

Dialogue on Diarrhoea

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Drugs and childhood diarrhoea

Oral rehydration therapy should be the priority treatment for childhood diarrhoea. Ninety five per cent of acute childhood diarrhoea, whatever the cause, can be successfully treated with ORT and continued feeding, and does not require treatment with drugs. Despite widespread promotion of this message, doctors continue to prescribe ineffective, expensive and unnecessary drugs to treat diarrhoea; families continue to ask their doctors for them or buy them over the counter from pharmacists; and manufacturers continue to promote and market a wide range of anti-diarrhoeals. In many countries, drugs are used more than ORT to treat diarrhoea (see pages 6 and 7). On pages 2, 3 and 4, *DD* reviews some of the antibiotics most

commonly used to treat diarrhoea, explaining why they are not appropriate for acute diarrhoea in children. The next two issues will include reviews of antimotility drugs and adsorbents.

Unnecessary prescribing

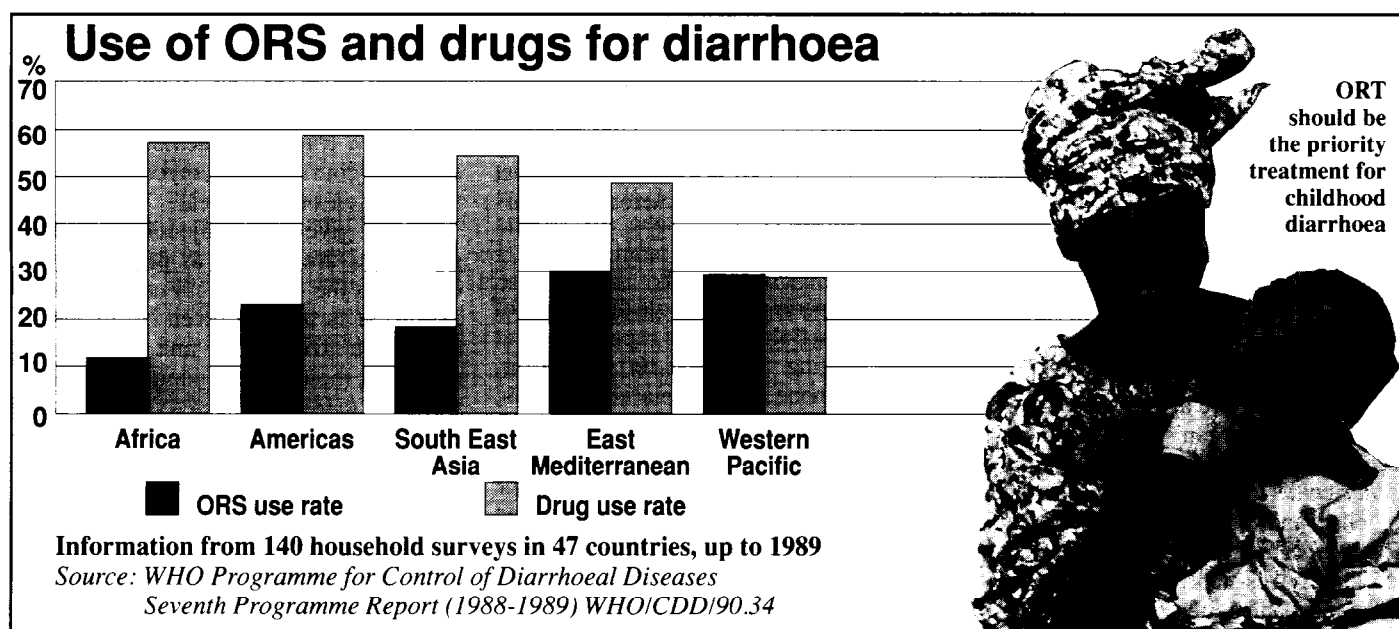
Unnecessary prescribing has several important disadvantages. First, giving powerful drugs to small children does not stop the diarrhoea, may cause dangerous side effects and can result in families neglecting to rehydrate and feed a sick child. Second, drugs are expensive for families and for the health system. The resources saved by reducing unnecessary prescribing could be better used in other ways and the drugs saved for when they

are really needed. Third, in some countries, widespread use of antimicrobials has led to high levels of antibiotic resistance – this means that the antibiotics are no longer effective. On page 5, *DD* describes how antibiotic resistance develops and why it is a serious problem.

Working together

To reduce inappropriate use of drugs for diarrhoea, a co-ordinated response is needed. This involves legislation, training and education of doctors and the public, and ensuring that messages about drug treatment for diarrhoea are consistent. The article on page 7 describes the co-ordinated approach being taken in Peru, where the Ministry of Health, health professionals and activists are working together to tackle the problem of widespread over-use of anti-diarrhoeal drugs in children.

