

EDITORIAL

**Unreasonable patient expectation –
one more reason behind irrational prescribing**

There was a time when life was simpler. Patients came to their doctors with faith. The doctors listened to their complaints with sympathy and did their best to diagnose the illness and prescribe medicines from the few that were available. There was not a plethora of drugs to choose from. The patients trusted their doctors and took the medicines which were meant mostly to provide symptom relief. A disciplined lifestyle combined with rest, relaxation and 'change' were advocated for very many chronic illnesses for which there were no cures and the patients expected none. Sick children enjoyed the comforts of home and a caring family.

Times have changed. Civilization has 'progressed'. Life has become faster. Most patients now have 'work' to do. They cannot remain idle because of illness. There are offices to attend, trips to undertake, meetings to participate in. Housewives have children to manage, shopping to complete, parties to organize, in addition to all their usual household chores. Even young children need a doctor's certificate if they are absent from school for more than 3 days and exams are always ahead.

The inevitable follows. In this age of instant everything, patients naturally expect and demand instant cures. Get well quick and never mind the disease is the motto. How often do we face situations like:

- The patient with pharyngitis who does not expect to cough any more right from the next day.
- The patient with gastroenteritis who comes with hourly loose stools in the morning and wants to be up and about in the evening.
- The patient with severe heartburn who is loathe to cut down on his smoking or tea/coffee but cannot understand why the doctor is only giving him medicines that do not work.
- The patient with viral hepatitis who is disappointed that the doctor is only prescribing rest and a simple diet and is not actively prescribing medicines.
- The stressed patient with a complaint of general weakness who thinks that he needs good vitamins to recharge.
- The patient with sleep disorder who thinks that sleep hygiene is a good idea but sedatives are so much more convenient.

Very often is the answer nowadays. So, most doctors in community practice, will agree that the pressure is on them to prescribe and prescribe they do – one, two, three, four – in fact as many drugs as there are complaints and some extra vitamins, antioxidants, food supplements and the like thrown in for good measure.

In India it is very easy to find examples of blatant polypharmacy and shotgun therapeutics – try a battery of medicines, surely one will work and the patient will be happy. Unfortunately patients do not realize, and we are too busy to educate them, that every illness has a natural history and will run its course. Apart from infections (that too if they are of a non-viral nature), there are few diseases currently where we can abort the natural history through treatment. Clamoring for instant relief and doctor-hopping complicates matters. For instance, it leaves the patient with more medicines to purchase and take, with corresponding chance of non-compliance and increased risk of adverse drug reactions.

There is no shortcut to solving this problem. It is our earnest request to all consumers of medicine that please be patient, cooperate with your doctor, and comply with the prescribed medication. Provide timely feedback and pay equal attention to the non-drug treatment advocated. If possible, spare some time to educate yourself about the illness so that you can take a more informed role in its management. You can expect to be cured only if you are diagnosed with a disease that is known to be curable. If not, you and your doctor must jointly evolve a strategy to limit further disability, get relief from symptoms and improve the quality of life as much as possible. After all medical science still has its limits.

Avijit Hazra

**RATIONAL
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Introduction

The internet is rapidly becoming a part of our daily lives - the computer already is. Millions of people around the world are routinely searching for information and conducting a variety of transactions using the worldwide network of networks, called the world wide web [WWW].

The web began its existence around 1989 with a document 'Information management: a proposal' by Tim Berners-Lee, a researcher at CERN - the European agency for nuclear research headquartered at Geneva, Switzerland. The proposal envisaged a network of remote documents in cyberspace linked logically using 'hypertext'. This network was to be called WWW. Berners-Lee's boss had this comment about the proposal, 'vague but interesting.' Today, this vague idea has grown into a phenomenon of revolutionary proportions and is set to affect the lives of each and everyone of us - whether we like it or not.

The internet software consortium [reachable at <<http://www.isc.org>>] estimates that as of July, 2001, there were 125,888,197 host computers on the internet serving almost 1 billion users around the globe.

What can we do through the Internet

We are limited only by our imagination in this regard:

- Communicate using e-mail / voicemail / real-time chat
- Search for information - text / graphics / audio / video
- Shop / transact
- Send applications
- Give examinations
- Play games
- Earn the daily livelihood

Web information retrieval

Web information retrieval [WebIR] is the process of extracting useful information from the petabytes of data that make up the WWW.

