Hitting the Target with Magic Bullets

Mass Chemotherapy in Disease Control

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PREFACE

The untimely death of Benjamin Oluwakayode Osuntokun was a sad blow to his family, his friends, his nation and to the scientific world at large. All of us are slowly adjusting to the post-Osuntokun era, realizing that we no longer have direct access to his knowledge and wisdom, to his caring concern, to his humour and to everything that made him a very special person to all of us who had the good fortune to know him. But like all great men and women, he has bequeathed to us his heirs and to generations to come, a large heritage of knowledge, wisdom, example and guidance.

World Health Organization
Adetokunbo O. Lucas
16 October 1996

I feel greatly honoured and I deeply appreciate the privilege of being selected to deliver the 5th B. O. Osuntokun Memorial Lecture. I cannot find any better words to express my feelings on this occasion than the statement that I made in 1996, when the World Health Organization honoured his memory.

Professor Osuntokun was most renowned for his erudite contributions to neurology but the most remarkable feature of his academic career was the wide scope of his scholarly work. He combined clinical observations with biochemistry, neurophysiology and other highly sophisticated biomedical research tools. He analysed problems, not as discrete isolated entities, but he used broad multidisciplinary approaches including epidemiological and community-based studies to put the issues in wider context of communities and populations. The central goal of his professional and academic work was to make people live longer and feel better.

Adetokunbo O. Lucas, Ibadan, 2002

In selecting the subject for this lecture, I was conscious of the fact that infectious and parasitic diseases remain a major cause of death, disease and disability in Nigeria. Professor Osuntokun's large portfolio of scientific publications included significant contributions on communicable diseases (Adeuja and Osuntokun, 1971; Bademosi and Osuntokun, 1979; Francis, Osuntokun and Kemp, 1972; Osuntokun, 1968, 1974, 1983; Osuntokun et al., 1971). All parts of the world have recorded major gains in the control of some of these diseases but major challenges persist (Lucas, 1985; Gilles and Lucas, 1998):

- The ***unfinished agenda*** of the traditional communicable diseases that have not been controlled; and
- The ***emergent threat*** of new infections, notably, HIV/AIDS.

The discovery of antibiotics and other anti-infective drugs revolutionized the control of some of these diseases but made little contribution in the control of other infections. It is therefore, worthwhile to review our experience over the past half century in this new antibiotic age. This lecture summarizes the experience gained so far in the use of mass chemotherapy as a tool for the control of infectious diseases. It will examine the value and the limitations of this strategy and will project future prospects globally, but with specific reference to the situation in Nigeria.

Historical Background

The discovery of microbes in the 19th century laid the foundation of modern chemotherapy. The so-called 'germ theory' postulated that small organisms, invisible to the naked eye, were the causes of many diseases – from the common cold to cholera from tetanus to typhoid, from the small pox to the great pox.

Magic bullets

Early in the 20th century, a German scientist, Paul Ehrlich (born 14 March 1854; died 20 Aug. 1915) introduced the concept of the *magic bullet* – chemicals that would selectively kill microbes without hurting the human host. He postulated that it should be possible to wage war against microbes using well-targeted weapons, the magic bullets, that would selectively destroy the invading organism without hurting the host. Using the military metaphor, he proposed a notion that is well captured in Chairman Mao's statement which seems equally applicable to war as it is to chemotherapy:

"The object of war is to destroy the enemy and preserve oneself."

The Little Red Book, Chairman Mao

Through his own research, Ehrlich produced two significant anti-infective agents that clearly illustrated the feasibility and value of his concept of the magic bullet:

Salvarsan (comppound 606) 1910 – this organic arsenical was the first effective treatment for syphilis; and

Antrypol – a chemical derived from urea for the treatment of trypanosomiasis and onchocerciasis.

Ehrlich opened the door by establishing the conceptual framework as well as two model drugs; others have followed with the discovery of new anti-infective agents. The early winners included:

1935 *Sulphonamides*

1940 *Penicillin* – the first antibiotic developed following the observation in 1928 that colonies of a penicillium organism inhibited the growth of certain bacteria.