KME, WAMC and KA



In this issue:

- Drug reviews and resources
- Antibiotic resistance
- Reports from Peru, Pakistan and Indonesia

AHRTAG

Appropriate Health Resources &
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Drugs and diarrhoea

In most cases of childhood diarrhoea, drugs are unnecessary and inappropriate. The WHO CDD programme has reviewed the literature on the efficacy and side effects of the most widely used drugs. In this issue *DD* previews the information available on three types of antimicrobial agents – neomycin, streptomycin and hydroxyquinolines.



Neomycin

Neomycin, an antibiotic contained in many oral anti-diarrhoeal preparations, has not been proved to be effective in the treatment of acute diarrhoea. Neomycin given by mouth has been associated with toxic effects on the gut and may worsen or prolong diarrhoea. Widespread use of antibiotics such as neomycin can increase antimicrobial resistance. Oral preparations containing neomycin are not recommended for use in the treatment of diarrhoea.

Formulations

Neomycin is an aminoglycoside antibiotic used either alone or in combination with intestinal adsorbents, antimotility agents, or other antibiotics*.

Pharmacology

Neomycin is classified as non-absorbable – most of a dose given by mouth is excreted unchanged in the stool, although some absorption does occur in the gastrointestinal tract. What is absorbed is primarily excreted in the urine.

How it works

Neomycin is rapidly bactericidal (it kills and inhibits reproduction of bacteria quickly). It is active against most aerobic Gram-negative organisms (see box) and staphylococci, but resistant strains of *Escherichia coli*, *Klebsiella*, *Proteus*, *Shigella*, and *Salmonella* are common. Streptococci and Gram-positive bacilli are also largely resistant.

The mechanism of resistance of Gram-negative organisms to neomycin can also confer resistance to other antibiotics (see page 5). These resistance factors, which can be transferred between bacteria, can sometimes also convey the ability to pro-

*With all drug preparations it is important to look carefully at the contents or ingredients as well as the brand name.

1 Diarrhoea can be caused by:

- Viruses – mostly rotavirus
- Bacteria – virtually all are Gram-negative aerobic pathogens
- Protozoa – especially *Cryptosporidia*, *Giardia* and amoeba

2 Antibiotics are, in general, only useful for bacteria. They are ineffective for viruses and have very limited value for protozoa, e.g. tetracycline is partly effective for amoeba. There are, however, anti-protozoals for amoeba and *Giardia*.

3 Antibiotics are ineffective for many food poisoning *Salmonella*. They are not practical for other bacterial diarrhoeas, except cholera and shigellosis, because one cannot determine clinically what bacterium is involved, if any, and thus what antibiotic to give.

duce enterotoxin. Widespread use of neomycin may therefore not only increase the frequency of antibiotic resistant microorganisms, but may also help bacteria that cause diarrhoea through enterotoxin to survive and spread.

Efficacy

Studies of neomycin in acute diarrhoea (of unknown aetiology) have reported 'cure' rates ranging from 50-100 per cent. However, none included placebo controls, and since most acute diarrhoeas are self-limiting, these reports of 'cures' are not meaningful.

One double blind, placebo-controlled trial (see box, page 4) of neomycin in acute diarrhoea indicated that neomycin may actually increase the severity and prolong the duration of the disease. There are no reported trials assessing neomycin in the treatment of diarrhoea caused by enterotoxigenic, entero-adherent, enterohaemorrhagic or entero-invasive *E. coli*. Some uncontrolled clinical observations have reported good response of EPEC infections to neomycin therapy, but others have noted little difference between neomycin and supportive therapy alone.

The role of some antibiotics in treating shigellosis is well established, but not all antibiotics are equally effective. Some early uncontrolled studies reported good results from treating shigellosis with oral aminoglycosides. Others showed bacterial and clinical cure rates of less than 50 per cent, and two suggested that streptomycin and neomycin were no better in shigellosis therapy than simple supportive care. A double blind trial comparing neomycin with ampicillin provided further evidence of the ineffectiveness of non-absorbable antibiotics such as neomycin in shigellosis treatment.

Studies have also shown that antibiotic therapy can actually prolong the carrier state in *Salmonella* gastroenteritis, and clinical relapse may be more frequent in patients treated with antibiotics. Placebo controlled trials of neomycin, ampicillin, and amoxycillin have confirmed that these antibiotics are ineffective in treating *Salmonella* gastroenteritis.

Adverse effects

Neomycin can damage the structure of the gut and interfere with its normal function. It can cause malabsorption of fats, sugars and calcium. After as little as three days, destruction of the microvilli lining the surface of the small intestine can appear; and after seven days, invasion of the sub-mucosal layer of the small bowel by eosinophilic white cells has been observed. Controlled trials have demonstrated that extended courses of neomycin prolonged the duration of diarrhoea.

