little cousin," in part because it causes an illness that is clinically indistinguishable from smallpox. First reported in captive monkeys in 1957, the virus typically lives, evidence suggests, in African rodents, possibly rope squirrels. Outbreaks have so far occurred mostly in Central Africa, with the notable exceptions of the U.S. in 2003 and Sudan in 2006.

University of California, Los Angeles, epidemiologist Anne W. Rimoin was in Kinshasa, Democratic Republic of the Congo, in 2002, when she first heard about local residents who had fallen ill with monkeypox. She did not know how many people were infected, how they were exposed to the virus

or whether the virus could spread to others. But she knew the disease was life-threatening and wanted to learn more.

With her blond hair and buff pedicure, Rimoin could hardly be mistaken for a local in the remote Congolese jungles. Yet she had studied the country's politics as an undergraduate in African history and was fluent in French, which is still spoken in the former Belgian colony, as well as Lingala and other local languages. She started asking around. "I just clicked with the right people and asked the right questions," she says. And "it became clear to me that there were probably a lot more cases than were being reported."

But how to find them? Unsurprisingly, given the dearth of health care facilities in rural Congo, few people who were sick sought out clinicians. And those who had recovered could not easily be identified with blood tests because there was no way of telling whether the presence of antibodies against poxvirus was the result of an earlier smallpox vaccination or another poxvirus infection. Assessing the incidence of monkeypox required finding people who were in the throes of an acute monkeypox infection, when it would be possible to test for the virus itself from the pustules on the skin.

Rimoin began her quest by establishing a research site deep in the forest. There were no roads, no cell-phone signals and no radio transmission. She chartered planes to get in and out and spent days walking and traveling by canoe and by motorcycle to track down monkeypox cases among the Lingala-speaking villagers of interior Congo.

The results were alarming. Compared with similar data collected by the World Health Organization in 1981-1986, Rimoin had found a 20-fold increase in the number of human monkeypox cases. Even so, she believes that her findings, which were published in 2010, are an underestimate. "It's the tip of the iceberg," she asserts. After all, the WHO had a much bigger and much better financed operation looking for monkeypox 30 years ago. Rimoin's team undoubtedly missed many more cases, relatively speaking, than that earlier, larger effort.

RISE OF MONKEYPOX

ALTHOUGH THE SPIKE in monkeypox cases was larger than anyone had anticipated, it was not unexpected. After all, most of the country's population is unvaccinated against poxviruses. (The Democratic Republic of the Congo stopped vaccinating against smallpox in 1980.)

Further research suggested that something else was going on as well. Ecologist James Lloyd-Smith, one of Rimoin's colleagues at U.C.L.A., uses computer models to study how diseases jump from animals to humans. According to his analyses of Rimoin's data, the withdrawal of the smallpox vaccine and subsequent loss of immunity to related poxviruses could not fully account for the spike in cases. There must have also been at least a fivefold increase in "spillover" events, he says, in which the virus jumped from infected rodents into humans.

Why monkeypox might be jumping into humans more frequently is a matter of conjecture. It could be that continued clearing of land for agricultural use and for burning wood has put more and more people in contact with infected squirrels, mice and other rodents. In addition, more local people may have been reduced to eating potentially infected animals as a result of the Congolese civil war. A 2009 survey, published in October 2011, found that a third of people in rural Congo eat rodents found dead in the forest and that, suggestively, 35 percent of monkeypox cases occur during hunting and farming season. (Most people contract monkeypox from close contact with infected animals, such as handling or eating them.)

Rimoin and other virologists worry that with expanded opportunities to infect people, monkeypox might better adapt to the human body. Buller studies the ways in which orthopoxviruses cause diseases in both humans and animals. Monkeypox "can already kill people," he says, and it can

spread between individuals, too -- just not that well. All that may be needed to transform monkeypox into a much more contagious human pathogen might be a few minor tweaks to a current viral trait.

SPREAD OF COWPOX Cowpox infections are mild in most people. After the virus enters cells and disarms the host's initial immune response, a fusillade of virus-hunting antibodies made by the victim prevents the pathogen from spreading to tissues throughout the body. Not so in people whose immune systems have been weakened, such as by HIV, cancer chemotherapy or treatment to prevent the rejection of transplanted organs. "They can get a smallpoxlike disease, and they can die," says Malcolm Bennett of the University of Liverpool in England. Since 1972, public health experts estimate, the number of immunocompromised people in the U.S. who are now susceptible to serious disease from cowpox and other poxviruses has grown 100-fold.

Bennett, a veterinary pathologist, studies the ecology and evolution of cowpox in wildlife. In the U.K., he says, cowpox normally resides harmlessly in bank voles, field voles and wood mice. Domestic cats pick up the virus from the rodents they hunt. They then expose the people who care for them (often at close range) to cow-pox, a chain of events that accounts for half of all human cowpox cases in the U.K.

Like monkeypox, cowpox has started making forays into creatures outside its normal reservoir hosts. With bank vole populations booming thanks to mild winters and other favorable climatic conditions, rats may have started playing an intermediary role in cowpox transmission similar to the one played by prairie dogs in the 2003 American outbreak of monkeypox. "There's been a proliferation of reports, either zoo-related or pet-related, associated with rats," says Mary Reynolds, an epidemiologist at the U.S. Centers for Disease Control and Prevention. That trend "is potentially quite concerning because black and brown rats sure make their way around the globe pretty efficiently," she notes. If cowpox becomes established in rats, as opposed to just voles and wood mice, millions more people could be readily infected by, for example, being bitten or coming into contact with their droppings.

Indeed, orthopoxviruses are notoriously adept at colonizing new species. The vaccinia virus, for example, which was used to create modern smallpox vaccines, now freely propagates in dairy cattle in Brazil, as well as in buffalo in India. And there are "a range of orthopoxviruses out there that have never been isolated or fully characterized," Reynolds points out. Given the right opportunities, those less familiar pox strains could extend their ranges into new regions and species. "Some will be pathogenic to people," Bennett adds. "They just haven't managed to make the species jump yet."

ARMED AND VIGILANT

AS THE CROWD of people who have never received a smallpox vaccination grows, pox virologists expect the incidence of human cases of monkeypox, cowpox and other poxviruses to continue to rise.

Should any of these poxviruses become adept at plaguing humans, new drugs and vaccines -- and the resources necessary to use them -- will be needed to contain the threat. Because of post-9/11 fears of intentional releases of smallpox, a spate of new vaccines and drugs are being developed to fight smallpox. These medications will likely provide protection against naturally emerging poxviruses as well. But producing and distributing them, as well as safeguarding against their inevitable side effects, will be a complex and costly undertaking. New smallpox vaccines, such as Bavarian-Nordic's Imvamune, have been designed to be safely administered even to immunocompromised people, but they must be given in higher doses and over the course of two shots instead of one, making them more expensive than traditional smallpox vaccines. A new drug, manufactured by Siga Technologies and known as ST 246, prevents orthopoxviruses from traveling from one cell to another in a host.

Despite not yet being approved by the U.S. Food and Drug Administration, the federal government has already purchased a large amount of ST 246 and added it to the national biodefense stockpile.

In places such as the rural Congo River basin, where health financing for cutting-edge new vaccines and drugs is limited, the best hope for now seems to be enhanced surveillance, combined with community education programs. For example, a monkeypox education program run by the CDC, in conjunction with local health officials and voluntary nongovernmental organizations in the Democratic Republic of the Congo, increased the proportion of local people able to recognize monkeypox cases from 23 to 61 percent. Rimoin's arduous surveillance of monkeypox continues as well, with new studies aimed at sequencing the genes in variants infecting animals and people today to see how the virus may be changing. Better detection means more opportunity to care for and isolate infected individuals, squelching chances for the virus to mutate into new forms that spread more efficiently between people.

The ancient war between poxviruses and humans may not have ended when that 21-year-old Somali hospital worker cleared his smallpox infection back in 1977. With new tools and better surveillance, scientists are better armed and more vigilant than ever before. But to prevent another pox from falling on humankind, society will need to maintain those defenses for some time to come.

Foam That Restores Breathing

Authors: Harmon, Katherin Source:Scientific American, Dec2012, Vol. 307 Issue 6, p36-37.

Injectable oxygen microbubbles could give asthma and choking victims precious minutes.

Only a few minutes after someone stops breathing -- whether it is from a piece of meat stuck in the throat, a severe asthma attack or a lung injury -- the brain starts to shut down. Cardiac arrest and death are imminent. Emergency responders and hospital workers have one primary recourse: insert a breathing tube through a patient's mouth. That procedure can be risky and time-consuming.

A new injectable solution could keep such people alive for 15 minutes or more, buying crucial time to get victims to a hospital or to do some surgical gymnastics in an operating room. The solution contains oxygen microbubbles, which the blood can absorb within seconds. The bubbles are too small to cause an air embolism -- a gas pocket that stops blood flow, thus causing a stroke or heart attack.

To create this lifesaving foam, John Kheir, a cardiologist at Boston Children's Hospital, and his colleagues adapted existing medical nanotechnology. Microparticles with lipid membranes already deliver drugs, as well as dyes for ultrasound imaging. Kheir's team propelled phospholipids through an oxygenated chamber and used sound waves to spur the ingredients to self-assemble into microparticles. The researchers then used a centrifuge to superconcentrate them into solution. Each four-micron-wide microbubble contains pure oxygen, surrounded by a lipid film that is just a few nanometers thick.

Because the bubbles contain oxygen at a pressure that is higher than in the bloodstream, the gas diffuses into red blood cells on contact. Once a bubble is depleted, the shell collapses to a disk that is less than a micron wide, easily passing through the circulatory system.

In a test, researchers blocked the airways of anesthetized rabbits for 15 minutes. Those injected with the solution were much less likely to go into cardiac arrest or have other organ damage than those who got saline solution -- despite not taking a single breath.

The approach is "a fairly innovative idea compared to what we have now," says Raymond Koehler of Johns Hopkins University, who is not involved in the work, because most emergency oxygen procedures require the pulmonary system to function at least at a minimal level.

One drawback is that because the blood absorbs the oxygen so quickly, a constant infusion is necessary, which involves a lot of saline to help the foam move smoothly into the bloodstream. The amount of solution that a patient would receive after 15 minutes could lead to edema, a fluid overload that can cause heart failure. Kheir's team is trying to improve the formulation so that it requires less saline.

Another concern is that without normal respiration, carbon dioxide builds up in the body, which can be toxic. As Koehler notes, however, the body can handle a little excess carbon dioxide better than it can handle a total lack of oxygen. If the microbubbles prove successful in further animal (and subsequent human) trials, the solution could help emergency crews or operating room technicians buy crucial minutes before they can implement other lifesaving treatments. In those situations, Koehler says, "you want to have a backup plan."

Early Treatment for Alzheimer's

Authors: Laber-Warren, Emily; Source: Scientific American, Dec 2012, Vol. 307 Issue 6, p38-39.

A drug trial of 300 Colombians could reveal a way to prevent the disease from ever starting.

Alzheimer's disease remains virtually untreatable. More than 100 experimental drugs have failed to halt the condition that robs people of their memories, their relationships and, ultimately, their identity. Now scientists will be testing a new strategy for preventing this horrific condition from starting in the first place. Just as healthy people take statins to lower their cholesterol and avoid heart disease, people at risk for Alzheimer's could conceivably pop pills to keep the disease at bay.

Researchers will be investigating a drug that flushes away an intrusive protein called amyloid, suspected as a primary contributor to Alzheimer's. Until recently, amyloid clumps could only be seen by dissecting the brain after death. Yet advanced positron-emission tomography scans of living people's brains, a recent innovation, show that by the time symptoms appear, amyloid has been silently accumulating for up to 20 years. Perhaps by then the brain is irreversibly damaged, making any drug useless. No one knows for sure, however, whether amyloid causes Alzheimer's or is merely a by-product of the disease. The new study may provide an answer to this mystery.

Set to start early in 2013 if all approvals are granted, the investigation will involve 300 members of distantly related families in Colombia whose rare and particularly devastating form of Alzheimer's strikes in the prime of life. By their 50s and 60s, many are as helpless as infants. Normally it is impossible to predict who will develop Alzheimer's, but in this extended family, a single genetic mutation, detectable by a blood test, spells doom.

Eric Reiman, executive director of the Banner Alzheimer's Institute in Phoenix, his colleague Pierre Tariot and their Colombian collaborator Francisco Lopera realized that the family provided a unique opportunity to test the benefits of early intervention. They plan to give an experimental drug, crenezumab, to 100 family members who are on the cusp of developing Alzheimer's symptoms and a placebo to 100 others. A third group not destined to get the disease will also receive the placebo.

Participants will receive biweekly injections for at least five years. Every few months they will undergo extensive testing: magnetic resonance imaging to track brain shrinkage; spinal taps to measure tau protein, which is associated with brain cell death; and memory and thinking tests designed to pick up subtle cognitive lapses, such as forgetting a list of words that were memorized only minutes or hours earlier, a marker of emerging Alzheimer's.

The study will also enlist up to three dozen patients in the U.S. The Americans, who will receive the same treatment, will be a less homogeneous bunch, possessing various mutations in any of three genes linked to early-onset Alzheimer's. Investigators hope to learn whether it is possible to

extrapolate from the Colombian family to others who are destined to develop dementia in middle age.

The \$100-million study is funded by the drug's maker, Genentech, as well as by philanthropists and the National Institutes of Health. Even if the drug succeeds, there is no guarantee that the results will translate to the much more common form of Alzheimer's that afflicts the elderly. Yet the researchers hope this trial will establish for Alzheimer's what cholesterol and high blood pressure are for cardiovascular disease -- intermediate signposts that aid research, diagnosis and treatment

The data they collect could mean that instead of having to wait years to see whether an experimental drug helps patients, researchers could quickly gauge results from subtle biological shifts such as smaller brain size or changes in tau or amyloid deposits. "We need to develop faster ways to test the range of promising therapies and find ones that work as soon as possible," Reiman says.

Sugar-Powered Pacemakers. (cover history)

Authors: Fessenden, Marissa; Source: Scientific American, Dec2012, Vol. 307 Issue 6, p42-43.

The glucose in our blood could drive medical implants

PACEMAKERS, insulin pumps and other medical devices of the future may run without batteries, powered instead by the same energy that fuels the body: sugar. Researchers first dreamed of glucose-powered implants in the 1960s, but the advent of lithium-ion batteries in the late 1970s provided a simpler, more powerful fix. Batteries have always had a major drawback, however: they must be surgically replaced -- every five to 15 years for pacemakers. Rechargeables connect to electronics outside the body with wires that pierce the skin and leave a person open to infection.

Several advances have prompted researchers to look again at glucose, which is plentiful in blood and the interstitial fluid that bathes our cells. More efficient circuitry in implants, for example, has reduced power requirements. And glucose biofuel cells are becoming much more efficient and body-friendly.

In most biofuel cells, enzymes at the anode strip electrons from glucose molecules. The electrons provide current as they flow to the cathode, where they react with oxygen, forming only small amounts of water. Unlike batteries, however, fuel cells need to be immersed in a constant supply of fuel -- which blood or interstitial fluid can readily provide.

Excitement started to build in 2003, when researchers at the University of Texas at Austin built a tiny biofuel cell that generated power from a grape. Since then, a handful of groups have demonstrated practical devices. Past models demanded acidic conditions not found in the body, but researchers at Joseph Fourier University in Grenoble, France, packed biocompatible enzymes on a graphite base, which produced a milder chemistry. Their diskshaped cell is half the diameter of a dime and slightly thinner. It is wrapped in material used for dialysis bags, which allows small molecules of glucose in but keeps enzymes from getting out. In a 2010 lab rat experiment, the device drew glucose from interstitial fluid and produced a stable power output of 1.8 microwatts for 11 days.

This year researchers at the Massachusetts Institute of Technology took another step toward commercialization. Engineer Rahul Sarpeshkar built a fuel cell as an integrated circuit on a silicon chip, using "the same easy-to-manufacture process as semiconductors," he says. His team wants to use cerebrospinal fluid to power brainmachine interfaces. The fluid, which cushions the brain and spinal cord, contains plenty of glucose yet few immune system cells that could work to reject the implant.

Sarpeshkar has crafted platinum electrodes, which do not irritate tissue or corrode, notes Sven Kerzenmacher, a chemical engineer at the University of Freiburg in Germany, who is also using the material in his designs. Still, the body can mount opposition to such an incursion; Kerzenmacher says biocompatibility is the biggest hurdle. His prototype fuel cell works well in buffer solutions in the lab, he says, but in body-fluid tests, amino acids in blood or serum caused the device to lose power.

While a Clarkson University group has implanted a biofuel cell in a snail, the Grenoble group is still the only one to successfully operate a glucose fuel cell inside a vertebrate. The M.I.T. design has not been tested in cerebrospinal fluid but in a buffer that approximates body-fluid chemistry. Yet Sarpeshkar is optimistic that biofuel cells could enter the market in 10 years. His silicon device produces a reliable power output of 3.4 microwatts per square centimeter. Current pacemakers need eight to 10 microwatts, a feasible goal. Cochlear implants require a few milliwatts, and artificial organs would require even more.

As sugar-powered implants advance, they are opening up the possibility of tiny medical devices. Perhaps nanoscale robots that run on glucose and dispense targeted drugs will one day swim from science fiction to reality.

A cure for what ails you.

Authors: Lewis, Ricki; Source: Scientific American, Jan2013, Vol. 308 Issue 1, p32-32.

Gene therapy, once off to a rocky start, transforms medicine by getting at the root cause of many diseases.

50 IT IS 2063. YOU WALK INTO THE DOCTOR'S OFFICE, AND A nurse takes a sample of saliva, blood or a prenatal cell and applies it to a microchip the size of a letter on this page on a handheld device. Minutes later the device reads the test results. The multicolored fluorescence pattern on its display reveals the presence of DNA sequences that cause or influence any of 1,200-plus single-gene disorders. Fortunately, regulatory authorities have approved a cure for each one of these diseases: gene therapy.

Gene therapy works by using the innate biological machinery of a virus to carry healthy versions of genes into the nucleus of a cell to replace a mutation that leads to illness. It was conceived shortly after the discovery of DNA's structure in 1953, but its path to a bona fide treatment was fitful. Early attempts worked sporadically at best. In 1999 an 18-year-old died when a type of gene-carrying virus used to treat a metabolic disorder triggered a deadly immune response; the molecular payload ignited a reaction in immune cells in the patient's liver. Also that year, two infants with an inherited immune deficiency received genes, onboard retroviruses, that veered into cancer-causing genes as well as their targets -- leukemia resulted.

These setbacks mired the development of gene therapy in a debate about which viruses could be used safely as a vector, the gene-bearing invader of a cell.

After a difficult start, gene therapy began to rack up milestones. In 2012 the European Commission approved the first gene therapy for lipoprotein lipase deficiency, which impairs fat digestion.

Then, in 2014, the U.S. Food and Drug Administration approved treatments for a form of inherited blindness (Leber's congenital amaurosis), an immune deficiency (adenosine deaminase, or ADA, deficiency) and a genetic disorder affecting the brain (adrenoleukodystrophy). Though rare, the conditions were relatively easy to target.

These endorsements affirmed adeno-associated virus (AAV) as the vector of choice. Most of us already carry it in some of our cells, which means our immune systems ignore it. Retroviruses, in contrast, were retooled to self-destruct but could still cause cancer, as they had in the

immunodeficient infants. And lentivirus, after winning FDA approval, failed to catch on because patients were reluctant to allow themselves to be injected with HIV, albeit in a form stripped of AIDS-related genes.

Arrival of gene therapy for hemophilia B, in 2016, proved the economic value of the technology: \$30,000 for a one-time gene treatment trumped a lifetime of clotting factor injections -- a bill that could tally up to an expenditure of \$20 million over the course of many years.

The ability to control the immune response to the vector meant that the most imposing technical barrier had been overcome: the chemical package delivered to patients not only provided a replacement gene, it also bolstered parts of the immune reaction against cancers and infections and dampened the aspects of the response that could lead to the rejection of viral vectors.

The floodgates now opened. Because the retina is shielded from the immune system, gene therapies for about 100 forms of blindness came first. In 2019 a dozen children with the ultra-rare giant axonal neuropathy became pioneers by receiving gene therapy to the spinal cord. Next on the list were spinal cord injury, amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) and spinal muscular atrophy. Intravenous, gene-laden AAV slipped across the blood-brain barrier, thereby preventing Parkinson's and other brain diseases. No longer was it necessary to bore holes in the skull, as happened in the early part of the century.