1943 *Streptomycin* – effective against tuberculosis.

Clinical applications of chemotherapy

The second half of the 20th century witnessed the discovery of a wide variety of antibiotics and other anti-infective drugs. The first obvious application of chemotherapy was in the treatment of individuals. In clinical application, penicillin and other antibiotics achieved 'miraculous', seemingly 'magical' cures of severe, life-threatening infections. These chemotherapeutic agents significantly altered the prognosis for many severe infections; septicemia (blood poisoning), pneumococcal meningitis and other diseases that previously were uniformly fatal, could now be cured by treatment with appropriate antibiotics. In medical practice, chemotherapy reduces the duration of illness and the frequency of complications; it also finds useful applications in surgery, obstetrics and other clinical branches of medicine.

Public health applications of chemotherapy

Beyond the treatment of the sick individual, the role of chemotherapy extends to public health applications.

Chemo-prophylaxis to protect vulnerable individuals who are exposed to infection, eg, malaria.

Mass chemotherapy aimed at reducing the reservoir of infection within the community and thereby eliminating the infection. This involves treating overt cases of the disease as well as persons with inapparent infection, carriers of infection who are potential sources of infecting other persons. Box 1 presents various options for applying mass chemotherapy.

Box 1

Options for Applying Mass Chemotherapy

Universal mass chemotherapy: Treating all persons in the community whether infected at the time of the survey or not. If a single examination shows a high infection rate, say 50 per cent or over, it may be more cost-effective to treat everyone without establishing the presence of infection in each subject.

Selective population chemotherapy: Treating all persons that are found to be infected at initial and subsequent surveys.

Targeted chemotherapy: Treating only those individuals harbouring heavy infections and/or high risk groups, eg, treatment of persons aged 5-20 years for *Schistosoma haematobium* infection.

Mass Chemotherapy

Early experience

Soon after the discovery of penicillin, the new wonder drug was applied in the epidemiological control of yaws – an infection that was highly endemic in the wet tropics. The World Health Organization (WHO) sponsored and directed the Yaws Campaign as the first example of mass chemotherapy for disease control. Yaws was highly prevalent in parts of the wet tropics including southern Nigeria. In highly endemic communities, most children showed signs of infection. The overt cases were easy to diagnose on simple inspection of skin lesions. A single dose of long acting penicillin aluminium monostearate (PAM) by intramuscular injection was a highly effective cure. Depending on the level of endemicity, the programme offered treatment to the entire community, both children and adults; or, in less affected communities, to all children and only adults who showed signs of infection. The yaws experience established important principles, notably that, in certain circumstances, one can use chemotherapy as an epidemiological tool for disease control; and that it may be acceptable and cost-effective to treat an entire group without establishing a diagnosis in each individual.

Recent Developments in Mass Chemotherapy

Leprosy

Until two decades ago, this ancient disease remained a persistent scourge in spite of massive efforts by governments and non-governmental organizations. Since its introduction in the 1940s for leprosy control, dapsone was widely deployed. National and international NGOs were spending US$ 30 million annually for

leprosy control and rehabilitation but the prevalence of the infection remained virtually unchanged during the three decades from the 1950's. There was also a threat that the situation would worsen as the organism developed resistance to dapsone, the drug that was the mainstay of leprosy control.

Research co-ordinated by the UNDP/World Bank/ WHO Special Programme for Research and Training in Tropical Diseases (TDR) led to the introduction of multiple drug therapy (MDT) as the new strategy for leprosy control (Milleron et al., 1998). In 1985, WHO established a programme aimed at the elimination of leprosy, using the MDT strategy. The programme has been highly successful and has achieved the goal of reducing prevalence to less than one case per 10,000 population. Globally, the number of active cases of disease has fallen by over 90% since the inception of the programme (WHO, 1982, 1993; see table 1).

