political in the sense that they ultimately involve competing or conflicting values, and therefore cannot be resolved by purely 'rational' (that is, empirical and logical-deductive) means."

If this view is accepted, there remains the problem of how values are to be incorporated into analysis if they cannot be quantified, or related to self interest. To the question "Does nature embody values apart from its usefulness in serving man's desires?", the answer seems to be, "Yes, but we are not clear, and cannot expect ever to be clear, what these values are." So Laurence Tribe proposes a fresh attitude to this issue. He concedes that most people are very vague about the values they hold on environmental matters and that "such inchoate values are crystallised into distinct preferences or criteria of choice only through the concrete process of seeking means to attain them and gradually discovering what such means entail." In other words, values evolve through the choices made in groping toward them, and it is an essential aspect of freedom that we can choose what we shall value.

The direction in which this argument leads is as follows. First, there are no sanctified principles upon which environmental decisions rest, no "axiom values"; but all decisions are rationalised in some provisionally held principles, and these provisionally held principles *evolve* in the light of the choices which are made and the observed consequences of these choices. (Consider, for instance, how our values about pesticides have evolved through experience of making decisions about the use of pesticides.) Second, the direction in which principles evolve in our attitude toward the environment is taking us beyond the crude criterion of self interest—witness the recent legislation in Britain to protect some species of wild animals and plants, so rare that not one in a hundred of the legislators is likely ever to have seen any of them! It is this sort of argument which leads Laurence Tribe to suggest that social values about environmental issues progress in a spiral (their direction depending upon their position in the spiral; a framework for choice, as he calls it, which "must incorporate procedures for its own evolution.") And as a starting point on the spiral, Tribe suggests that we "should avoid a premise of human domination—or indeed a premise of the total subservience of any form of being to any other."

A feeling of obligation toward organisms other than man and a responsibility for protecting natural objects—valleys, forests, wildernesses—is of course no novelty among individuals. It is the codification of this obligation or responsibility which is novel. Nearly ten years ago, for instance, there was a planning enquiry into the effect which a North Sea Gas terminal would have on an area of natural beauty on the Norfolk coast. It was the Minister of Housing and Local Government who had to decide whether the area of natural beauty would be damaged by the siting of the gas terminal. In a word, he had to act as the "guardian" of the area of natural beauty. This attitude to a natural object prompts one to ask whether natural objects, trees and woodlands, creatures other than man, should have "rights". At first sight this seems to be a sentimental and mystical attitude to nature. But that is not the view of some hard-headed practical lawyers. In 1972 an article by a professor of law in California, Christopher Stone, examined the singular thesis: Should Trees have Standing? The article has since been published as a book, together with judgement from the Supreme Court on the legal case which prompted Stone's article‡.

The circumstances which brought the action to the Supreme Court were these. The United States Forest Service had granted a permit to Walt Disney Enterprises Inc to "develop" Mineral King Valley in the Sierra Nevada mountains. The decision was challenged by the Sierra Club, which acts vigorously to defend natural objects in America. The Sierra Club lost its case for a reason which would apply to an analogous case if it were to be brought to the courts in Britain, namely because the Club had no sufficient "personal stake in the outcome of the controversy." But three members of the Supreme Court dissented from this decision, and one of the dissenting judgements, by Mr Justice Douglas, drew its inspiration from Stone's article in the California Law Review. He said: "The critical question of 'standing' would be simplified . . . if we fashioned a federal rule that allowed environmental issues to be litigated before federal agencies or federal courts in the name of the inanimate object about to be despoiled . . . Contemporary public concern for protecting nature's ecological equilibrium should lead to the conferral of standing upon environmental objects to sue for their own preservation."

In his lively essay, Stone examines the way rights in law have been conferred upon children (who have not always had rights in law), women, subject peoples formerly enslaved, and so on. He then reminds us that the "world of the lawyer is peopled with inanimate right-holders: trusts, corporations, joint ventures, municipalities . . ." So there is nothing unreasonable about putting natural objects, as the law puts other non-human things, into the category where their interests can be defended in courts by properly recognised guardians. Of course, before the principle could be adopted, many subsidiary questions (such as: Who should be the guardians?) would have to be settled. But the idea is worth serious reflection for it would be one more step in the evolution of an environmental ethic which does not rest on the assumption that nature is made for man. □

‡Stone, C. D., *Should Trees have Standing?* (Kaufmann, Los Altos, California, 1974).