The type of information retrieval depends upon the type of the web user:

- *Casual user.* Searches for something that is loosely defined and as per whims and fancies.
- *Academic user.* Searches for focused information to be utilized for teaching-learning, research or professional work. Information needs to be authentic and up-to-date.
- *Business user.* Searches for commercial information with commercial interests in mind. Also needs authentic and up-to-date information.

Problems in information search

WebIR is increasingly becoming a skilled activity. The chief problem for the novice user is that uninformed information searches tends to generate a deluge of data, much of which is probably irrelevant. Other problems are:

- Information can be from non-authentic sources.
- Commercial information can come disguised as academic information.
- Propaganda can be misconstrued as information.
- Not all information is free.

What are the search strategies

Searching can be in online or offline mode. The latter can be done at leisure and repeated as many times as one wants, provided access to the offline media is retained. More skill is required in online search. It can be done through various strategies:

- Know the URL e.g. <<http://www.mghmedical.com/harrison.htm>>.
- Join an Internet Discussion Group.
- Subscribe to a e-newsletter, e-bulletin, etc.
- Search through a search engine.
- Locate databases and search through them.

Searching through a search engine

At the heart of WebIR is the search engine. Numerous search engines exist (e.g. InfoMedical at <<http://www.infomedical.com>> and Medical Search Engine at <<http://www.medicalsearchengine.com>>). They employ different search strategies and are continually striving to upgrade their search capabilities. Table 1 depicts a comparison of salient features of 4 search engines popular among Indian net-surfers.

Searching in databases

Much of the content an academic web user needs is not directly retrievable by a web search engine. They are hidden in databases behind the search engine. Information has to be retrieved, often dynamically, by querying the database.

Popular medical databases available online include: MEDLINE, EMBASE, Cochran Database of Systematic Reviews, AIDSline, PopLine, ToxLine, CancerLit, PsycInfo, etc. These vary in scope and coverage. EMBASE and MEDLINE both attempt to cover all biomedical literature. EMBASE has less number of records – 6.5 million citations as opposed to 10 million in MEDLINE (as of 2000), but it is more comprehensive for pharmacology and psychiatry and gives better coverage of European and Asian literature. MEDLINE is free. EMBASE has a subscription or pay-per-record viewed system.

Table 1. Comparative features of some popular search engines

Feature	Google	Alta Vista	Lycos	Searchindia
Case-sensitive search	No	Yes	No	Yes
Search within results	Yes	Yes	Yes	No
Phrase search	Yes	Yes	Yes	Yes
Include / exclude phrases	Yes	Yes	Yes	Yes
Stemming	No	Yes	No	Yes
Logic expressions	Limited [automatic AND of search terms and OR operator]	Yes [AND, OR, NOT, NEAR]	Yes [AND, OR, NOT]	Limited [use "+ A or B" to prefer a page containing A and B over one containing only A]
Search scoping	Many qualifiers [site; intitle; link; inurl, etc.]	Limited [domain:]	Word filtering	Limited [url: (search within url); mailto: (search for contributions by user with e-mail address)]

Source Srinivasa S, Bhatt PC. Introduction to web information retrieval: A user perspective. Resonance 2002;7(6): 27-38.

About MEDLINE

- Most frequently accessed biomedical database.
- Maintained by the United States National Library of Medicine at Washington D.C.
- Indexes over 4000 biomedical journals currently.
- Dates back to 1966 literature.
- Over 11 million citations currently - about 70% are English language articles and about 70% are with abstracts.
- Allows various limits (filters) to refine searches.
- Searching facilitated by knowing MeSH keywords and Boolean operators.
- The PubMed portal <<http://pubmedcentral.nih.gov>> is most popular for accessing MEDLINE online. This facility is free - even registration is not required.
- Trying to provide free full-text access online through arrangement with publishers.
- Various agencies provide MEDLINE on offline media to which paid subscriptions can be taken.

Medical information retrieval in India

The National Library of Medicine [NLM] at All-India Institute of Medical Sciences, is the largest repository of medical information in India. Linking up with individual medical college libraries.

Indian National Scientific Documentation Centre [INSDOC], with headquarters at New Delhi, and a network of regional offices in the metro cities, can help in medical information searching and retrieving full-text articles.

