LEADING ARTICLE

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Drug Treatment of Tropical Parasitic Infections

Recent Achievements and Developments

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Abstract

Drug development offers potential solutions to a number of tropical health diseases, although the expense of pharmaceutical research and lack of return on investment has limited the production of new agents. The greatest successes have been through the development of single dose therapy and mass treatment control programmes for a number of diseases. We review some of the current treatment regimens for malaria, intestinal helminth infection, onchocerciasis, filariasis and schistosomiasis, and their use in clinical practice.

Geographical spread and emergence of drug resistant parasites have hindered the control of malaria, the most important global parasitic infection. Artemisinin compounds have proved effective antimalarial agents producing rapid reduction of parasite load and can be used in combination treatment regimens to combat multidrug resistance.

Intestinal helminth infections are widespread, giving rise to nutritional deficiencies and impaired childhood cognitive development. Pregnant women in developing countries are at increased risk of morbidity. Treatment with a single dose benzimidazole such as albendazole or mebendazole has beneficial effects on morbidity and rates of transmission.

Diethylcarbamazine has been used in the treatment of onchocerciasis and human filariasis. A complicated escalating dose regimen over several weeks is associated with systemic and allergic reactions and may require corticosteroid cover. Simplified regimens for mass population treatment with ivermectin have proved useful and been used in combination with single dose albendazole and diethylcarbamazine. The African Programme for Onchocerciasis Control in West and Central Africa has been one of the most successful mass control programmes virtually eliminating new infections by a combination of chemotherapy, education and vector control.

Schistosomiasis is of increasing importance as a result of the creation of new snail habitats by agricultural and economic development. Praziquantel has become the most widely available and effective chemotherapy for schistosomiasis. There have been a number of reports of persistent schistosome egg shedding after treatment posing concerns about the emergence of drug resistance.

Eflornithine has been successfully used in patients with human trypanosomiasis failing melarsoprol therapy however expense and availability have limited its potential.

Mass control treatment programmes have targeted schoolchildren, adolescents

and pregnant women. The integration of schistosomiasis, onchocerciasis, filariasis and helminth control programmes has been considered as a cost-effective method of delivering treatment. It is likely that future control will be based on this optimisation and integration of existing regimens, rather than the development of new agents.

Drugs and therapeutics offer the potential for simple and relatively cost-effective solutions to many tropical health problems. We already have the technology to effectively treat and control most common tropical infections, however, many resource poor countries in the tropics are unable to afford relatively expensive drugs and do not have the infrastructure to distribute medication to the target population. Poor quality and counterfeit drugs and vaccines have been responsible for lack of efficacy[1] and may contribute to emerging drug resistance. Lack of availability of cost-effective drugs is also a concern. There is no longer a guaranteed supply of intramuscular chloramphenicol oily suspension, which has been used as a cheap and effective treatment for *Neisseria meningitidis*[2] and availability of eflornithine, a useful new agent for combating African trypanosomiasis, is currently restricted.[3] The cost of highly active antiretroviral therapy is prohibitive in the developing world.

Large populations are therefore denied access to therapeutic and immunisation products. As a result the World Health Organization (WHO) has introduced the Revised Drug Strategy and essential drugs concept that is evidence based and promotes equity, public health principles and implementation of national policies.[4]

The expense of drug research and perceived poor investment return has restricted pharmaceutical developments against many of the diseases common in the tropics. The number of therapies released for tropical diseases over the last few decades has therefore been limited (see table I). Despite these many difficulties we now have a series of well tolerated and effective drugs that can be used as single dose therapy for mass treatment programmes. This article concentrates on successful developments for malaria and mass control programmes for helminth infection, filariasis, schistosomiasis and onchocerciasis.

1. Malaria

Malaria is the most serious global parasitic infection, with an estimated 300 million people infected annually, causing around 2 million deaths in endemic countries. Over recent years there has been geographical spread with cases of malaria in Asia and the Americas, and an increasing number of imported infections from endemic areas.[5,6]

Plasmodium falciparum infection is associated with life threatening complications including severe anaemia, renal failure, respiratory distress and cerebral malaria, which still has a mortality rate of 15 to 20% even when treated. In endemic areas *P. falciparum* infection is a major cause of childhood deaths. *P. falciparum* has been characterised by the development of drug resistant strains which now have a global distribution, although chloroquine sen-

Table I. New products developed for human use (1980-1998)