Over time researchers came to recognize that some conditions are best treated without replacing a gene. For cystic fibrosis, drugs that could untangle a protein with a faulty structure were better because gene-treated cells in the lungs and airway do not persist. And for Duchenne muscular dystrophy, reactivating silenced genes was easier than delivering healing genes to all the muscle cells in a child's body.

The successes only left room for more. By midcentury new therapies were targeted beyond rare, single-gene disorders to embrace common conditions that reflected genetic and environmental risk factors, such as mental illnesses, diabetes and most forms of heart disease.

By 2060 the ability to use gene testing to predict a patient's future health -- coupled with genetic interventions -- had reached an unprecedented level of precision, with profound repercussions. With diseases stopped in their tracks, health care costs plunged as a longer-lived, physically fit population emerged.

APPENDIX 3: Articles taken from the magazines National Geographic and National Geographic Italia

Influenza, la caccia ai nuovi vaccini - Katherine Hobson

http://www.nationalgeographic.it/scienza/medicina/2013/01/18/news/influenza_verso_un_vaccino_migliore_-1467156/

Immunizzarsi è sempre consigliabile, ma l'efficacia dei vaccini attualmente disponibili è limitata. Gli scienziati studiano nuovi prodotti in grado di proteggere l'organismo anche per diversi anni

Secondo uno studio condotto negli Stati Uniti, il vaccino anti-influenzale di quest'anno si è dimostrato efficace nel 62 per cento dei casi.

Come ogni anno, l'epidemia invernale di influenza si avvicina al suo picco, che in Italia dovrebbe arrivare tra la fine di gennaio e l'inizio di febbraio. Si calcola che dall'inizio di novembre la malattia abbia colpito circa 13 milioni di italiani. Anche se siamo alla "stretta finale", è ancora possibile vaccinarsi: il Ministero della Salute raccomanda di farlo soprattutto agli anziani e a persone che soffrono di particolari patologie.

Secondo uno studio del Centro studi della Federazione dei medici di famiglia, quest'anno la quota degli italiani che si sono sottoposti alla vaccinazione sarebbe scesa di circa il 25 per cento, soprattutto a causa dei timori suscitati dal ritiro, lo scorso ottobre, di alcuni lotti del vaccino che presentavano anomalie.

Ma perché contro l'influenza è necessario vaccinarsi ogni anno? Non sarebbe possibile farlo una volta per tutte, come avviene per altre malattie? La risposta sta nella natura "sfuggente" del virus dell'influenza.

Esistono virus che mutano molto poco nel tempo. Quello del morbillo, ad esempio, è "stabile come la roccia", sostiene William Schaffner, capo del dipartimento di medicina preventiva della Vanderbilt University di Nashville, negli Stati Uniti.

Anche la varicella subisce pochi cambiamenti da un anno all'altro.

Il virus dell'influenza, invece, è "geneticamente flessibile", spiega Shaffner. Muta continuamente, e può combinarsi con ceppi diversi dando vita a varianti sempre nuove. Può accadere così che il nostro sistema immunitario non riconosca la "versione" dell'influenza di quest'anno anche se l'anno scorso abbiamo contratto la malattia o ci siamo vaccinati.

"È come dover mettere un cappotto nuovo ogni inverno", spiega Shaffner, che ha anche presieduto la National Foundation for Infectious Diseases.

Occorre dunque aggiornare il vaccino per tener conto delle mutazioni del virus. Non sempre è facile. Ogni anno le autorità sanitarie tentano di prevedere come sono mutati i tre ceppi del virus - due dell'influenza A e uno dell'influenza B - che saranno più comuni nell'inverno seguente. L'operazione viene svolta con mesi d'anticipo, per dare il tempo di fabbricare, distribuire e somministrare i vaccini. "È marzo, ma devi cercare di capire che cosa circolerà nel febbraio seguente", spiega Shaffner.

Nei mesi seguenti, i ceppi circolanti del virus possono mutare abbastanza da ridurre l'efficacia del vaccino. E anche quando i vaccini distribuiti si rivelano efficaci, è sempre possibile essere infettati da un ceppo meno comune per il quale non è stata messa a punto una protezione. C'è inoltre una parte della popolazione - soprattutto tra gli anziani, i bambini e persone afflitte da particolari patologie - che anche dopo la vaccinazione non riesce a sviluppare una risposta immunitaria abbastanza forte da reprimere la malattia. E c'è chi contrae l'influenza prima che il vaccino possa fare effetto.

I Centers for Disease Control and Prevention, l'agenzia USA che si occupa di studiare e prevenire le patologie, hanno calcolato che il vaccino di quest'anno è stato efficace nel 62 per cento dei casi. La stima è stata effettuata monitorando per un mese lo stato di salute di un migliaio di adulti e bambini americani. Si tratta di una percentuale in linea con i risultati degli anni precedenti: analizzando i dati delle ricerche effettuate in passato, la rivista *Lancet Infectious Diseases* ha calcolato nel 2011 che sugli adulti sani di età pari o inferiore a 65 anni l'efficacia combinata dei vaccini è stata del 59 per cento: un risultato non proprio eccezionale.

Cambiare strada

Naturalmente i ricercatori sono al lavoro per mettere a punto metodi migliori per sconfiggere l'epidemia. "Quando mi chiedono se il vaccino attuale sia lo strumento più efficace che abbiamo a disposizione oggi, rispondo di sì. Bisogna usarlo», dice Michael Osterholm, principale autore della ricerca di Lancet e direttore del Center for Infectious Disease Research and Policy dell'Università del Minnesota. «Ma lo è anche per il futuro? No. Abbiamo bisogno di vaccini migliori».

E si tratta di un bisogno urgente. Secondo l'Organizzazione Mondiale della Sanità, ogni anno l'influenza stagionale fa tra i 250 mila e i 500 mila morti nel mondo. I casi gravi sono tra i tre e i cinque milioni. In Italia le vittime della malattia e delle sue complicazioni sono intorno alle 8.000 l'anno, in grande maggioranza anziani. In un recente rapporto, Osterholm ha lanciato l'appello perché nella ricerca sui vaccini "si cambi strada".

I tradizionali vaccini per l'influenza contengono pezzi della "testa" dell'emoagglutinina, una proteina che si trova sulla superficie del virus dell'influenza. Quando si imbattono in quei frammenti di proteina, dopo la vaccinazione, le cellule del sistema immunitario dette linfociti B imparano a produrre anticorpi contro di essi. Più tardi, se l'organismo viene a contatto con il virus, i linfociti sono già pronti a rispondere rapidamente per prevenire l'infezione.

Il problema è che questa parte della proteina muta rapidamente: per questo i vecchi anticorpi non sono più efficaci contro la nuova versione del virus.

Ricercatori e ditte biotech stanno quindi cercando di contrastare le proteine del virus che non mutano a seconda dei ceppi o degli anni. "Se troviamo un componente comune a tutti i virus dell'influenza che non muta col tempo, forse possiamo mettere a punto un vaccino che lo combatta", spiega Gregory Poland, direttore del gruppo di ricerca sui vaccini della Mayo Clinic, prestigioso centro di ricerca e di cura del Minnesota.

La speranza è che con questo approccio si riesca a mettere a punto un vaccino universale che protegga dall'influenza stagionale per diversi anni di fila e prepari l'organismo anche a combattere ceppi particolarmente aggressivi del virus, come quello della "spagnola", che a partire dal 1918 causò decine di milioni di morti in tutto il mondo, o quello della cosiddetta influenza suina, una variante del sottotipo H1N1 che provocò una pandemia globale nel 2009.

Per raggiungere l'obiettivo però, i ricercatori seguono anche altre strade. Sarah Gilbert, docente di vaccinologia all'Università di Oxford, sta lavorando con la sua équipe a un vaccino che interagisca con i linfociti T, che sono in grado di uccidere le cellule infettate dai virus. "Riescono a riconoscere le cellule infette perché riconoscono i piccoli segnali dell'infezione presenti all'esterno della cellula", spiega Gilbert. "È come se queste cellule mettessero fuori delle bandierine per dire che all'interno hanno qualcosa di non umano". Il vantaggio è che quelle "bandierine" sono più o meno le stesse per tutti i ceppi di virus influenzale.

L'équipe di Oxford ha pubblicato i risultati di alcuni piccoli esperimenti preliminari condotti su esseri umani, ma, precisa la studiosa, saranno necessari studi molto più estesi per dimostrare l'efficacia di questo approccio.

In ogni caso, anche se un vaccino più efficace fosse messo a punto, è molto improbabile che possa durare per la vita. L'efficacia dell'immunizzazione cala con il tempo, e quindi resterebbe la necessità di effettuare richiami.

"Probabilmente metteremo a punto un vaccino da richiamare ogni cinque anni circa", prevede Gilbert. Sarebbe inoltre disponibile tutto l'anno, in modo da evitare le tradizionali code negli studi medici tra settembre e marzo. C'è ancora da aspettare

Per ora però, l'attesa continua. "I possibili vaccini sono ancora nella fase dei primi test", precisa Poland. "Prima di diffonderne uno potrebbero passare dai quattro ai dieci anni".

Il rapporto dello scorso ottobre del Center for Infectious Disease Research and Policy ha sottolineato come per mettere un nuovo vaccino sul mercato possono occorrere anche 15 anni e un investimento di un miliardo di dollari. Nel rapporto, si prevede anche che un vaccino fondato su un approccio completamente diverso da quelli tradizionali dovrà sottostare a un processo di approvazione più lungo, con rischi finanziari "notevolmente più alti".

Nell'attesa, ci sono miglioramenti in vista anche per i vaccini tradizionali. A partire dal prossimo inverno sarà disponibile un vaccino quadrivalente, in grado di proteggere da due ceppi dell'influenza A e due della B. Entro un paio d'anni, assicura Poland, tutti i produttori di vaccini dovrebbero essere in grado di commercializzarlo.

(18 gennaio 2013)© RIPRODUZIONE RISER

How Far Off Is a Better Flu Shot?- Katherine Hobson

<http://news.nationalgeographic.com/news/2013/01/130116-flu-vaccine-immunity-virus-diseases-health-science/>

Someday you may only have to get a flu shot every five years.

The Centers for Disease Control estimates this year's flu vaccine to be 62 percent effective.

As you waited in line for your flu shot last weekend, you may have been wondering: Why must I go through this every year?

The answer is that the influenza virus is a slippery character. Some viruses barely change at all over time. The measles virus, for example, is "as stable as stone," said William Schaffner, chairman of the department of preventive medicine at Vanderbilt University.

Chicken pox, too, is consistent from year to year. But influenza is "genetically plastic," said Schaffner. It mutates all the time, and it can combine with other flu strains to regularly make new variants.

Those kinds of changes happen so frequently that the body's immune system won't necessarily recognize this year's iteration of the flu as a dangerous threat—even if you suffered from or were vaccinated against last year's version.

"It's like putting on a new sport coat every winter," said Schaffner, the past president of the National Foundation for Infectious Diseases.

The vaccine has to be updated every year to account for the flu's changes. But forecasting what those changes will be is tough.

Every year, public health officials try to predict the three flu strains—two of influenza A and one of influenza B—that will be common in the coming winter. They do this months in advance, giving manufacturers time to produce, distribute, and administer the vaccine.

"Here you are in March, trying to figure out what will be circulating next February," said Schaffner.

In the intervening months, circulating strains of the flu virus can change enough to reduce the vaccine's effectiveness.

Even when the seasonal vaccine is a good match, it doesn't offer complete protection. People may be infected by a less common strain not included in the vaccine.

Some, especially the elderly, very young, or those with certain health conditions, don't develop a strong immune response to the flu even after vaccination. Others get exposed to the flu before the vaccine can take effect.

The Centers for Disease Control and Prevention last week estimated the effectiveness of this year's vaccine to be 62 percent, based on a one-month survey of more than a thousand adults and kids.

That's in line with the historical average. A 2011 review of previous research published in *Lancet Infectious Diseases* found that vaccines had a combined efficacy of 59 percent against flu in healthy adults aged 65 and younger.

Trying to Change the Game

That less than stellar record has scientists working to develop better tools to fight flu.

"Is [the current vaccine] the answer for tomorrow? Yes, it's the best we have. Use it," said Michael Osterholm, lead author of the 2011 review and director of the Center for Infectious Disease Research and Policy at the University of Minnesota.

"Is this the answer for the next few tomorrows?" he continues. "No. We need better flu vaccines."

And that need is acute. The World Health Organization puts the global death toll from seasonal flu at 250,000 to 500,000 per year, out of 3 million to 5 million severe cases. In the United States, an estimated 3,000 to 49,000 people die each year from the flu, according to the CDC.

Osterholm was the lead author of an October Center for Infectious Disease Research and Policy report that called for "game-changing" influenza vaccines.

The traditional flu vaccine includes pieces of the "head" of the hemagglutinin protein, which is found on the surface of the flu virus. When immune cells called B cells run into those bits of protein after vaccination, the cells learn to make antibodies against them. Later, if the actual flu virus comes along, these prepared B cells can mount a speedy response and prevent infection.

The problem is that this part of hem agglutinin mutates rapidly, and the older antibodies are of no use against the newer version of the virus.

Researchers and some biotech companies are now trying to target proteins in the influenza virus that don't vary from strain to strain and from year to year.

"If this piece of the virus is the same among all influenza viruses and doesn't change over time, maybe we can make a vaccine against it," said Gregory Poland, director of the Mayo Clinic's Vaccine Research Group.

The hope is that the approach yields a universal vaccine that protects against seasonal flu without annual shots. Such a vaccine could also keep the body poised to fend off a major new flu virus, like the 1918 strain that killed tens of millions of people and the 2009 pandemic of a strain of H1N1, aka swine flu.

As they seek that silver bullet, researchers are taking a variety of approaches.

Sarah Gilbert, a professor of vaccinology at the University of Oxford, is working with colleagues on a vaccine that interacts with the body's T cells, which kill other cells that have been infected by a virus.

"T cells can recognize human cells infected with the virus because very small regions of the [infected cells'] contents are displayed on the outside," said Gilbert. "It's like putting little flags on the outside to say there is something nonhuman inside."

The advantage is that those little flags on the outside of infected cells don't vary much from flu strain to flu strain.

The Wait Continues

The Oxford group has published the results from some small, early studies in humans but will need many more studies to prove T cell approach is effective, Gilbert said.

Even if that or other new vaccines make it to market, the likelihood of a flu shot for life is low. Immunity declines over time, so people would probably need boosters.

"I think we'll probably move to a shot every five years," said Gilbert. Such a shot could be offered year-round, cutting down on lines at drugstores and doctors' offices between September and March.

For now, the wait continues. "Candidate vaccines are in early trials," said the Mayo Clinic's Poland. "It could be four to ten years before we see one."

The Center for Infectious Disease Research and Policy report from October noted that it can take as long as 15 years and as much as \$1 billion to bring a new vaccine to market.

It also predicted that flu vaccines taking an entirely new approach will face a longer approval process and "substantially higher" financial risk than more traditional vaccines. More studies will be needed, and regulators will need to figure out, for example, how to estimate the biological effectiveness of a vaccine that doesn't rely on the same mechanism as today's vaccines.

The October report urged changes to the U.S. government's regulatory process for approving new flu vaccines and "coordinated partnerships involving national governments, the pharmaceutical industry, the investment community, and academia." And it called on the U.S. government to "assume a primary leadership role" in spurring the development of new vaccines.

Can't wait for all that? There is an incremental improvement to the current flu vaccine coming soon.

Starting in the 2013-14 flu season, there will be a "quadrivalent" vaccine available that will protect against two influenza A and two influenza B strains. In a couple of years, all vaccine manufacturers will be making them, said Poland.

Avremo anche noi l'udito di Superman?- Ker Than

http://www.nationalgeographic.it/scienza/2011/05/18/news/un_superudito_anche_per_gli_esseri_umani_-338483/

Grazie a una nuova ricerca in futuro potremmo essere in grado di sentire suoni che oggi non percepiamo.

Sott'acqua l'udito dei subacquei percepisce una gamma di suoni che gli esseri umani non sentono fuori dall'acqua. Le ricerche su questo fenomeno potrebbero un giorno portare alla creazione di apparecchi che ci consentano di avere un superudito.

Secondo una nuova ricerca, gli esseri umani potranno sentire suoni che oggi non sono in grado di percepire. Nuovi esperimenti suggeriscono che facendo vibrare le ossa dell'orecchio si può creare una "scorciatoia" per far arrivare i suoni al cervello, potenziando l'udito.

La maggior parte della gente sente suoni nella gamma tra 20 hertz (Hz) al minimo, fino a circa 20 kilohertz (kHz) al massimo.

20 kHz, il suono più acuto, può suonare come il ronzio acuto di una zanzara mentre 20 Hz è ciò che sentiremmo "a un concerto rock se ci trovassimo vicino al bassista", spiega Michael Qin, ricercatore del Naval Submarine Medical Research Laboratory in Connecticut.

In alcuni casi, l'uomo può anche percepire frequenze al di fuori di questa gamma. Per esempio, chi fa immersioni subacquee può sentire suoni fino a 100 kHz, come dimostrato dagli esperimenti di Qin.

Non è chiaro perché l'udito dei subacquei migliori sott'acqua, ma ciò si può spiegare con il fatto che il suono viaggia direttamente attraverso le ossa al cervello, spiega Qin.

Le vibrazioni delle ossa del cervello potenziano l'udito

Nell'udito normale, le onde sonore che viaggiano attraverso l'aria o l'acqua entrano nel canale uditivo e colpiscono il timpano, facendolo vibrare. Il timpano è connesso a tre ossicini collegati tra loro: il martello, l'incudine e la staffa.

La staffa, oscillando, spinge contro una struttura contenente fluido chiamata coclea nell'orecchio interno. A forma di chiocciola, la coclea contiene strutture simili a peli che convertono la pressione nel fluido in segnali nervosi che vengono inviati al cervello e interpretati come suoni.

"Se consideriamo l'apparato uditivo come l'insieme di una lunga catena di eventi, ci sono molti punti in questa catena in cui la conduzione ossea o l'immersione subacquea possono scavalcare il normale avvicendamento nella catena di eventi", dice Qin.

Per esempio, la conduzione ossea avviene quando suoni ad alta frequenza stimolano direttamente le ossa dell'orecchio, inviando segnali al cervello senza attivare i timpani. È così che alcune specie di balene sentono sott'acqua.

"Il nostro studio mira essenzialmente a comprendere come funziona l'udito sott'acqua e la conduzione ossea dell'udito, e a stabilire inoltre se condividono lo stesso meccanismo.

In alternativa, alcune frequenze ultrasoniche potrebbero stimolare il fluido nella coclea.

"Il fluido stesso potrebbe oscillare, come l'acqua di un serbatoio colpito da un oggetto metallico", dice Qin.

Potremo usare apparecchi per avere un udito super?

Qin e il suo team stanno cercando di capire quali ossa dell'orecchio siano più sensibili alle vibrazioni ultrasoniche.

La ricerca porterà alla creazione di apparecchi che diano a tutti la possibilità di sentire come Superman o di migliorare notevolmente un udito normale? Qin non si lascia scappare una parola sull'argomento.

Alla fine di maggio Qin presenterà con il gruppo dei suoi ricercatori lo studio al congresso della Acoustical Society of America.

(18 maggio 2011)© RIPRODUZIONE RISERVATA

Superhuman Hearing Possible, Experiments Suggest- Ker Than

<http://news.nationalgeographic.com/news/2011/05/110516-people-hearing-aids-ears-science/>

Vibrating ear bones could someday boost hearing.

People may one day be able to hear what are now inaudible sounds, scientists say.

New experiments suggest that just vibrating the ear bones could create shortcuts for sounds to enter the brain, thus boosting hearing.

Most people can hear sounds in the range of about 20 hertz (Hz) at the low end to about 20 kilohertz (kHz) at the high end.

Twenty kHz would sound like a very high-pitched mosquito buzz, and 20 Hz would be what you'd hear if "you were at an R&B concert and you just stood next to the bass," explained Michael Qin, a senior research scientist at the Naval Submarine Medical Research Laboratory in Connecticut.

"It would be the thing that's moving your pants leg."

Under certain circumstances, humans can also hear frequencies outside of this normal range. For instance, divers underwater can detect sounds of up to a hundred kHz, according to Qin's recent experiments.

It's unclear why the divers have enhanced hearing underwater, but it may be because the sounds travel directly through the bones to the brain, he said.

Vibrating Ear Bones Boost Hearing

In normal hearing, sound waves traveling through the air or water enter our ear canals and strike our eardrums, causing them to vibrate. Our eardrums are connected to three tiny, connected bones called the malleus, incus, and stapes—popularly known as the hammer, anvil, and stirrup, due to their shapes.