Indian MEDLARS Centre [IMC] was set up in 1986 as a collaborative project between Indian Council of Medical Research [ICMR], New Delhi, and National Informatics Centre [NIC], New Delhi, to provide

Indian researchers with access to the Medical Literature Analysis and Retrieval System [MEDLARS] databases of the US National Library of Medicine. IMC's website was launched in August, 2000, (<<http://indmed.nic.in>) and since then is providing access to the IndMED database, which is an indigenously developed database of peer-reviewed Indian biomedical journals. Currently 76 journals are being indexed by IndMED. IMC also provides a chat room for medical professionals (Live@IndMED), ready-made lectures and tutorials, and links to a variety of internet health resources. Search requests can be submitted online through the webpage.

Some interesting websites

Index Medicus Journal Titles Abbreviation List

<<http://www.medscape.com/Home/Search/IndexMedicus/IndexMedicus.html>>.

FreeMedicalJournals.com.

<<http://www.freemedicaljournals.com>> Listing and links to medical journals providing free full-text access online.

CenterWatch Clinical Trials Listing Service.

<<http://www.centerwatch.com>> Latest drugs approved by US FDA and details of clinical trials in progress.

Evidence-based Medicine Website [eEBM].

<<http://www.evidence-basedmedicine.com>> Full text in <pdf> format and links to primary papers.

WHO Action Programme on Essential Drugs.

<http://www.who.ch/programmes/dap/DAP_Homepage.html>

British National Formulary online. <<http://www.bnf.org>>.

The Physician's Gen Rx site. <<http://www.genrx.com>> Online formulary of US prescription drugs.

British Medical Journal. <<http://www.bmj.com>>. Also provides links to all the journals published by the BMJ group most of which now allow free access.

Nobel Prizes. <<http://www.nobel.se>>. Official Nobel Prize website.

Tackling the menace of counterfeit drugs**Moitreyee Mondal**

Counterfeit drugs represent a serious problem affecting both developed and developing countries. The problem is more severe in countries where the manufacture, import, distribution, sale, and supply of drugs are weakly regulated, and enforcement is weak.

The magnitude of the menace can be gauged from a recent survey by the World Health Organization [WHO], which reveals that about 15% of drugs traded in the world are either counterfeit or substandard. Another survey by Division of Parasitic Disease of the Centers for Disease Control and Prevention in the United States reported that 38% of samples of the antimalarial Artesunate, purchased at retail counters in Cambodia, contained no active ingredients. In 1990 at least 30 malaria deaths in Cambodia could be linked to inadequate treatment due to counterfeit drugs.

Counterfeit drugs are often not efficacious, and in many cases, have been dangerous and harmful to public health. The factors facilitating the occurrence of counterfeit drugs differ in every country, and need to be correctly identified, to help governments to eradicate them. Common factors include the lack of laws prohibiting counterfeiting of drugs, weak penal procedures, weak drug regulatory authority [DRA], shortage/erratic drug supply, high cost of a drug, loose customs checking, increased sophistication in clandestine drug manufacture, corruption, etc. Counterfeiting takes place at regional, national and international levels. Each country has to develop a suitable strategy involving all concerned parties - government agencies, pharmaceutical companies, drug suppliers, doctors, pharmacists, other health care providers, consumers and non-governmental organizations [NGOs]. Governments and DRAs have to frame comprehensive drug legislation, including provisions prohibiting the manufacture, import, and sale of counterfeit drugs, and need to ensure that the manufacture, import, distribution, supply and sale of drugs are carried out under specific licenses in licensed premises, under the supervision of qualified persons. The points of drug entry, and drug establishments, including drug manufacturing units, wholesalers, and retailers must be regularly inspected and samples collected and tested by proper screening methods in consonance with legally accepted testing methods. Any imported drug suspected of being counterfeit should be placed in quarantine pending sampling and analysis in competent labs.

The WHO DMP-DAP Joint Project on Counterfeit Drugs, which ran from 1995-1997, has also developed guidelines for framing measures to combat counterfeit drugs. They have agreed on a definition of the term counterfeit drugs - "A counterfeit medicine is one, which is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply both to branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging". In view of the above, WHO has emphasized extensive education and training of drug inspectors and analysts involved in the detection and eradication of counterfeit drugs.

Counterfeiting of commercial products is an age-old practice which is motivated mainly by the huge profits made. Counterfeiting of drugs is growing sophisticated by the day, and strict vigilance is required to control it. Counterfeit drugs are generally not of the quality they claim to be, and may be mislabeled with respect to identity and/or source, and can be prepared both in large scale and small scale. Some counterfeit drugs contain the correct strength of the specified active ingredients, but its source is different to the one declared. Products may contain the specified active ingredients but in strengths different to those declared, they may also contain unacceptable levels of impurities.