Disease	Product	Year approved/ marketed
Malaria	Artemether	1997
	Atovaquone/proguanil	1994
	Halofantrine	1992
	Mefloquine	1987
African Trypanosomiasis	Eflornithine	1990
	Pentamidine	1984
Schistosomiasis	Oxamniquine	1981
	Praziquantel	1980
Helminths	Albendazole	1989
Onchocerciasis	Ivermectin	1987
Leishmaniasis	Liposomal amphotericin B	1996

sitivity is still found in certain parts of the world, particularly the Caribbean and the Americas.[7] With some exceptions in Oceania, benign malarias (*P. vivax*, *P. ovale* and *P. malariae*) remain generally sensitive to chloroquine.[8]

Chloroquine, a cheap and widely available drug, is active against the erythrocytic asexual stages of the malaria parasite. It appears to reduce detoxification of free haem released during haemoglobin digestion necessary for survival of the parasite. Multidrug resistance is associated with reduced concentration of chloroquine in the digestive vacuole of the parasite resulting from its increased removal from this site. This is associated with the P glycoprotein pump, however, the precise molecular basis for resistance has yet to be determined and remains controversial. The addition of pump inhibitors such as verapamil and fluoxetine can partially reverse this *in vitro*, however no clinical benefit has been shown.

The Cinchona alkaloids remain active against malaria despite use for over 300 years. Quinine resistance has slowly spread with cure rates declining to 80 to 90% in South East Asia using monotherapy, although combination with tetracycline[9] or atovaquone/proguanil can improve efficacy. Adverse effects such as bitter taste and cinchonism (nausea, tinnitus and deafness) often result in poor compliance over a seven day treatment course.

Mefloquine, a fluorinated quinoline methanol compound has been available as treatment for uncomplicated multidrug resistant falciparum malaria since 1984. Full treatment can be given in single or split administration but often induces nausea and vomiting. Minor central nervous system (CNS) disturbances including dizziness and insomnia are common, but more serious neuropsychiatric reactions have also been reported.[10,11] The development of resistance, associated with *Pfmdr 1* amplification, has necessitated the use of higher doses (25 mg/kg) and now monotherapy is associated with failure rates of over 50% in some areas, although the combination of mefloquine with an artemisinin derivative can be used to improve efficacy.[12,13]

Halofantrine is an active phenanthrene methanol compound but is associated with cardiotoxicity and ventricular tachycardia, which has restricted its use.[14] Resistance is also linked to the *Pfmdr 1* gene and is positively correlated with mefloquine resistance.

Atovaquone is a hydroxynaphthoquinone, with additional activity against *Pneumocystis carinii* and *Toxoplasma gondii*. It interferes with the plasma sodium cytochrome electron transport system. When used as a single agent, emergence of resistance conferred by a single point gene mutation occurs rapidly. It is available only in combination with proguanil, a biguanide dihydrofolate reductase inhibitor, giving high cure rates, however this does not entirely prevent resistant strains emerging.[15]

The artemisinin compounds, artemether, artesunate and dihydroartemisinin are derived from qinghaosu found in the sweet wormwood plant and an ancient Chinese herbal therapy. They are rapidly acting peroxidic agents achieving faster relief of fever and parasite reduction than other antimalarials.[16] Antiparasitic effects on the younger ring forms enhance their clearance and prevent development of the more pathogenic forms that induce rosetting and cytoadherence to cerebral vascular circulation.[17] In parts of South East Asia where there is 40% failure against mefloquine, the addition of 3 to 5 days artesumate improved cure rates to nearly 100%.[12,13] Two large trials including over 1000 patients with severe falciparum malaria compared intramuscular quinine to artemether and found similar cure rates with slightly prolonged recovery from coma in the artemether group.[18,19] High doses in rats have been associated with caudal brainstem lesions and a case report of cerebellar syndrome induced by artemether has raised concerns about neurological toxicity.[20,21]

The development of resistance is most likely to occur if a population of parasites encounters a subtherapeutic drug concentration and drugs with long half-lives such as mefloquine are most susceptible as low levels can persist for weeks. Recrudescence of infection or reinfection for those remaining in endemic areas may occur during this period of sub-

optimal drug concentration. The combination of mefloquine or other antimalarials with artemisinin derivatives is a more favourable therapeutic strategy as the parasite load is rapidly reduced by the artemisinin compound leaving relatively few parasites for the second drug to eliminate. This approach of combination therapy may be used increasingly frequently as new classes of antimalarial agents are unlikely to be available in the near future.[22,23] It remains to be seen if this approach is affordable and fulfils its potential in clinical practice.

