

Prevention

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Rheumatic fever and rheumatic heart disease in developing countries

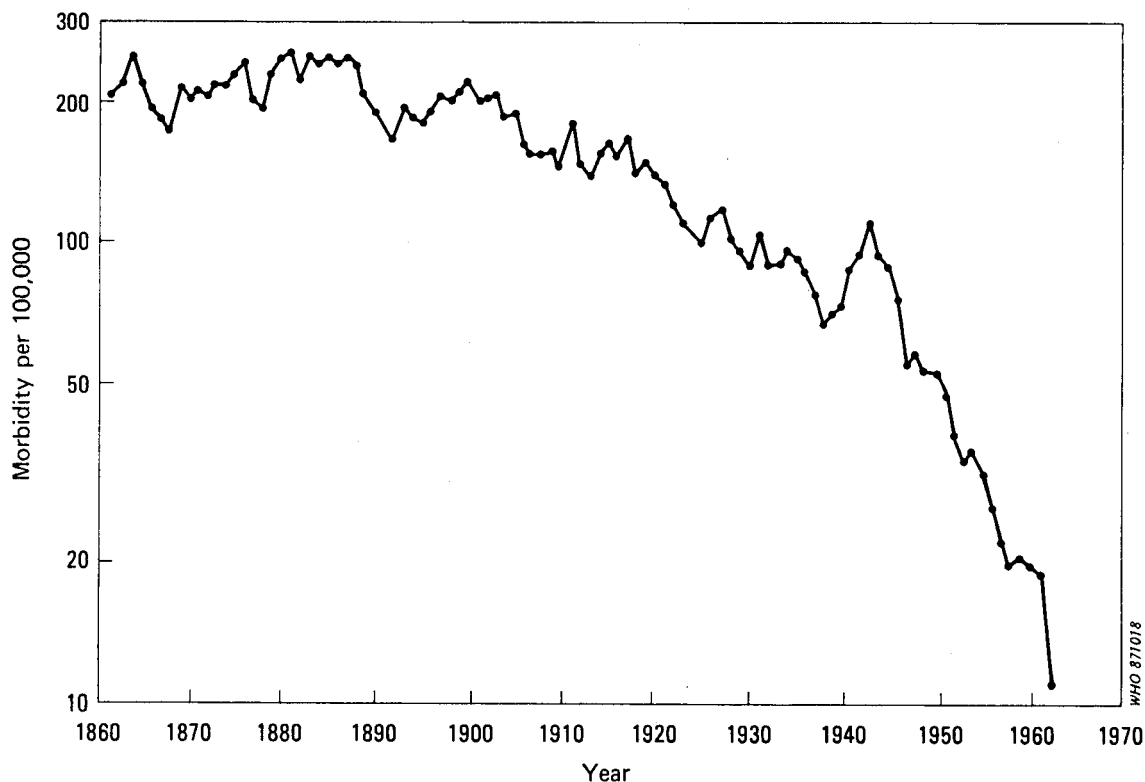
Rheumatic fever and rheumatic heart disease can be prevented by simple methods of primary health care. Well-organized prevention programmes can be cost-effective. Lasting benefit depends on the maintenance of both local interest and financial support from governments.

Rheumatic fever and rheumatic heart disease are common in both tropical and subtropical countries. Seasonal climatic factors can influence the spread of Group A streptococcal infections and thereby affect the incidence of rheumatic fever, but they cannot explain the distribution of the disease in the world at large in different communities of the same climatic area. Irrespective of climate, poor housing and overcrowding favour the spread of streptococcal upper respiratory infections and increase the risk of rheumatic fever.

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The most striking feature of the global epidemiology of rheumatic fever and rheumatic heart disease is the contrast between their progressive decline in the economically developed countries and their continuing intensity in the developing world. Rheumatic fever and rheumatic heart disease were widespread in Europe at the turn of the century, then began to decline. For example, between 1862 and 1900 the annual incidence of rheumatic fever in Denmark was over 200 per 100 000 population but by 1948 it had fallen to about 55 per 100 000. The decline subsequently accelerated and by 1962 the incidence was just over 10 per 100 000 population (see figure). Today, the mean annual incidence of rheumatic fever in the affluent countries is less than 5 per 100 000 and is still falling. As a result, the prevalence of rheumatic heart disease in

Reported rheumatic fever incidence in Denmark, 1862-1962.