As the stapes bone rocks back and forth, it pushes against a fluid-filled structure called the cochlea in the inner ear. Resembling a tiny snail, the cochlea contains tiny hair-like structures that translate the pressure waves in the jostling fluid into nerve signals that are sent to the brain and interpreted as sounds.

"If you think of the hearing system as one long chain of events, there are multiple places in which bone conduction or underwater hearing can bypass that chain," he said.

For example, bone conduction occurs when very high-frequency sounds directly stimulate the ear bones, sending signals to the brain without activating the eardrums. This is how some species of whales hear underwater.

"The core of our work is trying to understand underwater hearing and bone-conduction hearing, and to determine if they share the same underlying mechanism," he said.

Alternatively, certain ultrasonic frequencies might stimulate the fluid in the cochlea.

"It could be like hitting a wrench against a water tank," Qin explained. "The fluid itself could go into oscillation."

Superhuman Hearing Devices on the Horizon?

Qin and his team are now exploring which bones are most likely to be most sensitive to ultrasonic vibrations.

Could such research lead to devices that give us superhuman hearing or improved hearing aids? Qin is mum for now.

"That's the great thing about basic science, right? It lets you know how things work, and you can bend it to many applications."

APPENDIX 4: Doctor Shmerling's answers

- *What are the main difficulties in explaining to a patient the illness?*

I think the main difficulty is that physicians spend so much time immersed in the language doctors use that they forget that patients cannot understand them. And patients are often hesitant to ask for clarification. Much like translating a foreign language, doctors have to remember to slow down and communicate in terms their patients will understand. Conversely, patients need to understand that it's okay to ask their doctors to explain things more clearly.

- *Is it really difficult to provide an explanation using a "common/everyday language" to explain the diagnosis?*

I don't think it's difficult – after all, physicians once used common, everyday language themselves! But it does require a certain amount of attention and focus.

- *Could you give me some examples of "explanation request" so that I can see how specialists try to explain to patients an illness?*

If I tell a patient that she has “renal insufficiency and heart failure” she may have little understanding of what is actually happening. I would, instead, tell her that her kidneys are working at about 70% of normal and that her heart is not pumping as forcefully as it should. I can then provide more details about how these problems may affect her and what treatments are recommended.

- *To give you an example, how would you explain me what an hiatus hernia is?*

I would say: “The esophagus connects the mouth to the stomach by traveling through a small opening in the diaphragm. The stomach sits in the abdomen below the diaphragm. Sometimes, the stomach can slide up through this opening into the chest. This is called a hiatus hernia.”

All the best,

Rob Shmerling

Robert H. Shmerling, M.D.

Harvard Medical School

APPENDIX 6: Questionnaire for general practioners

APPENDIX 6: Questionnaire for general practioners.

1. Come potrebbe descrivere il linguaggio che utilizza mentre parla al paziente? (Alcuni esempi: utilizza un linguaggio carico di termini tecnici; un linguaggio semplificato ma comunque esprime alcuni concetti con termini tecnici; un linguaggio semplificato evitando l'uso di termini tecnici; un linguaggio fortemente figurato e carico di esempi facilmente comprensibili; un linguaggio colloquiale; utilizza anche il dialetto; utilizza solo l'italiano; controlla che il paziente la capisca; riassume spesso ciò che è stato detto durante la visita per agevolare la comprensione del paziente; adegua il suo linguaggio in base alla risposta del paziente;...)

USO LINGUAGGIO DELLA VITA
COMUNE TRADUCENDO IN FORMA SEMPLICE
I TERMINI TECNICI, IN FORMA COLLOQUIALE.
DATO IL TIPO DI POPOLAZIONE PREVALENTEMENTE
IN DIALETTO; ALLA FINE SINTETIZZO

2. Il suo paziente chiede spiegazioni riguardo il significato di termini specialistici?

- Sempre A volte
 Spesso Evito i termini tecnici

3. Utilizza un linguaggio molto diverso dal puro "linguaggio medico" con pazienti dell'età di:

- 20-40 anni 60-60>
 40-60 anni con tutti

4. Quali strategie utilizza per spiegare un concetto medico di difficile comprensione per il paziente? (Es.: si serve di esempi; di metafore/similitudini; lo spiega con un disegno; ripete più volte il concetto utilizzando parole diverse; si serve di foglietti illustrativi; di articoli riguardanti il tema trattato;...)

LINGUAGGIO COMUNE; ESEMPI DELLA VITA
QUOTIDIANA, RETATTORE, DISEGNI, ILLUSTRAZIONI
DA TESTI O RIVISTE, ANCHE CITAZIONI DOTTE,
PURE IN LATINO SE LA SITUAZIONE
LE CONSCIENTE DEL PAZIENTE SONO IN GRADO
DI COMPRENDERE. QUINDI UTILIZZO QUASI
TORNIA COMUNICATIVA ABBIA A DISPOSIZIONE
IN QUEL MOMENTO, ANCHE PER VIA INFORMATICA

5. Quali pazienti interagiscono di più durante la visita medica, interrompendo e chiedendo spiegazioni, instaurando così un rapporto più "alla pari"? Pazienti dell'età di:

- 20-40 anni 60-60>
 40-60 anni

6. A suo parere, negli ultimi 15 anni, quali mezzi di comunicazione (es. radio, tv, stampa, giornali specialistici, Internet) hanno influenzato maggiormente la relazione medico-paziente? Perché?

IN GENERALE PROBABILMENTE INTERNET,
PER LUSIANA, CON LA SUA POPOLAZIONE
PREVALENTEMENTE ANZIANA LA TELEVISIONE

7. La figura del medico, in un piccolo paesino come Lusiana, risente dell'influenza di Internet per le questioni strettamente legate alla salute?

- Troppo
 Molto
 Non troppo
 A volte
 No

8. Attualmente, nel paese di Lusiana, la figura del medico di base mantiene il suo ruolo di "punto di riferimento" per le questioni legate alla salute?

- Sì
 No
 E stata sostituita da

9. Cosa pensa delle informazioni mediche trovate dai pazienti su Internet?(sono esaustive, imprecise, confuse, parziali, incomplete, inaffidabili,...)

L'E' DI TUTTO BISOGNA SAPER SCEGLIERE
LE INFORMAZIONI AFFIDABILI E UTILI - LA
CONSCENZA CHE SPESSO LE PERSONE ACQUISISCONO
PER TALE VIA E' MAGARI ABBONDANTE PER
QUANTITA', MA FREQUENTEMENTE FUORVIANTE E
INOLTRA NON CENTRATA SULL'ESSENZA DEL PROBLEMA

10. Quanto spesso le capita di aver pazienti che discutono con lei di informazioni mediche trovate su Internet?

- Spesso
 Qualche volta
 Mai

11a. Ha mai proposto/indicato ai suoi pazienti siti web utili e affidabili per cercare informazioni su determinati problemi di salute/patologie?

- Sì
 No oppure MOLTO RARAMENTE (3-4 VOLTE)

11b. Perché?

PREFERISCO DARE IO LE SPIEGAZIONI
CHÉ RITENCO UTILI - SUL WEB ACQUISISCONO
VARIE CONSCENZE NON SEMPRE CORRETTE E COMUNQUE
ANCHE QUANDO SONO CORRETTE NON STANNO CONTESTUALIZZARLE

12. Il linguaggio utilizzato nei foglietti illustrativi dei medicinali è comprensibile per i pazienti?

- Sì
 Per la maggior parte dei pazienti
 Solo in alcune parti del foglietto illustrativo
 Non proprio
 Assolutamente no

13. A suo parere, quali sono le parti del foglietto illustrativo meno comprensibili per il paziente con un livello medio di istruzione?

- Composizione
 indicazioni terapeutiche
 Controindicazioni
 Precauzioni per l'uso
 Interazioni
 Avvertenze speciali
 Posologia
 Sovradosaggio
 Effetti indesiderati

FAANNO SPESSO CONFUSIONE FRA QUESTE SITUAZIONI

Questionario per medici di famiglia a Lusiana

1. Come potrebbe descrivere il linguaggio che utilizza mentre parla al paziente? (Alcuni esempi: utilizza un linguaggio carico di termini tecnici; un linguaggio semplificato ma comunque esprime alcuni concetti con termini tecnici; un linguaggio semplificato evitando l'uso di termini tecnici; un linguaggio fortemente figurato e carico di esempi facilmente comprensibili; un linguaggio colloquiale; utilizza anche il dialetto; utilizza solo l'italiano; controlla che il paziente la capisca; riassume spesso ciò che è stato detto durante la visita per agevolare la comprensione del paziente; adegua il suo linguaggio in base alla risposta del paziente;...)

Il linguaggio è necessariamente adattato alle fasce di età, alle condizioni alle scarse di comprensione del paziente.
Raramente uso il dialetto (solo con anziani con difficoltà per la lingua italiana).
Non uso linguaggio colloquiale - continuo sempre se il paziente ha compreso il discorso -

2. Il suo paziente chiede spiegazioni riguardo il significato di termini specialistici?

- Sempre
- A volte
- Spesso
- Evito i termini tecnici

3. Utilizza un linguaggio molto diverso dal puro "linguaggio medico" con pazienti dell'età di:

- 20-40 anni
- 40-60 anni
- 60-60>
- con tutti

4. Quali strategie utilizza per spiegare un concetto medico di difficile comprensione per il paziente? (Es.: si serve di esempi; di metafore/similitudini; lo spiega con un disegno; ripete più volte il concetto utilizzando parole diverse; si serve di foglietti illustrativi; di articoli riguardanti il tema trattato;...)

La maggior parte dei casi cerco di spiegare un concetto difficile addolendolo con disegni o schizzi che scarico in Rete reale da INTERNET

5. Quali pazienti interagiscono di più durante la visita medica, interrompendo e chiedendo spiegazioni, instaurando così un rapporto più "alla pari"? Pazienti dell'età di:

- 20-40 anni
- 40-60 anni
- 60-60>

6. A suo parere, negli ultimi 15 anni, quali mezzi di comunicazione (es. radio, tv, stampa, giornali specialistici, Internet) hanno influenzato maggiormente la relazione medico-paziente? Perché?

INTERNET e TV

84% dei giovani cerca informazioni mediche sul Web e preferisce i foglietti non sempre serio attendibile.

7. La figura del medico, in un piccolo paesino come Lusiana, risente dell'influenza di Internet per le questioni strettamente legate alla salute?

- Troppo
 Molto
 Non troppo
 A volte
 No

8. Attualmente, nel paese di Lusiana, la figura del medico di base mantiene il suo ruolo di "punto di riferimento" per le questioni legate alla salute?

- Sì
 No
 E stata sostituita da

9. Cosa pensa delle informazioni mediche trovate dai pazienti su Internet?(sono esaustive, imprecise, confuse, parziali, incomplete, inaffidabili,...)

Aumentano le proprie conoscenze in campo sanitario e sicuramente utile, un medico dovrebbe essere in grado di scegliere con attenzione le fonti di riferimento informatiche.

10. Quanto spesso le capita di aver pazienti che discutono con lei di informazioni mediche trovate su Internet?

- Spesso
 Qualche volta
 Mai

11a. Ha mai proposto/indicato ai suoi pazienti siti web utili e affidabili per cercare informazioni su determinati problemi di salute/patologie?

- Sì
 No

11b. Perché?

Preferisco discutere personalmente.

12. Il linguaggio utilizzato nei foglietti illustrativi dei medicinali è comprensibile per i pazienti?

- Sì
 Per la maggior parte dei pazienti
 Solo in alcune parti del foglietto illustrativo
 Non proprio
 Assolutamente no

13. A suo parere, quali sono le parti del foglietto illustrativo meno comprensibili per il paziente con un livello medio di istruzione?

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 Precauzioni per l'uso
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 Avvertenze speciali
 Posologia
 Sovradosaggio
 Effetti indesiderati

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uso spesso il dialetto - cerco di far comprendere, con
esempi e parole semplici il concetto da trasmettere -
chiedo al paziente se ha capito -

2. Il suo paziente chiede spiegazioni riguardo il significato di termini specialistici?

- Sempre A volte
 Spesso Evito i termini tecnici

3. Utilizza un linguaggio molto diverso dal puro "linguaggio medico" con pazienti dell'età di:

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uso alle volte dei disegni (o disegni) - uso parole
dialettali e esempi popolari

5. Quali pazienti interagiscono di più durante la visita medica, interrompendo e chiedendo spiegazioni, instaurando così un rapporto più "alla pari"? Pazienti dell'età di:

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TV - stampa non specializzata - per i più giovani

Internet

7. La figura del medico, in un piccolo paesino come Lusiana, risente dell'influenza di Internet per le questioni strettamente legate alla salute?

- Troppo Non troppo No
 Molto A volte

8. Attualmente, nel paese di Lusiana, la figura del medico di base mantiene il suo ruolo di "punto di riferimento" per le questioni legate alla salute?

- Sì No E stata sostituita da

9. Cosa pensa delle informazioni mediche trovate dai pazienti su Internet?(sono esaustive, imprecise, confuse, parziali, incomplete, inaffidabili,...)

sono troppo spesso specialistiche e quindi poco

comprendibili ai pazienti

10. Quanto spesso le capita di aver pazienti che discutono con lei di informazioni mediche trovate su Internet?

- Spesso Qualche volta Mai

11a. Ha mai proposto/indicato ai suoi pazienti siti web utili e affidabili per cercare informazioni su determinati problemi di salute/patologie?

- Sì No

11b. Perché?

o per parlarne con una sua specifica ^{infomatologica} ~~infomatologica~~ ^{malattia} di esperienza

12. Il linguaggio utilizzato nei foglietti illustrativi dei medicinali è comprensibile per i pazienti?

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 Per la maggior parte dei pazienti
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 Precauzioni per l'uso Effetti indesiderati
 Interazioni

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Utilizzo un linguaggio adeguato al
paziente ponendo attenzione per
le sue, grado di intelligenza e/o comprensione,
problematiche o altro...

2. Il suo paziente chiede spiegazioni riguardo il significato di termini specialistici?

- Sempre A volte
 Spesso Evito i termini tecnici

3. Utilizza un linguaggio molto diverso dal puro "linguaggio medico" con pazienti dell'età di:

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 40-60 anni con tutti

4. Quali strategie utilizza per spiegare un concetto medico di difficile comprensione per il paziente? (Es.: si serve di esempi; di metafore/similitudini; lo spiega con un disegno; ripete più volte il concetto utilizzando parole diverse; si serve di foglietti illustrativi; di articoli riguardanti il tema trattato;...)

cerco di spiegare in termini più semplici possibili...

5. Quali pazienti interagiscono di più durante la visita medica, interrompendo e chiedendo spiegazioni, instaurando così un rapporto più "alla pari"? Pazienti dell'età di:

- 20-40 anni 60-60>
 40-60 anni

6. A suo parere, negli ultimi 15 anni, quali mezzi di comunicazione (es. radio, tv, stampa, giornali specialistici, Internet) hanno influenzato maggiormente la relazione medico-paziente? Perché?

La TV - sono più informati -

7. La figura del medico, in un piccolo paesino come Lusiana, risente dell'influenza di Internet per le questioni strettamente legate alla salute?

- Troppo
 Molto
 Non troppo
 A volte
 No

8. Attualmente, nel paese di Lusiana, la figura del medico di base mantiene il suo ruolo di "punto di riferimento" per le questioni legate alla salute?

- Sì
 No
 E stata sostituita da

9. Cosa pensa delle informazioni mediche trovate dai pazienti su Internet?(sono esaustive, imprecise, confuse, parziali, incomplete, inaffidabili,...)

*C'è volte poco di aiuto
Tante volte confusione*

10. Quanto spesso le capita di aver pazienti che discutono con lei di informazioni mediche trovate su Internet?

- Spesso
 Qualche volta
 Mai

11a. Ha mai proposto/indicato ai suoi pazienti siti web utili e affidabili per cercare informazioni su determinati problemi di salute/patologie?

- Sì
 No

11b. Perché?

*nelle nostre realtà più difficili un
con unob*

12. Il linguaggio utilizzato nei foglietti illustrativi dei medicinali è comprensibile per i pazienti?

- Sì
 Per la maggior parte dei pazienti
 Solo in alcune parti del foglietto illustrativo
 Non proprio
 Assolutamente no

13. A suo parere, quali sono le parti del foglietto illustrativo meno comprensibili per il paziente con un livello medio di istruzione?

- Composizione
 indicazioni terapeutiche
 Controindicazioni
 Precauzioni per l'uso
 Interazioni
 Avvertenze speciali
 Posologia
 Sovradosaggio
 Effetti indesiderati

APPENDIX 7: Corpus of Italian patient information leaflets



PRIMA DELL'USO
LEGGERE CON ATTENZIONE TUTTE LE INFORMAZIONI CONTENUTE NEL FOGLIO ILLUSTRATIVO

Questo è un medicinale di AUTOMEDICAZIONE che potete usare per curare disturbi lievi e transitori facilmente riconoscibili e risolvibili senza ricorrere all'aiuto del medico.

Può essere quindi acquistato senza ricetta medica ma va usato correttamente per assicurare l'efficacia e ridurne gli effetti indesiderati.

- Per maggiori informazioni e consigli rivolgersi al farmacista.
- Consultare il medico se il disturbo non si risolve dopo un breve periodo di trattamento.

COMPOSIZIONE

100 g di unguento contengono:

PRINCIPI ATTIVI: Canfora 5,00 g, Olio essenziale di trementina 5,00 g, Mentaolo 2,75 g, Olio essenziale di eucalipto 1,50 g.

ECCIPIENTI: Timolo, Olio essenziale di legno di cedro, Olio essenziale di miristica, Vaselina bianca.

COME SI PRESENTA

VICKS VAPORUB si presenta in forma di unguento per uso inalatorio. Confezioni da 40 g, 50 g, 90 g e 100 g.

CHE COSA È

VICKS VAPORUB è un unguento balsamico per uso inalatorio.

TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO
PROCTER & GAMBLE S.r.l. - Viale Cesare Pavese, 385 - 00144 Roma.

PRODUTTORE E CONTROLLORE FINALE

Officina di produzione: PROCTER & GAMBLE GmbH - Procter & Gamble Strasse 1, 64521 - Gross Gerau, Germania.

PERCHÉ SI USA

VICKS VAPORUB si usa per il trattamento balsamico nelle affezioni delle prime vie respiratorie.

QUANDO NON DEVE ESSERE USATO

Il prodotto è controindicato nei bambini di età inferiore a due anni. Il prodotto non deve essere somministrato per inalazione ai bambini di età inferiore a sei anni, (ipersensibilità (allergia) ai principi attivi o ad uno qualsiasi degli eccipienti).

QUANDO PUÒ ESSERE USATO SOLO DOPO AVER CONSULTATO IL MEDICO

Vicks Vaporub deve essere utilizzato con cautela o dietro suggerimento medico dai pazienti che presentano:

reazioni di ipersensibilità a profumi o solventi,

Convulsioni o epilessia,

Asma e disturbi o pronunciata ipersensibilità delle vie respiratorie,

Gravidanza e allattamento. (vedere "Cosa fare durante la gravidanza e l'allattamento").

È opportuno consultare il medico anche nei casi in cui tali disturbi si fossero manifestati in passato.

COSA FARE DURANTE LA GRAVIDANZA E L'ALLATTAMENTO

In gravidanza Vicks Vaporub deve essere usato solo dopo aver consultato il medico e aver valutato con lui il rapporto rischio/beneficio nel proprio caso.

Consultate un medico nel caso sospettiate uno stato di gravidanza o pianificate una maternità.

Vicks Vaporub non deve essere applicato sul petto della madre durante l'allattamento per il potenziale rischio di riflesso apnoico nel lattante alimentato al seno.

QUALI MEDICINALI POSSONO MODIFICARE L'EFFETTO DEL MEDICINALE

Non è mai stato segnalato alcun tipo di interazione.
Se state usando altri medicinali chiedete consiglio al vostro medico o farmacista.

È IMPORTANTE SAPERE CHE

l'uso, specie se prolungato, di prodotti per uso topico, può dare origine a fenomeni di sensibilizzazione e produrre effetti indesiderati. In tal caso è necessario interrompere il trattamento e consultare il proprio medico.

COME USARE QUESTO MEDICINALE

Usare il prodotto secondo le istruzioni. Per solo uso esterno.