Table 1. Leprosy statistics in 32 endemic countries

End of year	Number of cases of active disease	Rate per 10, 000 population
1985	4,003,742	21.1
1986	4,047,385	20.9
1987	3,968,347	20.1
1988	3,729,982	18.5
1989	3,500,723	17.0
1990	2,916,407	13.9
1991	2,361,032	11.0
1992	1,820,302	8.3
1993	1,485,785	6.7
1994	1,171,711	5.2
1995	924,064	4.0
1996	838,718	3.5
1997	770,244	3.2

Source: WHO, *Elmination of leprosy programmes*

Schistosomiasis

In many respects, the various forms of schistosomiasis were good candidates for mass chemotherapy but initially, the available drugs such as antimony compounds were highly effective, but toxic, and thus unsuitable for mass treatment. Other non-antimonial drugs like lucanthone were less effective and poorly tolerated. A more recently discovered drug, hycanthone, was very promising; a single dose by intravenous injection achieved high cure rates. Unfortunately, fatalities resulting from acute liver necrosis occurred at an unacceptable rate and the drug was withdrawn. Niridazole (Ambilhar) was also used in some mass programmes but it required treatment over five days and it was associated with undesirable side effects. In spite of these disadvantages, it was used effectively in Iran.

The discovery of praziquantel offered the most attractive option: highly effective against the main human species of schistosomiasis; well-tolerated; and single day treatment by mouth; its high purchase price, however, made it unaffordable for use in poor endemic countries. Relatively inexpensive generic formulations of the drug are now available, as the patent for praziquantel has recently expired (WHO, 1998). This has rekindled interest in using the drug for mass control of the infection in endemic areas. Schistosomiasis is highly prevalent in parts of Nigeria. A study by Gilles, et al. in 1965 indicated that 20% of Nigerian school children were infected with *Schistosoma haematobium* and a high proportion of them showed evidence of renal damage.

Onchocerciasis

Until the mid-80s, only two drugs were available for the treatment of onchocerciasis: di-ethyl carbamazine (DEC) and *antrypol*. Both

drugs are notorious poisons and can only be safely used under close medical supervision; they are therefore unsuitable for mass therapy:

- **DEC** kills microfilariae but provokes severe allergic reactions. The most serious side effect occurs in the eyes. Communities in which the drug had been extensively used had a higher frequency of blindness than untreated communities!
- **Antrypol** is administered intravenously, usually once a week for 6 weeks. Side effects include renal damage.

The introduction of *ivermectin* radically altered the situation. Discovered by Merck and Co., ivermectin was developed in collaboration with WHO/TDR (Fujisaki & Reich, 1998). The usual treatment is an annual oral dose of 200 micrograms per kilogram body weight – about 12 mg for an adult. This single oral dose is highly effective in clearing microfilariae, but it does not kill the adult worm. The drug is well tolerated in most parts of the endemic area. Unlike DEC that provokes severe allergic reactions, side-effects from ivermectin are relatively mild. Generally, subjects feel much better after taking the drug and so they usually turn out in large numbers for follow-up treatment in subsequent years. In one area of Cameroon, severe neurological complications have been associated with mass campaigns of ivermectin distribution. Current evidence links these adverse effects to coincident high intensity of *Loa loa* infection.

Merck & Co., the manufacturers of ivermectin decided to make the drug available for the treatment of onchocerciasis at no cost to the subjects or their governments. Over the past 12 years, the company has kept its promise of making the drug available *as much*

as is required for as long as it takes. Currently, 30 to 40 million doses are made available each year.

WHO has been managing a large Onchocerciasis Control Programme in eleven West African countries, which was initially based on the extensive use of larvicides to control the breeding sites of the vector, *Simulium* flies. Ivermectin has made it possible to consolidate the gains made from the larvicide programme and to extend onchocerciasis control to other endemic countries that the WHO programme did not cover. There is now the prospect of eliminating onchocerciasis as a cause of blindness in all endemic areas (Abiose, 1998; Amazigo, 1994; Kale, 1998).