Drug distribution channels are often corrupted, so that counterfeit products have regularly been found alongside genuine drugs in legitimate channels, and also in illegitimate markets. New global trade arrangements, free trade policies and deregulation measures are dramatically changing the pharmaceutical market worldwide, and also encouraging the proliferation of pharmaceutical products. Factors like inequitable income and wealth distribution, and variable social and economic development, are also leading to increased cases of counterfeiting.

Counterfeit drugs are detrimental to public health in terms of human suffering and burden on the health services. A patient may respond inadequately to the spurious drug, or may not respond at all. Treatment with ineffective critical drugs like antibiotics can cause serious therapeutic failure. In extreme cases, counterfeit drugs may cause outright toxicity or exacerbate the condition being treated, due to the harmful ingredients they may contain. Reports abound in India of such mishaps. For instance, diethylene

glycol was incorporated fraudulently, or by mistake, in pharmaceutical formulations, and it resulted in death of more than 500 people, mostly children., due to its toxic effects on liver, kidney, etc. In another instance, placebo tablets containing no active ingredients were stolen, and sold as a contraceptive drug, leading to unexpected pregnancy.

As a result of such damaging effects, counterfeit drugs erode public confidence in health care systems, healthcare professionals, suppliers and sellers of genuine drugs, the pharmaceutical industry, and national drug regulators. Incorrect labeling as to the source can also be detrimental to the reputation and financial standing of the manufacturer whose name is being fraudulently used. Legitimate manufacturers thus have a direct stake in the fight against counterfeiting.

Legitimate drug manufacturers should develop measures, like securing their own stocks of medicines and packaging materials in order to prevent their diversion to illegal manufacturers and packagers. They must regularly check their own and the national drug distribution channels to detect any counterfeiting of their products. They must avoid promoting drugs in a manner that results in demands that can't be met by their own supply systems, thus leaving a gap, which can be exploited by counterfeiters. Taking up this cue, a group of pharmaceutical manufacturers in India are raising their voices against the fact that a large portion of drugs (about 20%) in the Indian market are counterfeit. According to an unofficial survey, North and North-Eastern states of India, along with pockets in North-Western India are flooded with spurious drug products. This alliance of pharmaceutical companies is also thinking of appointing private agencies to determine the exact status of counterfeit medicines in the Indian market.

Dissemination of information to health professionals, on the existence of counterfeit drugs in the national distribution channels, as fast as possible, is a necessary but neglected issue. Appropriate warnings should be issued through mass media. It is important to establish standard methods for reporting by licensed / authorized drug manufacturers / distributors, prescribers, and consumers, if they observe or suspect the presence of counterfeit drugs in the distribution channels. Procedures for the recall and immediate removal of counterfeit drugs should also be formulated.

Some other points also need to be acted upon to combat the growing menace of counterfeit drugs in the Indian pharmaceutical market:

- Drug laws should be made more stringent.
- A structured pharmacovigilance system should be developed, to identify sources of counterfeit drugs so that they can be stemmed.
- Capacity of drug testing laboratories must be increased to help analyze drugs other than for statutory purpose.
- Strength of the drug control authority must be upgraded.
- Coordination between enforcement agencies also needs to be increased.

Finally, at the consumer level too vigilance is necessary to prevent counterfeiters from gaining ultimate access to the patient. Consumers should procure drugs only from licensed retailers, insist on a proper invoice stating the lot number and expiry dates of the products being purchased, should inspect the packaging carefully for signs of duplication or tampering, and should be wary of unexpected low or bargain prices. These measures are not foolproof but will prevent them from being fooled most of the time.

Recent additions to our library

- **How to develop and implement a national drug policy. 2nd ed. Geneva: World Health Organization, 2001 [Updates and replaces Guidelines for developing national drug policies, 1998].**
- **Essential drugs for primary health care: A manual for health care workers. 3rd ed. New Delhi: World Health Organization – South East Asian Regional Office, 2000 [SEARO Regional Health Papers No. 16].**
- **Bulatao RA, Casterline JB, editors. Global fertility transition. New York: Population Council, 2001 [A supplement to Population and Development Review Vol 27, 2001].**
- **Haberland N, Measham D, editors. Responding to Cairo: Case studies of changing practice in reproductive health and family planning. New York: Population Council, 2002.**

Rabies and its prevention

Amitava Sen

Introduction

Rabies, known as hydrophobia in popular parlance, is an acute fatal viral disease of the nervous system. It is primarily a zoonotic disease of warm blooded animals such as dogs, cats, jackals and wolves but is transmitted to man through bites of rabid animals. The central nervous system is irreversibly affected resulting in death, despite intensive care. It is the only communicable disease of man that is always fatal.