L'unguento balsamico VICKS VAPORUB si può impiegare in due modi:

1. Applicare esternamente frizionando dapprima per 3-5 minuti il petto, la gola ed il dorso e poi stendere uno spesso strato sul petto. Ripetere il trattamento 2 volte al giorno, di cui una la sera prima di dormire. Non frizionare più di due volte al giorno sulla parte anteriore del torace, sul collo e sul dorso. Non applicare su ferite, abrasioni, e sulle mucose. Non ingerire e non applicare direttamente nelle narici o sul viso.
2. Sciogliere 2 cucchiaini da caffè in mezzo litro di acqua calda e aspirare il vapore liberato per un tempo non superiore a 10 minuti. Al fine di evitare il rischio di gravi ustioni non utilizzare acqua bollente per preparare le inalazioni. Non riscaldare la miscela una seconda volta. Non riscaldare la miscela durante l'inalazione. Non riscaldare la miscela nel microonde e non riscaldarla di nuovo durante e dopo l'uso.

IL PRODOTTO NON DEVE ESSERE INGERITO

Attenzione: non superare le dosi consigliate.

COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE

A) Somministrazione topica

Nell'eventualità di applicazione di una dose eccessiva, possono verificarsi:

raramente reazioni di irritazione a livello cutaneo. In tale eventualità rimuovere l'eccesso di prodotto con un tovagliolo di carta ed informare il proprio medico che provvederà a somministrare, se necessario, una terapia adeguata per tali reazioni.

B) Inalazione:

I sintomi ed il trattamento sono gli stessi previsti in caso di ingestione accidentale.

C) ingestione accidentale:

I sintomi sono dovuti principalmente alla presenza della canfora. Questi includono problemi a livello gastrointestinale quali nausea, vomito e diarrea.

Nell'eventualità in cui abbiate preso una dose fortemente eccessiva di Vicks Vaporub, avvertite immediatamente il medico o rivolgetevi al più vicino ospedale.

EFFETTI INDESIDERATI

A causa delle loro caratteristiche è prevedibile che alcuni componenti di Vicks Vaporub (canfora e mentolo) causino arrossamento ed una sensazione di calore a livello cutaneo.

Raramente possono verificarsi lievi irritazioni e reazioni allergiche. Più

specificamente: irritazione della pelle e prurito dopo uso topico e lievi irritazioni

dell'occhio a seguito di applicazione topica o inalazione.

Raramente si sono verificate reazioni di ipersensibilità a livello del sistema respiratorio

(dispnea e tosse).

Nel caso si verificano tali eventi, il trattamento va sospeso e va consultato il proprio

medico, che deciderà la cura più adatta.

Al fine di evitare il rischio di gravi ustioni non utilizzare acqua bollente per preparare

le inalazioni. Non riscaldare la miscela una seconda volta. Non riscaldare la miscela

durante l'inalazione. Non riscaldare la miscela nel microonde e non riscaldarla di

nuovo durante o dopo l'uso.

IL PRODOTTO NON DEVE ESSERE INGERITO

Altri eventi possono essere legati ad un uso improprio del prodotto (ingestione); a tal proposito si veda il paragrafo precedente.

Il rispetto delle istruzioni contenute nel foglio illustrativo riduce il rischio di effetti

indesiderati. Questi effetti indesiderati sono generalmente transitori. Quando si

presentano è tuttavia opportuna consultare il medico o il farmacista.

È importante comunicare al medico o al farmacista la comparsa di effetti

indesiderati.

Richiedere e compilare la scheda di segnalazione di effetti indesiderati disponibile in

farmacia (modello B).

SCADENZA E CONSERVAZIONE

Attenzione: non utilizzare il medicinale dopo la data di scadenza indicata sulla

confezione.

Tenere il medicinale fuori dalla portata dei bambini.

È importante avere sempre a disposizione le informazioni sul medicinale, pertanto

conservate sia la scatola sia il foglio illustrativo.

Revisione del foglio illustrativo da parte del Ministero della Salute: Agosto 2004

95181730



VICKS

Sinex

0,05% SPRAY NASALE SOLUZIONE
SOLUZIONE DECONGESTIONANTE
OSSIMETAZOLINA CLORIDRATO
Fiacone 15 ml

PRIMA DELL'USO
LEGGERE CON ATTENZIONE TUTTE LE INFORMAZIONI
CONTENUTE NEL FOGLIO ILLUSTRATIVO

Questo è un medicinale di AUTOMEDICAZIONE che potete usare per curare disturbi lievi e transitori facilmente riconoscibili e risolvibili senza ricorrere all'aiuto del medico. Può essere quindi acquistato senza ricetta medica ma va usato correttamente per assicurare l'efficacia e ridurre gli effetti indesiderati.

- Per maggiori informazioni e consigli rivolgersi al farmacista.
- Consultare il medico se il disturbo non si risolve dopo un breve periodo di trattamento.

COMPOSIZIONE

1 ml di prodotto contiene:
PRINCIPIO ATTIVO: Ossimetazolina cloridrato 0,5 mg, per un totale di 7,5 mg per flacone di 15 ml.
ECCIPIENTI: Levomentolo, Sodio clorato bivalente, Tioxapolo, Acido citrico anidro, Cinnexidina gluconato, Benzalconio cloruro, Canfora, Acido etilendiamminotetraacetico (sale di sodio), Eucalipto, Ispessante di sodio, Acqua purificata.

COME SI PRESENTA

VICKS SINEX SPRAY NASALE SOLUZIONE si presenta in forma di soluzione nasale, contenuta in un flacone di materiale plastico da 15 ml.

CHE COSA È

VICKS SINEX SPRAY NASALE SOLUZIONE è un decongestionante nasale per uso locale, cioè libera il naso chiuso.

TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

PROCTER & GAMBLE S.r.l. - Viale Cesare Pavese, 385 - 00144 Roma.

PRODUTTORE E CONTROLLORE FINALE

Procter & Gamble Manufacturing GmbH, Procter & Gamble Strasse 1, 64521 - Gross Gerau, Germania.

PERCHÉ SI USA

VICKS SINEX SPRAY NASALE SOLUZIONE si usa per alleviare gli sgradevoli sintomi legati alla congestione della mucosa nasale (naso chiuso) tipici del raffreddore e dell'influenza.

QUANDO NON DEVE ESSERE USATO

Ipersensibilità (allergia) verso i componenti del prodotto, ipertrofia prostatica (rigonfiamento della prostata), malattie cardiache ed ipertensione arteriosa grave (elevata pressione arteriosa), glaucoma (elevata pressione dell'occhio), ipertiroidismo (aumento dell'attività della tiroide).
Bambini di età inferiore ai 6 anni.


QUANDO PUÒ ESSERE USATO SOLO DOPO AVER CONSULTATO IL MEDICO

Nai pazienti con malattie cardiovascolari, e specialmente negli ipertesi (pazienti con elevata pressione arteriosa).
È opportuno consultare il medico nel caso in cui tali disturbi si fossero manifestati in passato.
Gravidanza: vedere "Cosa fare durante la gravidanza e l'allattamento".

COSA FARE DURANTE LA GRAVIDANZA E L'ALLATTAMENTO

Impiegare con cautela nei primi mesi di gravidanza, per cui si consiglia di consultare il medico nel caso sospettate uno stato di gravidanza o desiderate pianificare una maternità.




PRECAUZIONI PRIMA DELL'USO

Impiegare con cautela negli anziani per il pericolo di ritenzione urinaria (difficoltà ad urinare). Non deve essere usato oralmente. Evitare il contatto del liquido con gli occhi.

QUALI MEDICINALI O ALIMENTI POSSONO MODIFICARE L'EFFETTO DEL MEDICINALE

Esiste la possibilità di interazione con farmaci antidepressivi (anti-MAO) per cui si sconsiglia l'uso durante o nelle due settimane successive al trattamento con tali farmaci. È opportuno evitare il contemporaneo consumo di alcool. Se state usando altri medicinali chiedete consiglio al vostro medico o farmacista.

È IMPORTANTE SAPERE CHE

L'uso protratto del vasoconstrictori (sostanze che riducono i vasi sanguigni dilatati in seguito ad una infiammazione) può alterare la normale funzione della mucosa del naso e dei seni paranasali, inducendo anche assuefazione al farmaco.

Ripetere le applicazioni per lunghi periodi può risultare dannoso, in quanto l'uso prolungato dei prodotti ad uso locale può dar luogo a reazioni allergiche; in tal caso è necessario interrompere il trattamento e consultare il proprio medico.

Il prodotto se accidentalmente ingerito o se impiegato per lungo periodo in dosi eccessive, può determinare fenomeni tossici.

Il prodotto va tenuto lontano dalla portata dei bambini, poiché l'ingestione accidentale può provocare sedazione spiccata (stato di eccessiva calma).

Attenzione per chi svolge attività sportive: il prodotto contiene sostanze vietate per doping. È vietata un'assunzione diversa, per schema posologico e per via di somministrazione, da quelle riportate.

COME USARE QUESTO MEDICINALE

Attenzione: non superare le dosi indicate senza il consiglio del medico.

Adulti e bambini di età superiore ai 6 anni: 1-2 spruzzi per narice, ogni 6-8 ore.

Tenere il flacone in posizione verticale, introdurre nella narice la sua estremità e premere il nebulizzatore stesso con moto rapido e deciso. Dopo la nebulizzazione, inspirare profondamente a bocca chiusa.

Lo spazio vuoto sovrastante il liquido è necessario per ottenere la migliore nebulizzazione.

Non usare per più di 4 giorni, in assenza di risposta terapeutica completa entro tale termine, consultare il medico.

Inoltre, consultare il medico se il disturbo si presenta ripetutamente o se avete notato un qualsiasi cambiamento recente delle sue caratteristiche.

COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE

In caso di dose eccessiva, può comparire ipertensione arteriosa (aumento della pressione arteriosa), tachicardia (aumento della frequenza dei battiti cardiaci), fotofobia (fastidio per la luce), mal di testa, oppressione toracica e, nei bambini, ipotermia (abbassamento della temperatura corporea) e grave depressione del sistema nervoso centrale con spiccata sedazione, che richiedono l'adozione di adeguate misure d'emergenza.

In caso di ingestione/assunzione accidentale di una dose eccessiva di VICKS SINEX SPRAY NASALE avvertite immediatamente il medico o rivolgersi al più vicino ospedale.

EFFETTI INDESIDERATI

Il rispetto delle istruzioni contenute nel foglio illustrativo riduce il rischio di effetti indesiderati.

Il prodotto può determinare localmente reazioni allergiche e rigonfiamento delle mucose. Per rapido assorbimento dell'ossimetazolina (principio attivo) attraverso le mucose infiammate, possono insorgere: ipertensione arteriosa (aumento della pressione arteriosa), bradicardia riflessa (diminuzione della frequenza dei battiti cardiaci), mal di testa, disturbi della minzione (difficoltà a urinare). Questi effetti indesiderati sono generalmente transitori. Quando si presentano è tuttavia opportuno consultare il medico o il farmacista.

È importante comunicare al medico o al farmacista la comparsa di effetti indesiderati non descritti nel foglio illustrativo.

Richiedere e compilare la scheda di segnalazione degli Effetti Indesiderati disponibile in farmacia (modello B).

SCADENZA E CONSERVAZIONE

Attenzione: non utilizzare il medicinale dopo la data di scadenza indicata sulla confezione.

La data di scadenza, riportata sull'etichetta esterna e interna, si riferisce al prodotto in confezionamento integro, correttamente conservato.


TENERE IL MEDICINALE FUORI DALLA PORTATA DEI BAMBINI.

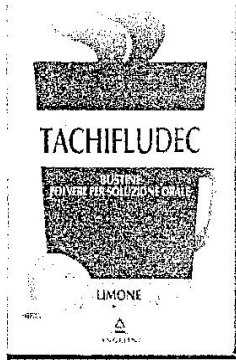
È importante avere sempre a disposizione le informazioni sul medicinale, pertanto conservare sia la scatola che il foglio illustrativo.

REVISIONE DEL FOGLIO ILLUSTRATIVO DA PARTE DEL MINISTERO DELLA SALUTE:

Maggio 2000

95459415





PRIMA DELL'USO LEGGETE CON ATTENZIONE TUTTE LE INFORMAZIONI CONTENUTE NEL FOGLIO ILLUSTRATIVO

Questo è un medicinale di AUTOMEDICAZIONE che potete usare per curare disturbi lievi e transitori facilmente riconoscibili e risolvibili senza ricorrere all'aiuto del medico. Può essere quindi acquistato senza ricetta ma va usato correttamente per assicurarne l'efficacia e ridurre gli effetti indesiderati.

- Per maggiori informazioni e consigli rivolgetevi al farmacista
- Consultate il medico se il disturbo non si risolve dopo un breve periodo di trattamento



TACHIFLUDEC
polvere per soluzione orale

COMPOSIZIONE

TACHIFLUDEC polvere per soluzione orale (confezione gusto limone).
Una bustina da 6 g contiene: Principi attivi: paracetamolo 600 mg, acido ascorbico 40 mg, fenilefrina cloridrato 10 mg. Eccipienti: saccarosio, acido citrico, sodio citrato, amido di mais, sodio ciclamato, saccarina sodica, silice colloidale, aroma limone, curcumina (E 100).

TACHIFLUDEC polvere per soluzione orale (confezione gusto miele limone).

Una bustina da 6 g contiene: Principi attivi: paracetamolo 600 mg, acido ascorbico 40 mg, fenilefrina cloridrato 10 mg. Eccipienti: saccarosio, acido citrico, sodio citrato, amido di mais, sodio ciclamato, saccarina sodica, aroma limone, aroma miele, caramello (E 150).

COME SI PRESENTA

Il prodotto si presenta in forma di polvere per soluzione orale. Il contenuto della confezione è di 10 bustine.

CHE COSA È

TACHIFLUDEC polvere per soluzione orale è un prodotto ad attività analgesica, antipiretica e decongestionante nasale.

TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

Azienda Chimiche Riunite Angelini Francesco - A.C.R.A.F. S.p.A. - Viale Amelia, 70 - 00181 Roma.

PRODUZIONE, CONFEZIONAMENTO E CONTROLLI

A.C.R.A.F. S.p.A. - Via Vecchia del Pinocchio, 22 - 60137 Assisi (Perugia)

LABORATORIO S.A. - Avda de Ajalvir km 2,5 - Alcalá de Henares - Madrid (Spagna).

FAMAR ITALIA S.p.A. - Via Zambelletti, 25 - Baranzate di Bollate (MI).

PERCHÉ SI USA

TACHIFLUDEC polvere per soluzione orale si usa per il trattamento sintomatico dell'influenza, del raffreddore e degli stati febbrili e dolorosi ad essi correlati, con azione decongestionante sulle prime vie aeree superiori.

QUANDO NON DEVE ESSERE USATO

Ipersensibilità verso i componenti o altre sostanze strettamente correlate dal punto di vista chimico. Nei pazienti che assumono beta-bloccanti, inibitori delle monoaminoossidasi ed antidepressivi triciclici. Nei pazienti affetti da insufficienza epatica o renale, diabete, ipertirodismo, ipertensione e malattie cardiovascolari. I prodotti a base di paracetamolo sono controindicati nei pazienti con manifesta insufficienza della glucosio-6-fosfato deidrogenasi ed in quelli affetti da grave anemia emolitica. Grave insufficienza epatocellulare.

QUANDO PUÒ ESSERE USATO SOLO DOPO AVER CONSULTATO IL MEDICO

In gravidanza e allattamento (vedere "Cosa fare durante la gravidanza e l'allattamento").

Nei bambini al di sotto dei 12 anni (vedere "È importante sapere che").

È opportuno consultare il medico anche nei casi in cui tali disturbi si fossero manifestati in passato.

COSA FARE DURANTE LA GRAVIDANZA E L'ALLATTAMENTO

In gravidanza e nell'allattamento TACHIFLUDEC polvere per soluzione orale deve essere usato solo dopo aver consultato il medico e aver valutato con lui il rapporto rischio/beneficio nel proprio caso. Consultate il medico nel caso sospettiate uno stato di gravidanza o desideriate pianificare una maternità.

PRECAUZIONI PER L'USO

Durante il trattamento con paracetamolo, prima di assumere qualsiasi altro farmaco controllare che non contenga lo stesso principio attivo, poiché se il paracetamolo è assunto in dosi elevate si possono verificare gravi reazioni avverse, tra cui una grave epatopatia ed alterazioni a carico del rene e del sangue. Inoltre prima di associare qualsiasi altro farmaco contattare il medico. Vedere anche la voce "Quali medicinali o alimenti possono modificare l'effetto del medicinale." È sconsigliato l'uso del prodotto se il paziente è in trattamento con antinfiammatori.

QUALI MEDICINALI O ALIMENTI POSSONO MODIFICARE L'EFFETTO DEL MEDICINALE

L'effetto epatocitossico del paracetamolo può essere potenziato dall'assunzione di altri farmaci attivi sul fegato. I pazienti in trattamento con flupirtina, cimetidina o con farmaci antiipertensivi quali glu-

telimmide, fenobarbital, carbamazepina, devono usare il paracetamolo con estrema cautela e solo sotto stretto controllo medico. Il paracetamolo aumenta l'attività del cloramfenicolo. Il paracetamolo assunto in dosi elevate può potenziare l'effetto degli anticoagulanti cumarinici. La fenilefrina può ridurre l'efficacia dei farmaci beta-bloccanti ed ipertensivi e può potenziare l'azione degli inibitori delle monoaminoossidasi. Se state usando altri medicinali chiedete consiglio al vostro medico o farmacista.

È IMPORTANTE SAPERE CHE

Nei bambini al di sotto dei 12 anni TACHIFLUDEC polvere per soluzione orale deve essere usato solo dopo aver consultato il medico e aver valutato con lui il rapporto rischio/beneficio nel proprio caso. La somministrazione di paracetamolo può interferire con la determinazione della uricemia (mediante il metodo dell'acido fosicotungstico) e con quella della glicemia (mediante il metodo della glucosio-ossidasi-perossidasi). Per la presenza di sodio, il prodotto deve essere usato con cautela nei pazienti sottoposti a dieta povera di sodio. Per la presenza di saccarosio (3725 mg per bustina in TACHIFLUDEC confezione gusto limone e 3802 mg per bustina in TACHIFLUDEC confezione gusto miele limone), il prodotto deve essere usato con cautela nei pazienti con intolleranza ereditaria al fruttosio, sindrome da malassorbimento di glucosio-galattosio o in caso di deficienza di sucralasi-isomaltasi. Il medicinale non è controindicato per i soggetti affetti da malattia celiaca. TACHIFLUDEC polvere per soluzione orale non interferisce sulla capacità di guidare e di usare macchinari.

COME USARE QUESTO MEDICINALE

Quanto

Adulti e bambini al di sopra dei 12 anni: 1 bustina ogni 4-6 ore e fino ad un massimo di 3 bustine nelle 24 ore. **Bambini al di sotto dei 12 anni:** il prodotto non va somministrato ai bambini al di sotto dei 12 anni se non sotto il controllo medico (vedere "È importante sapere che").

Attenzione: non superare le dosi indicate senza il consiglio del medico.

Quando e per quanto tempo

Attenzione: usare solo per brevi periodi di trattamento.

Consultate il medico se il disturbo si presenta ripetutamente o se avete notato un qualsiasi cambiamento recente delle sue caratteristiche.

Come

Sciogliere una bustina in un bicchiere d'acqua molto calda e, a piacere, diluire con acqua fredda per raffreddare e dolcificare come si desidera.

COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE

Alle dosi consigliate, o anche nell'ipotesi in cui si dovesse assumere l'intera confezione, non dovrebbero comparire sintomi da sovradosaggio di paracetamolo. Tuttavia, in caso di ingestione di dosi molto elevate di paracetamolo (superiori a 15 g), la complicanza più comunemente riscontrata è il danno epatico, che si manifesta in genere 2-4 giorni dopo l'assunzione. I sintomi precoci sono nausea, vomito e dolori addominali: la terapia idonea consigliata è la lavanda gastrica usando antidoti specifici quali acetilcisteina o metionina. Oltre 10 ore dall'ingestione potrebbe rendersi necessaria una emoperfusione. Altri sintomi da sovradosaggio, sono causati dalla fenilefrina e si manifestano con irritabilità, emicrania e aumento della pressione arteriosa. In caso di ingestione/assunzione accidentale di una dose eccessiva di TACHIFLUDEC polvere per soluzione orale avvertire immediatamente il medico o rivolgetevi al più vicino ospedale.