Source: Public Health Board of Denmark, Copenhagen. The decline in incidence started early in the twentieth century, and accelerated after sulfonamides and penicillin became available.

these countries has shown an equally dramatic decline; among schoolchildren it is now between 0.1 and 0.5 per 1000 (1). This trend was triggered and maintained by improvements in socioeconomic conditions and general living standards. The benefits of improved medical care and the introduction of antimicrobial agents came later and contributed to the accelerated decline in the incidence of rheumatic fever which has occurred in the developed countries since the end of the Second World War. Even here, however, rheumatic fever still exhibits pockets of relatively high frequency in many inner city areas. There is also the potential risk of occasional flare-

ups in communities where the disease has virtually disappeared. Thus an unexpected epidemic was recently reported in middle-class, suburban families in the USA (2). There should be no complacency about the risk of rheumatic fever, even in affluent populations.

In developing countries the incidence of rheumatic fever is difficult to establish. However, rheumatic heart disease is a common clinical problem and rheumatic fever presumably occurs with corresponding frequency. The available information suggests that incidence rates of rheumatic fever approaching 100 per

Table 1. Reported incidences of rheumatic fever

Country	Period	Age group (years)	Annual rate/100 000
Iran (Teheran) (3)	1972-74	5-19	80
New Zealand (North Island) (4)	1969-81	under 20	24 (non Maori) 116 (Maori)
Sri Lanka (5)	1977-78	5-19	143
USA (New York City) (6)	1963-65	5-14	61

Table 2. Prevalence rates of rheumatic heart disease among schoolchildren

Country	Year	Age group (years)	Rate/1000
Egypt (Qualab) (7)	1972	6-12	10
India (8)	1978	Schoolchildren	6-11
Japan (9)	1971	6-15	0.1
Morocco (Rabat) (10)	1970	6-14	9.5
Bolivia (La Paz) (11)	1973	Schoolchildren	17

100 000 in younger age groups are to be expected in most developing countries (Table 1). Lower figures are frequently reported because many cases go unrecognized.

The prevalence of rheumatic heart disease in developing countries is easier to determine. Reliable estimates have been obtained by screening schoolchildren (Table 2). Differences in the ages of the populations studied and in the methodologies of surveys make it difficult to compare results. Nevertheless, a mean prevalence rate of 10 per 1 000 for the age group 5-15 years can be taken as a reasonable and convenient approximation for planning purposes in countries where data are not yet available.

Public health implications

Rheumatic heart disease interferes with the quality of life of many children and young adults in developing countries. Employability and economic output are diminished, and death usually occurs before the age of 45 years. Patients with fully established rheumatic heart disease are a financial and social burden on their families; those who can afford it, or are fortunate enough to have a health facility close by, become regular attenders at outpatient clinics. These people may have to spend several weeks in hospital every

year, but their expectation of cure is never fulfilled. Drug therapy does not improve damaged heart valves but only provides symptomatic and supportive treatment. Valve replacement surgery offers some hope and improves the five-year survival rate in selected patients. However, few developing countries can provide facilities for open heart surgery or guarantee the long-term anticoagulant treatment and surveillance required after such surgery. Very few families can afford to send their children abroad for heart surgery.

The only way to achieve a real breakthrough is to combat the root causes of the disease in the population, a matter for public health action. Rheumatic heart disease is relatively common, especially in young people, and has high morbidity and

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fatality rates. There is no permanent cure and the cumulative expense of repeated hospitalization for supportive medical care is a considerable drain on human and material resources. Remedial surgery can

improve the quality of life but the cost is beyond the reach of most patients and governments. Surgery does not reduce the incidence of the disease in the community, or the individual's susceptibility to further

Nurses have proved to be both reliable and efficient in identifying children who require medical examination.

attacks of rheumatic fever. Although attacks of rheumatic fever can be treated, even the best treatment has no effect on the subsequent development and course of rheumatic heart disease. The prevention of rheumatic fever is the only solution, and the methods are simple, well-tried and relatively inexpensive. Some developing countries are already implementing prevention programmes in designated areas. A planned, coordinated effort is now needed to initiate more programmes and to extend existing ones towards nationwide coverage.

It is to be hoped that widespread improvements in socioeconomic conditions will eventually help to diminish poverty-related diseases, but few developing countries can expect the incidence of rheumatic fever and rheumatic heart disease to decline significantly for this reason alone in the near future. The emphasis in these countries must be on direct medical approaches to prevent rheumatic fever. This involves the recognition and treatment of streptococcal pharyngitis to prevent first attacks of rheumatic fever, i.e., primary prevention, and the provision of regular, long-term anti-streptococcal prophylaxis to ward off second attacks or recurrences, i.e., secondary prevention.

