

Acute rheumatic fever and rheumatic heart disease: a prevention program for the Pacific

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Introduction

The Pacific countries like many developing countries, suffer from high rates of Acute Rheumatic Fever (ARF) and its principle long term sequelae of Rheumatic Heart Disease (RHD). Since the underlying causal agent group A streptococcus (*S. pyogenes*) and the disease streptococcal pharyngitis are easily treated, ARF should be preventable. This paper outlines a prioritized stepwise program to prevent ARF and RHD. The purpose of presenting these suggestions is to provide a framework for discussion and to allow individual health departments to determine their own policies.

How bad is the problem of ARF and RHD in Micronesia?

Dr. Alto¹ and colleagues at the Pacific Basin Medical Officers Training Program (PBMOTP) tried to determine an incidence rate of ARF by conducting a retrospective review of existing medical record in four states of the Federated States of Micronesia (FSM). Applying strict criteria to avoid over counting they estimated the rate of at least 10.4/100,000. As they acknowledge, this is certainly way too low given the many probable cases that had to be excluded due to insufficient documentation (lack of availability of streptococcal testing, incomplete charts, etc.) And the likelihood that other cases never came to the hospital from remote areas.

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Another, and somewhat more standardized, way to measure the severity of the problem is to look at the prevalence rate of RHD among school age children. In Pohnpei and Kosrae states in the FSM, all school children are screened for heart murmurs, generally in grades 1, 4, and 8. Children with suspicious murmurs are referred to be examined by physicians at the local hospital. All suspect cases of RHD are seen once a year by a visiting pediatric cardiologist who makes the final diagnosis. A list of all children diagnosed with RHD is kept by the Public Health Department in order to provide monthly benzathine penicillin prophylaxis (see below). From this list we were able to calculate the prevalence rate of RHD among 5 to 15 year old children in Kosrae and Pohnpei. This is the same method, school-based screening for murmurs with follow-up diagnosis by expert physicians, by which WHO and others have calculated RHD rates in many developing and industrialized countries (see Table 1).

Thus, it would appear that the school-age prevalence rate of RHD is relatively high in Pohnpei and Kosrae, even when compared to other developing countries. These high rates, especially in Kosrae, are not likely to be due to over diagnosis given the careful review by several physicians including a pediatric cardiologist. Many children with questionable diagnoses were excluded. In fact, the high rate in Kosrae is most likely due to its small

size and population, with a more thorough and complete school-based screening program than is found in most other countries.

How can we prevent ARF and RHD in the Pacific?

A six part ARF/RHD prevention program is described below. These make up a prioritized step-wise program. Steps 1-3 are universally acknowledged minimal action that should be part of any public health, community health and primary care program. Steps 4-6 are progressively more aggressive actions which have been tried with success in specific settings elsewhere, and which may be appropriate for the situations in many Pacific nations. The purpose of presenting these suggestions is to provide a framework for

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Table 1. Rheumatic heart disease: school age prevalence rates

Geographic site	Rate per 1,000 5-15 year olds		
	Average	Country range	Reference
Africa (Mali, Zambia, Zimbabwe)	4.7	3.4 - 12.6	2
Americas (Bolivia, El Salvador, Jamaica)	1.5	0.1 - 7.9	2
Mediterranean (Egypt, Iraq, Pakistan, Sudan)	4.4	0.9 - 10.2	2
South-East Asia (India, Sri Lanka, Thailand)	0.12	0.1 - 1.3	2
Asia-Pacific (China, Philippines, Tonga)	0.7	0.6 - 1.4	2
Soweto, South Africa	7.1		3
India	1.5		4
Pohnpei	5.5		5
Kosrae	11.9		5

discussion and to allow individual health departments to determine their own policies.

1. Intramuscular benzathine penicillin injection given every 21–28 days to all persons having had one or more episodes of ARF or RHD prevent recurrent episodes of ARF and RHD.

This is recommended because the risk of secondary ARF with subsequent episodes of streptococcal pharyngitis is 50%. This compares to a rate of only 1–3% of primary ARF following untreated streptococcal pharyngitis in a person who has never had ARF before. There is typically progression of RHD with each episode of ARF.

This is usually accomplished by having community level clinics keep a registry of all children known to have had an episode of ARF or to have RHD. The registry is then actively used to ensure compliance either by home or school visits by a health care worker or having the child come to the clinic. Intramuscular benzathine penicillin should be given every 21 to 28 days. Scheduling on a calendar month basis may be simpler but is spaced too far apart allowing the penicillin level to fall too low for too long.