The attack on tropical disease

Alex Dorozynski looks at the World Health Organisation's efforts to relieve man of one of his major burdens

In spite of recent expressions of concern about the new economic order, interdependence of nations, and co-operation, there is one area of enormous importance to the developing world that has largely been ignored: that of tropical diseases. They affect several hundred million people, represent a permanent human burden, and a major obstacle to development. Tropical disease research has hardly benefited from the explosion of knowledge in bio-medical sciences that has taken place in the developed world.

In fact, some of the tropical diseases are now recrudescent, because parasites have become resistant to drugs and vectors to insecticides, because agricultural development sometimes contributes to the creation of conditions required for a disease to become endemic, and because international aid toward the control of tropical diseases has shrunk in the face of increasing costs. In the past year, the World Health Organisation (WHO) has been mounting a new attack on these diseases. The approach is novel, and the outlook promising, although one major element of uncertainty still remains: will there be enough money to carry out this long term programme?

The global annual investment in tropical disease research is estimated by the WHO at about $30 million, which is a mere pittance of money in comparison to huge budgets devoted to other areas of bio-medical research. Advances in treatment and control of tropical diseases have been painstakingly slow, in spite of the fact that most of the causative agents are relatively simple parasites belonging to the lowest orders, protozoa or worms, that in most cases are completely incapable of independent life and rely for survival on the highly specialised environment provided by two or three or sometimes more successive hosts.

"According to the law that viability is inversely proportional to the stringency of ecological requirements," says Professor Christian de Duve, "the pathogenic parasites certainly occupy the bottom of the scale. They are puny enemies indeed." He is the director of the International Institute of Cellular and Molecular Pathology, Brussels, and a member of Rockefeller University, New York. A consultant of the WHO in the new "Programme of Research and Training in Tropical Diseases", he is one of the scientists who has suggested a new approach to tropical diseases research in which the basic biology of the parasite becomes the prime target.

The diseases

Six diseases have been selected as the initial targets of the WHO's Special Programme: malaria, schistosomiasis, trypanosomiasis, filariasis, leprosy, and leishmaniasis.

● Malaria is one of the most widespread diseases in the world, affecting some 200 million people. In Africa, about one-fourth of all adults suffer from malarial fever at one time or another, and at least one million children die of the diseases every year. In several areas of Asia and South America, *Plasmodium falciparum* (one of the four human malaria parasites, responsible for the severest forms of the diseases), has developed resistance to 4-aminoquinolines, major anti-malarial drugs. In Asia resistant strains have progressed westward to reach the Indo-Pakistani subcontinent, and they represent a great threat to Africa, where *P. falciparum* is the main malaria parasite.

In addition, mosquitoes have developed resistance to some insecticides and, as a result of increased costs and reduced international assistance programmes, many countries cannot afford to carry out intensive anti-malarial campaigns.

India is an example. The number of cases there of malaria had been reduced to a low of 60,000 in 1962, but last year it exceeded four million (a 70-fold increase). In Africa, there appears to be no hope of malaria control in the near future. Dr Adetokunbo O. Lucas, former president of the Nigerian Medical Research Council, who in April become the director of the WHO Special Programme, points out that several intensive pilot projects have shown that infection is so deeply entrenched in the environment that spraying of insecticides and drug distribution are not sufficient to interrupt transmission.

In some parts of the world, malaria has inadvertently been promoted by irrigation. A typical example is that of the Gezira, the region between the White Nile and the Blue Nile south of Khartoum. Irrigation had turned the Gezira into the most densely populated and most prosperous agricultural region of Sudan, and the periodical drying out of peripheral irrigation ditches, possible when the area was almost exclusively planted to cotton, had to be abandoned when other crops (notably, rice) were introduced. In 1950, an outbreak of malaria affected more than half of the total labour force, and since then malaria has been endemic. A major effort is now under way to keep the diseases under control.

● Schistosomiasis, caused by trematodes (or fluke worms) also affects about 200 million people. Free-swimming larvae (or cercariae) penetrate through the skin of a person entering the water, migrate to the liver where they mature into adult worms that settle inside blood vessels and go on laying eggs for several years. Infected people may become emaciated, with an enlarged spleen and bloated abdomen, and many develop cancer. It is possible to treat individual cases with injections of antimonials and other compounds, but most of these can cause severe side effects. There is no adequate method for mass treatment.