Rabies is enzootic in India. It constitutes a major but neglected public health problem in India with an estimated mortality of 30,000 a year, while 1.1 to 1.5 million receive postexposure prophylaxis each year. The incidence of the disease in animals is of far greater magnitude but the true extent is unknown.

Agent, host and environment factors in rabies

The causative agent of rabies is a bullet shaped RNA virus that is excreted in the saliva of affected animals. The virus recovered from naturally occurring cases of rabies is called street virus. It is pathogenic for mammals and shows a long and variable incubation period. Serial brain-to-brain passage of the street virus in rabbits modifies the virus such that its incubation is reduced progressively till it becomes constant between 4 to 6 days – this is the fixed virus used in preparation of antirabies vaccines. There is evidence that fixed virus can also be pathogenic for human and mammals under certain conditions, for instance the parenteral injection of antirabies vaccine that is inadequately inactivated.

Rabies exists in three epidemiological forms depending upon the reservoir of infection:

- **Urban rabies:** Transfer of infection from wildlife to domestic dogs results in the creation of the urban cycle which is maintained by the dog and is responsible for 99 % of human cases in India. Cats can also be source of human infection.
- **Wildlife rabies:** Also known as sylvatic form of rabies, this presents an intractable problem. The true reservoir of infection is unknown.
- **Bat rabies:** This type is more prevalent in Latin America.

All warm-blooded animals, including man, are susceptible to rabies. In dogs and cats the virus may be shed in the saliva for 3 to 4 days. The source of infection in man is the saliva of rabid animals. Rabies in man is usually a dead-end infection and has no survival value for the virus. Children account for a large proportion of severely exposed cases. Laboratory staff working with rabies virus, veterinarians, dog handlers, animal keepers and hunters face a bigger risk of rabies than do the general public. Medical and nursing staff treating rabies cases are also at risk.

The modes of transmission include:

- **Animal bites** – Rabid dog bite is the usual source. As a prerequisite to transmission, the saliva of dog (or the biting animal) must contain the virus at the time of the

bite. the possibility of contracting rabies occasionally from animals other than the dog should borne in mind.

- **Licks** – Licks on abraded skin and mucosa [abraded or unabraded] can transmit the disease if the animal has a high virus load.
- **Aerosols** – Aerosolized transmission through the respiratory route has been observed in nature only in relation to certain caves harboring rabies infected bats. In the laboratory, aerosol created during homogenization of infected animal brains can infect laboratory workers.
- **Person-to-person** – Man-to-man transmission, although rare, is possible. A case of a child biting his parent and transmitting the disease is on record. There is also report of transmission of rabies by corneal and organ transplants.

Clinical features in man

Rabies begins with prodromal symptoms such as headache, soar throat, malaise and slight fever lasting for 3-4 days. This is followed by widespread excitation and stimulation of all parts of nervous system, usually involving, in order, the sensory, the motor, the sympathetic nervous systems and the brain and mental faculties. The symptoms progressively intensify and all attempts at swallowing liquids become unsuccessful. At a later stage the mere sound of water may provoke spasm of muscle of deglutition. This has earned the synonym of hydrophobia for rabies. The duration of acute illness is for 2-3 days, but may be prolonged to 5-6 in exceptional cases. The patient may die abruptly in one of the convulsion or may pass on to the stage of paralysis and coma. Till date, only 3 people are on record who have been afflicted with rabies but have survived.

Prevention and treatment

There is no specific treatment for rabies. The mainstay of prevention rests on diligent vaccination [post-exposure] after bites by potentially rabid animals and partly on appropriate first aid for the wound. It is also important to know that persons who run a high risk of exposure, such as veterinarians, should be protected by [pre-exposure] immunization. Vaccines available in India are:

- **Nerve tissue vaccines** derived from sheep-brain, are available in Government Institutions, and are cheap. Unfortunately, the vaccine is of low potency, vaccination requires several doses, is painful and the vaccine being a relatively crude preparation, is capable of causing severe reactions. Recently, the Government of India has decided to withdraw this vaccine.
- **Cell culture vaccines** including second generation tissue culture vaccines and the human diploid cell vaccine. These are now available in India.