When given by injection, aminoglycosides are known to produce toxic effects on the kidneys and ears. Because neomycin is usually given by mouth in diarrhoea treatment and is poorly absorbed, these complications are uncommon, but there have been reports of toxic effects with prolonged therapy or high doses, especially when kidney function is already impaired.

Source: the text on pages 2 to 4 has been adapted by *DD* from draft material prepared by the Control of Diarrhoeal Diseases Programme of the World Health Organization (WHO). A series of nine reviews is in preparation covering drugs commonly used in the treatment of diarrhoea. They will be grouped in three sections: antimicrobials, antimotility drugs and adsorbents, and published together as a WHO publication entitled *The rational use of drugs in the management of acute diarrhoea in children*, to be available early in 1991 from: CDD/WHO, 1211 Geneva 27, Switzerland.

Drugs and diarrhoea

Formulations and drug interactions

Neomycin is usually sold in combination with a variety of adsorbents or other antibiotics. None of these combination products has been shown to be effective in clinical trials. The hydroxyquinolines contained in many of them have been withdrawn and prohibited in many countries because of their dangerous effect on the nervous system, while kaolin and pectin components can interfere with the absorption of certain useful antibiotics and antimalarials.



Streptomycin

Streptomycin (or dihydrostreptomycin) has no proven value in the treatment of any diarrhoea. It may increase the severity or prolong the duration of some cases of diarrhoea. The widespread use of antibiotics such as streptomycin promotes resistance to a variety of antimicrobial agents. Streptomycin (and dihydrostreptomycin) are not recommended for the treatment of diarrhoea.

Formulations

Streptomycin is an aminoglycoside antibiotic which is important in tuberculosis (given by injection), but which is also widely marketed as an oral preparation for diarrhoea treatment. It is often combined with a variety of adsorbents, vitamins, or other antibiotics. Dihydrostreptomycin is a related antibiotic with similar properties but greater toxicity. Despite the absence of studies on its efficacy in diarrhoea, it is also widely marketed as a diarrhoea treatment.

Pharmacology

Streptomycin is not absorbed from the gastrointestinal tract, except when the mucosa is damaged. Most of the drug is excreted unchanged in the stool.

How it works

Like neomycin, streptomycin kills and inhibits reproduction of many bacteria quickly. Streptomycin is extremely useful in the treatment of tuberculosis. It is also active against aerobic Gram-negative bacteria and some strains of *Staphylococcus aureus*. Extensive use of streptomycin to treat other infections is associated with the development of widespread antimicrobial resistance. Current reports of streptomycin resistance



J. Mohr/WHO

Families and health workers need to know that ORT, not drugs, should be given for most childhood diarrhoea.

range from 36 per cent for *Escherichia coli* and 67 per cent for *Shigella* in Boston, USA, to almost 100 per cent for enteropathogenic *E. coli* in New Delhi, India. As with neomycin, widespread use may also lead to selection of organisms with enhanced pathogenicity.

Efficacy

Most trials to assess the efficacy of oral streptomycin in the treatment of acute diarrhoea have been uncontrolled, hence the results are not useful. In one controlled trial, streptomycin therapy was associated with increased severity and duration of diarrhoea.

Despite the lack of evidence of efficacy from controlled clinical trials, streptomycin was widely used in the 1950s to treat diarrhoea due to *Escherichia coli*. Since the emergence of widespread resistance, other antibiotics have been used to treat *E. coli* infections.

Early uncontrolled trials suggested that streptomycin might be effective to treat

shigellosis; but other reports showed high failure rates or detected no difference between streptomycin and supportive therapy alone. Some treatment failures have been attributed to high rates of microbial resistance, but failure rates of 60 per cent in the treatment of *Shigella* dysentery have been noted even when the infecting organisms are sensitive to streptomycin when tested in the laboratory.

Comparison of ampicillin and neomycin suggest that non-absorbable antibiotics*, such as neomycin and streptomycin, do not have much effect on organisms that invade the intestinal mucosa, and hence are of little use in treating *Shigella* infections. (*It is better to use an absorbable antibiotic — one that can get into the blood and tissues.)

High failure rates have also been reported with streptomycin in the treatment of *Salmonella* gastroenteritis. Antibiotic therapy alone can actually prolong the carrier state in acute gastroenteritis due to salmonella. (In contrast, *Salmonella typhae*, the organism that causes typhoid

Drugs and diarrhoea

How do we know if a drug really works?

