

Rationalizing pharmacology education

Medical students today are a harried lot. A typical medical school in India proposes to convert a high school student to a basic [MBBS] doctor in 4-5 years of formal study, with an additional year of internship rotating through various clinical departments. During this period, the student is exposed to barely 18 months of training in pharmacology. By the time he graduates and proposes to actually apply this knowledge he has forgotten whatever pharmacology he had learnt and therefore, to survive, he has to depend upon the pharmaceutical company retailer (medical representative) to learn afresh about drugs and to copy the prescribing habits of his peers. Add to this the continued proliferation of drugs in the therapeutic jungle. Over the past decade more than 500 new single ingredient formulations have been added to the pharmaceutical market in India. In contrast, the attrition rate of old molecules through obsolescence is low.

The results of this type of education is not difficult to guess:

- In their formative years, students are forced to mug up the classifications, mechanisms of action, contraindications, and other pharmacological characteristics of a multitude of drugs, mostly with an eye on exams.
- In their clinical years, students are busy memorizing doses and picking up the prescribing habits of their seniors.
- Tendency to prescribe by brand name comes automatically.
- New drugs are automatically assumed to be better drugs and therefore prescribed at every available opportunity.
- Idea about pricing of drugs remains vague, and in many cases the financial burden being imposed on the patient and his family, through the prescription, is not appreciated.
- Seminars and other events sponsored by pharmaceutical companies are looked upon as prime learning opportunity, with the added incentives of free gifts, lunches and dinners.
- Most damaging of all, pharmacology is looked upon as a basic science irritant, with scant relation to therapeutics, that needs to be memorized, regurgitated on the examination answer sheets, and then happily forgotten.

Pharmacology education for medical students in India is therefore not playing an optimum role in their careers. They do not see it as more than a data bank needed for the examination, with much of the data being irrelevant to day-to-day patient care in practice. Furthermore, as the data bank grows prodigally, it is looked upon with awe, generating fear and apprehension rather than encouragement to delve deeper when the need arises. Ten years down the line it is quite possible that medical students will have nervous breakdowns from the sheer volume of data.

Contrast this with what experts have observed. Most doctors do not use a repertoire of more than 200 drugs in their daily practice. Those in some specialties, like anesthesia, surgery, radiology, ophthalmology, etc., use much less. So for practice purposes, it is best to encourage students to adopt the P-drug concept – select your own preferred drugs and know these thoroughly along with the basic standard treatments in your field. Use this knowledge to cover your day-to-day practice demands. If you decide to use a non-standard drug or one falling outside your P-drug basket, familiarize yourself beforehand and then use the drug.

Urgent steps are also needed to reduce the undue burden of the pharmacology syllabus. First and foremost, like the vital-essential-non-essential [VEN] strategy for drug selection, it must be compartmentalized into core-essential-non-essential components. The Medical Council of India [MCI] has provided guidelines in this regard. However, leaving it to individual universities to decide upon the compartmentalization is perhaps not working and MCI can think of doing this task itself with the help of the Indian Pharmacological Society and invited experts. Examiners must be instructed to follow these guidelines while framing questions or examining candidates. Pharmacology practical syllabus must also be modernized, deleting obsolete items such as compounding and including more useful items such as demonstration of dosage forms and drug delivery devices (e.g. nebulizers), monitoring devices (e.g. glucometers), therapeutic problem solving exercises, case studies of prescribing in complex situations, prescription analysis for possible adverse drug reactions and interactions. This may entail inputs from clinical colleagues or taking the students on ward rounds. This would make pharmacology less daunting and more interesting for the already harassed student.

Avijit Hazra

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Drug price games in India

Amitava Guha

The Government of India constituted a Committee on 'Review of Drug Prices Control Order, 1996' to develop a new policy on drug prices. The committee traveled to several countries in the west to gather knowledge on their system of drug pricing. Whether this travelling was necessary is a moot point, since in these developed age of informatics one can gather such information without going abroad. Leaving this aside, what was their observation? The committee mentioned in their report that all developed countries have some form of control on prices of medicines, directly or indirectly. However, they ignored this very observation totally while making their own recommendations. They directed that control on prices should be gradually abolished and the present basket of price controlled drugs should be immediately shrunk so that the rigor of price control does not affect production. To reach such a conclusion, why did the committee ostensibly explore systems prevailing in the developed countries, particularly when they were destined to follow the dictates of the pharmaceutical industry?