EFFETTI INDESIDERATI

Con l'uso del paracetamolo sono state segnalate reazioni cutanee di vario tipo e gravità, inclusi casi di entema multiforme, sindrome di Stevens Johnson e necrosi epidermica. Sono state segnalate reazioni di ipersensibilità quali ad esempio angioedema, edema della laringe, shock anafilattico. Inoltre sono stati segnalati i seguenti effetti indesiderati: trombocitopenia, leucopenia, anemia, agranulocitosi, alterazioni della funzionalità epatica ed epatiti, alterazioni a carico del rene (insufficienza renale acuta, nefrite interstiziale, ematuria, anuria), reazioni gastrointestinali e vertigini. Con i simpaticomimetici (fenilefrina) possono manifestarsi occasionalmente stati di irritazione cutanea, tachicardia, ipertensione e molto più raramente nausea, vomito o anoressia. Quando si presentano questi effetti indesiderati è opportuno consultare il medico o il farmacista. Il rispetto delle istruzioni contenute nel foglio illustrativo riduce il rischio di effetti indesiderati. È importante comunicare al medico o al farmacista la comparsa di effetti indesiderati non descritti nel foglio illustrativo. Richiedere e compilare la scheda di segnalazione degli Effetti Indesiderati disponibile in farmacia (modello B).

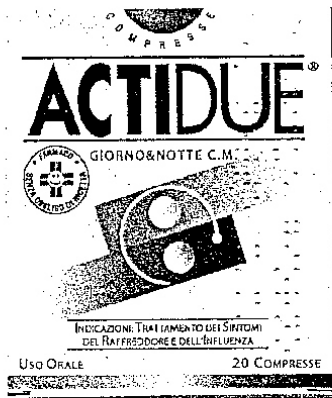
SCADENZA E CONSERVAZIONE

Attenzione: non utilizzare il medicinale dopo la data di scadenza indicata sulla confezione.

Tenere il medicinale fuori dalla portata dei bambini.

È importante avere sempre a disposizione le informazioni sul medicinale, pertanto conservare sia la scatola che il foglio illustrativo.

REVISIONE DEL FOGLIO ILLUSTRATIVO DA PARTE DELL'AGENZIA ITALIANA DEL FARMACO:
Luglio 2005



ACTIDUE®

GIORNO & NOTTE C.M.

PRIMA DELL'USO

LEGGETE CON ATTENZIONE TUTTE LE INFORMAZIONI CONTENUTE NEL FOGLIO ILLUSTRATIVO

Questo è un medicinale di AUTOMEDICAZIONE, che potete usare per curare disturbi lievi e transitori facilmente riconoscibili e risolvibili senza ricorrere all'aiuto del medico.

Può essere quindi acquistato senza ricetta ma va usato correttamente per assicurarne l'efficacia e ridurre gli effetti indesiderati.

- Per maggiori informazioni rivolgersi al farmacista
- Consultare il medico se il disturbo non si risolve dopo un breve periodo di trattamento.

DENOMINAZIONE DEL MEDICINALE

ACTIDUE Giorno & Notte C.M. compresse.

COMPOSIZIONE

Una compressa bianca (giorno) contiene: principi attivi: paracetamolo mg 500, pseudoefedrina cloridrato mg 60; eccipienti: cellulosa microcristallina, amido di mais pregelatinizzato, croscarmellosa sodica, magnesio stearato, povidone, crospovidone, acido stearico.

Una compressa rivestita azzurra (notte) contiene: principi attivi: paracetamolo mg 500, difenidramina cloridrato mg 25; eccipienti: cellulosa microcristallina, amido di mais, amido glicolato sodico, idrossipropilcellulosa, amido di mais pregelatinizzato, croscarmellosa sodica, acido stearico, magnesio stearato, ipromellosa, glicole propilenico, Opapray M-1F-4315B.

COME SI PRESENTA

Atteuccio contenente 20 compresse, di cui 15 bianche "giorno" e 5 azzurre "notte".

CHE COSA È

ACTIDUE Giorno & Notte C.M. appartiene alla categoria degli analgesici, antipiretici ed associa l'azione analgesica (riduzione del dolore) ed antipiretica (riduzione della febbre) del paracetamolo con l'azione decongestionante nasale della pseudoefedrina e quella difenidramina.

TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

Pfizer Consumer Health Care S.r.l. - Latina

Produttore e controllore finale:

Godecke GmbH - Freiburg (Germania)

PERCHÉ SI USA

Actidue Giorno e Notte C.M. si usa per il trattamento dei sintomi del raffreddore e dell'influenza.

QUANDO NON DEVE ESSERE USATO

Non usare questo medicinale in caso di ipersensibilità ai principi attivi o ad uno qualsiasi degli eccipienti, o ad altre sostanze strettamente correlate dal punto di vista chimico, in particolare verso altri analgesici ed antipiretici.

Il prodotto è inoltre controindicato nei bambini al di sotto dei 12 anni; nei pazienti in trattamento con farmaci inibitori delle monoamminossidasi (IMAO) e nelle due settimane successive a tale trattamento; in caso di asma, glaucoma, ipertrofia prostatica, stenosi dell'apparato gastro-enterico (stomaco e intestino) ed urogenitale, ipertiroidismo, diabete, epilessia, malattie del cuore e della circolazione, ipertensione (pressione sanguigna elevata), gravi malattie del fegato.

Per il contenuto in paracetamolo il prodotto è controindicato nei pazienti con manifesta insufficienza della glucosio-6-fosfato deidrogenasi ed in quelli affetti da grave anemia emolitica.

Non usare nei casi di grave insufficienza epatica.

Non usare in gravidanza accertata o presunta, né durante l'allattamento.

QUANDO DEVE ESSERE USATO SOLO DOPO AVER CONSULTATO IL MEDICO

Durante l'adolescenza (da 13 a 18 anni), nei soggetti con insufficienza renale od epatica e in età avanzata (vedere "Come usare questo medicinale").

In caso di qualsiasi contemporanea terapia è opportuno consultare il medico (vedere "Quali medicinali o alimenti possono modificare l'effetto del medicinale").

PRECAUZIONI PER L'USO

Utilizzare con cautela e sotto il diretto controllo del medico in caso di insufficienza renale od epatica.

Durante il trattamento con paracetamolo (uno dei principi attivi di Actidue Giorno & Notte C.M.), prima di assumere qualsiasi altro farmaco controllare che non contenga lo stesso principio attivo, poiché se il paracetamolo è assunto in dosi elevate si possono verificare gravi reazioni avverse.

Non assumere il medicinale insieme ad altri analgesici, antipiretici o antinfiammatori non steroidei.

Inoltre, prima di associare qualsiasi altro farmaco, contattare il medico. Vedere anche la voce successiva "quali medicinali o alimenti possono modificare l'effetto del medicinale".

QUALI MEDICINALI O ALIMENTI POSSONO MODIFICARE L'EFFETTO DEL MEDICINALE

Se state usando altri medicinali chiedete consiglio al vostro medico o farmacista.

416 293





E' sconsigliato l'uso del prodotto in caso di trattamento contemporaneo con altri analgesici, antipiretici e antinfiammatori non steroidei.

Nel corso di terapia con anticoagulanti orali le dosi vanno ridotte.

L'uso degli antistaminici (come la difenidramina contenuta nel prodotto) contemporaneamente a certi antibiotici ototossici (dannosi per l'orecchio) può mascherare i primi segni di danno all'apparato uditivo, che può rivelarsi solo quando il danno è irreversibile. Gli effetti degli antistaminici sono resi più evidenti dall'alcol, dagli ipnotici, sedativi o tranquillanti, ecc., che pertanto non vanno assunti contemporaneamente.

I pazienti in trattamento con rifampicina, cimetidina o con farmaci antiepilettici quali glutebimide, fenobarbital, carbamazepina, devono usare il paracetamolo (uno dei principi attivi di Actidue Giorno & Notte C.M.) con estrema cautela e sotto stretto controllo medico.

La somministrazione di paracetamolo può interferire con la determinazione dell'uricemia (mediante il metodo dell'acido fosforungitico) e con quella della glicemia (mediante il metodo della glucosio-ossidasi-perossidasi) (due tipi di esami del sangue).

E' IMPORTANTE SAPERE CHE

Se i sintomi non migliorano entro 3 giorni o se compare febbre alta o altri effetti indesiderati, interrompere il trattamento e consultare il medico.

Il prodotto, nella forma in compresse azzurre, contenente difenidramina, sostanza antistaminica, può dare sonnolenza; di ciò debbono tener conto coloro che potrebbero condurre autoveicoli, attendere ad operazioni richiedenti integrità del grado di vigilanza, i quali dovranno astenersi da tali mansioni dopo l'assunzione del prodotto. Dosi elevate o somministrazioni prolungate del paracetamolo, presente nel prodotto, possono provocare un'epatopatia (malattia del fegato) ad alto rischio ed alterazioni a carico del rene e del sangue anche gravi.

Nei rari casi di comparsa di reazioni allergiche la somministrazione va sospesa.

COME USARE QUESTO MEDICINALE

Quanto

Non superare le dosi consigliate senza il consiglio del medico.

Adulti e bambini con età superiore ai 12 anni: una compressa bianca tre volte al giorno, al mattino, a mezzogiorno e al pomeriggio, più una compressa azzurra alla sera prima di coricarsi.

Durante l'adolescenza (da 13 a 18 anni), in caso di insufficienza renale od epatica e in età avanzata occorre rivolgersi al medico.

Quando e per quanto tempo

Le compresse bianche vanno assunte esclusivamente durante il giorno, quelle azzurre alla sera, prima di coricarsi per il riposo notturno.

Attenzione: usare solo per brevi periodi di trattamento.

Dopo 3 giorni di impiego continuativo, senza risultati apprezzabili, consultare il medico.

Consultare il medico anche se il disturbo si presenta ripetutamente o se avete notato un qualsiasi cambiamento recente delle sue caratteristiche.

Come

Assumere le compresse con un bicchiere d'acqua.

COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE

In caso di ingestione accidentale di una dose eccessiva di ACTIDUE Giorno & Notte C.M., avvertite immediatamente il medico o rivolgetevi al più vicino ospedale.

EFFETTI INDESIDERATI

Con l'uso della pseudoefedrina si può verificare eccitazione del sistema nervoso centrale, inclusi disturbi del sonno; raramente sono stati riportati casi di allucinazione. Possono manifestarsi casi di ritenzione urinaria in pazienti in cui l'ipertrofia prostatica rappresenta un fattore predisponente. Eruzioni cutanee.

Con l'uso di paracetamolo sono state segnalate reazioni cutanee di vario tipo e gravità, inclusi casi di eritema multiforme, sindrome di Stevens Johnson e necrolisi epidermica.

Sono state segnalate reazioni di ipersensibilità quali ad esempio angioedema, edema della laringe, shock anafilattico. Inoltre sono stati segnalati i seguenti effetti indesiderati: trombocitopenia, leucopenia, anemia, agranulocitosi, alterazioni della funzionalità epatica ed epatiti, alterazioni a carico del rene (insufficienza renale acuta, nefrite interstiziale, ematuria, anuria) reazioni gastro-intestinali e vertigini.

Effetti indesiderati legati all'assunzione di difenidramina possono essere: sonnolenza, astenia, vertigini, disturbi gastrointestinali, secchezza delle fauci, del naso e della gola, ritenzione urinaria. Eruzioni cutanee su base allergica, prurito, rash cutanei, eritema e urticaria.

Il rispetto delle istruzioni contenute nel foglio illustrativo riduce il rischio di effetti indesiderati.

Questi effetti indesiderati sono generalmente transitori. Quando si presentano è tuttavia opportuno consultare il medico o il farmacista.

E' importante comunicare al Medico o al Farmacista la comparsa di effetti indesiderati non descritti nel foglio illustrativo.

Richiedere e compilare la scheda di segnalazione degli effetti indesiderati disponibile in farmacia (Modello B).

SCADENZA E CONSERVAZIONE

Conservare a temperatura non superiore a 25°C, nel contenitore originale per tenerlo al riparo dalla luce e dall'umidità.

Attenzione: non utilizzare il medicinale dopo la data di scadenza indicata sulla confezione. Tale data si riferisce al prodotto in confezionamento integro correttamente conservato.

Tenere il medicinale fuori dalla portata dei bambini.

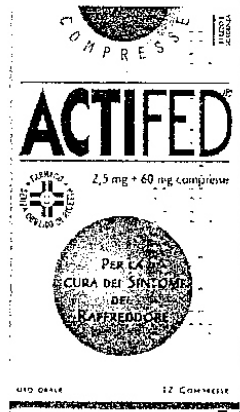
E' importante avere sempre a disposizione le informazioni sul medicinale, pertanto conservate sia la scatola che il foglio illustrativo.

Revisione del Foglio illustrativo da parte del Ministero della Salute:

Giugno 2003.

Actidue
Consumer Health Care 446 293





Foglio illustrativo

PRIMA DELL'USO

LEGGETE CON ATTENZIONE TUTTE LE INFORMAZIONI CONTENUTE NEL FOGLIO ILLUSTRATIVO

Questo è un medicinale di AUTOMEDICAZIONE che potete usare per curare disturbi lievi e transitori facilmente riconoscibili e risolvibili senza ricorrere all'aiuto del medico.
Può essere quindi acquistato senza ricetta ma va usato correttamente per assicurarne l'efficacia e ridurre gli effetti indesiderati.

- Per maggiori informazioni rivolgersi al farmacista
- Consultare il medico se il disturbo non si risolve dopo un breve periodo di trattamento.

DENOMINAZIONE DEL MEDICINALE

ACTIFED®

COMPOSIZIONE

Ogni compressa contiene:

Principi attivi:	Tripolidina cloridato	2,5 mg
	Pseudoefedrina cloridrato	60,0 mg

Eccipienti: Lattosio, Amido di mais, Polivinilpirrolidone, Magnesio stearato.

Ogni flacone da 100 ml di sciroppo contiene:

Principi attivi:	Tripolidina cloridrato	25 mg (pari a 0,25 mg per ml)
	Pseudoefedrina cloridrato	600 mg (pari a 6 mg per ml)

Eccipienti: Glicerina, Saccarosio, Metile p-idrossibenzoato, Sodio benzoato, Giallo chinidina (E104), Giallo tramonto (E110), Acqua depurata.

COME SI PRESENTA

Astuccio contenente un blister da 12 compresse
Flacone da 100 ml di sciroppo con misurino dosatore tarato a 5 e 10 ml

CHE COSA È

La **Tripolidina cloridrato** è un antistaminico.
La **Pseudoefedrina cloridrato** è un decongestionante nasale (libera le vie respiratorie superiori).
L'Actifed associa queste due sostanze in un prodotto efficace nel liberare il naso chiuso e le prime vie respiratorie rapidamente e per oltre 6 ore.

TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

Pfizer Consumer Health Care S.r.l. - s.s. 156 Km 50 - 04010 Borgo San Michele (LT)

Produttore e controllatore finale delle compresse:

Goedekes - Friburgo (Germania)

Produttore e controllatore finale dello sciroppo:

Pfizer PGM - 5, Avenue de Concy - 45071 Orléans Cedex 2 (Francia)

PERCHÉ SI USA

Actifed si usa per decongestionare la mucosa nasale (libera il naso chiuso), specie in caso di raffreddore.

QUANDO NON DEVE ESSERE USATO

ACTIFED non deve essere usato in caso di ipersensibilità nota verso i componenti e verso altri antistaminici di analoga struttura chimica. Il prodotto non deve essere usato nei bambini al di sotto dei 6 anni, durante la gravidanza, l'allattamento, nei pazienti in trattamento con farmaci inibitori delle monoamminossidasi (MAOI) o nelle due settimane successive a tale trattamento, e nella terapia delle affezioni delle basse vie respiratorie (bronchi e polmoni), compresa l'asma bronchiale. Per i suoi effetti anticolinergici non utilizzare in caso di glaucoma, nell'ipertrofia prostatica (ingrossamento della prostata), nell'ostruzione del collo vescicale, nelle stenosi (restringimenti) piloriche (valvola dello stomaco) e duodenali (primo tratto dell'intestino) o di altri tratti dell'apparato gastroenterico ed urogenitale. È inoltre controindicato nelle affezioni cardiovascolari (malattie del cuore e della circolazione), ipertensione arteriosa (pressione arteriosa elevata), ipertiroidismo (eccessiva attività della tiroide), nonché epilessia e diabete. Leggere anche il paragrafo "Cosa fare durante la gravidanza e l'allattamento".

QUANDO DEVE ESSERE USATO SOLO DOPO AVER CONSULTATO IL MEDICO

Bambini: Nei bambini dai 6 ai 12 anni il prodotto in sciroppo deve essere usato solo sotto il controllo del medico. Le compresse non devono essere somministrate nei bambini di età inferiore ai 12 anni.

Anziani: Consultare il medico per determinare la dose negli anziani per la loro maggiore sensibilità verso gli antistaminici e verso la Pseudoefedrina.

Soggetti con ridotta funzionalità di fegato e reni: L'ACTIFED® non dovrebbe essere usato neppure da pazienti con gravi malattie del fegato o dei reni.

Cosa fare durante la gravidanza e l'allattamento: Non usare in caso di gravidanza o durante l'allattamento

QUALI MEDICINALI O ALIMENTI POSSONO MODIFICARE L'EFFETTO DEL MEDICINALE

Se state usando altri medicinali chiedete consiglio al vostro medico o farmacista.

Gli effetti degli antistaminici sono resi più evidenti dall'alcool, dagli ipnotici, dai sedativi, dai tranquillanti, e da altre sostanze ad azione anticolinergica o ad effetto depressivo sul sistema nervoso centrale, che non vanno pertanto assunte durante la terapia. Gli antistaminici possono ridurre la durata d'azione degli anticoagulanti orali. L'uso degli antistaminici può mascherare i primi segni di otosistite (tossicità a carico dell'orecchio) di certi antibiotici.

447 308

Il Furazolidone causa una progressiva inibizione della monoamminossidasi, per cui non va assunto contemporaneamente all'ACTIFED®. L'effetto degli antipertensivi che interferiscono con l'attività del sistema nervoso simpatico (per es. metildopa, alfa e beta bloccanti, debrisoquina, guanetidina, betanidina e breltilo) può essere parzialmente annullato dall'ACTIFED®, che pertanto, anche in questo caso, non va contemporaneamente assunto.

E' IMPORTANTE SAPERE CHE

Se i sintomi non migliorano entro 7 giorni o se compaiono o altri effetti indesiderati, interrompere il trattamento e consultare il medico.

Alle comuni dosi terapeutiche gli antitamirici presentano reazioni secondarie assai variabili da soggetto a soggetto e da composto a composto. Poiché l'effetto secondario più frequente è la sedazione che può manifestarsi con sonnolenza, di ciò debbono essere avvertiti coloro che possono condurre autoveicoli o svolgere operazioni che richiedono integrità del grado di vigilanza.

Lo sciroppo contiene saccarosio, di ciò si tenga conto in caso di diete ipocaloriche (a basso contenuto calorico).

Sebbene la Pseudoefedrina non abbia prodotto effetti importanti sulla pressione arteriosa di soggetti normotesi (con normali valori di pressione), l'ACTIFED® non dovrebbe essere assunto da pazienti in terapia con antipertensivi, antidepressivi triciclici, agenti simpaticomimetici, quali i decongestionanti, gli anoreizzanti, gli amfetaminosimili.

L'Actifed non dovrebbe essere usato da pazienti con gravi malattie dei reni o del fegato.

Tenere lontano dalla portata dei bambini

Il medicinale non è controindicato per i soggetti affetti da malattia celiaca.

COME USARE QUESTO MEDICINALE

Quanto

Non superare le dosi consigliate.

Sciroppo:

Adulti e ragazzi al di sopra dei 12 anni: una dose da 10 ml di sciroppo 2 - 3 volte al giorno.

Bambini di età compresa tra i 6 e i 12 anni: una dose da 5 ml di sciroppo 2 - 3 volte al giorno, solo dopo aver consultato il medico.

Compresse:

Adulti e ragazzi al di sopra dei 12 anni: una compressa 2 - 3 volte al giorno.

Quando e per quanto tempo

Attenzione: usare solo per brevi periodi di trattamento

Consultare il medico se il disturbo si presenta ripetutamente o se avete notato un qualsiasi cambiamento recente delle sue caratteristiche.

Come

Sciroppo:

Alla confezione è annesso un misurino dosatore con indicate tacche di livello rispondenti alle capacità di 5 e 10 ml.

COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE

In caso di eccessivo dosaggio si osservano in genere spiccati effetti depressivi o stimolanti sul Sistema Nervoso Centrale, sonnolenza, letargia, depressione respiratoria, ipertensione, iritabilità, convulsioni. Nei bambini l'azione dominante è quella eccitante con accentuati tremori, insonnia, iperattività e convulsioni.

In caso di ingestione di una dose eccessiva di Actifed, avvertite immediatamente il medico o rivolgetevi al più vicino ospedale.