Primary prevention

The ultimate goal should be primary prevention, but broad community programmes based on primary prophylaxis are difficult to apply. In the vast majority of cases, soreness of the throat is of viral origin and does not require antibiotic treatment. However, 10-20% of cases are caused by streptococci, and 1-3% of these are associated with rheumatic fever. There is no reliable way of identifying individuals who are susceptible to rheumatic fever before they have succumbed to the first attack; primary prevention programmes must therefore be directed at the whole community. Cases of streptococcal sore throat ("strep throat") must be recognized and treated whenever they occur. This means that a large number of acute throat infections must receive appropriate medical care in order to prevent a few cases of rheumatic fever. It would be unrealistic to expect many developing countries to mount successful population-wide programmes of this sort. However, less ambitious programmes limited to defined groups, e.g., schoolchildren, are feasible.

For the individual patient, primary prevention of rheumatic fever is much less difficult and can be a regular feature of clinical care. This involves early recognition of "strep throat" and treatment with drugs that can eradicate the streptococci from the throat if given in appropriate doses for an adequate period of time. Penicillin is the antibiotic of choice, a single injection of benzathine penicillin G maintaining sufficiently high blood levels for long enough to eradicate the infection. If oral medication is used, e.g., penicillin V or— for those allergic to penicillin— erythromycin, treatment should continue for 10 days (Table 3); treatment for shorter periods may not eradicate the streptococci and may thus fail to prevent rheumatic

Table 3. Treatment of streptococcal pharyngitis for primary prophylaxis^a of rheumatic fever

Antibiotic	Dose	Duration and route
Benzathine penicillin G	1.2 million units for adults and children over 30 kg 600 000-900 000 units for children weighing less	Single dose i.m.
Penicillin V	250 mg 4 times daily 125 mg 4 times daily for small children, e.g., 3 years old (15 kg)	10 days by mouth
Erythromycin (for patients allergic to penicillin)	250 mg 4 times daily 40 mg/kg/day in 2 to 4 divided doses for children	10 days by mouth

^a Sulfonamides, tetracyclines, chloramphenicol and trimethoprim are contraindicated.

fever. Sulfonamides, tetracyclines and other bacteriostatic drugs do not eradicate the organisms from the throat and should not be used.

It is often difficult to distinguish "strep throat" from viral pharyngitis on clinical grounds alone. Furthermore, many clinics do not have laboratory facilities for throat culture and are also not able to use services available elsewhere. In such circumstances, the decision to treat a sore throat with antibiotics should be based on clinical suspicion (Table 4) and a consideration of what is going on in the environment, e.g., whether there is a local outbreak of streptococcal pharyngitis.

The recognition and proper treatment of "strep throat" prevents rheumatic fever and minimizes the spread of the disease in the community; it also avoids the dangers and cost of giving antibiotics uncritically or unnecessarily to every case of acute pharyngitis. Test kits for the rapid detection of Group A streptococcal

antigens in throat swabs by direct methods are commercially available. A result is usually obtainable in under 15 minutes. If these kits fulfil their early promise and also become easily procurable at low cost, they could make an important contribution to the primary prevention of rheumatic fever.

Secondary prevention

Programmes based on secondary prophylaxis are the most practical because the target group is limited to those who are known to be susceptible to rheumatic fever, namely, people with a past history of the disease and patients with rheumatic fever or rheumatic heart disease. Successful secondary prophylaxis prevents infection of the upper respiratory tract by Group A streptococci and therefore the subsequent development of rheumatic fever. WHO has consistently advocated this as the main thrust of prevention programmes for communities in developing countries.

The most reliable method of secondary prophylaxis is the intramuscular injection of long-acting benzathine penicillin G at monthly intervals. Oral antimicrobial agents, e.g., penicillin V, or sulfadiazine or erythromycin for patients allergic to penicillin, can be used, but long-term prophylaxis by mouth is much less effective

Table 4. Common features of streptococcal and viral pharyngitis

	Streptococcal	Viral
Season	Cool, rainy months	Varies
Age	5-15 years	All ages
Onset	Often abrupt	More gradual
Initial symptoms	Painful to swallow	Mild sore throat
Other symptoms	Tender cervical lymph nodes	Runny nose, cough, hoarseness
Pharyngeal appearance	Redness, oedema, exudate	Redness, ulcers, vesicles

than benzathine penicillin in preventing streptococcal infections and recurrences of rheumatic fever (1). The dosage schemes indicated in Table 5 have been endorsed and recommended by a recent WHO study group (12).