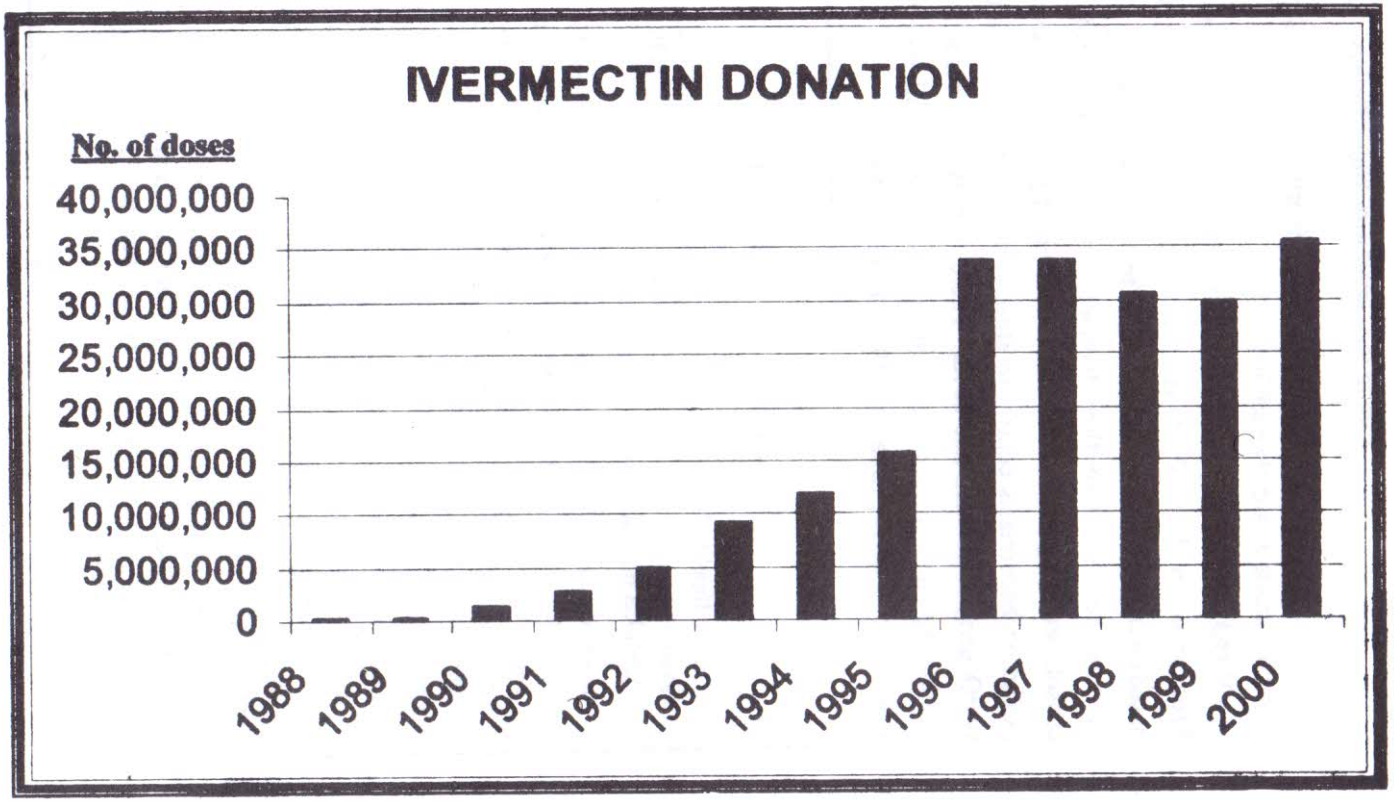
Box 2
IVERMECTIN COMES FREE

On 20 June 1986, Robert D Fluss, Division of International Public Affairs, Merck & Co. telexed the Director of TDR, Adetokunbo Lucas, with this message:

...Merck and the WHO have collaborated extensively on the development of Ivermectin for onchocerciasis. We are very encouraged by the prospects that this drug will be the first new agent available in several decades which will allow for the safe and effective treatment of patients on a mass scale.