Drugs need to be tested objectively; the proper way to do this is a 'controlled clinical trial'. The steps are as follows:

- Define the patients to be treated, making sure that they have the disease for which they are to be treated, not some other illness.
 - Randomly allocate patients to two (or more) treatment groups.
 - It is best if treatments are given 'blind', i.e. neither the patients nor the health workers know which treatment is given to specific individuals. This is called a 'double blind' clinical trial.
 - Assess recovery by objective measurements (such as duration of symptoms, amount of stool passed, etc.) rather than because patients say they 'feel better'.
- If there is no effective treatment for the illness, test the new drug against a 'placebo' (an inert substance, with no pharmacological action, but which looks like the treatment drug).
 - If a recognised effective drug exists and the trial is to see whether a new product is better, the standard and new drugs should be compared with each other in a 'double blind' assessment.
 - Assess the results of the two groups (standard treatment or placebo versus new treatment) statistically, to see whether any difference in outcome is likely to be caused by the drug, and not to have occurred by chance.
 - Unless trials of drugs are done following these rules, it is not likely that their results will be valid.

fever, requires appropriate antibiotic treatment. Typhoid fever is not normally associated with diarrhoea.)

Adverse effects

Streptomycin, like neomycin, if given by injection, may have toxic effects on the ears and kidneys. If given orally, these complications are unlikely, but the extent of drug absorption, and its toxicity in children with acute diarrhoea, have not been fully evaluated.

Formulations and drug interactions

For diarrhoea treatment, streptomycin is usually sold in combination with other ingredients such as kaolin, pectin, hydroxyquinolines, sulphonamides, or chloramphenicol. These combination products have not been shown to be effective and the multiple agents they contain cause additional side effects or undesirable drug interactions.



Hydroxyquinolines

Hydroxyquinolines are useful in the treatment of some parasitic infections. They are, however, widely used for the routine treatment of diarrhoea, even though they have not been shown to be effective. They have some effect on amoebic dysentery, but must be used with other drugs to obtain satisfactory results. Side effects include severe eye and nervous system disorders. Hydroxyquinolines are not recommended for diarrhoea because they are ineffective

and toxic: they are no longer used at all in developed countries. For amoebic dysentery, less toxic, more effective amoebicides are available and are much preferred.

Formulations

A range of products is available, the most popular being clioquinol (iodochlorhydroxyquinoline) and iodoquinol (di-iodohydroxyquinoline); also dibromohydroxyquinol (broxyquinoline) and chlorquinaldol (dichloromethylhydroxyquinoline). These are sold under various trade names, either alone or combined with vitamins, antibiotics or other agents.

Pharmacology

Hydroxyquinolines are well absorbed by the body. Though most of the drug is excreted in the stools, up to 25 per cent of an oral dose is broken down in the liver and can be recovered in the urine.

How they work

The way in which hydroxyquinolines work is unknown. They are active against both motile and cyst forms of amoeba. They have also been shown to be active against a number of enteric bacteria in the laboratory, but their effect on the bacteria within the gut is not well understood.

Efficacy

Hydroxyquinolines function only within the intestinal lumen. When used alone to treat amoebic dysentery, failure rates are high; in combination with antibiotics such as tetracycline or erythromycin, treatment seems to be more successful, although

most of these antibiotics are not amoebicidal, and the rationale for combination therapy is therefore unclear. No well-controlled trials have compared these combinations with metronidazole, the current treatment standard for amoebiasis.

Hydroxyquinolines have also been advocated to treat asymptomatic amoebic cyst passers, but failure rates of up to 25 per cent have been seen and therapy for up to three weeks is usually needed. Metronidazole produces comparable cure rates after only ten days of treatment. However, therapy for asymptomatic cyst passers is not recommended because most are colonised with non-pathogenic *E. histolytica* and up to 90 per cent of infections terminate spontaneously without treatment. Moreover, in areas of high endemicity, the probability of reinfection is high.

With nitroimidazoles such as metronidazole (now available as a low cost generic), tinidazole, ornidazole and nimorazole widely available, hydroxyquinolines are not needed to treat amoebic diseases.

Hydroxyquinolines are still used widely and non-selectively in acute diarrhoea, even though no studies have shown them to be effective. The results of different trials give no basis for recommending hydroxyquinolines for prevention or treatment of traveller's diarrhoea or other diarrhoeas.

Adverse effects

Adverse effects include abdominal discomfort, diarrhoea, skin rash, acne, headaches and enlargement of the thyroid gland. More serious are the many reports of neurological complications linked to hydroxyquinolines. Between 1955 and 1970, about 10,000 cases of subacute optic neuropathy (SMON) were diagnosed in Japan: five per cent of affected persons died and up to 15 per cent were left completely disabled; 75 per cent of the cases were associated with taking clioquinol. SMON is characterised by abdominal pain or diarrhoea followed by painful sensations in the arms and legs and impaired vision. Removal of clioquinol from the Japanese market led to a dramatic fall in the number of cases of SMON. Similar neurological disorders associated with hydroxyquinolines have been reported from Europe, the USA, Australia and India.