2. Intestinal Helminths and Benzimidazoles

The most frequent infecting human helminths include *Ancylostoma duodenale*, *Necator americanus*, *Ascaris lumbricoides* and *Trichuris trichiura*. Intestinal geohelminths may globally infect almost a quarter of the world population (1.5 billion people). A recent review has suggested that over 10% of the world population experience helminth-induced disease, giving rise to considerable morbidity and economic loss.[24] Around 44 million pregnant women have iron deficiency anaemia secondary to hookworm infestation. Intestinal helminth infections have a detrimental effect on cognition and school achievement in children as a result of anaemia and undernutrition.[25,26] Worm burden is unevenly distributed, with most individuals carrying few worms and relatively few hosts harbouring a high worm intensity. Around 70% of the worm population is carried by 15% of the host population. Those most heavily infected are at the highest risk of morbidity and are the major sources of environmental contamination and subsequent transmission.[27]

Almost all geohelminth infections can be treated with one of 5 antihelmintic drugs: albendazole, mebendazole, ivermectin, praziquantel and diethylcarbamazine (DEC). These are well tolerated, affordable and effective treatments with broad-spectrum activity. There is evidence that mass treatment of populations with high worm intensity can reverse deficits in nutrition, growth, physical fitness and mental development of children.[25,26,28,29] However, a recent meta-analysis of 30 trials involving over 1500 children has found limited evidence of improvements in weight and cognitive performance after antihelminth drug treatment.[30] The WHO Division of Control of Tropical Diseases and UNICEF have recognised community based antihelmintic treatment as an efficient use of healthcare funds, and have designed and implemented control and intervention programmes in a number of countries. Although helminths affect all members of the community, specific groups have been targeted for treatment including preschool and school age children, adolescent girls and pregnant women.[31,32]

Single dose therapy of the benzimidazoles (albendazole and mebendazole) is effective against trichuriasis, ascariasis and hookworm infection. These agents can be used safely above the age of one year using standard doses of albendazole 400mg and mebendazole 500mg. Such treatment may not eliminate heavy infection, but significantly reduces the worm burden and associated morbidity.[32,33] Mebendazole and albendazole have been associated with teratogenicity in rats[32] and therapy is recommended after the first trimester of pregnancy where intervention could improve birth outcomes and reduce maternal morbidity.

Hookworm related anaemia is a serious and common antenatal problem in many tropical countries. In Sri Lanka, a national programme which commenced in 1994 has successfully offered single dose mebendazole to all pregnant women after the first trimester, with a significant reduction in the rate of stillbirth and perinatal deaths.[34] No increase in congenital defects was identified in infants born to women taking the drug during the second trimester.

Simultaneous administration with cimetidine increases the serum concentration of benzimidazoles and enhances the therapeutic effect in hydatid disease.[35,36] In areas where helminth and schistosome infections co-exist combination therapy of praziquantel with a benzimidazole offers effective treatment against both parasites.[37]

3. Ivermectin and Diethylcarbamazine

3.1 Onchocerciasis

Onchocera volvulus infection (onchocerciasis) is a major cause of visual impairment, skin depigmentation, localised scrotal swelling and general debilitation in countries throughout Africa and South America. Onchocerciasis is transmitted by the blackfly, *Simulium damnosum*, which breeds in fast flowing rivers. Infection causes severe morbidity in localised endemic areas and is known as 'river blindness'. The African Programme for Onchocerciasis Control (APOC) was formed in 1974 and geographically extended in 1986 to include 19 endemic countries in West Africa. Initially, 1 million people in the region were affected, but the programme has now reduced the incidence of onchocerciasis to almost nil.[38]

The recent Merck ivermectin donation programme, allowing large scale mass treatment, has prevented ocular problems. Ivermectin is a highly effective semisynthetic macrocyclic lactone with broad spectrum activity against a range of helminthic parasites. Originally developed for veterinary use, it became available for human use during the 1980s and is an effective treatment for a number of human infections including strongyloides, ascaris, onchocerciasis and lymphatic filariasis. It disrupts locomotor function by inducing paralysis and inhibits feeding by interruption of pharyngeal movement.[39] Ivermectin kills microfilaria but not the adult worms, and subsequent retreatment is usually required to maintain control of filarial infection. Adverse effects are usually due to an allergic or inflammatory response to microfilarial death, and include arthralgia, fever, lymphadenopathy, skin rashes and fever. Until the 1980s, the standard treatment for onchocerciasis and other filarial infections was diethylcarbamazine (DEC). This agent also has little effect against adult worms and requires initial dose escalation because of similar adverse effects. DEC may cause initial worsening of ocular lesions, anaphylaxis and neurological disturbance.