We need to explore inside our own country whether price control has prevented the industry from making profit. For that purpose we need to find out what profit margin exists in selling drugs in India. It is also required to study how far the existing Drug Prices Control Order [DPCO], however small its coverage in different therapeutic segments, has been effective in controlling of prices.

The review committee has focused on some areas and expressed their concern but have not provided any solution. They expressed serious concern that the same drugs are often sold, in different brand names, at different prices. The price range from the lowest priced to the highest priced brand can be singularly wide. It cannot be denied that the brand with the lowest price also earns profit for its manufacturer, otherwise it would not have been on the market. It is also observed that brand leaders (highest selling brands) are generally sold at higher price.

Table 1. Price differential of selected brands in the Indian pharmaceutical market

Drug & packing	Higher priced brand	Price [Rs.]	Lower priced brand	Price [Rs.]	Price difference [%]
Amlodipine Tab 5 mg X 10	STAMLO [Dr. Reddy's]	24.75	AMADAY [Ajanta Pharma]	7.50	230.0
Cephalexin Cap 500 mg X 10	CEFF [Lupin]	123.27	BLUCEF [Bluecross]	60.00	105.5
Ethambutol Tab 400 mg X 10	COMBUTOL [Lupin]	21.37	COXYTOL [Stadmed]	6.79	214.0
Isosorbide mononitrate Tab 20 mg X 10	ISMO [Nicholas Piramal]	27.00	ANGIMON [Globus]	4.20	542.9
Pyrazinamide Tab 750 mg X 10	PYZINA [Lupin]	66.20	PIRALDINA [Pharmed]	20.48	223.0

Source: Price list of different companies.

Trade margins

The pharmaceutical industry in India always complains of low or no profit in production and selling of drugs due to price control and in fact, they have tried their best to stall any kind of price control on medicines from the very inception of DPCO. They have even sometimes tried to pressurize the government for waiver of DPCO totally by reducing production / supply of a large number of essential drugs. Even now the industry blames the DPCO as a monstrous deterrent to the growth of the industry.

In the DPCO of 1995, in clause 19, which has not yet been altered, it is stated that: "Prices of formulation sold to the dealer - A manufacturer, distributor or wholesaler shall sell a formulation to a retailer, unless otherwise permitted under the provision of this Order or any order made thereunder, at a price equal to the retail price, as specified by an order or notified by the Government, (excluding excise duty, if any) minus

sixteen per cent thereof in the case of Scheduled drugs."

The above was applicable only to 76 drugs initially and later, it was reduced to 63 drugs. But for drugs outside the price control order, the industry was allowed to fix trade margin with the traders associations. It was an agreed principle that the wholesale margin would be 10% and the same for retailers would be 20% maximum.

However, recent trends show that most of the companies are giving a large amount of discounts to the trade apart from the government norm and also beyond the agreed norm. Apart from the usual trade margins, almost all companies throughout the year give extra offers, usually in the form of free bonus for many of their products. These offers vary from 10 percent to more than 100 percent. Table 2 shows that even for price controlled category of drugs, apart from the stipulated 16% margin, trade bonus is given. For example, amikacin sulfate

which was under the price controlled category, apart from the usual 16% margin, for purchase of 100 vials, 125 vials are given free!

For all newly introduced drugs, the industry always has very high trade offer by way of additional free incentives. It is obvious that new drugs are only introduced if they have high profit margin and equally obviously the cost for consumers is high. The profit margin of such drugs are so high that whenever a new drug is introduced, a large number

of companies jump to market it together and promote it vigorously. In marketing terms, this is creating a high noise level which hopes to bewilder the prescribers into dishing out prescriptions for the new drug. The prices of these drugs are, however, brought down soon simultaneously with the high amount trade offer over and above the usual trade margin. This has two implications - the fabulous trade incentives given never reach the end users and by free offers the state governments lose sales tax revenue.