The company concluded that, in this case, the best way to achieve the full potential of ivermectin was to ensure that the economic circumstances of patients and governments in onchocerciasis-endemic areas would not prevent or restrict widespread use of the product once it is approved. Consequently, Merck is undertaking to make appropriate arrangements, if necessary with other interested parties, to make needed quantities of the drug available to these governments and patients at no cost to them for the treatment of onchocerciasis...

Figure 1
Showing the number of doses of ivermectin donated by Merck & Co. for onchocerciasis control



In summary, the Mectizan (Ivermectin) Donation Programme is rapidly eliminating onchocerciasis as a public health problem. It is relieving the unpleasant cutaneous symptoms and the blinding complications (Amazigo, 1994, Foege, 1998). The Nigerian programme is being implemented with the support of various non-governmental organizations.

Trachoma

Trachoma is the commonest cause of preventable blindness in the world. In the past, tetracycline ointment instilled daily into the eyes for six weeks, was the main control measure. More recently, a new broad spectrum antibiotic, azithromycin, has proved highly effective in single day treatment. WHO, in association with other partners, has developed a comprehensive strategy – **S.A.F.E.** – for trachoma control consisting of four elements:

Surgery – to reverse trichiasis which damages the cornea. In order to promote access to trichiasis surgery, some countries are training nurses to perform the surgery, providing service through mobile teams.

Antibiotic – azithromycin where available; tetracycline ointment where azythromycin is contraindicated or not available.

Face-washing – to reduce attractiveness of dirty faces to flies.

Environmental sanitation – to reduce fly breeding and provide adequate water supply for personal hygiene.

Pfizer Co., the manufacturer of azithromycin (Zithromax), is donating the drug in support of the global programme. The drug company sponsored the International Trachoma Initiative (ITI) that is now operating in several highly endemic countries: Ghana, Mali,

Morocco, Tanzania, Sudan, Vietnam, and more recently, Ethiopia and Nepal. The initial results of the ITI programme are most encouraging. For example, with ITI support, Morocco reported a 50% reduction in the prevalence of active cases at the end of the first year of operation.

Comment

These five diseases – yaws, schistosomiasis, onchocerciasis, trachoma and leprosy – illustrate the successful application of mass chemotherapy as the main tool for disease control. It is also interesting to review three other infectious diseases in which chemotherapy plays a role – malaria, intestinal helminths and HIV/AIDS.

Malaria

The role of chemotherapy has been less successful but still significant in the control of malaria. In parts of the world where malaria was not highly endemic, the infection was eliminated through the combined application of vector control measures and chemotherapy. In the highly endemic areas, chemotherapy has been less successful; the emergence of drug resistance in the parasites has limited the effectiveness of malaria chemotherapy. However, drugs still play a major role in the protection of highly susceptible persons – children, pregnant women and foreigners (that is people with little natural immunity). Chemotherapy will play a key role in the World Health Organization's renewed effort (**Roll Back Malaria**) to deal with this infection that still kills one to two million persons a year. In order to intensify the search for new anti-malarial drugs, a new public-private partnership, the Medicines for Malaria Venture (MMV) aims to develop effective and affordable anti-malarial drugs. Through MMV, global public health organizations, the

pharmaceutical industry, government ministries, research institutions and foundations will combine their expertise and resources to ensure the research, development and release of new anti-malarial drugs.

Intestinal helminths

It is estimated that 170 to 400 million school-age children harbour the common intestinal parasites: roundworms, hookworms and whipworms. Some recent publications suggest that public health practitioners may have underestimated the morbidity attributable to these infections. Recent reports have drawn attention to physical stunting, but more importantly, to the impairment of cognitive and other intellectual skills. The authors of these papers claim that when children are dewormed, significant improvement occurs in their physical and intellectual status. There is no consensus about the precise measure of the intellectual impairment resulting from infestation with intestinal worms. However, now that highly effective, broad-spectrum anthelmintics are available, there is a strong case for mass treatment of whole communities; a more cost-effective approach is the selective targeted treatment of school children. Because of the logistic convenience, this approach is highly cost-effective.