Double-blind, placebo-controlled trials showed that single dose ivermectin (200 μg/kg) produces sustained reduction in skin microfilarial counts with less systemic and ocular adverse effects than DEC. However, these studies confirmed that it had no effect on the viability of adult worms up to 12 months after treatment.[40,41]

Mass population treatment with ivermectin has been attempted in a number of locations worldwide. A Malawian study of the effect of ivermectin on skin nodules showed a reduction in severity and extent of the lesions but it was felt that annual treatment did not produce full cure.[42] A Ghanaian study showed that 97% reduction in skin microfilarial counts was sustained over a 12-month period after single dose administration with either 150 or 200 μg/kg.[43] There was also an impact on the reproductivity of the parasite. Ivermectin is well tolerated. The main adverse effects reported in a 3-year, placebo-controlled trial of over 7000 patients were minor but included significant increases in papular rashes, facial oedema and musculoskeletal pains.[44] The national onchocerciasis control programme of biannual ivermectin in Ecuador gained high compliance of up to 98% at some centres and produced a significant impact on the prevalence of ocular disease and onchodermatitis.[45] The blackfly infection rate declined from 1.1 to 0.08%, a level below the vectorial capacity with interruption of transmission. This was confirmed clinically as there were no new cases in children under 5 years and a lack of nodules developing in patients after 1994.[45]

A trial carried out in Zanzibar of 301 children with *Strongyloides stercoralis* and helminth infection found single dose ivermectin resulted in a cure rate of 83% compared with 45% with 3 days of albendazole. Both drugs were effective against Ascaris but ivermectin was ineffective against hookworms and produced only a 11% cure rate of *T. trichuria*.[46]

3.2 Human Filariasis

Human lymphatic filariasis is a mosquito borne parasitic infection which affects over 90 million

people worldwide. *Wuchereria bancrofti* and *Brugia malayi* may each result in fever, lymphadenitis and chronic lymphoedema. Adult worms survive in hosts for up to 18 years releasing large numbers of microfilaria into the circulation. DEC has rapid microfilaricidal activity but limited effect on adult worms.[47] Reducing the microfilaria count decreases mosquito uptake and interrupts transmission. Treatment requires a course of 2- to 3-weeks duration with an escalating dose regimen to 6 mg/kg and is associated with systemic and local allergic reactions as microfilariae die.[48-50] Corticosteroids may be required to attenuate the severity of these reactions. This complicated regimen makes mass treatment impractical. A single dose regimen of DEC 6 mg/kg was less successful in maintaining microfilarial clearance 6 months after treatment,[51-53] although one study comparing single to 12 day administration suggested equivalent clearance with 40% of treated patients remaining amicrofilaraemic at 1 year after treatment.[52]

Single dose ivermectin (100-400 μg/kg) clears the blood of microfilaria more rapidly than DEC, however this effect is not sustained beyond 3 to 12 months after treatment.[48-50] Multiple dose administration of ivermectin (400 μg/kg every 2 weeks for 3 months) produced a more rapid reduction in microfilaria count than DEC, but again this was not sustained.[54] Comparative studies show that higher single doses of ivermectin (200-400 μg/kg) produce faster microfilariae clearance rates and may suppress recrudescence over 1 to 2 years.[49,53,55] Adverse effect profiles of the drugs are similar, but ivermectin is better tolerated than DEC causing more generalised symptoms (headache, myalgia and fever) than local reactions (testicular pain and nodular formation).[48,49]

The combination of low dose ivermectin and single dose DEC has a synergistic or additive effect compared to either agent alone, reducing microfilarial concentration to 1.7% of pre-treatment concentrations after 1 year and sustained at 2.4% after 2 years.[49,53] Enhanced suppression of microfilaraemia has also been found with ivermectin in combination with albendazole, although the mechanism is unclear.[56] In a recent study,[56] 832 Haitian children infected with *W. bancrofti* were treated with ivermectin, albendazole, both or placebo. After 4 months, 17% of children in the combination group remained positive for microfilariae compared to 76, 69 and 61% of the albendazole, placebo and ivermectin groups, respectively. No excess adverse effects were noted in the dual therapy group. Even individuals who remain clear of microfilariae 2 years after treatment have persisting circulating filarial antigen suggesting that living adult worms persist in almost all patients treated with DEC or ivermectin.[51]