EFFETTI INDESIDERATI

L'ACTIFED® può causare soprattutto sonnolenza, poi astenia, vertigini, eruzioni cutanee su base allergica, fotosensibilizzazione, secchezza della fauci, ritenzione urinaria, ispessimento delle secrezioni bronchiali, disturbi gastroenterici come nausea, vomito e diarrea, eventualmente riducibili somministrando il prodotto dopo i pasti, eccitazione del Sistema Nervoso Centrale, specie nei bambini, accompagnate da insonnia, euforia e tremori; molto raramente alterazioni ematiche (del sangue) e, specie negli anziani, cefalea, extrasistole (battito anomalo), tachicardia (battito cardiaco accelerato) e ipotensione (abbassamento della pressione arteriosa).

Il rispetto delle istruzioni contenute nel foglio illustrativo riduce il rischio di effetti indesiderati.

Questi effetti indesiderati sono generalmente transitori. Quando li presentano è tuttavia opportuno consultare il medico o il farmacista.

E' importante comunicare al Medico o al Farmacista la comparsa di effetti indesiderati non descritti nel foglio illustrativo.

Richiedere e compilare la scheda di segnalazione degli effetti indesiderati disponibile in farmacia (Modello D).

SCADENZA E CONSERVAZIONE

Compresse: Conservare a temperatura non superiore a 25°C, in luogo asciutto.

Sciroppo: Conservare al riparo dalla luce.

Attenzione: non utilizzare il medicinale dopo la data di scadenza indicata sulla confezione. Tale data si riferisce al prodotto in confezionamento integro correttamente conservato.

Tenere il medicinale fuori dalla portata dei bambini.

E' importante avere sempre a disposizione le informazioni sul medicinale, pertanto conservate sia la scatola che il foglio illustrativo.

Ultima revisione del foglio illustrativo da parte dell'Agenzia Italiana del Farmaco:

Luglio 2005.



447 308



Benagol[®]

**PRIMA DELL'USO LEGGERE CON ATTENZIONE TUTTE LE INFORMAZIONI
CONTENUTE NEL FOGLIO ILLUSTRATIVO**

Questo è un medicinale di AUTOMEDICAZIONE che potete usare per curare disturbi lievi e transitori facilmente riconoscibili e risolvibili senza ricorrere all'aiuto del medico. Può essere quindi acquistato senza ricetta ma va usato correttamente per assicurarne l'efficacia e ridurre gli effetti indesiderati.

- Per maggiori informazioni e consigli rivolgetevi al farmacista.
- Consultare il medico se il disturbo non si risolve dopo un breve periodo di trattamento.

DENOMINAZIONE DEL MEDICINALE

BENAGOL Pastiglie
BENAGOL Pastiglie gusto Miele e Limone
BENAGOL Pastiglie gusto Limone Senza Zucchero

COMPOSIZIONE

BENAGOL Pastiglie

Ogni pastiglia contiene:

Principi attivi: 2,4-diclorobenzil alcool 1,2 mg; amilmetacresolo 0,6 mg.

Eccipienti: saccarosio, glucosio liquido, mentolo, anetolo, essenza di menta, acido tartarico.

BENAGOL Pastiglie gusto Miele e Limone

Ogni pastiglia contiene:

Principi attivi: 2,4-diclorobenzil alcool 1,2 mg; amilmetacresolo 0,6 mg.

Eccipienti: essenza di menta, essenza di limone, acido tartarico, miele, glucosio liquido, saccarosio.

BENAGOL Pastiglie gusto Limone Senza Zucchero

Ogni pastiglia contiene:

Principi attivi: 2,4-diclorobenzil alcool 1,2 mg; amilmetacresolo 0,6 mg.

Eccipienti: aroma di limone, saccarinato sodico, acido tartarico, sciroppo di maltitolo, isomaltosio.

COME SI PRESENTA

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero si presenta in forma di pastiglie. Il contenuto della confezione è di 24 pastiglie.

CHE COSA E'

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero è un antisettico del cavo orofaringeo (disinfettante della bocca e della gola).

TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

Boots Healthcare International Ltd - 1, Thane Road West - Nottingham NG2 3AA (UK)

Rappresentante per l'Italia:

Boots Healthcare S.p.A. - Via Caldera, 21 - 20153 Milano

PRODUTTORE E CONTROLLORE FINALE

The Boots Company Plc - 1, Thane Road - Nottingham NG2 3AA (UK)

PERCHÉ SI USA

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero si usa come antisettico del cavo orale per disinfettare la bocca e la gola, dove svolge una rapida azione battericida (elimina rapidamente batteri e funghi causa di disturbi) con un effetto prolungato.

QUANDO NON DEVE ESSERE USATO

Ipersensibilità al principio attivo o ad uno qualsiasi degli eccipienti.
Non somministrare ai bambini di età inferiore ai due anni.

Cosa fare durante la gravidanza e l'allattamento.

In gravidanza o nell'allattamento BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero deve essere usato solo dopo aver consultato il medico.

PRECAUZIONI PER L'USO

Non sono necessarie particolari precauzioni d'uso.

E' IMPORTANTE SAPERE CHE

In caso di comparsa di fenomeni di sensibilizzazione o irritativi occorre interrompere l'assunzione del farmaco e consultare il medico.

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone contiene saccarosio. Di ciò si tenga conto in caso di diabete o di diete ipocaloriche.

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero non interferisce sulla capacità di guidare veicoli o sull'uso di macchinari.

Il medicinale non è controindicato per i soggetti affetti da malattia celiaca.

QUALI MEDICINALI O ALIMENTI POSSONO MODIFICARE L'EFFETTO DEL FARMACO

Non sono note interazioni con altri farmaci.

In ogni caso, se state usando altri medicinali chiedete consiglio al vostro medico o farmacista.

COME USARE QUESTO MEDICINALE

Quanto

Attenzione: non superare le dosi consigliate senza consultare il medico. 1 pastiglia ogni 2-3 ore. Nei bambini al di sopra dei due anni di età consultare il proprio medico per un'appropriata posologia.

Quando e per quanto tempo

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero può essere assunto a qualsiasi ora della giornata.

Attenzione: usare solo per brevi periodi di trattamento. Consultate il medico se il disturbo si presenta ripetutamente o se avete notato un qualsiasi cambiamento recente delle sue caratteristiche.

Come

Ogni pastiglia va sciolta lentamente in bocca. Fare attenzione ai bambini piccoli in quanto se le pastiglie vengono degluite intere possono provocare soffocamento.

COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI FARMACO

In caso di ingestione/assunzione accidentale di una dose eccessiva di BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto Limone Senza Zucchero avvertite immediatamente il medico o rivolgetevi al più vicino ospedale. L'ingestione accidentale di una dose eccessiva di farmaco potrebbe causarvi solamente disturbi gastrointestinali.

EFFETTI INDESIDERATI

~~BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone / BENAGOL Pastiglie gusto~~

Limone Senza Zucchero solo raramente può indurre disturbi gastrointestinali, fenomeni locali di ipersensibilità, irritazione della lingua. Questi effetti indesiderati sono generalmente transitori. Quando si presentano è tuttavia opportuno consultare il medico o il farmacista.

Il rispetto delle istruzioni contenute nel foglio illustrativo riduce il rischio di effetti indesiderati.

E' importante comunicare al medico o al farmacista la comparsa di effetti indesiderati non descritti nel foglio illustrativo. Richiedere e compilare la scheda di segnalazione degli effetti indesiderati disponibile in farmacia (modello B).

SCADENZA E CONSERVAZIONE

BENAGOL Pastiglie / BENAGOL Pastiglie gusto Miele e Limone: Conservare ad una temperatura non superiore ai 30°C.

Attenzione: non utilizzare il medicinale dopo la data di scadenza indicata sulla confezione.

Tenere il medicinale fuori dalla portata dei bambini.

E' importante avere sempre a disposizione le informazioni sul medicinale, pertanto conservate sia la scatola che questo foglio illustrativo.

REVISIONE DEL FOGLIO ILLUSTRATIVO DA PARTE DELL'AGENZIA ITALIANA DEL FARMACO

Giugno 2004

LNZC6

APPENDIX 8: Corpus of English patient information leaflets



ANADIN EXTRA

Contains Paracetamol, Aspirin and Caffeine

Read this leaflet carefully because it contains important information for you.

This medicine is available without a prescription, for you to treat a mild illness without a doctor's help. Nevertheless, you still need to use ANADIN EXTRA tablets carefully to get the best results. Ask your pharmacist if you need more information or advice.

You must see a doctor if your symptoms worsen or do not improve.

Keep this leaflet. You may need to read it again.

WHAT IS IN THIS MEDICINE?

Each tablet contains: 300mg of Aspirin BP, 200mg of Paracetamol Ph Eur and 45mg of Caffeine Ph Eur.

Aspirin and paracetamol work by relieving pain and reducing high temperature and fever. Aspirin belongs to a group of medicines called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and has anti-inflammatory properties. In addition, ANADIN EXTRA tablets contain caffeine, which increases the pain-relieving effect of the product.

Each tablet also contains: maize starch, microcrystalline cellulose (E460), hydrogenated vegetable oil, hydroxypropyl methylcellulose (E464), polyethylene glycol, pregelatinised starch and povidone.

WHO MAKES AND SUPPLIES THIS MEDICINE?

ANADIN EXTRA is distributed by Wyeth Consumer Healthcare, Huntercombe Lane South, Taplow, Maidenhead, Berkshire, SL6 0PH.

Licence Holder: Wyeth Consumer Healthcare, Huntercombe Lane South, Taplow, Maidenhead, Berkshire, SL6 0PH.

Manufacturer: Wyeth Lederle S.p.A. - Via Nettunense 90, 04011 Aprilia (LT) Italy.

ANADIN EXTRA is available in packs containing 8, 12, 16 or 32 tablets. The 32 tablet pack is available only from your pharmacy.

WHAT IS THIS MEDICINE USED FOR?

Fast effective relief from:-

- | | | | |
|------------------|------------------|------------------|---------------|
| • Headache | • Migraine | • Sprains | • Period pain |
| • Dental pain | • Strains | • Joint swelling | • Colds & Flu |
| • Stiffness | • Muscular aches | • Sore throat | • Sciatica |
| • Rheumatic pain | • Feverishness | • Lumbago | • Neuralgia |

WILL THIS MEDICINE SUIT ME?

Do not take this medicine if any of the following apply to you:

- You have had or are suffering from stomach ulcers.
- You are taking any other products that contain paracetamol and/or any other NSAID.
- You are allergic to aspirin, or any other NSAID, or any of the other ingredients.
- You are breast-feeding
- You suffer from haemophilia or are taking medicines that reduce clotting of the blood (e.g. Warfarin).

Talk to your doctor before taking this medicine if any of the following applies to you:

- *You suffer from asthma, allergic disease, kidney or liver disease, or dehydration.*
- *You are pregnant.*
- *You are taking water tablets, methotrexate, cholestyramine, chloramphenicol, metoclopramide, domperidone, corticosteroids, phenytoin, valproate, or any other NSAID.*

There is a possible association between aspirin and Reye's syndrome when given to children. Reye's syndrome is a very rare disease, which can be fatal. For this reason aspirin should not be given to children aged under 16 years, unless on the advice of a doctor.

Always ask your pharmacist or doctor whether this medicine is suitable for you if you are taking any other medicines.

HOW TO USE THIS MEDICINE

Adults, the elderly and young persons aged 16 and over:

Take 2 tablets with a drink of water.

Repeat every 4 to 6 hours as required.

Do not take more than 8 tablets in 24 hours.

Do not give to children aged under 16 years, unless on the advice of a doctor.

Do not take with any other paracetamol containing products.

Do not exceed the stated dose.

If symptoms persist for more than 3 days, contact your doctor.

OVERDOSE

Taking too many tablets may be harmful. Immediate medical advice should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

POSSIBLE SIDE EFFECTS

Side effects are rare. However, susceptible individuals may experience unwanted effects. If you experience any side effects mentioned below or any other side effects, stop taking this medicine immediately and contact your doctor.

Allergic reactions: difficulty in breathing, skin rash, swollen facial features and a runny nose.

Gastro-intestinal: abdominal pain, nausea, digestive problems, constipation, diarrhoea and rarely peptic ulcer and bleeding in the stomach, shown by the vomiting of blood, or the passage of black stools.

Blood: the blood does not clot well, which may result in easy bruising or bleeding. Rarely agranulocytosis, a disease of the blood may occur, which lowers the body's natural resistance to infections.

Breathing: wheezing and breathing difficulties may be triggered in patients suffering from or with a previous history of asthma.

Other rare side effects include changes in skin colour or shortness of breath.

High caffeine intake can result in tremor and palpitations. Aspirin may trigger gout in susceptible individuals.

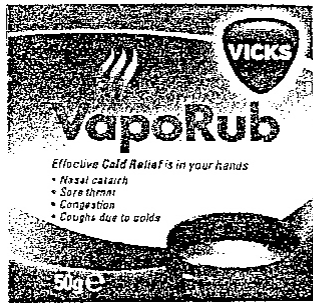
HOW SHOULD THIS MEDICINE BE STORED?

*Do not use this medicine after the expiry date shown on the end of the carton.
Do not store above 25°C.*

*If you have any queries or comments about Anadin Extra please contact the Careline by phone, or write to:
Careline, Wyeth Consumer Healthcare, Huntercombe Lane South,
Taplow, Berkshire SL6 0PH, UK. or Careline@wyeth.com*





**KEEP ALL MEDICINES IN A SAFE PLACE
OUT OF THE SIGHT AND REACH OF CHILDREN**




VapoRub

Please read this leaflet carefully before you start to use this medicine. If you are not sure about anything or have any questions please ask your pharmacist or doctor.

 This product can be used with other medicines.

**What's in it?**

 Vicks VapoRub contains levomenthol (2.75% w/w), camphor (5.00% w/w), eucalyptus oil (1.50% w/w) and turpentine oil (5.00% w/w) as the active ingredients. These aromatic ingredients work by relieving nasal congestion (a blocked nose), soothing irritated linings in the nose to effectively ease breathing and relieve cough.

Vicks VapoRub also includes thymol, nutmeg oil, cedarwood oil and white soft paraffin.

The product licence for Vicks VapoRub is held by;
Procter & Gamble (Health & Beauty Care) Limited
The Heights
Brooklands
Weybridge
Surrey
KT13 0XP
UK

Vicks VapoRub is manufactured at;
Procter & Gamble GmbH & Co. Manufacturing OHG
H-S Richardson Strasse
64521 Gross Gerau
Germany

This pack may contain 25g, 50g or 100g of ointment.

What's it for?

Vicks VapoRub is used to relieve nasal catarrh and congestion, sore throat and coughs due to colds. It contains:

- Menthol and camphor to calm a cough
- Eucalyptus and menthol to relieve nose congestion
- Eucalyptus to relieve catarrh



**Check before use**

DO NOT use Vicks VapoRub on babies under 6 months of age. DO NOT swallow or place in nostrils. If symptoms persist or in case of fever, consult your doctor.

If you are pregnant or breast-feeding ask your doctor or pharmacist for advice before taking any medicine.

Directions for use**Adults:**

Rub Vicks VapoRub liberally on the chest, throat and back. Cover whole area for maximum effect. Leave nightclothes loose to allow vapours to be inhaled easily.

Or

Melt two teaspoons of Vicks VapoRub in very hot (not boiling) water. Inhale the medicated vapours for 10-15 minutes.

Caution: Never re-heat the mixture.

Children (infants and babies over 6 months):

Apply lightly to chest and back. Rub in gently. Leave clothes loose for easy inhalation.

For external use only

While using it

Occasionally Vicks VapoRub can cause a temporary reddening of the skin in the region where the product has been rubbed in. This "skin reddening" fades and disappears within hours without any further action from yourself. If the reddening does not disappear or if you notice anything else unusual / have any unexpected effects please talk to your doctor or pharmacist.

Storage

Do not store Vicks VapoRub above 25°C.

Do not use Vicks VapoRub after the expiry date on the carton and jar.

Remember, keep all medicines safely away from children.

You may want to read this leaflet again. Please DO NOT throw it away until you have finished using this medicine.

Vicks and VapoRub are registered trademarks.

P/L 0129/0130

Date of preparation: December 2006.

95727639





Sinex

DECONGESTANT NASAL SPRAY
Oxymetazoline



Please read this leaflet carefully before you start to take your medicine. If you are not sure about anything or have any questions, please ask your pharmacist or doctor.

What is in your medicine?

This pack may contain 15ml or 20ml of nasal spray solution

Vicks Sinex contains 0.05% w/v oxymetazoline hydrochloride. It also contains sodium citrate dihydrate, tyloxapol, citric acid anhydrous, chlorhexidine digluconate, menthol, benzalkonium chloride, camphor, disodium edetate, eucalyptol, sodium hydroxide and purified water.

Vicks Sinex contains oxymetazoline hydrochloride. This works by relieving nasal congestion (a blocked nose) to effectively ease breathing.

The product licence for Vicks Sinex is held by:

Procter & Gamble (Health & Beauty Care) Limited
The Heights
Brooklands
Weybridge
Surrey
KT13 0XP, UK



Vicks Sinex is manufactured by

Procter & Gamble
Manufacturing GmbH
Procter & Gamble Strasse 1
64521 Gross-Gerau
Germany





About your medicine

Vicks Sinex relieves a blocked nose caused by a cold, hayfever or sinusitis.

Before taking your medicine

Do NOT use this medicine if;

- you suffer from high blood pressure
- you suffer from any heart complaint
- you suffer from diabetes
- you suffer from thyroid disease,
- you suffer from any liver or kidney disorder



Ask your doctor before taking Vicks Sinex Decongestant Nasal spray if;

- you feel worse or do not feel better after 7 days
- you develop new symptoms
- you are pregnant or breast feeding

Directions for use

Adults and children, over six years: 1-2 sprays per nostril every 6-8 hours unless otherwise directed by your doctor.

For topical nasal use.

Do not give Vicks Sinex to children under six years of age.

See your doctor if you feel worse or do not feel better after seven days, you develop new symptoms or if you accidentally take too much product.

While taking your medicine

Most people have no side-effects with Vicks Sinex but as with all medicines it may not suit everyone. If you notice anything unusual or have any unexpected effects talk to your doctor or pharmacist.



Storage

DO NOT use Vicks Sinex after the expiry date.

Keep out of reach and sight of children.

Vicks is a registered trademark.

PL 0129/5011R

Date of preparation: December 2006

95727631



PACKAGE LEAFLET: INFORMATION FOR THE USER

Lemsip Max Lemon Flavour Tablets

(Paracetamol and Phenylephrine hydrochloride)

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to take Lemsip Max Lemon Flavour Tablets carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact your doctor if your symptoms worsen or do not improve after 3 days.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What this medicine is and what it is used for.
2. Before you take this medicine.
3. How to take this medicine.
4. Possible side effects.
5. How to store this medicine.
6. Further information.

1. WHAT THIS MEDICINE IS AND WHAT IT IS USED FOR.

This medicine is a combination of active ingredients which are effective in relieving the symptoms associated with colds and flu, including relief of aches and pains, sore throats, headache, nasal congestion and lowering of temperature.

Paracetamol is a well-known painkiller (analgesic). It is effective against mild to moderate aches and pains, including headache. It can also reduce raised temperatures or fever (antipyretic).

Phenylephrine hydrochloride (nasal decongestant) reduces swelling in the passages of the nose, relieving nasal congestion and reducing pressure which may cause a headache.

2. BEFORE YOU TAKE THIS MEDICINE.

Do not take this medicine if you:

- are allergic to paracetamol, phenylephrine hydrochloride or any of the other ingredients listed in Section 6.
- have a serious heart condition.
- have an overactive thyroid.
- have high blood pressure (hypertension).
- are taking or have taken within the last 14 days a medicine called a monoamine oxidase inhibitor (MAOI), usually used to treat depression.
- have taken another medicine for the treatment of cold and flu.

Take special care with this medicine if you:

- suffer from liver or kidney problems, heart disease.
- have non-cirrhotic liver disease (liver disease that is not associated with changes to the structure of the liver).
- suffer from Raynaud's syndrome (poor blood circulation which makes the fingers or toes pale and numb), or diabetes mellitus.
- are taking beta blockers for high blood pressure, or vasodilators (drugs used to treat high blood pressure, leg pain due to vascular problems or Raynaud's syndrome).
- are a woman with a history of pre-eclampsia (a condition of high blood pressure and swelling in pregnancy).
- have glaucoma or enlarged prostate.
- are taking tricyclic antidepressants (a specific class of drugs used to treat depression).
- are taking other decongestants, or barbiturates (used to treat sleep problems or epilepsy).