The dose of benzathine penicillin is, as it is for the other measures listed below, is 600,000 units for children up to 30 pounds (about up to age 4 years), 900,000 units for children up to 60 pounds (about ages 4–8 years), and 1.2 million units for children and adults over 60 pounds.

The question of when to stop is difficult and guidelines may in practice depend upon financing. Ideally, people who have had a single episode of ARF without any permanent heart damage (no RHD) should remain on benzathine penicillin until they are at least 18 years of age, but at least for 5 years. That is, if they had their one bout of ARF at age 17 then they

should continue on prophylaxis until age 22. If they had their one bout at age 7 then they should continue on prophylaxis until age 18. Ideally, people who have had more than one episode of ARF or have RHD should remain on prophylaxis indefinitely. In addition, any person with ARF or RHD should remain on prophylaxis so long as they are in school or sharing a residence with a school-age child, since this puts them at continued risk for streptococcal pharyngitis.

This has been found to very cost-effective. In the United States, the savings are \$5 for every \$1 spent. In the Pacific Islands the saving is even greater because benzathine penicillin is available from UNICEF for about 20 cents per dose or \$9/year/case treated. This compares to a cost of about \$11,000 for an off-island referral for valve surgery.

Use of benzathine penicillin is safe. WHO in its multi-country trials of this program reported very low rate of anaphylactic reactions. In 30,000 ARF patients from 16 countries over 4 years they had only 11 cases of anaphylactic reactions (0.09% patient-years, 2 per 10,000 injections) and 4 deaths (0.03% patient-years, 0.8 per 100,000 injections).

2. Screen all children ages 5 to 18 years for heart murmurs.

This is most simply done by school-based screening for heart murmurs by primary health care workers. Any child even a slightly suspicious murmur may then be referred to a higher level worker for further evaluation. A brief history for acute or recurrent sore throats and/or migrating arthralgia or arthritis may also be done. This school-based screening serves as active surveillance for possible RHD and allows for referral to the secondary prevention program cited in number 1 above. The school-based screening can also be used as one opportunity for the health education measure listed in number 3 below.

3. Educate parents and children to recognize and seek care for all sore throats, and also for all arthralgia or arthritis.

The measures in 1 and 2 above, at best, only prevent further secondary attacks of ARF and progression of RHD. Primary prevention of ARF depends on early and complete treatment of all cases of streptococcal pharyngitis. This requires that the child and parents recognize "sore throats" when they occur, and then seek and receive care. Although some cases may be truly asymptomatic, most cases are not. In the United States 20-30% of ARF cases did not report a prior sore throat. However in the FSM the great majority of cases either did not seek care or did not recognize that they had a sore throat. This suggests a need to understand community

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education: Sore throats make sick hearts?

sooner a child is seen for ARF the less likely offer heart disease. In the FSM, as in most parts acute migrating arthralgia or arthritis is the most y symptom. Rash is also a common presenting somewhat less specific.

children with clinical pharyngitis (sore throats) single dose of intramuscular benzathine penicil-

two recommendations:

all sore throats with antibiotics without bother-determine whether there is *streptococcus* (no es or antigen tests).

single dose of intramuscular benzathine penicil-ner than a course of oral antibiotics.

sore throats without testing for streptococcus is y place with a high rate of ARF and RHD and ces are limited. In most developing countries tococcus, whether by culture or antigen test kit available, too expensive, or likely to be inaccur-ore, delays in treatment increase the likelihood ment. The percentage of sore throats due to pathogens rather than viral pathogens is greater in eloping countries than in temperate-climate ountries so the rate of over treatment is less. The reating, at the UNICEF price of 20 cents a dose e penicillin, is less than the cost of testing.

reatment with a single intramuscular dose of enicillin, rather asking a child (or adult) to take ion 3 to 4 times a day for 14 days is justified n the world. This provides complete treatment rather than depending upon difficult patient Even in special controlled studies where compli-ect, benzathine has a higher cure rate than oral

penicillin. Furthermore, the UNICEF price of 20 cents for the single dose of benzathine penicillin is less than the \$5 to \$50 that 42 to 56 oral doses of any antibiotic, even generic oral penicillin, will cost.