HIV/AIDS

The discovery of anti-retroviral drugs has brought new hope for persons infected with the HIV virus. The current strategy is to use a combination of three drugs. In the best cases, 'triple therapy' has brought clinical relief to the patients and prolonged their lives but there are severe limitations and dangers.

Suppression not cure. Highly active anti-retroviral treatment (HAART) suppresses but does not eliminate the infection and so treatment has to be continued indefinitely.

High toxicity. The drugs are toxic; careful monitoring of the patients clinically and with laboratory tests is absolutely mandatory for safe use of the drug. Treatment is abandoned in up to 40% of the patients.

Complex treatment schedules. The treatment regimes are complex requiring a total of several dozen tablets each day

Poor compliance. It is difficult to maintain the compliance of patients because of the occurrence of unpleasant side-effects.

Cost of drugs. The high cost of the brand drugs was a major barrier to their use in developing countries. Initially costing over US$10,000 per patient per annum, generic equivalents are now available at a much lower price, around US$500 per patient, per annum.

The most vital role of anti-retroviral chemotherapy for HIV/AIDS is in reducing the risk of mother to child transmission (MTCT). There is a strong interest in the prophylactic use of the drug nevirapine; it is relatively inexpensive and the treatment schedule is simple.

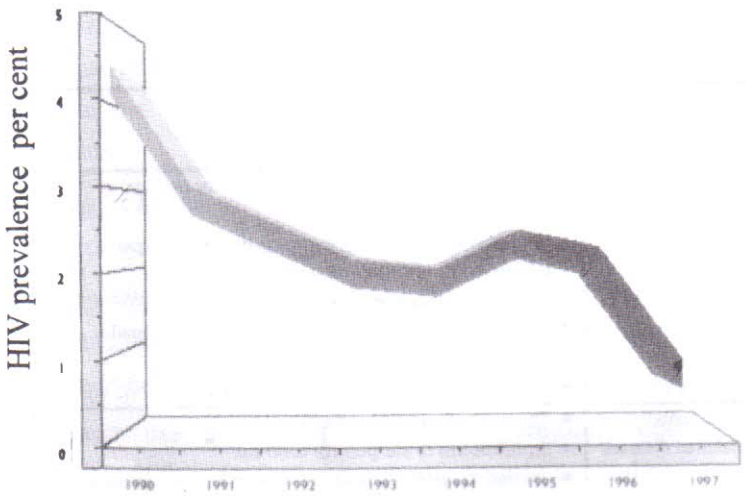
It is clear that anti-retroviral chemotherapy has a limited role in the control of HIV/AIDS. Experience from other African countries has demonstrated the value of public health interventions. For example, in Uganda, intensive public health interventions have resulted in a steep decline in the prevalence of HIV and similar improvements have been reported from other parts of the world where public health measures have been vigorously pursued (figure 2). Through early and intensive interventions, Senegal kept HIV

prevalence below 2%. Nigeria can and should follow the examples of Senegal and Uganda and intensify public health measures to stem the advance of the epidemic of HIV/AIDS in this country.