References for the studies referred to in these reviews are available from DD/AHRTAG and CDD/WHO.

Antibiotic resistance

Q What is an antibiotic?

A Antibiotics are drugs that prevent or restrict bacterial growth, and so they are useful in treating infections caused by bacteria. Some antibiotics have a 'broad spectrum' of action, that is they work against a wide variety of micro-organisms. Others work only against specific groups of organisms, and are not effective against others. This is because many bacteria are naturally insensitive to some antibiotics. Antibiotics have no effect on viral infections such as rotavirus diarrhoea.

Q When should antibiotics be given for diarrhoea?

A Antibiotics are useful for diarrhoea treatment if there is blood in the stool, indicating that *Shigella* is the likely cause; or cholera (diarrhoea caused by *Vibrio cholerae*) is suspected: the patient has severe dehydration due to watery diarrhoea, is over two years old, and cholera is known to be occurring in the area.

Antibiotics should never be given routinely for diarrhoea: they can be harmful, especially in young children, and may prolong an episode of diarrhoea.

Q What is antibiotic resistance?

A Bacteria that were originally sensitive to an antibiotic may become resistant to it. Resistance can be demonstrated in the laboratory, but may also be seen clinically because the antibiotic will have little or no beneficial effect on the illness.

Q Why is antibiotic resistance important?

A If bacteria become resistant to particular antibiotics, then those drugs will be ineffective — they will no longer treat the infection caused by the bacteria. Because of this, some antibiotics are no longer useful in many parts of the world. Newer antibiotics which are effective may not be available, or may be very expensive. Some strains of bacteria have adapted to new antibiotics almost as soon as they become available, thus greatly limiting their usefulness. In many countries, most *E. coli*

bacteria are resistant to cotrimoxazole, tetracyclines and other antimicrobials; and most *Shigella* to ampicillin.

Q How does resistance develop?

A There are two main ways in which bacteria can resist the effects of antibiotics.

1. The bacteria themselves can change so that antibiotics are no longer effective against them — they become *drug-tolerant*. Because bacteria reproduce rapidly they are very adaptable and able to change fast in order to survive. When antibiotics are given, the more sensitive bacteria are rapidly eliminated, but if a few adapt and become resistant, these will reproduce and soon replace the ones that were sensitive.

2. The bacteria can develop ways to reduce the effectiveness of the antibiotics — they become *drug-destroying*. For example, bacteria can produce substances which inhibit the action of some antibiotics e.g. betalactamases which make penicillins ineffective, and cephalosporinases or aminoglycoside-inactivating enzymes which make cephalosporin antibiotics (gentamicin and kanamycin) ineffective.

Resistance is more likely to develop if antibiotics are widely and frequently used; and antibiotics are used in doses which are not large enough or are used for too short a time, so that not all the disease-causing bacteria are destroyed.

Antibiotic resistance often develops because a bacterium acquires a component known as a plasmid. A bacterium which is resistant to an antibiotic because it possesses a resistance factor (R-factor) can pass this on, by means of a plasmid, to a bacterium which was previously sensitive to the antibiotic. The plasmid contains genetic material which is transferred from one bacterium to another. If antibiotics are used after a resistant strain develops, that strain survives, continues to multiply and can quickly become predominant.

Q What can be done to prevent resistance from developing?

A The correct use of antibiotics is extremely important. Antibiotics should never be used when they are not needed,

What the patient can do:

- remember that ORT is the correct treatment for most diarrhoea;
- never use antibiotics for diarrhoea unless they are prescribed by a doctor or health worker, never give anti-diarrhoeal drugs to children or infants;
- if an antibiotic is prescribed, be certain you understand the instructions for its use and follow them carefully: take it for the recommended time, and do not stop even if the symptoms clear up;
- never try to save money by buying less than the prescribed amount.

What the doctor can do:

- never prescribe antibiotics or antibacterial agents unless they are absolutely necessary; for diarrhoea, give antibiotics only for dysentery or when cholera is suspected;
- explain to the patient that they must complete the full course of treatment, even though the symptoms may go away or become less before the end of the treatment.

What the health authority can do:

- do not allow 'prescription only' medicines (such as antibiotics) to be sold without a prescription;
- ensure that antibiotics are only prescribed by trained health workers, and that advice is given on their use;
- ensure that drug legislation is adequate and that it is enforced;
- as part of the strategy to control diarrhoeal disease, make sure that ORT is promoted as the best and most important treatment for diarrhoea.

because resistance becomes more likely if a drug is used more widely. Antibiotics should always be taken in the right doses and for the recommended amount of time.

If a drug is prescribed to be taken for five days, it is important to continue taking it for five days. Often a patient may begin to feel better and symptoms may be lessened in only two or three days, but the bacteria are unlikely to have been fully eliminated in this time. Stopping the drug early helps resistance to develop, and symptoms may return because the bacteria are able to grow again. Often, people will be tempted to take less than the recommended amount of a drug if it is cheaper for them to buy less, and they do not understand why a full course is needed.