Table 2. Additional trade incentives for select products in the Indian pharmaceutical market

Drug	Company	Additional trade incentive
Amikacin 500 mg vial	Bio Drug	125 %
Ceftriaxone sodium 1 g vial	Nicholas Piramal	28.6 %
Ceftriaxone sodium 1 g vial	Bio Drug	60 %
Chloramphenicol range	Nicholas Piramal	20 %
Ciprofloxacin 100 ml infusion	Ranbaxy	114 %
Gatifloxacin Infusion	Nicholas Piramal	100 %
Gentamicin 80 mg vial	Nicholas Piramal	20 %

Additional trade discounts offered to the wholesalers: (July, '02 to September, '02)

Apart from the above, a serious phenomenon has developed recently. Many companies, in addition to the said benefits to the trade, are giving unannounced trade incentives. In order to reach their arbitrarily fixed business targets, many companies offer trade benefits according to local conditions. To some wholesalers they offer some more incentives for purchase of large quantities. Some wholesalers use this opportunity to dump the drugs where interstate differences in sales taxes exist. Thus a type of black marketing has started functioning. It was even found that some companies tactfully evade central excise duties and sneak out unscrupulous methods to market their non-excise paid drugs to the large wholesale markets like in Kolkata (Baghree market), Mumbai (Princep street market), Delhi (Bhagirath place market), Agra, Banaras, etc. This unhindered trail has also allowed influx of spurious drugs with serious connotations for public health. Even the Drugs Controller General of India, in a confidential circular, has alerted the state Drug Controllers about a huge cache of spurious

drugs sized in the wholesale market of Delhi. This also has become a concern for the industry to the extent that it has decided to appoint a group headed by former police official Mr. K. P. S. Gill to act as watchdog. It remains to be seen whether these steps taken by the industry and the government are effective in curtailing the spurious drugs menace.

Confusion over 'branded generics'

The other significant gray area in pricing is generic drugs where a total anarchy exists. Many large and medium companies are selling their drugs as 'branded generics'. These drugs are not promoted like simple branded drugs. These drugs are given a brand name but the generic name is focused mostly and since they enjoy certain duty exemptions, they are sold mostly in a manner as if they are generics. Prices offered to the end users are similar to the usual branded drugs but the prices offer to the wholesalers are phenomenally low. The industry states that these drugs are sold to institutions as bulk supply and generally under rate contract.

Table 3. Margin of profit offered for selected 'branded generic' drugs in the Indian market

Drug	Brand [of tablet formulation]	Company	Unit	Sale Price [Local taxes extra] to wholesalers	Maximum retail price to consumers	Price difference [%]
Amlodipine 5 mg	AGINAL-5	Alembic	1 X 10	2.90	17.60	506.9
Amoxicillin 250 mg	ALMOX DT	Alkem	10 X 10	57.28	247.00	331.2
Cetirizine	CETRAL	Alembic	1 X 10	2.20	25.60	1063.6
Cisapride 10 mg	CISACHEM	Alkem	25 X 10	119.78	902.5	653.5
Diclofenac 50 mg + Paracetamol 325 mg	ZEDONAC	Alkem	20 x 10	51.60	320.00	520.2
Nimesulide 100 mg	PYRIMIDE	Alkem	25 X 10	39.10	625.00	1498.5
Nimesulide 100 mg	PYRIMIDE	Alkem	25 X 10	60.90	725.00	1090.5
Nimesulide 100 mg	PYRESTAT	Ranbaxy	1 X 10	1.70	25.00	1370.6
Piroxicam 20 mg	OXICAM DT	Alembic	1 X 10	3.45	31.50	813.0

- Compiled from the price lists (as circulated by various companies) collected from the wholesalers.
- Prices are in Indian Rupees.