This policy has been a proven and safe success in Costa Rica, a small developing Central American country. There, a program that combined public education and improved community clinics, with a national protocol to treat all clinically diagnosed exudative pharyngitis immediately with a single dose of benzathine penicillin resulted in a decreased incidence of ARF by a factor of 10 fold, from 9 to 0.9 per 100,000.⁶ There were no cases of fatal anaphylaxis and no emergence of penicillin resistant streptococcus after 10 years. Although the

data presented in the paper does allow us to determine the relative importance of different factors, such a policy of universal single dose intramuscular benzathine penicillin for all cases of sore throats will prevent many cases of ARF and RHD from ever occurring.

As noted in recommendation 3, this is still dependent upon the parent and child recognizing the presence of a sore throat, and seeking and receiving care. These recommendations build one upon the other to make a complete program.

Parenthetically, it should be noted that combining rifampin with penicillin or another drug (but never rifampin alone) can be considered as a secondary line of therapy for persons who are streptococcal positive despite a course of penicillin, or are suspected of chronic streptococcal carriage, or who have recurring episodes of ARF.

5. Treat all contacts of ARF presumptively with a single dose of intramuscular Benzathine penicillin (contact/exposure based).

The purpose of this is to reduce the presumed high rate of streptococcal infections and carriage among close contacts of the person already known to have had recent streptococcal infection by virtue of their now having ARF. Close contacts may include household members, playmates, immediate neighbors and schoolmates sharing the same classroom. Such a policy has multiple benefits: It will reduce the likelihood of recurrent ARF from reinfection in the index case. It also reduces the prevalence of streptococcal infection and carriage in the population. It targets a cohort likely to have a higher rate of streptococcus and a strain proven to be rheumatogenic.

6. Presumptive treatment of high prevalence areas and groups with a single dose of intramuscular benzathine penicillin (community/population based).

The idea is a one time treatment, with a single dose of

active appro-educations makes de-tes

Similarly, they are to su- of the world, a common early symptom, if se-

4. Treat all children with a single dose of intramuscular benzathine penicillin.

This is really

- 1) Treat all children with a single dose of intramuscular benzathine penicillin.
- 2) Use a single dose of intramuscular benzathine penicillin rather than a course of oral antibiotics.

Treating all children with a single dose of intramuscular benzathine penicillin is justified in areas where resources are limited. In most developing countries, tests for streptococcus are either unavailable or too expensive. Furthermore, the cost of non-treatment of bacterial pathogens in tropical developing countries is high. The cost of over treatment with benzathine penicillin is low.

Primary treatment with a single dose of intramuscular benzathine penicillin is justified everywhere in the world. This provides complete treatment rather than depending upon difficult patient compliance. Even in special controlled studies where compliance was per-

intramuscular benzathine penicillin, of a population or site known to have a high incidence of ARF or prevalence of RHD. This could be school-based in selected villages, municipalities or islands found to have a high rate after instituting measure 1, 2, 3, and 4. Similar to measure 5, but even more aggressive, the purpose is to reduce the population burden of streptococcal carriage and infection. This in turn will reduce the number of people who get ARF or RHD.

Although it might appear to be extreme, such a policy has been successful in comparable settings elsewhere.⁷⁻¹⁰ It seems especially appropriate in the small geographically isolated population of the Pacific. It is, in principle, not very different from other population-based strategies to reduce the burden of disease such as the use of universal prophylaxis with vitamin A, vermoz or diethylcarbamazepine for vitamin A deficiency and ascariasis in high prevalence populations. It can even be compared to immunization against vaccine preventable diseases where the risk of disease to any single individual is low, but universal coverage is sought to protect the population. It also harkens back to the Pacific experience with the eradication of yaws.

This is admittedly a very aggressive step to take, and would best be done after measures 1-4 have been implemented and in conjunction with a study measuring pre- and post-streptococcal carriage and infection rates and rates of ARF. There will inevitably be some remaining cases of streptococcus and some subsequent reintroduction from outside populations. However the prevalence and burden of streptococcal infections, ARF and RHD will decline. It is likely that the rates would never reach their prior high levels.

Finally, we should also acknowledge that other independent socioeconomic and demographic changes now desired and sought in most Pacific jurisdictions — such as decreased birthrates, increased childbirth spacing, decreased house-

hold and school size and crowding, and improved nutrition, ventilation and sanitation — are likely to cause a natural decline in the incidence and transmission of streptococcal pharyngitis and hence in the incidence and prevalence of ARF and RHD.

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After 20 years one is no longer quoted in medical literature.
Every 20 years one sees a re-publication of the same ideas.

Bela Schick (1886 - 1947)