Schistosomiasis is often associated with rural development. Thus the incidence of the disease has been increasing in Egypt and Sudan since the creation of Lake Nasser, and in Ghana since the construction of the Akosombo Dam on Lake Volta. In Northern Nigeria there has been a three-fold increase in three years around the lake created by the Kainji dam, and even in the semi-arid Arabian Peninsula irrigation has introduced schistosomiasis to regions where it did not previously exist.

● Filariasis affects about 300 million people. The two major filarial parasites, *Wucheria bancrofti* and *Brugia malayi*, transmitted by mosquitos, infect about 250 million people (mainly in Africa, the Indian subcontinent, South-East Asia, the Philippines, China, and the Pacific Islands). They cause elephantiasis of the legs, arms and genitals, by obstructing the flow of lymph.

One form of filariasis is onchocerciasis (or river blindness), caused by *Onchocerca volvulus*, transmitted by *Simulium damnosum*—the blackfly. In the upper basin of the Volta river, more than a million people are infected and thousands are blind. A costly control programme has been initiated in seven of the most affected countries; it involves the spraying from helicopters of the often inaccessible fast-flowing streams where the blackflies hatch, and the treatment of infected persons, but there is a need for better drugs, with less side effects and more effective against adult worms.

● Trypanosomiasis affects some 10 million people. The African form of the disease, sleeping sickness, is endemic over about 10 million square kilometres of land, much of it fertile but abandoned to the tsetse fly, vector of the disease. (It is estimated that this land could provide for a cattle population of 125 million.) The South American form of trypanosomiasis is Chagas' disease, incurable and fatal (it destroys the heart).

● Leprosy, one of the most perplexing infectious diseases, also affects at least 10 million people. Although Hansen's bacillus, or *Mycobacterium leprae*, was described more than a hundred years ago, it has not been grown *in vitro* (or, at least, no reported culture has yet been confirmed). Even the mode of transmission of the disease is not well understood, and although it is generally believed that infection is from man to man, Hansen's bacillus has also been identified in insects, and some researchers believe their bite may also be involved.

● Leishmaniasis, the sixth disease included as a target in the initial stages of the Special Programme, is caused by various protozoa of the genus *Leishmania*. Two of its forms are lethal: the South American *espundia*, which kills by destroying the face, and visceral leishmaniasis, or kala azar.

The programme

There are several reasons why the timing for a renewed effort to develop remedies against these diseases is propitious.

The means to control and treat them are limited, and there is relatively little research directed towards new remedies. A number of recent findings, however, both in parasitology and fundamental biology, can be used to explore new approaches. Several such approaches have been identified, and "task forces", or scientific working groups, have been formed by the WHO, consisting of top scientists in various disciplines, to pursue specific goals.

One group, for instance, is concerned with immunology of malaria, and its ultimate goal is to develop reliable, long-acting vaccines, which would undoubtedly revolutionise the control of malaria. Infection has long been known to produce a certain degree of immunity, and some experimental vaccines have already been produced. Last year, it was shown that some people possess a genetic factor that prevents the invasion of red blood cells by malaria parasites. This genetic trait conferring resistance to malaria is called "Duffy negative", because red cells lack the Duffy antigen, named after the first person in whom it was discovered. It appears that this antigen leads the parasites into the red blood cells, and that in Duffy negative people the absence of the antigen protects the blood cells against the parasites. Some preliminary experiments indicate that certain enzymes can block the antigen, thus conferring anti-malarial protection to the cells.

An even more important finding was announced only last April by Professor William Trager of the Rockefeller University in New York, who is a member of the Special Programme's "task force" on immunity to malaria: he has succeeded in maintaining a laboratory culture of *Plasmodium falciparum* for three months. This is the first time that a continuous culture of any of the malaria parasites has been successfully established *in vitro* and gone through a large number of multiplication cycles. Large amounts of pure *P. falciparum* can now be available, and this is a significant step towards the development of a vaccine.

The harvest of a large number of *Mycobacteria leprae* is also possible since researchers in Louisiana found in 1971 that injection into nine-banded armadillos caused massive infection of the animals. (Previously, infection had been achieved only in mouse footpads, and it was very limited.)

The WHO's scientific working group on immunology of leprosy has already engaged in antigen preparation and purification, and three promising antigens have been isolated, one in Venezuela, one in the United Kingdom, and one in the USA. As with other task forces, the specialists from several countries meet periodically, either at the WHO headquarters in Geneva or elsewhere, to coordinate their efforts. There is good hope that a practical vaccine, providing long-term protection against *M. leprae* can be developed, and a tentative schedule has already been established: if all goes well, field trials should start in four or five years.