Unfortunately, these drugs are also openly sold in the retail market and in the packaging the retail prices are clearly mentioned, which of course are similar to branded drugs. Trade margins offered for these drugs remain anywhere from 70 to 1700%. It may be noted that these drugs are not obsolete and despite such high margins, the industry can retain profit. Chronicle Pharmabiz, a widely circulated pharmaceutical industry and trade periodical in India, informs that the industry has voluntarily announced that they may stop selling such branded generic drugs. It is thus established that a huge profit margin exists even for old widely sold drugs. Table 3 gives examples of profit margins associated with 'branded generics'

Rising drug prices for consumers

The price rise trend for medicines for Indian consumers remains high. In recent years this trend has escalated significantly across many therapeutic segments. When, for some essential drugs, the price escalation has been 50 to 110% in a year, it becomes obvious that the DPCO has failed to control prices. One suspects that this fact has been deliberately ignored by the review committee. CDMU maintains serial data to monitor prices of different brands in different therapeutic groups. Some instances are given in Table 4 from the data bank.

Table 4. Price escalation of selected products in the Indian pharmaceutical market

Product	Drug / Therapeutic group	Manufacturer	Strength & Pack	Retail 1998	Price 2002	Per cent increase
AVIL tablet	Chlorpheniramine	Aventis	25 mg X 10	1.80	2.64	46.67
BENADRYL capsule	Cough Syrup	Parke-Davis	25 mg X 10	19.86	20.32	2.32
BEPARINE injection	Heparin	Biological E	5000 IU / ml - 5 ml	67.94	98.00	44.24
BETADINE ointment	Povidone iodine	Win Medicare	15 g	18.85	29.75	57.82
BRICANYL inhalation	Terbutaline	Astra-IDL	200 dose MDI	75.81	86.60	14.23
CALPOL liquid	Paracetamol	Burroughs Wellcome	120 mg / 5 ml - 60 ml	11.67	13.84	18.59
DIGENE liquid	Antacid	Knoll	200 ml	17.50	30.50	74.29
DOLONEX DT tablet	Piroxicam	Pfizer	20 mg X 10	24.64	34.32	39.29
GARDENAL tablet	Phenobarbital	Rhone-Poulenc	30 mg X 10	5.04	8.15	61.71
ISORDIL tablet	Isosorbide dinitrate	Wyeth Lederle	10 mg X 100	12.10	30.50	152.07
OVRAL-L tablet	Oral contraceptive	Wyeth Lederle	21	14.20	30.00	111.27
PARAXIN capsule	Chloramphenicol	Nicholas Piramal	500 mg X 6	20.00	21.50	7.50
PRACTIN tablet	Cyproheptadine	Wockhardt- Merind	4 mg X 10	5.45	9.90	81.65
PROFASI injection	Human chorionic gonadotropin	Serum Institute	5000 IU X 3	1078.35	1278.63	18.57
PUBERGEN injection	Human chorionic gonadotropin	Uni-Sankyo	5000 IU X 1	312.50	385.00	23.20
PYZINA tablet	Pyrazinamide	Lupin	750 mg X 10	37.00	49.50	33.78
RABIPUR injection	Rabies vaccine	Aventis	Unit dose vial	250.00	294.00	17.60
SHIELD ointment	Antihemorrhoidal	Glaxo	15 g	18.85	32.25	71.09
TEGRETOL tablet	Carbamazepine	Novartis	200 mg X 10	17.83	18.47	3.59
TRYPTOMER tablet	Amitriptyline	Wockhardt- Merind	25 mg X 10	11.31	17.90	58.27
UNICONTIN tablet	Theophylline	Modi Mundi Pharma	400 mg CR X 10	33.10	44.00	32.93
UNIWARFIN tablet	Warfarin	Unichem	5 mg X 10	5.30	22.45	323.58
WYSOLONE tablet	Prednisolone	Wyeth Lederle	10 mg X 10	13.20	14.72	11.52
ZOSTA tablet	Simvastatin	USV	20 mg X 10	58.00	79.50	37.07