With thanks to Professor P D'Arcy, The School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, UK.

Country reports

PAKISTAN

Should ORS be marketed like other drugs?

Why do people use 'anti-diarrhoeal' drugs when ORS is better and cheaper? Camille Saade and Maggie Huff-Rousselle argue that understanding commercial sales techniques could help to increase the use of ORS.

Commercial marketing is a powerful force. It is, for example, a factor in persuading women to use powdered milks and infant formulas instead of breastfeeding. To promote ORT successfully, it is essential to understand the commercial forces used to promote the drugs which are often used instead of ORT. Figure 1 shows the results of a study in Pakistan (carried out by the PRITECH project) on the market for commercial treatments for diarrhoea. It is estimated that at least US\$7.5 million is spent on these products each year, with only about nine per cent of this spent on ORS packets (of which eight different brands are available). Over 90 per cent of the total was spent on 'anti-diarrhoeal' drugs which are ineffective and potentially dangerous. As well as the 82 different combination drugs which include antibiotics in their formula, this 90 per cent share included motility inhibiting drugs and intestinal adsorbents such as combina-

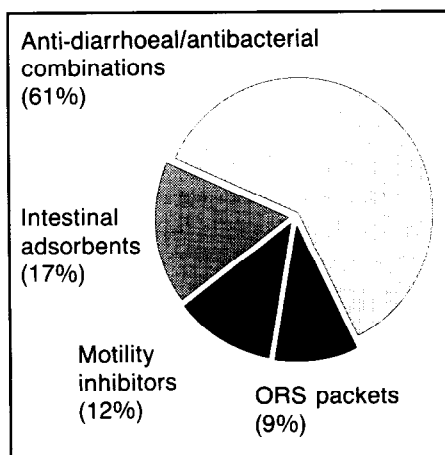


Figure 1: the market shares of commercial treatments for diarrhoea in Pakistan

tions of kaolin and pectin.

The best-selling 'anti-diarrhoeal' drugs in Pakistan are all produced by subsidiaries of multinational companies with tremendous marketing strength and experience. The main marketing technique in Pakistan is 'detailing', which involves members of the 50 to 80 person sales force of each company making regular visits to most doctors in the country.

Before and during the diarrhoea season, company representatives increase the emphasis on 'anti-diarrhoeal' drugs by handing out promotional literature and free samples. This activity is backed up by advertising in medical journals and by techniques aimed at pharmacists: giving free goods, bonus offers and sales incentives.

Only one company carried out promotion of ORS. This company was responsible for 80 per cent of ORS sales, and employed 41 'detailmen' to visit doctors. In urban areas, company staff visited drug retailers and wholesalers to encourage orders for ORS packets, as well as to promote ORS by talking to doctors. In rural areas, a further 120 sales staff worked with a network of regional distributors, and also with paramedical workers.

The relatively weak market position of ORS may be one reason why it is not used more often. In many places, increased marketing of ORS might help to increase both its sales and use. Health workers and others concerned with public health can also take action. Those targeted by representatives promoting 'anti-diarrhoeal' drugs must understand that these drugs are promoted to increase sales, not necessarily because they have proven value for treating diarrhoea. This is especially important because 'anti-diarrhoeal' drugs are potentially dangerous. Also their high costs waste health service resources, and the over-use of antibiotics encourages the development of resistant strains of bacteria. Those involved in marketing of ORS need to analyse the competition in the commercial sector, and develop strategies to increase the demand for ORS.

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INDONESIA

Drug prescribing for diarrhoea

In 1987 the Ministry of Health (with support from USAID) began a study of drug selection and procurement procedures for health facilities. Part of the study looked at the prescribing of drugs in 4,060 cases of childhood illness, including diarrhoea. The results of the study⁽¹⁾ revealed that:

- nearly 60 per cent of all patients received prescriptions for four or more drugs;
- the average number of drugs per case for all diagnoses was 3.8, and one in four drugs used was given by injection;
- 88 per cent of children under five were treated with an antibiotic, but

the average prescription was for only two days.

Specifically for diarrhoea treatment, the average number of drugs prescribed per case was similar (4.0 for children under five, 3.8 for older children). Also:

- antibiotics were prescribed more than twice as often as ORS, and over 50 per cent of cases that received an antibiotic were given two or more of these agents;
- more vitamins and minerals were prescribed than ORS.

1. *Child Survival Pharmaceuticals of Indonesia, Part II ("CSP-II"), 1988. Jakarta, Ministry of Health. Source: WHO/CDD/90.34 Seventh Annual Report.*

PERU

Co-ordinated national action

Inappropriate use of drugs for childhood diarrhoea is a major problem in Peru. Patricia Paredes and Hildebrand Haak report on recent steps taken to improve the situation.