Less is known of the immunological aspects of schistosomiasis, filariasis, trypanosomiasis and leishmaniasis, but there is, nevertheless, hope that vaccines can also be developed against at least some of these diseases.

Recent research has shown, for instance, that the *Schistosoma* parasite has a very sophisticated system to ensure its survival in spite of the immunological defences of the organism it invades. When a free-swimming pre-adult cercaria penetrates through the skin of a person, it does trigger antibody production. But within a few days, by the time the parasite reaches maturity, it appears to cover its antigens with proteins that mimic the host's own antigens. Thus, if immunisation could increase the organism's reaction against the pre-adult cercaria, the schistosoma could be destroyed before it had time to protect itself.

High technology

At the same time, other participants in the Special Programme are exploring the possibility of entirely new approaches, relying on recent bio-medical knowledge. Professor de Duve, for instance, is attempting to apply "lysosome therapy" to some of the tropical diseases. "Lysosomes," he says,

> are essentially miniature little stomachs, which occur in all cells. One of their principal functions is to serve in the digestion of food 'eaten' by the cells by a special capture process, called phagocytosis or pinocytosis, depending on the size of the food particles taken in. As with humans, cells may be greedy or frugal, and they may exhibit a wide variety of tastes. Our purpose is to take advantage of these differences to kill certain cells selectively by poisoning their favourite food. To do this, we bind the poison to a carrier molecule in such a way that it will be released when it gets in the lysosome, that is, in the stomach of the cells that have eaten this poisoned food.

Experiments in mice carried out at the International Institute of Cellular and Molecular Pathology in Brussels have shown that such "selective poisoning" can be effective against at least one *Trypanosoma* parasite. A similar approach can be tried for the treatment of diseases such as schistosomiasis or onchocerciasis, caused by worms with very tough skins, whose weak points may be their "stomachs". Even the leprosy bacillus, which has no lysosomes of its own, may be susceptible to similar "poisoning" because it develops within membrane-bound vacuoles resembling lysosomes in the macrophages of its host.

Enzyme therapy is another possible approach. It is known, for instance, that fertilised eggs of the nematode worm, another parasite of man, manufacture chitin, a substance that protects the cell; since mammals do not produce chitin, interference with the enzymes needed to produce it could destroy nematode eggs without affecting the human host.

Interference with the parasites' nervous system could also be explored —notably by acting on chemotaxis, an important determinant of behaviour, or on neurotransmitters (experiments with *Caenorhabditis elegans*, a free-living soil nematode, have shown that tetramysole, an agonist of acetylcholine, a major neurotransmitter, effectively paralyses the worms, arresting feeding and mobility).

Vector control, likewise, can benefit from goal-oriented research, notably in the area of biological vector control. It is known that parasites can be infected by other parasites (for instance, mermithid worms can infect and kill the tsetse fly). But basic research into the biology of the insect and its predator, and into the ecological impact of such an approach, must first be carried out.

These are "high technology" approaches, that require the commitment of skilled manpower and adequate budgets. Their goal is the development of remedies on the basis of knowledge of parasite function and biology, rather than through often empirical, large-scale screening, such as has been widely used until now in anti-parasitic drug research.

The purpose of the Special Programme of Research and Training in Tropical Diseases is not, however, limited to such research, much of which must be carried out in institutes, universities, and pharmaceutical laboratories in the developed world. The very countries most affected by tropical diseases will be associated with the programme.

At the beginning, the focus will be on Africa, which has the highest prevalence of the six diseases and where multiple infection is almost the rule. Several African countries have expressed their willingness to participate in and contribute to the programme, and Zambia has offered laboratories in the large Ndola hospital complex for the creation of a multidisciplinary research centre bringing under the same roof different aspects of laboratory research and clinical medicine. Strengthening of existing laboratories, creation of new ones if necessary, and training of additional indigenous personnel, are planned as part of the programme to promote self-reliance in the very parts of the world where tropical diseases are prevalent.

Several meetings devoted to the Special Programme, co-sponsored by the WHO and the United Nations Development Programme, have already been held, and scientific work has started with the help of initial funds contributed last year by several nations and organisations. But a long-term commitment is needed, as the programme cannot be financed from the shrinking budgets of the WHO or UNDP. This is why a meeting with potential donor nations and agencies will be held later this year. In view of the magnitude of the problem being tackled, and the results that can be expected, the initial annual budget of \$15–\$20 million (the price of a jet fighter or a few miles of superhighway) seems reasonable enough. □