Data source: CIMS 61 Apr-Jun 1998 and CIMS 77 Apr-Jun 2002

It is thus painfully clear that prices of many drugs are rising and in many instances they have more than doubled. This is not seen with any other commodity. It is also found that even in the price controlled category, margin of profit remains high. The review committee has mentioned ORG-MARG retail survey in many places of their report. One can find in the last chapter of the same report list of drugs for which additional trade incentives are offered by almost all companies. The committee

also ignored this. The question naturally arises for whose purpose was the committee set-up. It is also surprising that not a single member has dissented to the recommendations finally made by the committee. Whose interest has the committee served – public health or drug industry? When a child, woman or man dies because of failing to secure medicines owing to high price, will it be unjust to attribute part of the responsibility for this to each member of the committee?

Cholera

Amitava Sen

Cholera is an acute diarrheal disease caused by *Vibrio cholerae*, a gram-negative comma shaped bacterium. The pathogen has two types biotypes, namely classical and El Tor. The clinical spectrum of the disease varies widely – ranging from asymptomatic infection to severe debilitating disease characterized by sudden onset of profuse watery diarrhea, vomiting, rapid dehydration, muscular cramps and suppression of urine, that may lead to hypovolemic shock and death if not treated appropriately. The advent of oral rehydration therapy, however, has simplified the management of cholera and substantially reduced the mortality due to dehydration.

Cholera occurs in both epidemic and endemic form in tropical countries. Epidemics of cholera are characteristically abrupt and often present an acute public health problem. They have a high potential to spread fast and cause deaths. Endemic cholera undergoes seasonal fluctuations with variations between countries and even between regions of the same country.

Since the introduction of cholera El Tor biotype in India in 1964, the distribution of this disease has changed considerably in our country. West Bengal has lost its reputation as the home of cholera as many of the states which never had cholera or were free from it for a long time got infected and became endemic foci of El Tor infection. A new strain of cholera, namely *V. cholerae* 0139, emerged in India in 1992. It spread west to Pakistan and East to China and the early months of 1993 caused an estimated 1,00,000 cases and 1000 deaths in southern Bangladesh. The pathophysiology and clinical course of disease caused by *V. cholerae* 0139 Bengal, have not been characterized well but have been reported to be similar to those of *V. cholerae* 01.

Epidemiology

V. cholerae multiplies in the lumen of the small intestine and produces an exotoxin, which induces diarrhea through its effect on the adenylate cyclase-cyclic AMP system in mucosal cells of the small intestine. There is no effect on any tissue other than the intestinal epithelial cells. Man is the only reservoir of cholera infection. An infected individual may be a case or carrier – cases range from inapparent infection to life-threatening disease. However, it is the mild and symptomatic cases that play a significant role in maintaining the endemic reservoir. Carriers are usually temporary, rarely chronic. They also make an important contribution to the reservoir of infection. Since carriers excrete fewer cholera vibrios than clinical cases they are best detected by bacteriological examination of the purged stool. There are four types of cholera carriers

- Preclinical or incubatory carrier – since the incubation period of cholera is short [1-5 days], incubatory carriage is of short duration. These carriers are potential patients.

- Convalescent carrier - patients who have recovered from an attack of cholera may continue to excrete vibrios during the convalescence period of 2 to 3 weeks. Convalescent state has been found to occur in patients who have not received antibiotic treatment. Convalescent carriers can often become chronic and long-term carriers.
- Contact or healthy carrier – this is the result of subclinical examination contracted through association with a source of infection. The duration of the contact carrier state is usually less than 10 days. Contact carriers probable play an important role in the spread of cholera.
- Chronic carrier – this state occurs infrequently. The longest carrier state known to occur is more than 10 years.

The period of communicability in a case of cholera is 7 - 10 days. Convalescent carriers are infectious for 2 - 3 weeks, the chronic carrier state may last for a month upto 10 year or more.

In addition to direct contact, which is an important mode of transmission in developing countries, cholera transmission may occur from man to man through fecally contaminated water and contaminated food and drinks. Uncontrolled water sources like wells, lakes, ponds, streams, river, etc., may be particularly dangerous during epidemics. Ingestion of contaminated food and drink has been associated with major outbreaks of cholera. Bottle feeding could be a significant risk factor for infants.