In India, in the prophylaxis of rabies, the lack of proper health education compounds the fear of injections. Once bitten by a dog, a person is often confused as to what he / she should do immediately. By the time the person acquires some knowledge of the disease there is a often a

considerable lag period which could be dangerous in some circumstances. Considering the magnitude of the problem, the concept of dog bite clinics catering to especially the underprivileged population is attractive. The clinics can offer proper counseling, first aid and affordable immunization against rabies. They can also spearhead mass education campaigns.

Treatment

Local treatment is necessary for all bite / scratch wounds. The wound must be cleaned immediately by flushing with water, preferably under a running tap, and applying soap. After cleansing antiseptics must be applied such as surgical spirit, tincture of iodine or povidone iodine. The last is non-irritating and has good efficacy. There is no firm evidence that cauterization with phenol, or other substances, helps and so this is not necessary. Booster doses of tetanus toxoids (or the full course if tetanus immunization status is unsatisfactory or uncertain) should be administered if necessary. Large, lacerated wounds may require systemic antibacterial treatment to tackle secondary infections.

Antirabies treatment should be started / continued in case:

- The animal shows signs of rabies / dies within 10 days of observation.
- The biting animal cannot be traced / identified.
- Unprovoked bites from street dogs.
- All bites by wild animals.

Combined vaccine and immunoglobulin (antirabies serum) treatment offers the best prophylaxis of rabies in exposed persons. However, the cost of rabies immunoglobulin is very high and may be beyond the reach of the subject. Hence guidelines have been developed by the World Health Organization [WHO] to guide the vigorousness of treatment depending on the degree of exposure (see box).

Classification of exposure to rabies

Class I [slight risk]

- Licks on healthy unbroken skin.
- Consumption of unboiled flesh of the suspected animal [unlikely nowadays].
- Scratches without oozing of blood.

Class II [moderate risk]

- Licks on fresh cuts or nibbling of uncovered skin.
- Scratches with oozing of blood.
- All bites except those on head, neck, face, palms and finger.
- Minor wounds less than 5 in number.

Class III [severe risk]

- All bites or scratches with oozing of blood on neck, head, face palms and finger.
- Lacerated wounds on any part of the body.
- Multiple wounds 5 or more in number.
- Bites from wild animals.

Vaccination schedules with cell culture vaccines

Conventional schedule: 5 doses (0.5 or 1 ml each, depending on the preparation) on days 0, 3, 7, 14 and 28 and an optional booster dose on day 90. Day 0 should ideally be the day of the bite. Injections are given by intramuscular [IM] route in the deltoid region (or anterolateral thigh in small children) and must not be given in the buttock. Dosing is the same for children.

In addition to antirabies vaccine, Class III exposures should additionally be treated with rabies immunoglobulin [RIG] at the same time as the first dose of the vaccine. The usual dose of human RIG is 20 IU/kg and as much as possible should be infiltrated in and around the wound site. Equine RIG dose is 40 IU/kg but it is less preferable to human RIG. Vaccine and immunoglobulin should not be combined in the same syringe or given at the same site

The ideal way to monitor the efficacy of antirabies vaccine is to monitor the antibody titer serologically following vaccination. An inadequate titer calls for booster doses. In practice, vaccination more than 5 y back calls for a fresh course on re-exposure.

In case of individuals with well-documented previous rabies immunization within past 5 year, 2 dose on Days 0 and 3 IM in the deltoid area are sufficient in case of another dog bite.

Multisite schedule: 2-1-1 regimen - one dose (0.5 or 1 ml) is given IM in the right arm and another in the left arm at day 0 followed by one dose given IM in the deltoid region on days 7 and 21. The 2-1-1 schedule includes an early antibody response and may be particularly effective when post-response treatment does not include administration of rabies immunoglobulin.

Intradermal schedule: This is an alternative regimen which costs lower than the conventional IM schedule. It is also known as 2-2-2-1-1 regimen. It consists of one dose [0.1 ml] of vaccine given by intradermal route at each of two sites on days 0, 3, 7 and at one site on days 28 and 90. Separate syringes and needles must be used for each dose. However, intradermal injection should be administered only by staff who have been trained in this technique. Vaccine vials should be stored between 4 C and 8 C after reconstitution and total content should be used as soon as possible.