Table 2. Key elements of national HIV/AIDS programmes

Interventions	Comment
1. Health education	■ Promote community wide awareness of the problem of HIV/AIDS ■ Inform people how they can protect themselves against infection with emphasis on sexual abstinence and monogamous relationships ■ Promote safe sex including the use of male and female condoms ■ Promote safer habits among illegal drug users
2. Control sexually transmitted diseases	■ Promote safe sexual habits (see #1) ■ Ensure access to inexpensive condoms ■ Prompt diagnosis & treatment of other sexually transmitted diseases
3. Manage surveillance programme	■ Promote voluntary counseling and testing ■ Collate & analyse data from sentinel sites & groups to determine trends ■ Identify high-risk groups including commercial sex workers
4. Prevent mother to child transmission	■ General prevention of HIV infections ■ Voluntary screening of pregnant women ■ Prevent unwanted pregnancies in infected persons ■ Use anti-retroviral therapy to protect the child and care for the mother
5. Provide & manage anti-retroviral therapy	■ Give high priority to treatment of pregnant woman and her child ■ Need to define a treatment programme that is feasible in the particular country, given three important considerations – complexity of schedules – need for careful monitoring of patients, including laboratory tests – high cost of the drugs

Figure 2
HIV Prevalence among 13-19 year olds, Masaka, Uganda



Lessons Learnt

The illustrative cases enable us to sum up global experience on the role of chemotherapy in disease control. Clearly, for some diseases, chemotherapy plays an important or even decisive role, eg, leprosy and onchocerciasis. In other cases it makes significant contribution to a package of interventions, eg, trachoma. For some diseases, its role is limited or non-existent.

In what circumstances is mass chemotherapy indicated?

Mass chemotherapy can be applied in a cost-effective way when:

- the drug is efficacious, safe, acceptable, has a simple regime, and is affordable
- the disease is endemic or during an epidemic outbreak

- infected persons can be easily identified, clinically or with simple laboratory tests.

Given the circumstances under which various chemotherapy will be administered, the ideal drugs for use in developing countries should meet the following specifications.

Efficacy. The drug should be effective against all strains of the pathogen; the occurrence or emergence of resistant strains would limit the usefulness of the drug.

Safety. The drug should be easy to use safely by health personnel who have limited skills; it should be safe to administer to persons who are not under continuous medical supervision; there should be a wide margin between the effective and the toxic dose; and there should be no dangerous side-effects.

Simple treatment schedules. The treatment schedule should be simple and the drug should be administered preferably by mouth; single dose treatments should be available.

Acceptable. The drug should be well tolerated by persons of the target age group and should have no unpleasant side-effects.

Affordable. The cost of the drug should permit its use within the limited budgets of developing countries.

Few drugs have all these qualities, but the specifications serve as a checklist for assessing the value of any drug that is proposed for large-scale use. Two important risks occur when there is such widespread use of drug therapy: resistant strains may emerge and some individuals may develop undesirable side-effects.

Selecting control strategies

Table 3 is a clear reminder that control strategies have to be carefully selected on the basis of the scientific knowledge of what

works. It would be a grave error for example to try to use chemotherapy as the main intervention for the control of HIV/AIDS.

Table 3. Interventions for controlling infectious diseases

Main intervention	Examples	Comments
Chemotherapy	Leprosy	Marked reduction in active cases through the use of multiple drug therapy
	Onchocerciasis	Highly successful mass chemotherapy with ivermectin
	Schistosomiasis	Major control programmes being planned using generic praziquantel.
	Trachoma	Azithromycin being used in integrated S.A.F.E. programmes
Vaccine	Smallpox	Eradicated globally
	Poliomyelitis	Eliminated from Western hemisphere; significant progress in other regions
Sanitation	Guineaworm	Eliminated from most endemic areas through improvement of water supplies.
Behavioural modification	HIV/AIDS	Safe sex, safe blood transfusion and injection practices have successfully controlled the disease in some countries. Crucial role of chemotherapy in preventing mother to child transmission.