Taking other medicines:

- Do not take with any other paracetamol-containing products.
- Some drugs may affect the way paracetamol works including:
 - Cholestyramine - used to treat blood cholesterol
 - Metoclopramide and domperidone - used to treat nausea and vomiting.
- The effect of blood thinning drugs (warfarin and other coumarins) may be increased by paracetamol. Ask your doctor or pharmacist for advice before taking this medicine.
- Phenylephrine hydrochloride may adversely interact with other sympathomimetics (such as those used to treat blood pressure, glaucoma or nasal congestion), vasodilators (drugs used to treat high blood pressure) and beta-blockers.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking this medicine with food and drink:

- Do not consume large quantities of alcohol while taking this medicine.

Pregnancy or breast-feeding:

- If you are pregnant or breast-feeding, ask your doctor or pharmacist for advice before taking this medicine.

Important information about some of the ingredients in your medicine:

- This product contains aspartame, a source of phenylalanine, which may be harmful for people with phenylketonuria (an inherited genetic disorder).

3. HOW TO TAKE THIS MEDICINE.

To remove the tablet, tear along the perforations and peel back to reveal the tablet. Follow the instructions on the blister. Replace unopened blisters back into carton.

There are two possible ways to take this medicine.

Either

Swallow whole with water. Do not chew.

Or

Make into a hot drink: Dissolve in half a mug of hot (not boiling) water. Stir until dissolved. If preferred sweeten to taste using sugar, honey or your usual sweetener. Once prepared the drink should be taken as soon as possible and should not be stored.

It is important to drink plenty of liquid when suffering from colds and flu.

Age	Dose and how often to take
Adults and children 16 years and over	Take two tablets every 4-6 hours. Do not take more than eight tablets in a total of 24 hours.
Children aged 12 to 15 years old	Take one tablet every 4-6 hours. Do not take more than four tablets in a total of 24 hours.
Do not give to children under 12 years of age.	

If the symptoms persist for more than three days, or worsen, consult your doctor.

If you take more of this medicine than you should:

Immediate medical advice should be sought in the event of an overdose, even if you feel well because of the risk of delayed, serious liver damage.

If you forget to take this medicine:

This product should only be used when necessary. Do not take a double dose to make up for a forgotten dose.

-- If you have any further questions on the use of this product, ask your doctor or pharmacist. --

4. POSSIBLE SIDE EFFECTS.

Like all medicines this product can cause side effects, although not everybody gets them.

- Allergic reactions (such as skin rashes).
- Changes in the number of blood cells, such as thrombocytopenia (reduction in blood platelets which might mean that you bleed or bruise more easily) or agranulocytosis (reduction in white blood cells which makes infection more likely).
- High blood pressure with headache.
- Nausea and vomiting.
- Irregular or fast heartbeats.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE THIS MEDICINE

Keep out of the reach and sight of children.

Do not store above 30°C.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste.

Ask your pharmacist how to dispose of medicines no longer required.

These measures will help protect the environment.

6. FURTHER INFORMATION.

What this medicine contains:

- The active ingredients per tablet are: paracetamol 500mg and phenylephrine hydrochloride 6.1mg.
- The other ingredients are: crospovidone, citric acid (E330), aspartame (E951), microcrystalline cellulose, magnesium stearate (E470b), quinoline yellow lake (E104), lemon flavour, pre-gelatinised maize starch, povidone (E1201).

What the medicine looks like and the contents of the pack:

The product is a convex pale yellow oval shaped tablet with lemon odour.

The product is available in cartons of 6 and 12 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:

Marketing Authorisation Holder/Manufacturer: Reckitt Benckiser Healthcare (UK) Limited, Hull, HU8 7DS. (PL00063/0555).


This medicinal product is authorised in the Member States of the EEA under the following names:

United Kingdom: Lemsip Max Lemon Flavour Tablets

Ireland: Lemsip Decongestant & Flu Lemon Tablets Paracetamol 500mg Phenylephrine Hydrochloride 6.1mg

Alternative format patient information for the visually impaired is available on request from the marketing authorisation holder.

Leaflet last revised April 2010.

Lemsip, Lemsip Max and  are trade marks.



Day & Night Tablets

Read all of this leaflet carefully because it contains important information for you. This medicine is available without prescription, for you to treat a mild illness without a doctor's help. Nevertheless, you still need to use Benylin Day & Night Tablets carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve.

What Benylin Day & Night Tablets are and what they are used for

Benylin Day & Night Tablets come in a carton containing 15 white day-time tablets and 5 blue night-time tablets.

Each day-time tablet contains the active ingredients: Paracetamol 500 mg, and Pseudoephedrine hydrochloride 60 mg per tablet. Each night-time tablet contains the active ingredients: Paracetamol 500 mg, and Diphenhydramine hydrochloride 25 mg per tablet.

The day-time tablets also contain pregelatinised maize starch, povidone, crospovidone, stearic acid, microcrystalline cellulose, croscarmellose sodium and magnesium stearate.

The night-time tablets also contain microcrystalline cellulose, maize starch, sodium starch glycolate, pregelatinised maize starch, hydroxypropylcellulose, croscarmellose sodium, stearic acid, magnesium stearate and are coated with methylcellulose (methocel ES), Opaspray M-1F-43158 containing indigo carmine (E132), titanium dioxide (E171) and propylene glycol.

Product licence holder: Pfizer Consumer Healthcare, Walton-on-the-Hill, Surrey, KT20 7NS.

Manufacturer: Gödecke GmbH, Mooswaldallee 1, 79090 Freiburg, Germany.

Benylin Day & Night Tablets relieve the symptoms of colds and flu.

The day-time tablets contain paracetamol, a painkiller which also helps to reduce fever and pseudoephedrine, a decongestant, that clears stuffy noses and blocked sinuses.

The night-time tablets contain paracetamol and diphenhydramine, an antihistamine which helps clear catarrh and so aid sleep.

Before you take Benylin Day & Night Tablets

Do not take Benylin Day & Night Tablets if:

- You are allergic to any of the ingredients
- You are taking or have taken within the last two weeks, drugs for depression known as Monoamine Oxidase Inhibitors (MAOIs)
- You have high blood pressure or heart disease

Take special care with Benylin Day & Night Tablets if:

- You have diabetes, an over-active thyroid, glaucoma (pressure in the eye) or prostate problems
- You have liver or kidney disorders

Please consult your doctor, even if these statements were applicable to you at any time in the past.

Pregnancy and breast-feeding

Do not take during pregnancy, or whilst breast-feeding.

Driving and using machines

The blue night-time tablets can cause drowsiness or difficulty in concentration. If affected do not drive or operate machinery. Avoid alcoholic drink.

447 263

Taking other medicines

Take special care if you are taking other medicines including

- paracetamol or pseudoephedrine. Do not take with any other paracetamol or pseudoephedrine containing products
- antidepressants known as Monoamine Oxidase Inhibitors (MAOIs) or tricyclic antidepressants
- colestyramine (to lower blood cholesterol)
- metoclopramide and domperidone (to treat nausea and vomiting)
- anti-coagulants (to thin the blood e.g. warfarin)
- sedatives or alcohol
- appetite suppressants, other depressants or stimulants
- medicines to treat high blood pressure (e.g. α and β blockers, bretylium, betanidine, guanethidine, debrisoquine and methyldopa)
- anticholinergics (e.g. atropine or some psychotropic drugs used to treat anxiety, depression or other mental illnesses)
- anticonvulsants or oral contraceptives ("the pill")

You can use Benylin Day & Night Tablets while you are taking oral contraceptives ("the pill") or tablets for epilepsy but they may not work so well on your pain and fever.

If you are unsure if another medicine you are taking is one of those mentioned above, then show the pack to your pharmacist.

Please consult your doctor or pharmacist, even if these statements were applicable to you at any time in the past.

Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine – even those not prescribed.

How to take Benylin Day & Night Tablets

For oral use. Swallow tablet whole with a glass of water.

Adults and children over 12 years: Take one white, day-time, tablet every 4 to 6 hours (one tablet in the morning, at mid-day and in the afternoon). Do not take more than 3 day-time tablets in 24 hours.

One blue, night-time, tablet may be taken at night. Do not take the night-time tablet during the day.

Children under 12 years: This medicine is not suitable for children under 12 years.

If you forget to take a dose, take it as soon as you remember unless it is time for your next dose. Do not take two doses at the same time.

If you take more Benylin Day & Night Tablets than you should

If you may have taken more Benylin Day & Night Tablets than you should, talk to a doctor or pharmacist immediately. Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

Possible side-effects

Like all medicines Benylin Day & Night Tablets can have side-effects. Although these are rare, when they do occur they are usually mild and temporary. Tell your doctor if you notice any of the following:

Very rarely people may develop hypersensitivity reactions. These may include reddened skin, itching or skin rashes.

The white day-time tablets may cause symptoms associated with stimulation of the nervous system such as difficulty sleeping and rarely hallucinations. Difficulty passing urine has occasionally been reported in men, although prostate problems may have been an important factor.

The blue night-time tablets may also cause drowsiness, dizziness, blurred vision, stomach upset, dry mouth, nose and throat or urinary retention. If affected do not drive or operate machinery.

There have been rare reports of blood disorders in people taking products containing paracetamol, although these were not necessarily caused by paracetamol.

If you notice any side-effects not mentioned in this leaflet, please tell your doctor or pharmacist

Storing Benylin Day & Night Tablets

Keep Benylin Day & Night Tablets out of the reach and sight of children.

Do not use after the expiry date on the label. Return any out-of-date medicine to your pharmacist.

Keep the pack tightly closed in a dry place in the packaging that it comes in.

Do not store above 25°C.

This leaflet was revised: February 2005.

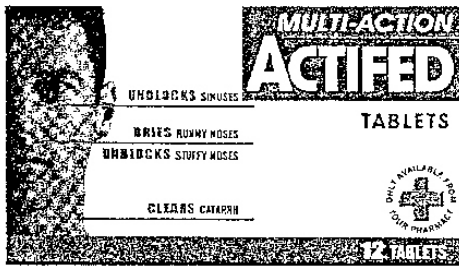
Benylin is a registered trade mark of Pfizer Consumer Healthcare.



Consumer Healthcare

121-201073

447 263



Multi-Action Actifed Tablets

Read all of this leaflet carefully because it contains important information for you. This medicine is available without prescription for you to treat a mild illness without a doctor's help. Nevertheless, you still need to use Multi-Action Actifed Tablets carefully to get the best results from them.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve.

What Multi-Action Actifed Tablets are and what they are used for

Multi-Action Actifed Tablets are off-white, biconvex, branded and scored tablets, coded M2A. Each tablet contains the active ingredients: Pseudoephedrine hydrochloride 60 mg and Triprolidine hydrochloride 2.5 mg. They also contain: lactose, maize starch, povidone and magnesium stearate.

Multi-Action Actifed Tablets contain a decongestant to relieve nasal congestion as well as blocked sinuses and catarrh. They also contain an ingredient which works in two ways: an antihistamine action to relieve the symptoms of allergies, such as sneezing and a drying action to relieve other symptoms of colds, flu and hayfever such as runny noses and watery eyes.

Product Licence holder: Pfizer Consumer Healthcare, Walton-on-the-Hill, Surrey, KT20 7NS.

Manufacturer: Gödecke GmbH, Mooswaldallee 1, 79090 Freiburg, Germany.

They are available in packs of 12 tablets.

Before you take Multi-Action Actifed Tablets

Do not take Multi-Action Actifed Tablets if:

- You have ever had a bad reaction to any of the ingredients.
- You are taking, or have taken in the last two weeks, drugs for depression including Monoamine Oxidase Inhibitors (MAOIs).
- You have high blood pressure or heart disease.
- You have an inherited intolerance to lactose or related conditions.

Take special care with Multi-Action Actifed Tablets if:

- You have kidney or liver problems.
- You have prostate disease, diabetes, glaucoma (increased pressure in the eye) or an over-active thyroid.
- You are taking any other medicines including:

- tricyclic antidepressants
- the antibacterial agent furazolidone
- decongestants, appetite suppressants, stimulants or sedatives
- medicines for high blood pressure (e.g. methyldopa)

If you are unsure if the medicine you are taking is one of those mentioned above, then show the pack to your pharmacist.

Please consult your doctor or pharmacist, even if the statements were applicable to you at any time in the past.

Driving and using machines

Do not drive or operate machinery if Multi-Action Actifed Tablets make you drowsy or make it difficult for you to concentrate. Avoid alcoholic drink.

If you take medicines which make you drowsy while you are taking Multi-Action Actifed Tablets, the chances of getting these side-effects are increased.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking Multi-Action Actifed Tablets in pregnancy or whilst breast-feeding.

How to take Multi-Action Actifed Tablets

For oral use:

- Adults and children over 12 years of age: Take one tablet every 4 - 6 hours up to 4 times a day. Maximum of 4 tablets in 24 hours.

If you take more Multi-Action Actifed Tablets than you should

_____ If you have taken more tablets than you should, talk to a doctor or pharmacist immediately.

_____ If you forget to take Multi-Action Actifed Tablets

_____ Do not take a double dose to make up for forgotten individual doses.

_____ Possible side-effects

_____ Like all medicines, Multi-Action Actifed Tablets can have side-effects, although these are rare and usually mild. Tell your doctor or pharmacist if you notice any of the following:

Sleep disturbances, drowsiness, hallucinations, dry mouth, nose or throat, skin rash with or without irritation, nausea and vomiting, upset stomach, difficulty in passing urine, or palpitations.

If you notice any side-effects not mentioned in this leaflet, please inform your pharmacist or doctor.

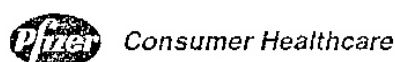
Storing Multi-Action Actifed Tablets

Keep out of reach and sight of children.

Keep the medicine in the original blister in a dry place, below 25°C. Protect from light.

Do not use after the expiry date on the label.

This leaflet was approved January 2004.



121-200664

4/6 (3)

STREPSILS Original Lozenges
2,4-Dichlorobenzyl alcohol
Amylmetacresol

Read all of this leaflet carefully because it contains important information for you. This medicine is available without prescription. However, you still need to take Strepsils Original Lozenges carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 3 days.
- If any of the side effects become serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Strepsils Original Lozenges are and what they are used for
2. Before you take Strepsils Original Lozenges
3. How to take Strepsils Original Lozenges
4. Possible side effects
5. How to store Strepsils Original Lozenges
6. Further information

1. WHAT STREPSILS ORIGINAL LOZENGES ARE AND WHAT THEY ARE USED FOR

Strepsils Original Lozenges contains two antiseptic ingredients for use in throat medications. These are used for the symptomatic relief of mouth and throat infections. These ingredients are both mild antiseptics which kill the bacteria associated with mouth and throat infections. The action of sucking the lozenge allows the active ingredients to work in the area of the discomfort and also helps lubricate and soothe the painful area. This helps relieve the soreness and discomfort of mouth and throat infections.

2. BEFORE YOU TAKE STREPSILS ORIGINAL LOZENGES

This product is recommended for adults, children (over 6 years old) and the elderly. Children under 6 years old should not use this product.

Do not take this product if you:

- are allergic (hypersensitive) to 2,4-dichlorobenzyl alcohol, amylmetacresol, or any of the other ingredients shown in Section 6 – Further Information.
- are under 6 years old.

Do not take this product if:

- You have an intolerance to certain sugars such as fructose, glucose-galactose and sucrose-isomaltose. These would be normally confirmed by your doctor. Intolerance would lead from conditions such as deficiency of the enzyme fructose-1-phosphate aldolase (leading to fructose intolerance), glucose-galactose malabsorption and sucrose-isomaltase deficiencies.

Tell your doctor or pharmacist if you:

- are taking or have recently taken any other medicines, including medicines obtained without a prescription.
- suffer or are suffering from any other throat problems.

Pregnancy and breast-feeding

It is not recommended to use this product if you think you are pregnant, are pregnant or are breastfeeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Important information about some of the ingredients in this product

This product contains sucrose and glucose. If you have been told by your doctor that you have an intolerance to some sugars contact your doctor before taking this product.

3. HOW TO TAKE STREPSILS ORIGINAL LOZENGES

Remove one lozenge from the foil blister packaging. Replace the foil blister back into the cardboard carton. Place lozenge into the mouth allowing it to dissolve slowly.

Dissolve one lozenge slowly in the mouth every 2 – 3 hours.

Adults, Children (over 6 years old) and the elderly – One lozenge to be dissolved slowly in the mouth every 2 – 3 hours up to a maximum of 12 lozenges in 24 hours.

It is not recommended that children under 6 years use this product.

Remember that young children can choke on lozenges.

If symptoms persist for more than 3 days or if anything unusual happens please consult your doctor.

If you take more of this product than you should

You may experience stomach discomfort. Do not take any more of this product and consult your doctor or pharmacist.

If you forget to take this product

Do not take a double dose to make up for a forgotten lozenge. Continue to use this product normally.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Strepsils Original Lozenges can cause side effects, although not everybody gets them. If you experience any hypersensitivity to this product i.e. itching, stop taking this product and consult your doctor or pharmacist. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Also you can help to make sure that medicines remain as safe as possible by reporting any unwanted side effects via the internet at www.mhra.gov.uk/yellowcard. Alternatively you can call Freephone 0800 100 3352 (available from 10 a.m. to 2 p.m. Mondays to Fridays) or fill in a paper form available from your local pharmacy.

5. HOW TO STORE STREPSILS ORIGINAL LOZENGES

Keep out of the reach and sight of children. Do not use this product after the expiry date which is stated on the carton. The expiry date refers to the last day of that month and the year. Do not store above 25°C. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Strepsils Original Lozenges Contain

The active substances are: 2,4-Dichlorobenzyl alcohol 1.2mg Amylmetacresol 0.6mg

The other ingredients are: Star Anise oil, Peppermint oil, Menthol natural or menthol synthetic, Tartaric acid, Ponceau 4R edicol (E124), Carmoisine edicol (E122), Liquid Sucrose, Liquid Glucose Syrup, Water (potable).

What Strepsils Original Lozenges looks like
A red circular lozenge.

Marketing Authorisation Holder:

Reckitt Benckiser Healthcare (UK) Limited, Slough, SL1 3UH

Manufacturer

Reckitt Benckiser Healthcare International Limited, Nottingham, NG90 2DB

Licence Number: PL 00063/0396

Date of preparation February 2013



Pharmaceuticals
to action on the
front of the leaflet.

Please recycle empty
boxes to help on the
back of the leaflet.



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APPENDIX 9: Concordance results

1.