For ten years, the national Control of Diarrhoeal Diseases (CDD) Programme in Peru has promoted oral rehydration therapy (ORT) for diarrhoea, and the use of a few selected antimicrobials for dysentery only. National surveys have, however, found that ORT use is still low, while the use of drugs for diarrhoea in children under five is very high.^(1,2)

To address the problem, a workshop was organised in Lima by scientific profes-

sionals and the Pan American Health Organization (PAHO) in collaboration with the Ministry of Health. Health professionals, health administrators, international agencies, Peruvian researchers, health activist groups and others attended, contributing much information on drug use for childhood diarrhoea.

Research findings

Workshop participants presented results of research studies. Two national surveys showed that, in 1984, 50 per cent, and in 1986, 62 per cent of all diarrhoeal episodes in children under five were treated with some kind of drug. The drugs most frequently used were antibiotics such as chloramphenicol, tetracycline, neomycin and cotrimoxazole, and antimotility agents like loperamide^(1,2). A study of beliefs and behaviour, conducted in the outskirts of Lima in 1987-88, showed that traditional remedies were widely used for diarrhoea, but that modern pharmaceuticals were often also used in combination with them. Loperamide was the most widely used drug, followed by a combination tablet containing chloramphenicol and tetracycline. These tablets can easily be bought without prescription in local shops.

Inappropriate drug use for diarrhoea is not just a result of so-called 'self-medication' by families. Doctors also frequently prescribe ineffective drugs. A survey of patterns in drug prescribing found that, of patients attending a health facility or a private surgery for diarrhoea treatment, 57 per cent received a prescription for antibiotics, and 55 per cent for an 'anti-diarrhoeal' drug.⁽³⁾

Dangerous and expensive

Most of the medicines described above are never appropriate for diarrhoea, and the remainder are being greatly overprescribed. Over-use of antibiotics increases the chances of resistant bacterial strains developing, and drugs such as loperamide are dangerous and may be fatal in young children.

As well as being ineffective or harmful, such overprescribing and over-use of drugs is also extremely expensive. Data from the pharmaceutical industry show that between June 1988 and June 1989, approximately US\$2.5 million was spent on drugs to treat diarrhoea. Only 1.4 per cent of spending on rehydration solutions was on official ORS packets, which are cheap and made according to the WHO formula. The rest was spent on more expensive commercial preparations of glucose-electrolyte solu-



Many children in Peru are prescribed inappropriate drugs for diarrhoea.

WHO/J Vizcarra

tions, most of which differ substantially from the approved formula.⁽³⁾

During discussion of these data it became clear that inappropriate drug use is a complex problem involving many interests. For example, even when mothers, pharmacists and doctors are aware of ORT and correct diarrhoea management, they give a variety of reasons for using other treatments which seem to them to be better. Although there is still no safe treatment which stops the diarrhoea quickly, doctors will prescribe a remedy which claims to give a rapid 'cure', because this is what the mother wants. However, there is little awareness of the possible dangers of these drugs, of their unnecessary cost, especially for poor families, and the role they play in delaying the use of effective rehydration therapy.

Action

The workshop led to a series of actions.

1. PAHO/WHO published a report of the data and the discussion which has been distributed within Peru and in the PAHO region.⁽³⁾ The workshop is presented as an example for other national programmes.⁽⁴⁾
2. The Ministry of Health organised a series of paediatric forums throughout the

country where correct case management of diarrhoea and the disadvantages of 'anti-diarrhoeal' drugs were discussed with doctors, nurses, pharmacists and students.

3. Messages about ORT and inappropriate drugs were reinforced through additional teaching sessions and radio interviews.

4. Inappropriate use of antibiotics and other drugs during diarrhoea is now recognised as important by the Ministry of Health, and there are plans to focus on the problem in the next update of the national diarrhoea treatment guidelines.

5. A local health activists group, in collaboration with the Ministry of Health, has organised several forums for medical and pharmaceutical students on inappropriate drug use. This group has also prepared a popular information folder on 'anti-diarrhoeals', which includes, among other printed materials, the workshop report and a WHO document on proper case management of diarrhoea.

6. The workshop report has also been used as a basis for discussion in regional seminars of the National Pharmacists Association. The Association has recognised the problem and is willing to collaborate in efforts to reduce the inappropriate dispensing of pharmaceuticals for childhood diarrhoea.

Working together

One strength of this effort has been the willingness of the scientific community, the Ministry of Health, international agencies and health activist groups to work together and recognise the seriousness of the problem. The positive attitude of those involved in trying to find solutions, each in their own field and in collaboration with others, deserves special attention and has been one of the most encouraging results of the initial workshop.