* See page 11

Rational Use of Drugs

Future prospects

Antibiotics and other anti-infective agents are powerful tools that serve us well, but we must not take them for granted. Abuse of these drugs leads to treatment failure in individual cases and promotes the emergence of drug resistant strains of the infective agents. In Nigeria, there is widespread inappropriate self-treatment, but doctors and other health personnel also abuse the drugs. Common errors include:

Malaria

- Misdiagnosis of cases of other causes of febrile illness
- Unnecessary use of injection of chloroquine instead of oral dosage
- Use of halofantrine without paying attention to potential serious adverse effects

Typhoid

- Misdiagnosis of typhoid on the basis of a single Widal test

Common cold

- Unnecessary use of antibiotics for treating the common cold and other viral infections

Prophylaxis

- Using antibiotics to cover surgical operations instead of maintaining good aseptic techniques
- Using prophylactic antibiotics to cover exposure to unprotected sex

Chemotherapy in Disease Control

Future prospects

What is the future of specific chemotherapy in disease control? Health research can contribute by enabling us to make more effective use of available technologies and generate new technologies:

Situation analysis – knowledge generated from surveillance and the study of the dynamics of transmission can enhance control strategies

Health care – Health systems research can help to develop and refine methods for delivering health care including chemotherapy. For example, the development of community-based distribution

networks for ivermectin is a major breakthrough that has increased the coverage and cost-effectiveness of the programme.

Improved tools for disease control – Research and development of new and improved tools for disease control including drugs, vaccines, diagnostic methods and innovative vector control measures is essential. Research on tropical diseases is still grossly underfunded. According to a recent analysis of the 1233 new drugs identified as reaching the market between 1975 and 1997, only 13 were approved for tropical diseases. Of these 13, six were developed with TDR support. An additional seven chemical entities or drug combinations have also been brought for registration or recommendation for use in the control of tropical diseases with input from TDR (Mattock, 2001).

Contributions from Nigeria

Nigerian scientists and institutions have made significant contributions to the development and application of chemotherapy in disease control. The first clinical trials on the efficacy of dapsone were conducted in 1947 in a Nigerian leprosarium and it was in this country that the anti-malarial effect of dapsone was first discovered. In the post-independence period, Nigerian scientists, from the University of Ibadan and other academic institutions, have made significant contributions to the developments that this lecture has reviewed.

- A Ghanaian physician, **Dr. Kwablah Awadzi**, a graduate of Ibadan, working in Tamale, Ghana, made major contributions to the clinical evaluation and development of ivermectin. (Awadzi, 1980; Awadzi et al, 1980)

- **Professor A. Abiose**, another Ibadan graduate headed a team that investigated the ophthalmological aspects of ivermectin treatment (Abiose, 1998).
- In the 1960s, an Ibadan research team – **Lucas, Oyediran Cockshott** and others demonstrated that in children, chemotherapy of vesical schistosomiasis leads to reversal of obstructive uropathy (**Lucas** et al. 1966; **Oyediran**, 1975). Initially a contentious issue, but with accumulated evidence from other centres, the phenomenon is now well recognised. The reversibility of obstructive uropathy served to establish chemotherapy as the prime intervention for control of the infection.
- Data obtained from a study of pyrimethamine alone and in combination with sulfadoxine and dapsone were used in obtaining the registration of Fansidar (**Lucas** et al., 1969).
- Nigerian scientists contributed to the evaluation of anthelminthic drugs (**Lucas** and **Oduntan**, 1972).
- TDR involved a global network of researchers and institutions A Nigerian scientist, **A Lucas**, directed the programme during its first decade, 1976-86. Distinguished Nigerians played a significant role in various committees and projects – **Professor O Kale** (filariasis), **Professor ABO Oyediran** (schistosomiasis), **Professor L Salako** (malaria), **Dr U Amazigo,** (onchocerciasis), etc.

Conclusion

Winning the war against the microbes

The great foresight of Paul Ehrlich in proposing the feasibility of magic bullets has been clearly realised. Chemotherapy alone or in combination with other interventions, has scored major successes in disease control. Chemotherapy is, however, no panacea. Basic public health measures are still vitally important for the control of diseases that are associated with poor environmental sanitation and bad personal hygiene. Behavioural modification such as the adoption of safe sex practices is critical for controlling sexually transmitted diseases including HIV/AIDS. To rely solely on chemotherapy for the control of cholera, typhoid and other diarrhoeal diseases or HIV/AIDS would be a grave error.

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