A further study from Sri Lanka compared albendazole alone with single dose combinations of albendazole, ivermectin and DEC in patients with *W. bancrofti* infection and found that albendazole/ivermectin therapy was the most effective for clearing microfilariae with 69% patients remaining amicrofilaraemic at 15 months compared with only 30% in the DEC/ivermectin group.[57] The additional benefits of the single dose combination of albendazole and ivermectin include the lack of serious adverse effects and a wide spectrum of activity against filarial disease and intestinal helminths, making this an attractive option for mass treatment campaigns in many tropical areas.[46,57] The most cost effective delivery system could be the school-based system already in place for intestinal helminth control programmes.

4. Praziquantel: Schistosomiasis

The incidence of schistosomiasis (bilharziasis) is rising globally with over 200 million infected people.[58] Environmental developments such as reservoir and irrigation projects create ideal habitats for the snail intermediate vectors. Successful control of schistosomiasis has been achieved in North Africa, the Caribbean region and parts of Asia by the integration of WHO endorsed strategies including health education, water sanitation and chemotherapy.[58] Diagnosis, often based on inexpensive indirect evidence such as dipstick positive haematuria, followed by chemotherapy with

praziquantel is the cornerstone of many control programmes.

Praziquantel is the drug of choice because of its efficacy against all species of schistosomes, tolerability and cost.[59] Its antischistosomal activity appears to be related to the alteration of calcium homeostasis within the parasite. However, the efficacy and increasing availability of praziquantel, has led to a reduction in supply of the existing alternative drugs (oxamniquine and metrifonate), reduced interest in the search for novel therapies and concerns over possible resistance.

Individual case reports of returning travellers who continue to pass schistosome eggs despite several courses of praziquantel have been published in the US and Australia.[60,61] Laboratory reports have demonstrated selection of resistant strains of *Schistosoma mansoni* in mice under experimental conditions.[62] Concern over praziquantel resistance was raised where complete cure was achieved in only 36 to 39% of individuals in a very intense *S. mansoni* focus in Senegal, at either standard (40 mg/kg) or higher (60 mg/kg) doses, despite an expected 79% cure rate for oxamniquine.[63,64] A further study in the same area treated 130 infected adults with 2 doses of praziquantel 40 mg/kg 40 days apart, and found that the cure rate after the first dose was 42.5%, rising to 76% one month after the second dose with 88% reduction in the intensity of infection.

The failure to eradicate infection after single dose of praziquantel may be a result of high intensity and maturation of prepatent infections rather than drug resistance,[65] and reassessment of the original data with different mathematical models suggested that the low cure rate could be explained by the high intensity of the focus.[66] However, a large study of 1987 infected Egyptian patients found that 2.3% continued to excrete eggs after 3 doses of praziquantel (2 at 40 mg/kg then 60 mg/kg 6 weeks apart) and 80% of the schistosomes isolated from these patients had higher ED_{50} (dose effective against 50%) values than those from successfully cured patients.[67,68] Further field monitoring is urgently required to assess the impact and development of praziquantel resistance.

Other studies have found single low dose praziquantel effective against *Echinochasmus fujianensis*, taeniasis in Taiwan and paragonimiasis in Thailand.[69-71]

There has been little in the way of development of new agents but the relatively new antimalarial artemisinin derivatives have also demonstrated activity against immature schistosomes.[66] Cyclosporin has also been found to exhibit antiparasitic activity against *Schistosoma* spp. Interestingly, the antischistosomal activity appears to be long lasting; up to 100 days. This antiparasitic action is unrelated and distinct from the immunosuppressive effects of cyclosporin and its mechanism remains unclear.[72]