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1. ENNSA: *INE: Informe General Peru 1986*. pp 145-146.

2. ENNSA: *INE: Informe General Peru 1988*. pp 118-121.

3. *Medicamentos inapropiados en diarrea: la magnitud del problema*. PAHO/WHO, Lima, 1989.

4. *Programme for Control of Diarrhoeal Diseases. Seventh Programme Report*. WHO, 1988-1989.

Resources

More information on drugs, including drugs for diarrhoea, can be obtained from the organisations and publications listed below.

- All India Drug Action Network (AIDAN). Contact: Voluntary Health Association of India, 40 Institutional Area, South of ITT, New Delhi 110016, India. AIDAN is a network of health, consumer, legal aid, and human rights organisations.
- *Drug Disease Doctor*. Subscription. Published by Drug Action Forum, P 254, Block B, Lake Town, Calcutta 700089, India. Quarterly journal on rational drug therapy and prescribing practice.
- *The Drug Monitor*. Free. Published by the Health Action Information Network (HAIN), 9 Cabanatuan Road, Philam Homes, Quezon City, Philippines.
- *Drug Information*. Free. Published by the Pharmaceuticals Unit, World Health Organization, 1211 Geneva 27, Switzerland. A bulletin for the international transfer of information on current drug topics.
- *Essential Drugs Monitor*. Free. Published by the World Health Organization, 1211 Geneva 27, Switzerland. The newsletter of the WHO Action Programme on Essential Drugs and Vaccines.
- *HAI News*. Subscription. Published by Health Action International (HAI), IOCU, PO Box 1045, 10830 Penang, Malaysia. Regional offices at HAI-Europe, Jacob van Lennepkade 334 T, 1053 NJ Amsterdam, Netherlands; and IOCU Regional Office for Latin America and the Caribbean, Casilla 10993, Sucursal 2, Montevideo, Uruguay. The newsletter of HAI, a network of consumer, development action and other public interest groups worldwide.
- *INRUD News*. Free. Published by the International Network for Rational Use of Drugs, 165 Allandale Road, Boston, Massachusetts 02130, USA.



- INRUD is a co-operative organisation of health workers, administrators and researchers in developing countries aiming to improve drug use. There are several different national groups.
- *WHO Drug Information*. Subscription. Published in English and French by the World Health Organization, 1211 Geneva 27, Switzerland. Journal of drug development and regulation.
 - WHO CDD Programme.

Further reading

- Chetley, A, 1987. *Antibiotics: the wrong drugs for diarrhoea*. Health Action International. Available from HAI Europe.
- Cutting, W A M, 1989. *Self-prescribing and promotion of anti-diarrhoeal drugs*. *Lancet* 8646:1080.
- Dean, P and Ebrahim, G J, 1986. *Practical care of sick children: a manual for use in small tropical hospitals*. Macmillan, 348 pages.
- Ghai, O P, 1987. *Understanding and*

managing acute diarrhoea in infants and young children. All-India Inst of Medical Sciences, 25 pages.

- Laing, R O, 1990. *Rational drug use: an unsolved problem*. *Tropical Doctor* 20(3): 101-103. A short and recent overview.
- Merson, M H, 1987. *Proper treatment of diarrhoea: role of the pharmacist*. *International Pharmacy Journal* 1: 52-56.
- Quinby Rush, C and White, K, 1988. *Control of diarrhoeal diseases: an annotated bibliography of PRITECH holdings*. PRITECH, 333 pages.
- Rylance, G (ed), 1987. *Drugs for children*. Non-serial publication available from WHO. 185 pages.
- *Banned and Bannable Drugs*, 1986 (third revised edition, 1989). The Voluntary Health Association of India (VHAI), 40 Institutional Area, South of IIT, New Delhi 110016, India. 106 pages. Available from VHAI.
- *Drugs in the management of acute diarrhoea in infants and young children*, 1989. *Bull. WHO* 67(1): 94-96. A short overview. Based on the unpublished document WHO/CDD/CMT/86.1 Rev 1 (1988).
- WHO, 1988. *The use of essential drugs: third report of the WHO expert committee*. Technical report series 770. 63 pages. Includes a model list of essential drugs designed for individual countries to use to develop their own lists.
- WHO, 1988. *Essential drugs for primary health care: a manual for health workers in South-East Asia*. SEARO Regional Health Papers No 16, 105 pages. SwF10/US\$8, order no. 1580016.
- WHO, 1987. *Use of drugs in the treatment of diarrhoea*. CDD/TAG/87.5.
- WHO, 1987. *The rational use of drugs*. Report of the Conference of Experts, Nairobi, 25-29 November 1985, 329 pages. SwF52/US\$41.60, order no. 1150271.
- WHO, 1988. *The world drug situation*. 123 pages. SwF20/US\$16.00.

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