Cholera affects all ages and both sexes. In endemic areas, attack rate is highest in children. Movement of population [e.g. pilgrimages, marriages, fairs and festivals] result in increase risk of exposure to the infection. The incidence of cholera tends to be the highest in lower socioeconomic groups and this attributed mainly to poor hygiene. Regarding immunity, natural infection confers quite effective immunity. Vaccination, as of now, gives only temporary, partial immunity for 3 - 6 months.

Clinical features

The severity of cholera depends on the rapidity and duration of fluid loss. A typical case of cholera shows three stages:

- Stage of evacuation: This is characterized by the onset of abrupt, profuse painless watery diarrhea followed by vomiting. The stools have a characteristic 'rice water' appearance.
- Stage of collapse: The patient soon passes into a stage of collapse due to dehydration. The classical signs are sunken eyes, hollow cheeks, subnormal temperature, loss of skin turgor, feeble pulse, hypotension, and reduced urine output. The patient becomes restless and complains of intense thirst and cramps in the

legs and abdomen. Shock may appear due to dehydration and acidosis can also result. Death occurs if the patients is not adequately rehydrated.

- Stage of recovery: If death does not occur, the patient begins to show signs of clinical improvement. Blood pressure begins to rise, temperature returns to normal and urine secretion is re-established. However, if anuria persists the patient may die of renal failure despite apparent recovery from collapse.

Today, the classical stages of cholera occur only in 5 to 10% of cases. In the rest, the disease tends to be milder, characterized by diarrhea with or without vomiting or marked dehydration. As a rule mild cases recover in one to three days and may not even be recognized as cholera.

Treatment

Cholera is simple to treat; only the rapid and adequate replacement of fluids and electrolytes is required. Antimicrobials have an important adjunctive role. Mildly dehydrated patients, who account for over 90% of cases can be treated at home with oral rehydration fluid [ORS]. Severely dehydrated patients may require intravenous fluid replacement and should be shifted to nearest health facility. If possible, they should received oral rehydration on the way to hospital or treatment

centre. Ever since the introduction of ORS by WHO in 1971, it has become the mainstay of treatment of mild to moderately dehydrated cholera patients. Oral fluid replacement is based on the observation that glucose orally enhances the intestinal absorption of salt and water and is capable of correcting the electrolyte and water deficit. The composition of ORS includes sodium chloride – 3.5 g, trisodium citrate dihydrate 2.9 g, potassium chloride 1.5 g, glucose 20 g made up in 1 L of potable water. Earlier, the ORS bicarbonate variety was used. However, the use of ORS citrate results in less stool output, specially in high output diarrhea, probably reflecting a direct effect of trisodium citrate in increasing intestinal absorption sodium and water. It is noteworthy that many over the counter ORS formulations do not contain electrolytes in optimum proportion. Packets of WHO recommended ‘oral rehydration salts’ are freely available at all primary health centers, subcenters and hospitals in India, free of cost. The contents of the packets are to be dissolved at one go in one liter of drinking water, the solution should be made fresh daily and used up within 24 hours. It should not be boiled or otherwise sterilized. In developing countries, cholera and other diarrheal diseases tend to cause more dehydration in children under the age of 5. Therefore it is very essential to initiate the treatment with ORS as early as possible.

Table 1. Guidelines for oral rehydration therapy [for all ages] during the first four hours

Age	< 4 months	4-11 months	12-23 months	2-4 years	5-14 years	15 years or over
Weight [kg]	< 5	5-7.9	8-10.9	11-15.9	16-29.9	30 or over
ORS needed [ml]	200-400	400-600	600-800	800-1200	1.200-2.200	2.200-4.000

The patient's age should be only be used if weight is not known. The approximate amount of ORS required in ml may be calculated by multiplying the patient's weight [in kg] by 75.