The target population for pre-exposure prophylaxis has been mentioned earlier. It requires three IM doses in the deltoid area on days 0, 7 and 28, a booster at 1 year and subsequent boosters every 5 years. Pre-exposure vaccination should be postponed in case fever, acute disease, pregnancy and known hypersensitivity to ingredients in the currently available vaccines. Since declared rabies infection is fatal, there is no absolute contraindication to post-exposure vaccination. The adverse reactions to second generation tissue culture vaccines which are now being used in India (e.g. purified chick embryo cell vaccine, Vero cell vaccine and human diploid cell vaccine) are generally infrequent and minor.

GlaxoSmithKline Under Watch

A briefing paper on the global pharmaceutical conglomerate GlaxoSmithKline [GSK] prepared by Oxfam reports that over 1.2 billion people, or about 20% of the world population, do not have access to modern healthcare. One third do not have access to basic medicines. In one year, 110 lakh (11 million) people would die from infectious diseases like malaria, pneumonia, diarrhea, respiratory infections, tuberculosis – an astounding 30000 deaths each day! Almost half of the victims will be children and the vast majority will be poor. Apart from malnutrition and poor living conditions, the major cause of such death would include the high cost of drugs. Peter Singer wrote in the 'The Economist' that if large drug manufacturers like GSK do not do not reduce prices of anti-retroviral for HIV-AIDS patients, then their 'Chief Executive will have the deaths of millions of men, women and children on their hands'.

GSK has manufacturing units in 41 countries, sells products in 140 countries, employs almost a 1,000,000 people and has market capitalization of 107.3 billion pounds. GSK alone now accounts for 7% of the global pharmaceutical market and enjoys \$6.8 billion pre-tax profit yearly. This multinational is now under strong and bitter criticism by international health action organizations. They have found that the GSK empire is expanding on over-pricing of drugs. Despite desperate need and crippling constraints in African health budgets, the report on 'Patents and Prices' shows that GSK's lamivudine, an essential drug for treatment of HIV-AIDS, is on an average 20% more expensive in Africa than in ten advanced industrial countries surveyed.'

GSK has discovered a gold mine in Africa, the continent where most HIV-AIDS patients are found, and this has earned the company a profit of \$588 million by selling only one drug, COMBIVIR, for HIV-AIDS patents in Africa. The company patented three-drug regimen for HIV-AIDS patents and charged \$11,000 a year per patient. This reckless over charging got exposed when Indian companies offered same drugs in generic version at the rate of \$350 per year. For approaching Indian companies to market cheap version of this combination drug,

GSK mobilized 37 other multinational companies to file lawsuits against the South African Government. Protesters started forming international coalition against such reckless profiteering by multinationals which compelled the MNC to withdraw the case. Now under global public pressure, companies like GSK and Bristol-Myers Squibb have reduced prices of anti HIV-AIDS drugs.

GSK is also known to be heavily spending for political purpose. Between 1997 and 1999, GlaxoWellcome spent \$9.6 million and SmithKline-Beecham \$7.9 million for the senators in the USA. GlaxoWellcome ranked 35th in the list of 250 contributors to the republication party in the CIS elections of 2000, donating \$1 million. These generous donations have helped GSK's empire building.

However, in recent times GSK has not been able to conceal all its misdeeds. Wall Street Journal reported that the US Tax Court has started pretrial interview against GSK for deceiving US revenue department for a decade from 1989 for six top selling drugs including the blockbuster ranitidine. GSK had tactfully avoided paying taxes amounting to \$2.4 billion by simply using transfer pricing between GSK [UK] and GSK [USA]. This may land GSK into a lengthy litigation and payment of the full amount or the matter may be negotiated for an out-of-court settlement.

Not only the Government, the Wall Street Journal also reported that AIDS Healthcare Foundation of California has recently filed a case against GSK seeking damages of \$66 million on over charging of antiretrovirals in USA. This organization has also demanded that the patent claim of GSK for the drug zidovudine should be invalidated because of its 'obviousness'. GSK is now in the docks and is under scrutiny by many organizations globally.

Source: Oxford Briefing paper on GlaxoSmithKline.
Dare to lead: Public health and company watch.
London: Oxfam GB, 2002.



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