5. Human African Trypanosomiasis

Human African Trypanosomiasis (HAT) or sleeping sickness is a protozoal parasite transmitted by the tsetse fly throughout tropical Africa. Recent resurgence of the disease, especially in Angola, Congo and Uganda,[73,74] has been associated with population movements as a result of economic decline and civil unrest. *Trypanosoma brucei rhodesiense* characteristically gives rise to a progressive, and usually fatal, meningoencephalitis that occasionally responds to suramin sodium. *T. brucei gambiense* has a more protracted course, often extending for several months.[75] Melarsoprol is associated with a cure rate of around 94%, however treatment is associated with a marked encephalopathic reaction most frequently seen in those with severe cerebrospinal fluid (CSF) abnormalities. This can be reduced by concurrent prednisolone administration.[76-78] Pentamidine has been found to give comparable cure rates to melarsoprol in early CNS stages of HAT.[79]

Eflornithine, a polyamine synthesis inhibitor, has demonstrated antitrypanosomal activity. It has been used successfully in patients with CNS disease relapsing after melarsoprol.[3,80,81] First line treatment failures occur in 10% and are associated with low CSF penetration.[82,83] It is well tolerated and adverse effects include mild diarrhoea, hair loss and transient bone marrow depression. Unfor-

Table II. Integrated treatment schedule for *Schistosoma haematobium*, filariasis and intestinal helminths in Zanzibar (reproduced from Savoli et al.,[85] with permission)

Schistosomiasis	Intestinal helminths	Filariasis
Drug		
Praziquantel 40 mg/kg single dose	Mebendazole 500mg single dose or Albendazole 400mg single dose	Ivermectin 200 mg/kg plus Albendazole 400mg single dose
Target group		
Schoolchildren (annual): mass treatment in areas with >20% prevalence of microhaematuria; selective treatment in areas with <20% prevalence of microhaematuria	Schoolchildren: three annual doses Preschool age: two annual doses Pregnancy: one dose after first trimester	Older than 2 years: annual dose

tunately eflornithine prohibitively expensive and is no longer manufactured, leaving sleeping sickness difficult to treat effectively and safely.

6. Integrated Control Programmes

Children are one of the most accessible groups available for mass treatment campaigns using the existing school infrastructure and teachers who are able to assist in the delivery of education and treatment packages. Integration of schistosomiasis control into existing health programmes against helminth infection, onchocerciasis and filariasis has been considered a cost efficient way of delivering treatment. Better coordination and combining of resources should enhance the health impact of mass treatment and reduce transmission of many tropical diseases. Combination therapy of praziquantel with a benzimidazole is an effective method of offering treatment against the main helminths and schistosomes. A double-blind placebo-controlled study of concurrent albendazole and praziquantel in over 1500 children in China, the Philippines and Kenya found the efficacy of each drug and degree of adverse effects was unaffected by dual therapy.[37]

Cost analysis studies of dual annual mass treatment in Ghana and Tanzania have shown that school-based delivery can treat each child for less than US$1.00.[84] This has led the WHO to recommend that mass treatment for schoolchildren should be carried out in communities where the estimated prevalence of helminth infection exceeds 50%.[33]

Mass treatment programmes do not provide a complete cure for all infected people but should be regarded as an effective strategy for reducing the parasite burden of the population and subsequent transmission of infection. Reinfection rates are often high and further mass treatment must be given at appropriate intervals. These campaigns are most effective when they are combined with health education and public health measures including provision of clean drinking water, sanitation and use of insecticides/mollucicides. Table 2 shows an integrated treatment schedule of control of filariasis, intestinal helminths and schistosomiasis used in Zanzibar, Tanzania.[85]

Perhaps the most successful mass control campaign has been the WHO onchocerciasis control programme in West Africa, which included mass treatment with ivermectin through a partnership with the manufacturers (Merck), insect control and local public health training. This programme has virtually eliminated transmission of onchocerciasis and prevented infection of an estimated 12 million children. Vector control has been one of the most important factors in the success of the programme and large tracts of valuable agricultural land have been rescued from previous black fly infestation.[86]

7. Conclusion

This article has highlighted some of the more important recent advances in the drug treatment of tropical parasitic infections. Effective drugs are available for many of the widespread parasitic diseases affecting the tropics and these can often be administered as a single dose treatment. Single

dose drug combinations have the potential to treat a range of infections and are attractive for mass population treatment as they are reasonably cheap with few serious adverse effects.

The relatively low priority given to research into tropical disease by many multinational drug companies will limit the number of new drug treatments developed in the future. Cost-effective therapies are required for there to be any significant impact on disease burden in most tropical countries. The development of vaccinations for malaria and schistosomes offer alternative strategies. It is likely that future control will be based on improving and optimising existing treatment regimens and integration of mass treatment programmes.

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