Table 2. Recommended dosing for IV fluids in cholera in children

Age	First 30 ml/kg body weight in	Then give 70 ml/kg body weigh in
Infants	1 hour	5 hours
Older children	30 minutes	2½ hours

The initial rehydration should be fast until an easily palpable pulse is present. Reassessment must be every 1 to 2 hours. When the condition of the patient improves he or she can be given ORS. If dehydration persists, the IV infusion is given more rapidly.

Mothers should be taught how to administered ORS solution to their children. It is best to if a nurse or a trained health worker can give an initial demonstration. Following are to be noted.

- For children under two years, a teaspoon-full every 1 to 2 minutes is to be given. Older children should be encouraged to take frequent sips out of a cup. Adults may drink as much as they can. Efforts are to be made to give the estimated requirement of ORS within a 4 hour period.
- If the child vomits, wait for 10 minutes then try to give the solution again slowly i.e. a spoon-full every 2 to 3 minutes.
- If the child wants to drink more ORS solution than the estimated amount and does not vomit, there is no harm in giving more.

- If the child refuses to drink the required amount and the signs of dehydration have disappeared, then rehydration is complete.
- In breast-fed children, breast feeding should be continued along with ORS.
- For non-breast fed infants under 6 months, an additional 100 to 200 ml of water may be given during first 4 hours.

For severely dehydrated cases, where the patient is unable to drink or in a stage of imminent shock, intravenous [IV] rehydration is essential. The recommended fluids are:

- Ringer's lactate solution [Hartman's solution]: It supplies adequate concentration of sodium and potassium and other essential components for correction dehydration

- Diarrhea Treatment Solution [DTS] is recommended by WHO as an ideal poly-electrolyte solution. It contains in 1 liter, sodium chloride 4 g, sodium acetate 6.5 g, potassium chloride 1 g and glucose 10 g.

Use of antibiotics

Although not necessary for cure, the use of an antibiotic to which the cholera vibrio is susceptible will diminish the volume and duration of fluid loss and will hasten clearance of the organism from stool. Single dose of doxycycline [300 mg] or tetracycline [2 g] is effective in adults. But tetracyclines are not recommended for children under 8 years of age and pregnant patients. Emerging drug resistance is an ever present concern. It is to be noted that the *V cholerae* 0139 has been resistant to doxycycline but susceptible to quinolones, erythromycin and ampicillin. For adults with cholera, in an area where tetracycline resistance is prevalent, ciprofloxacin either in a single dose [30 mg / kg body weight, but not exceeding 1 g] or in a short course [15 mg / kg body weight] of 3 days [not exceeding a total daily

dose of 1 g]. Erythromycin [40 mg / kg body weight in three divided doses for 3 days] is also a clinically effective substitute. WHO recommends erythromycin as the first alternative to tetracycline. For children, furazolidone has also been recommended. It is the antibiotic of choice for pregnant woman.

Conclusion

Although cholera can manifest as a life-threatening diarrheal illness, timely and appropriate intervention can considerably reduce the mortality and morbidity burden. The most effective prophylactic measure is proper health education, with emphasis on timely and appropriate use of oral rehydration therapy. The community must be made aware of the importance of early reporting of cholera cases. At the individual level, the habit of hand washing after defecation and before eating, consumption of only safe water and hygienic food practices, can do a lot in reducing the risk of cholera and breaking the transmission cycle if there has been a case in the family or neighborhood.