Concordance Results 5: tak*	
Hit	KWIC
1	o Neuralgia WILL THIS MEDICINE SUIT ME? Do not take this medicine if any of the following apply to yo
2	or are suffering from stomach ulcers. . You are taking any other products that contain paracetamol and/o
3	st-feeding. . You suffer from haemophilia or are taking medicines that reduce clotting of the blood (e.g.
4	lood (e.g. Warfarin). Talk to your doctor before taking this medicine if any of the following applies to
5	ase, or dehydration. You are pregnant You are taking water tablets, methotrexate, cholestyramine, chlo
6	ther this medicine is suitable for you if you are taking any other medicines. HOW TO USE THIS MEDICINE A
7	, the elderly and young persons aged 16 and over: Take 2 tablets with a drink of water. Repeat every 4 t
8	er. Repeat every 4 to 6 hours as required. Do not take more than 8 tablets in 24 hours. Do not give to c
9	6 years, unless on the advice of a doctor. Do not take with any other paracetamol containing products. D
10	more than 3 days, contact your doctor. OVERDOSE Taking too many tablets may be harmful. Immediate medica
11	s mentioned below or any other side effects, stop taking this medicine immediately and contact your doctor
12	g ask your doctor or pharmacist for advice before taking any medicine. Directions for use Adults: Rub Vick
13	e read this leaflet carefully before you start to take your medicine. If you are not sure about anything
14	e caused by a cold, hayfever or sinusitis. Before taking your medicine Do NOT use this medicine if; - you
15	y liver or kidney disorder Ask your doctor before taking Vicks Sinex Decongestant Nasal spray if; - yo
16	, you develop new symptoms or if you accidentally take too much product. While taking your medicine Most
17	if you accidentally take too much product. While taking your medicine Most people have no side-effects wi
18	without prescription. However. you still need to take Lemsip Max Lemon Flavour Tablets carefully to get
19	medicine is and what it is used for. 2.Before you take this medicine. 3.How to take this medicine. 4.Pos
20	ed for. 2.Before you take this medicine. 3.How to take this medicine. 4.Possible side effects. 5.How to
21	ressure which may cause a headache. 2. BEFORE YOU TAKE THIS MEDICINE. Do not take this medicine if you:
22	eadache. 2. BEFORE YOU TAKE THIS MEDICINE. Do not take this medicine if you: are allergic to paracetamo
23	d. have high blood pressure (hypertension). are taking or have taken within the last 14 days a medicine
24	lood pressure (hypertension). are taking or have taken within the last 14 days a medicine called a monoa
25	r (MAOI), usually used to treat depression. have taken another medicine for the treatment of cold and flu
26	nother medicine for the treatment of cold and flu. Take special care with this medicine if you: suffer f
27	r toes pale and numb), or diabetes mellitus. are taking beta blockers for high blood pressure, or vasodil
28	nancy). have glaucoma or enlarged prostate. are taking tricyclic antidepressants (a specific class of dru
29	fic class of drugs used to treat depression). are taking other decongestants, or barbiturates (used to tre
30	rates (used to treat sleep problems or epilepsy). Taking other medicines: Do not take with any other para
31	ems or epilepsy). Taking other medicines: Do not take with any other paracetamol-containing products.
32	. Ask your doctor or pharmacist for advice before taking this medicine. Phenylephrine hydrochloride may a
33	Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, inclu
34	or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained
35	luding medicines obtained without a prescription. Taking this medicine with food and drink: Do not consu
36	Do not consume large quantities of alcohol while taking this medicine. Pregnancy or breast-feeding: If y
37	, ask your doctor or pharmacist for advice before taking this medicine. Important information about some o
38	tonuria (an inherited genetic disorder). 3.HOW TO TAKE THIS MEDICINE. To remove the tablet, tear along t
39	back into carton. There are two possible ways to take this medicine. Either Swallow whole with water. D
40	sual sweetener. Once prepared the drink should be taken as soon as possible and should not be stored. It
41	ing from colds and flu. Age Dose and how often to take Adults and children 16 years and over Take two ta
42	ten to take Adults and children 16 years and over Take two tablets every 4-6 hours. Do not take more tha
43	and over Take two tablets every 4-6 hours. Do not take more than eight tablets in a total of 24 hours. C
44	tal of 24 hours. Children aged 12 to 15 years old Take one tablet every 4-6 hours. Do not take more than
45	years old Take one tablet every 4-6 hours. Do not take more than four tablets in a total of 24 hours. Do
46	three days, or worsen, consult your doctor. If you take more of this medicine than you should: Immediate
47	of delayed. serious liver damage. If you forget to take this medicine: This product should only be used w
48	roduct should only be used when necessary. Do not take a double dose to make up for a forgotten dose. If
49	helps clear catarrh and so aid sleep. Before you take Benylin Day & Night Tablets Do not take Benylin
50	fore you take Benylin Day & Night Tablets Do not take Benylin Day & Night Tablets If: * You are allergi

51 are allergic to any of the ingredients * You are taking or have taken within the last two weeks, drugs fo
 52 o any of the ingredients * You are taking or have taken within the last two weeks, drugs for depression k
 53 * You have high blood pressure or heart disease Take special care with Benylin Day & Night Tablets If:
 54 in the past Pregnancy and breast-feeding Do not take during pregnancy, or whilst breast-feeding. Drivi
 55 ive or operate machinery. Avoid alcoholic drink. Taking other medicines Take special care if you are taki
 56 y. Avoid alcoholic drink. Taking other medicines Take special care if you are taking other medicines in
 57 king other medicines Take special care if you are taking other medicines including * paracetamol or pseudo
 58 ncluding * paracetamol or pseudoephedrine. Do not take with any other paracetamol or pseudoephedrine con
 59 can use Benylin Day & Night Tablets while you are taking oral contraceptives ("the pill) or tablets for e
 60 er. If you are unsure if another medicine you are taking is one of those mentioned above, then show the pa
 61 lease inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine - eve
 62 or pharmacist if you are taking, or have recently taken, any other medicine - even those not prescribed.
 63 ther medicine - even those not prescribed. How to take Benylin Day & Night Tablets for oral use. Swallow
 64 lass of water. Adults and children over 12 years: Take one white, day-time, tablet every 4 to 6 hours (o
 65 morning, at mid-day and in the afternoon). Do not take more than 3 day-time tablets in 24 hours. One blu
 66 in 24 hours. One blue, night-time, tablet may be taken at night. Do not take the night-time tablet durin
 67 night-time, tablet may be taken at night. Do not take the night-time tablet during the day. Children un
 68 ble for children under 12 years. If you forget to take a dose, take it as soon as you remember unless it
 69 ren under 12 years. If you forget to take a dose, take it as soon as you remember unless it is time for
 70 mber unless it is time for your next dose. Do not take two doses at the same time. If you take more Beny
 71 e. Do not take two doses at the same time. If you take more Benylin Day & Night Tablets than you should
 72 y & Night Tablets than you should If you may have taken more Benylin Day & Night Tablets than you should,
 73 ve been rare reports of blood disorders in people taking products containing paracetamol, although these w
 74 are available in packs of 12 tablets. Before you take Multi-Action Actified Tablets Do not take Multi-A
 75 ore you take Multi-Action Actified Tablets Do not take Multi-Action Actified Tablets if: You have ever ha
 76 a bad reaction to any of the ingredients. You are taking, or have taken in the last two weeks, drugs for d
 77 o any of the ingredients. You are taking, or have taken in the last two weeks, drugs for depression inclu
 78 ted intolerance to lactose or related conditions. Take special care with Multi-Action Actified Tablets if
 79 re in the eye) or an over-active thyroid. You are taking any other medicines including: . tricyclic antide
 80 yldopa) If you are unsure if the medicine you are taking is one of those mentioned above, then show the pa
 81 you to concentrate. Avoid alcoholic drink. If you take medicines which make you drowsy while you are tak
 82 ake medicines which make you drowsy while you are taking Multi-Action Actified Tablets, the chances of gett
 82 ake medicines which make you drowsy while you are taking Multi-Action Actified Tablets, the chances of gett
 83 g Ask your doctor or pharmacist for advice before taking Multi-Action Actified Tablets in pregnancy or whil
 84 ets in pregnancy or whilst breast-feeding. How to take Multi-Action Actified Tablets For oral use: * Adul
 85 use: * Adults and children over 12 years of age: Take one tablet every 4-6 hours up to 4 times a day. M
 86 s a day. Maximum of 4 tablets in 24 hours. If you take more Multi-Action Actified Tablets than you should
 87 ion Actified Tablets than you should If you have taken more tablets than you should, talk to a doctor or
 88 octor or pharmacist immediately. If you forget to take Multi-Action Actified Tablets: Do not take a doubl
 89 rget to take Multi-Action Actified Tablets: Do not take a double dose to make up for forgotten individual
 90 without prescription. However. you still need to take Strepsils Original Lozenges carefully to get the
 91 ges are and what they are used for. 2. Before you take Strepsils Original Lozenges 3. How to take Streps
 92 re you take Strepsils Original Lozenges 3. How to take Strepsils Original Lozenges 4. Possible side effe
 93 omfort of mouth and throat infections. BEFORE YOU TAKE STREPSILS ORIGINAL LOZENGES this product is recom
 94 r 6 yeras old should not use this product. Do not take this product if you: . are allergic (hypersensiti
 95 rther information.. are under 6 yeras old. Do not take this product if: . you have an intolerance to cer
 96 cies. Tell your doctor or pharmacist if you: .are taking or have recently taken any other medicines, inclu
 97 r pharmacist if you: .are taking or have recently taken any other medicines, including medicines obtained
 98 . Ask your doctor or pharmacist for advice before taking any medicine. Important information about some of
 99 lolerance to some sugars contact your doctor before taking this product. HOW TO TAKE STREPSILS ORIGINAL LOZE
 100 ct your doctor before taking this product. HOW TO TAKE STREPSILS ORIGINAL LOZENGES Remove one loozenge f
 101 usual happens please consult your doctor. If you take more of this product than you should. You may exp
 102 ld. You may experience stomach discomfort. Do not take any more of this product and consult your doctor
 103 nsult your doctor or pharmacist. If you forget to take this product. Do not take a double dose to make u
 104 acist. If you forget to take this product. Do not take a double dose to make up for a forgotten lozenge.
 105 persensitivity to this product i.e. itching, stop taking this product and consult your doctor or pharmaci

Concordance Results 10: assu*

Hit	KWIC
1	Durante il trattamento con paracetamolo, prima di assumere qualsiasi altro farmaco controllate che non conte
2	stesso principio attivo poiché se paracetamolo è assunto in dosi elevate si possono verificare gravi reazi
3	consiglio del medico. Quando e per quanto tempo Assumere il prodotto a stomaco pieno, usare solo per brevi
4	se eccessiva, di medicinale In caso di ingestione/ assunzione accidentale di una dose eccessiva di Neo-Cibalg:
5	a del naso e dei seni paranasali, inducendo anche assuefazione al farmaco. Ripetere le applicazioni per lungi
6	ontiene sostanze vietate per doping. È vietata un' assunzione diversa, per schema posologico e per via di som
7	adeguate misure d'urgenza. In caso di ingestione/ assunzione accidentale di una dose eccessiva di VICKS SiNEI
8	late dal punto di vista chimico. Nei pazienti che assumono beta-bloccanti. Inibitori delle monoaminoossidasi
9	Durante il trattamento con paracetamolo, prima di assumere qualsiasi altro farmaco controllare che non conte
10	esso principio attivo, poiché se il paracetamolo è assunto in dosi elevate si possono verificare gravi reazi
11	ssico del paracetamolo può essere potenziato dall' assunzione di altri farmaci attivi sul fegato. I pazienti in
12	nta l'emivita del cloramfenicolo. Il paracetamolo assunto in dosi elevate può potenziare l'effetto degli an
13	nsigliate, o anche nell'ipotesi in cui si dovesse assumere l'intera confezione, non dovrebbero comparire sin
14	ico, che si manifesta in genere 2-4 giorni dopo l' assunzione . I sintomi precoci sono nausea, vomito e dolori
15	della pressione arteriosa. In caso di ingestione/ assunzione accidentale di una dose eccessiva di TACHIFLUDE
16	attivi di Actidue (Giorno 6 Notte C.M.), prima di assumere qualsiasi altro farmaco controllare che non conte
17	esso principio attivo, poiché se il paracetamolo è assunto in dosi elevate si possono verificare gravi reazi
18	si possono verificare gravi reazioni avverse. Non assumere il medicinale insieme ad altri analgesici, antipi
19	ivi o tranquillanti, ecc., che pertanto non vanno assunti contemporaneamente. I pazienti in trattamento con
20	quali dovranno astenersi da tali mansioni dopo l' assunzione del prodotto. Dosi elevate o somministrazioni p:
21	do e per quanto tempo Le compresse bianche vanno assunte esclusivamente durante il giorno, quelle azzurre
22	ramento recente delle sue caratteristiche. Come Assumere le compresse con un bicchiere d'acqua. COSA FARE
23	ali e vertigini. Effetti indesiderati legati all' assunzione di difenidramina possono essere: sonnolenza, ast
24	sistema nervoso centrale, che non vanno pertanto assunte durante la terapia. Gli antistaminici possono rid
25	inibizione della monoaminoossidasi, per cui non va assunto contemporaneamente all'ACTIFED. L'effetto degli a
26	, anche in questo caso, non va contemporaneamente assunto . E' IMPORTANTE SAPERE CHE Se i sintomi non migli
27	lori di pressione), l'ACTIFED non dovrebbe essere assunto da pazienti in terapia con antipertensivi, antide
28	ibilizzazione o irritativi occorre interrompere l' assunzione del farmaco e consultare il medico. BENAGOL Pas
29	Pastiglie gusto Limone Senza Zucchero può essere assunto a qualsiasi ora della giornata. Attenzione: usare
30	DOSE ECCESSIVA DI FARMACO In caso di ingestione/ assunzione accidentale di una dose eccessiva di BENAGOL Pa

Concordance Results 27: preso

Hit	KWIC
1	re, con acqua o altri liquidi. Cosa fare se avete preso una dose eccessiva, di medicinale In caso di inge
2	trine (vedere anche alla voce "Cosa fare se avete preso una dose eccessiva di medicinale). Con l'uso dei
3	superare Le dosi consigliate. COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE A) Somministrazi
4	vomito e diarrea. Nelleventualità in cui abbiate preso una dose fortemente eccessiva di Vicks Vaporu
5	nte delle sue caratteristiche. COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE In caso di dose
6	dolcificare come si desidera. COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE Alle dosi consig
7	esse con un bicchiere d'acqua. COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE In caso di inges
8	alle capacità di 5 e 10 ml. COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI MEDICINALE In caso di ecces
9	ossono provocare soffocamento. COSA FARE SE AVETE PRESO UNA DOSE ECCESSIVA DI FARMACO In caso di ingesti

2.

Concordance Results 6: treat	
Hit	KWIC
1	e is available without a prescription, for you to treat a mild illness without a doctor's help. Nevertheless
2	noamine oxidase inhibitor (MAOI), usually used to treat depression. have taken another medicine for the
3	gh blood pressure, or vasodilators (drugs used to treat high blood pressure, leg pain due to vascular pro
4	antidepressants (a specific class of drugs used to treat depression). are taking other decongestants, or
5	ing other decongestants, or barbiturates (used to treat sleep problems or epilepsy). Taking other medicin
6	cetamol works including: -Cholestyramine -used to treat blood cholesterol -Metoclopramide and domperidone
7	lesterol -Metoclopramide and domperidone -used to treat nausea and vomiting. the effect of blood thinnin
8	ith other sympathomimetics (such as those used to treat blood pressure, glaucoma or nasal congestion), va
9	or nasal congestion), vasodilators (drugs used to treat high blood pressure) and beta-blockers. Please te
10	ine is available without prescription, for you to treat a mild illness without a doctor's help. Neverthel
11	cholesterol) » metoprolol and domperidone (to treat nausea and vomiting) anti-coagulants (to thin t
12	other decongestants or stimulants * medicines to treat high blood pressure (e.g. a and B blockers, bret
13	(e.g. atropine or some psychotropic drugs used to treat anxiety, depression or other mental illnesses) *
14	cine is available without prescription for you to treat a mild illness without a doctor's help. Neverthel

Concordance Results 8: per il trattamento	
Hit	KWIC
1	nnunziata (NA) Perché si usa Neo-Cibalgina si usa per il trattamento sintomatico di mal di testa, nevralgie, mal di de
2	rau, Germania. PERCHÉ SI USA VICKS VAPORUB si usa per il trattamento balsamico nelle affezioni delle prime vie respira
3	TACHIFLUDEC polvere per soluzione orale, si usa per il trattamento sintomatico dell'influenza, del raffreddore e deg
4	PERCHE'SI USA Actidue Giorno e Notte CM. si usa per il trattamento dei sintomi del raffreddore e dell'influenza. QUA

3.

Concordance Results 14: kidney*	
Hit	KWIC
1	you: You suffer from asthma, allergic disease, kidney or liver disease, or dehydration. You are pregn
2	thyroid disease, - you suffer from any liver or kidney disorder Ask your doctor before taking Vicks Sine
3	with this medicine if you: suffer from liver or kidney problems, heart disease. have non-cirrhotic live
4	the eye) or prostate problems * You have liver or kidney disorders Please consult your doctor, even if the
5	re with Multi-Action Actifed Tablets if: You have kidney or liver problems. You have prostate disease, dis

Concordance Results 15: renale	
Hit	KWIC
1	io, ulcera gastro-duodenale). Asma, Insufficienza renale . L'uso di questo medicinale è controindicato nei
2	ello stomaco o dell'intestino o con insufficienza renale o epatica, devono consultare il medico prima dell
3	arterioso e ipertensione polmonare); - disfunzione renale , che può progredire in insufficienza renale con o
4	zione renale, che può progredire in insufficienza renale con oligo-idroamminosiosi, - la madre e il neonato,
5	strare con cautela nei soggetti con insufficienza renale o epatica. Durante il trattamento con paracetamol
6	osi, alterazioni a carico del rene (insufficienza renale acuta, nefrite interstiziale, ematuria, anuria), r
7	. Nei pazienti affetti da insufficienza epatica o renale , diabete, ipertiroidismo, ipertensione e malattie
8	(da 13 a 18 anni), nei soggetti con insufficienza renale od epatica e in età avanzata (vedere "Come usare
9	ttutto controllo del medico in caso di insufficienza renale od epatica. Durante il trattamento con paracetamo
10	enza (da 13 a 18 anni), in caso di insufficienza renale od epatica a in età avanzata occorre rivolgersi
11	iti, alterazioni a carico del rene (insufficienza renale acuta, nefrite interstiziale, ematuria, anuria) r

4.

Concordance Results 18: experience	
Hit	KWIC
1	ts are rare. However, susceptible individuals may experience unwanted effects. If you experience any side effe
2	dividuals may experience unwanted effects. If you experience any side effects mentioned below or any other sid
3	ake more of this product than you should. You may experience stomach discomfort. Do not take any more of this
4	effects, although not everybody gets them. If you experience any hypersensitivity to this product i.e. itching

Concordance Results 30: compar*	
Hit	KWIC
1	mpportante comunicare al medico o al farmacista la comparsa di effetti indesiderati non descritti nel foglio
2	mpportante comunicare al medico o al farmacista la comparsa di effetti indesiderati. Richiedere e compilare l
3	SSIVA DI MEDICINALE In caso di dose eccessiva può comparire ipertensione arteriosa (aumento della pressione
4	mpportante comunicare al medico o al farmarista la comparsa di effetti indesiderati non descritti nel foglio
5	esse assumere lintera confezione, non dovrebbero comparire sintomi da sovradosaggio di paracetamolo. Tuttavi
6	mpportante comunicare al medico o al farmacista la comparsa di effetti indesiderati non descritti nel foglio
7	E Se i sintomi non migliorano entro 3 giorni o se compare febbre alta o altri effetti indesiderati, interro
8	l rene e del sangue anche gravi. Nei rari casi di comparsa di reazioni allergiche la somministrazione va sos
9	mpportante comunicare al Medico o al Farmacista la comparsa di effetti indesiderati non descritti nel foglio
10	mpportante comunicare al Medico o al Farmacista la comparsa di effetti indesiderati non descritti nel foglio
11	uzioni d'uso. E' IMPORTANTE SAPERE CHE In caso di comparsa di fenomeni di sensibilizzazione o irritativi occ
12	mpportante comunicare al medico o al farmacista la comparsa di effetti indesiderati non descritti nel foglio

5.

Concordance Results 33: ini*	
Hit	KWIC
1	range di dosaggio. - Dosi di 500 mg/die e oltre Linibizione della sintesi di proslaglandine può interessare n
2	zione cardiaca e di gastroschisi dopo luso di un inibitore della sintesi dalle proslaglandine, nelle prime f
3	la terapia. Negli animali, la somministrazione di inibitori della sintesi di proslaglandine ha mostrato di pr
4	rtata in animali a cui erano siati som-ministrati inibitori di sintesi delle prostaglandine durante il period
5	rante il terzo trimestre di gravidanza, tutti gli inibitori della sintesi di prostaglandine possono esporre:
6	nte che può occorrere anche a dosi molto basse; - inibizione delle contrazioni uterine risultanti in ritardo
7	himico. Nei pazienti che assumono beta-bloccanti. Inibitori delle monoaminoossidasi ed antidepressivi tricicl
8	ti ed ipertensivi e può potenziare lazione degli inibitori delle monoaminoossidasi. Se state usando altri me
9	12 anni; nei pazienti in trattamento con farmaci inibitori delle monoaminossidasi (IMAO) e nelle due settima
10	ttamento, nei pazienti in trattamento con farmaci inibitori delle monoaminossidasi (IMAO) o nelle due settima
11	tibiotici. Il Furazolidone causa una progressiva inibizione della monoaminossidasi, per cui non va assunto c

Concordance Results 26: inhi*	
Hit	KWIC
1	ast 14 days a medicine called a monoamine oxidase inhibitor (MAOI), usually used to treat depression. have t
2	, drugs for depression known as Monoamine Oxidase Inhibitors (MAOIs) * You have high blood pressure or heart d
3	ucts * antidepressants known as Monoamine Oxidase inhibitors (MAOIs) or tricyclic antidepressants * colestyram
4	drugs for depression including Monoamine Oxidase Inhibitors (MAOIs). You have high blood pressure or heart di

6.

AAE GDR		Concordance Results 19: develop*
Hit	KWIC	
1	el worse or do not feel better after 7 days - you develop new symptoms - you are pregnant or breast feeding	
2	worse or do not feel better after seven days, you develop new symptoms or if you accidentally take too much	
3	tice any of the following: Very rarely people may develop hypersensitivity reactions. These may include red	
AAE GDR		Concordance Results 31: evolv*
Hit	KWIC	
1	di cellule del fegato (citolisi epatica) che può evolvere verso la massiva ed irreversibile necrosi. Per la	

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