The duration of secondary prophylaxis should be based on individual needs and circumstances, but the following general principles apply (12).

- Patients with no evidence of cardiac involvement should receive prophylaxis for a minimum period of five years after the last attack of rheumatic fever.
- Patients with evidence of carditis during the initial attack should continue regular prophylaxis at least until they are 25 years old, but longer if the environmental conditions so warrant.
- Patients with chronic rheumatic heart disease, including those who have had cardiac surgery, require secondary prophylaxis indefinitely, sometimes even for life; the actual duration needed will vary between individuals.

In prevention programmes it is important to educate the general public, especially schoolchildren and their parents and teachers, about the need to treat "strep throat". The aim is to encourage people to seek medical advice when they have a sore throat, so that "strep throat", if present, will be recognized and treated. Primary health care workers should receive health education and the training and back-up support necessary for practising primary prophylaxis. Health education programmes should also be designed to motivate such patients and their families to accept secondary prophylaxis on a regular long-term basis and to enlist their cooperation for maintaining a high level of patient compliance.

Table 5. Antibiotic regimen for secondary (continuous) prophylaxis of rheumatic fever/rheumatic heart diseases (12)

Mode of administration	Penicillin	Sulfadiazine
Intramuscular	Benzathine penicillin G Single injection once a month ^a For children <30kg: 600 000 I.U. For larger children and adults: 1 200 000 I.U.	
Oral ^a	Penicillin V 250 mg twice daily	For children <30kg: 0.5 g daily For larger children and adults: 1 g daily

^a For the unusual patient who may be allergic to penicillin and sulfonamides, erythromycin 250 mg twice daily is suggested.

^b For special circumstances or high-risk patients, one injection every three weeks may be used.

From 1970 to 1975, WHO coordinated a research project based on secondary prophylaxis in seven developing countries (13). This study demonstrated that secondary prevention programmes were feasible and cost-effective. A comprehensive manual of operational standards for extending programme coverage at different levels of care has also been prepared (14). Yet few developing countries have gone beyond the pilot study stage, and fewer still have taken up the challenge in the context of their national health development priorities. How can such programmes be implemented and what are the barriers to success?

Every country in which rheumatic fever and rheumatic heart disease are a significant problem needs a national plan for secondary prevention, with objectives, targets, and a time-based programme for extending activities in realistic stages towards nationwide coverage. The plan of operation is usually prepared by a national programme manager appointed by the ministry of health. A multidisciplinary national advisory committee, similarly

appointed, provides general policy guidance and advises government on the fiscal and other requirements for maintaining and extending the programme in accordance with the approved plan of operation.

In many situations, the only hard data available on which to base initial planning come from hospital statistics which show that rheumatic fever and rheumatic heart disease account for up to 4.5% of general admissions and for 30-45% or more of the cardiac patients in wards. Hospital departments of paediatrics or medicine are therefore well placed to extend their regular registration and follow-up procedures into more widely based secondary prevention programmes. The choice depends on local circumstances, the important consideration being that the programme manager can liaise effectively with schools, school health services, primary health care centres and maternal and child health services, as well as with departments of medicine and paediatrics and laboratory services in hospitals.

A fully established programme centre should:

- operate a central register for patients with rheumatic fever and rheumatic heart disease;
- promote cooperation between participating physicians, school health services, maternal and child health centres, hospitals and laboratories;
- plan and coordinate case-finding surveys, including training of survey teams;
- establish and maintain a system of regular secondary prophylaxis and, wherever feasible, promote primary prophylaxis;
- promote health education and keep health personnel at all levels informed

about rheumatic fever and rheumatic heart disease in general and the programme in particular;

- evaluate methods of programme operation and submit periodic reports to the ministry of health;
- analyse, as far as possible, the cost of the programme.

Satellite or programme subcentres with limited but similar functions can be established from the very start or as part of a phased programme to extend activities to additional regions.