History of the hypodermic syringe

The history of the hypodermic syringe is complex. Investigators in the 17th century, including Sir Christopher Wren (1632–1723), used trocars and bladders for intravenous injections on dogs. But the modern hypodermic syringe is derived from attempts to deliver medication near the site of the pathology. In the 1830s, French physicians were forcing morphine paste down grooved trocars to treat neuralgia, or implanting subcutaneous pellets with darning needles, but these devices could hardly be called syringes. In 1844, Francis Rynd (1803–61) of Dublin made subcutaneous injections, also for neuralgia. A slender trocar and cannula, it was inserted subcutaneously and the trocar retracted by means of a spring. Narcotic liquid descended from the hollow handle into the puncture site as the instrument was withdrawn. The Edinburgh physician Alexander Wood (1817–84) was apparently first to publish on subcutaneous therapeutic injection of drugs, in 1855. He used one of the “elegant little syringes constructed by Mr. Ferguson of Giltspur Street”, and was championed as the inventor of the hypodermic syringe, especially by those anxious that the honor should not go to Charles Gabriel Pravaz (1791–1853), a veterinary surgeon of Lyons. Pravaz attached a hollow metal needle to an all-metal syringe barrel to inject aneurysms with a sclerosing agent in 1852. Quickly modified with a glass barrel, and a screw thread instead of a slip joint, this was perhaps the nearest precursor to the modern hypodermic syringe. By the end of

the 19th century, syringes like these were widely available. Plungers were still of leather (or asbestos) and had to be protected from dehydration. Sir George Buckston Browne (1850–1945) had a travelling syringe, which he carried in his walking stick, but the number of preparations available for injection in his day was small.

In 1905, only 20 (1.8%) of the 1039 drugs in the United States Pharmacopoeia were injectable. But this proportion soon rose, and in the 1920s insulin brought a whole new market for manufacturers. “Automatic” syringes, devised in the 1870s with a spring activated plunger, were soon revamped for nervous diabetics. The disposable syringe has unmistakable military origins. Many incorporated “single shots” of drugs or vaccines and had complex delivery mechanisms. The AMPIN, for example, devised in 1948, contained a glass ampoule attached to a needle via flexible tubing and filter. The ampoule had to be broken after the needle was inserted in the patient. Compressed inert gas in the upper part of the device was then released to force the medication down the needle. This was apparently a modification of apparatus used for blood transfusion in the Spanish Civil War. Ubiquitous cheap, sterile plastic syringes, and disposable needles, have done away with all such contraptions, making injecting drugs easy - some would say all too easy.

Adapted from: Lawrence G. The hypodermic syringe. *Lancet* 2002; 359. [Online version accessed May 25, 2002].

New drugs approved by Drugs Controller General of India during the period January to June, 2002

Name of the drug	Therapeutic category	Name of the drug	Therapeutic category
Abacavir	Antiretroviral	Mifepristone	Progesterone antagonist
Alprostadil [Inj]	For erectile dysfunction	Miltefosine	Kala-azar
Apraclonidine [ED]	Antiglaucoma agent	Mizolastine	Antiallergic
Bicalutamide	Anticancer	Montelukast	Antiasthmatic
Bimatoprost [ED]	Antiglaucoma agent	Nadifloxacin [Top]	Antibacterial [For acne]
Dexarazoxane [Inj]	Cardioprotective agent	Nateglinide	Antidiabetic
Divalproex sodium	Antiepileptic	Quetiapine	Antipsychotic
Famciclovir	Antiviral	Tamsulosin	For BPH
Isotretinoin	Retinoid [For acne]	Thymogen [Inj]	Anticancer
Itopiride	GI prokinetic agent	Tizanidine SR	Multiple sclerosis
Lercanidipine	Antihypertensive	Tranexamic acid	Antifibrinolytic
Loteprednol etabonate [ED]	Steroid [For ophthalmic use]	Vimocetine	Vasodilator
Meropenem [Inj]	Antibiotic [Beta-lactam]	Zaleplon	Sedative-hypnotic
Mesalazine SR	Inflammatory bowel disease	Ziprasidone	Antipsychotic

Abbreviations: BPH = Benign prostatic hyperplasia; ED = Eye drop; GI = Gastrointestinal; Inj = Injection; SR = Sustained release; Top = Topical use

Source: Office of State Drugs Control – West Bengal

It is to be noted that this list is exclusive of new fixed dose combinations and products approved for veterinary use. Further, approval of a new drug does not necessarily result in immediate introduction of the corresponding formulation in the Indian pharmaceutical market, whether imported or indigenously manufactured. Even if available, prescribers should exercise due caution in the use of these drugs for obvious reasons, particularly for those drugs which are new in the global pharmaceutical market too.

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