Case-finding, an important component of programme activities, may involve retrospective surveys of hospital records and the screening of schoolchildren. In many countries, nurses are trained to recognize certain criteria for referral, e.g., heart murmurs, and have proved to be both reliable and efficient in identifying children who require medical examination. Surveys targeted only on rheumatic fever and rheumatic heart disease are likely to be cost-effective where there is a high risk of these conditions in the community. They

Programmes for the secondary prevention of rheumatic fever and rheumatic heart disease can be implemented through primary health care facilities, without major additional cost.

can be made more so if performed as part of a general purpose health survey of schoolchildren. The ultimate aim should be to incorporate screening surveys into the routine school health examination system

on a regular basis or to help establish such services where they do not yet exist. The epidemiological data acquired from case-finding surveys provide a useful basis for estimating the size of the problem and for planning future extension of the programme. This by-product further justifies regular school screening surveys.

Constraints

The common barriers facing community prevention programmes in developing countries include lack of personnel, equipment and supplies, and inadequate managerial and infrastructural support. However, programmes for the secondary prevention of rheumatic fever and rheumatic heart disease can be implemented through existing primary health care facilities, without major additional cost; the obstacles to their development must therefore be sought elsewhere. Health administrators and policy-makers are possibly unimpressed by the size of the problem or perhaps there are no locally relevant data to persuade them that it merits concerted public health action. It may also be that there are so many other problems high up on the list of traditionally established health priorities that rheumatic heart disease does not get a proper hearing.

There are other obstacles to success at the level of the programme itself. A common cause of failure is poor patient compliance, often aggravated by the lack of a well-organized method for following up patients who drop out or miss their appointments. Poor compliance may arise because of the long distances that patients sometimes have to travel to reach treatment centres, or because of the cost of travelling regularly to them. In some countries, benzathine penicillin is not always available, with the result that there are recurrences of

rheumatic fever. Some doctors do not use this drug because they fear allergic reactions, yet serious reactions are rare, particularly in children, and are no more frequent or severe than those following treatment with other forms of parenteral penicillin.

Cost-effectiveness

In principle, it is desirable to implement health improvement procedures that are effective and inexpensive, and at the same time prevent illness for which costly treatment would otherwise be sought. Examples of such measures include immunization against common diseases, the provision of safe water, and antibiotic treatment of streptococcal sore throat (15).

The socioeconomic, psychological and emotional consequences of rheumatic heart disease are substantial and the potential benefits of prevention programmes directed against rheumatic fever are well known but difficult to express in monetary terms. It has been shown that a mean of 3.14 prophylactic injections of penicillin per patient are required to avert one day in hospital (13). Assuming that the cost of delivering one injection is US\$ 1.25, and that the average cost of hospitalization in a developing country is \$ 25 per day, then \$ 4.00 spent on prophylaxis will avert the expenditure of \$ 25 in hospital. Using a slightly different approach, a Nigerian study showed that the money spent on medical treatment for one case of rheumatic heart disease for one year could have prevented 5.4 cases in the same period (16). These examples do not take into account the costs related to surgical treatment, nor do they express benefits, such as reduced disability and increased years of healthy life, which can be attributed to preventive measures.

WHO global action to prevent rheumatic fever and rheumatic heart disease

Sixteen countries in five WHO Regions are participating in a global effort to prevent rheumatic fever and rheumatic heart disease. The WHO programme is partly supported by funds from the Arab Gulf Programme for United Nations Development Organizations. All the collaborating countries have national advisory committees and national plans of operation.

The local programmes are based on case-finding, registration, surveillance of suspected cases, and follow-up of known and newly identified patients. The aim is to prevent recurrences of rheumatic fever by providing regular secondary prophylaxis to at least 70% of registered patients.

The total target population, i.e., children aged 5-15 years, in the designated programme areas is over 3 million. At the end of the first phase of the programme (1985-86) some 200 000 schoolchildren in 12 countries had been screened and 329 cases confirmed and registered. A further 4625 cases were uncovered from retrospective surveys of case records and from other sources. Data on penicillin coverage during the first six months of field activities were available from 13 countries and the average coverage rate was 76.6% of the expected maximum, the range being 32-100%.^a

Although the initial reports are promising, there are still many obstacles to success, among them the difficulty of consolidating and extending programmes when financial support from external sources comes to an end. It remains to be seen whether the countries will continue the programmes at an effective level.

^a WHO global programme for the prevention of rheumatic fever/rheumatic heart disease in sixteen developing countries (AGFUND supported). Report of a meeting of national programme managers, Geneva, 4-6 November 1986. World Health Organization, 1987 (unpublished document WHO/CVD/87.1).

The effects of rheumatic heart disease in terms of illness, disability and death can be quantified as the number of days of healthy life which are lost. The data required for this type of analysis include estimates of incidence, case fatality rate, average ages of onset and death, life expectancies, and the extent and duration of disability and illness. In Ghana, a rank order of 48 diseases was prepared on the basis of estimates of the numbers of healthy days of life lost per 1000 persons per year because of the diseases (17). The top three were malaria, measles and pneumonia, which together accounted for nearly a quarter of the total number of days of healthy life lost.

Rheumatic heart disease was ranked 32 and accounted for 1% of the total.

Priorities for public health action should not, of course, be based solely on the ranking of disease problems in this way. Other factors, such as preventability and the cost of the proposed health improvement procedure expressed in terms of effects achieved per unit cost, must also be considered.

Assuming 66% programme coverage and 90% effectiveness of penicillin in preventing rheumatic heart disease, it is

possible to calculate that every dollar spent on delivering penicillin in a programme for the secondary prevention of rheumatic fever and rheumatic heart disease in Ghana would achieve a saving of 51 days of healthy life per 1000 population per year. Measles immunization achieved a saving of 918 healthy days per 1000 per year under comparable conditions (17).

Such comparisons, and the assumptions on which they are based, are perhaps open to challenge. However, they illustrate the use of cost-effective analysis and suggest the need for more studies of this kind to enable health administrators to estimate the relative costs and benefits of prevention programmes and the priority that should be given to the prevention of rheumatic fever and rheumatic heart disease. □

References

1. **Taranta, A. & Markowitz, M.** *Rheumatic fever—a guide to its recognition, prevention and cure—with special reference to developing countries.* Boston, MTP Press, 1981.
2. **Veasey, L.G. et al.** Resurgence of acute rheumatic fever in the intermountain area of the U.S. *New England journal of medicine*, **316**: 421-427 (1987).
3. **Gharagozloo, R.A. et al.** RF and RHD among 56 800 inhabitants in south-east Teheran from 1972-74. *Acta tropica* (Basel) **33**: 215-222 (1976).
4. **Flight, R.J.** The Northland rheumatic fever register. *The New Zealand medical journal*, **97**: 671-673 (1984).
5. **Wallooppillai, N.J.** *The community control of rheumatic fever and rheumatic heart disease.* Report of a WHO meeting held in New Delhi, 21-27 November 1979. Geneva, World Health Organization, 1980 (unpublished document WHO/CVD/80.3, p.25).
6. **Brownell, K.D. & Bailen-Rose, F.** Acute rheumatic fever in children. Incidence in a borough of New York City. *Journal of the American Medical Association*, **224**: 1593-1597 (1973).
7. **El Kholy, A.** *Prevention of RHD.* VII World Congress of Cardiology, Buenos Aires, 1-7 September 1974.
8. **Padmavati, S.** Rheumatic fever and rheumatic heart disease in developing countries. *Bulletin of the World Health Organization*, **56**: 543-550 (1978).
9. **Shiokawa, Y.** Epidemiology of rheumatic fever and rheumatic heart disease in Japan. *Japanese circulation journal*, **39**: 185-186 (1975).
10. **Tazi, M.A.** *Progress of rheumatic fever prevention in Morocco.* Geneva, World Health Organization, 1972 (unpublished document CVD/72.2).
11. **Ibarnegaray, J. et al.** *Informe de Bolivia a la V Conferencia Panamericana de Estudio y Prevención de la Fiebre Reumática.* [Report from Bolivia to the 5th Pan American Conference on the Study and Prevention of Rheumatic Fever.] Buenos Aires, 1974.
12. *Rheumatic fever and rheumatic heart disease. Report of a WHO Study Group, 30 March-4 April 1987.* Geneva, World Health Organization, 1988 (Technical Report Series No.764).
13. **Strasser, T. et al.** The community control of rheumatic fever/rheumatic heart disease: report of a WHO international cooperative project. *Bulletin of the World Health Organization*, **59**: 285-294 (1981).
14. *Prevention and control of rheumatic fever in the community.* Washington, Pan American Health Organization, 1985 (Scientific Publication No. 399).
15. **Shepard, D.S. & Thompson, M.S.** First principles of cost-effectiveness analysis in health. *Public health reports*, **94**: 535-543 (1979).
16. **Jaiyesimi, F.** Chronic rheumatic heart disease in childhood: its cost and economic implications. *Tropical cardiology*, **8**: 55-59 (1982).
17. **Morrow, R.H., et al.** A quantitative method of assessing the health impact of different diseases in less developed countries. *International journal of epidemiology*, **10**: 73-80 (1981). Reproduced in *World health forum*, **3**: 331-335 (1982).