EPIDEMIOLOGIC PATTERNS AND CONTROL STRATEGIES IN TYPHOID FEVER

INTRODUCTION
Human beings are the only reservoir and host for typhoid fever, caused by Salmonella typhi and less commonly S. paratyphi B and S.paratyphiA. Typhoid fever is a serious disease occurring in many developing countries. It kills young adults at the beginning of their productive years, these people frequently are the main wage earners in the family which further magnifies the socioeconomic impact of the disease. Control of the disease requires uncontaminated water, effective sewage disposal and prompt diagnosis and treatment of patients as well as asymptomatic carriers. Unfortunately these are not readily available in many countries where typhoid fever is endemic.

HISTORICAL OVERVIEW
First described by P Ch A Louis in 1829\(^1\), later William Budd provided evidence that bowel discharges were the main source of infection; that the disease was water borne and insisted that germs cause typhoid\(^2\). S.typhi was first cultured in 1884 and the first vaccine for human use was prepared with heat killed organisms in 1896\(^3\). In 1903 Robert Kochs outlined three principles of typhoid control-disinfect excreta at its source\(^3\), improve sewage handling and isolate convalescent patients until they are bacillus free. It was as late as 1948 that chioromycetin was first used in typhoid\(^4\).

EPIDEMIOLOGY
Typhoid could be prevented by blocking the passage of bacilli from the intestine or urinary tract of one person to the mouth of another was well established in 1880s. The results of putting this knowledge to practice resulted in a dramatic fall in the incidence of (Table I and II).
1) Typhoid fever incidence:
It has been estimated that 33 million cases and 500,000 deaths occur annually throughout the world.
developing world due to typhoid fever with a worldwide incidence of 365 /100,000 and 540 /100,000 (0.5%) in the
developing world. In countries where reliable system of reporting exists such as Japan and U.S.A the annual incidence is 0.24 - 3.7 /100,000 population.

2) Basic epidemiologic parameters:
   i) Incubation period: range 7-21 days, mean 14 days;
   ii) Duration of sickness: range 14-35 days, mean 28 days;
   iii) Frequency of relapse: 5% of cases;
   iv) Duration of relapse: range 7-28 days, mean 18 days;
   v) Proportion of cases: symptomatic (typical, febrile):20% asymptomatic (and mild):80%;
   vi) Case fatality rate: 1-10%, average 3%;
   vii) Carrier rate: chronic, range 2-5%, average 3%; temporary, (mean duration 90 days) range 7-20%, average 10%.

3) Patterns of transmission:
a) Water-borne versus water-washed infection:
   Typhoid fever is a water-borne as well as a water-washed (or water-scarce) disease. The latter are
diseases of the intestinal tract which can be significantly reduced following improvement in domestic
and personal hygiene and increased availability of water. They depend on the quantity of water rather
than its quality. There has also been some suggestion that epidemic typhoid is water borne while
endemic typhoid is water-washed.
b) Food-borne infection:
   Polluted water is the source of organisms in many food-borne epidemics not only of typhoid but also
paratyphoid B infection. Milk and other dairy products follow close on water as an important source of
explosive epidemics. Recently lettuce, cabbage and celery, vegetables that are eaten raw in salad were
traced to be the prime source of S.typhi during the summer months in Santiago. The incubation period
in food-borne epidemics is generally short and the attack rate higher than in water-borne epidemics.
c) Infection by contact:
   There is no doubt that both S.typhi and S.paratyphi B can be transmitted from one person to another
without the interposition of water and food. The house fly is an important vehicle for transferring the
bacilli from excreta to food. The danger of contamination from the soiled feet or proboscis appears to
be far less important, than when the fly itself becomes infected and carries the bacilli for some days in
its intestinal canal. The only high risk people in developed countries, are the laboratory workers and
are known to have contracted the fever on several occasions.

Epidemiologic patterns of typhoid fever:
In the 1960s four epidemiologic patterns of exposure to S.typhi had been suggested.
a) where hygiene and sanitation are appalling S.typhi is prevalent, but typhoid epidemics are rare
because of immunity acquired during asymptomatic or unrecognised infection in infancy or early
childhood;
b) where hygiene and sanitation are poor, S. typhi is common and typhoid fever is particularly
prevalent in children;
c) where hygiene and sanitation are a mixture of primitive and modern (often in association with ur-
banisation) outbreaks of typhoid fever may involve all age groups;
d) where hygiene is excellent S.typhi and typhoid fever are rare.
In large cities such as Mexico City, Karachi and Santiago the second and third epidemiologic patterns
exist and typhoid fever is frequent among children and adolescents. A major problem is the continuous
migration of indigent rural people into the cities. In the urban fringe areas where these people
congregate the supply of drinking water is inadequate. Typhoid fever remains endemic in such areas,
with epidemics occurring from time to time. Water-borne outbreaks of typhoid are typically explosive.
in onset. The curve for the whole epidemic is characteristically skew, the primary cases due to direct infection from the water supply being followed by secondary crops of contact cases. Less often when infection of water is slight or intermittent, there is a series of single cases or small groups of cases occurring over a considerable period of time affecting a small proportion of consumers. Contamination may occur at the water source, during storage or distribution. Suspicion of the water should always arise if building operations, repairs or any alterations have been going on in the water services.

**Clinical severity of typhoid fever**

Whether clinical severity of typhoid fever is increasing in the developing world is at present an unanswerable question. The reported case fatality ratios, in the pre-antibiotic era, appeared to decrease to 1-12% in the years after the introduction of chloramphenicol. Reports from Nigeria, Indonesia and India show case fatality ratios of 9-32% during the last 10 to 15 years. In some areas of Indonesia, the incidence of typhoid fever is 1% per year and typhoid fever is among the five major causes of death. Countries that show increased typhoid severity share several characteristics in common.

a) rapidly increasing population and urbanisation;
b) inadequate facilities for processing human waste;
c) decreasing water supply per capita;
d) intimate contact between humans, food and heavily contaminated water supplies;
e) over burdened health care delivery systems.

**Typhoid carriers**

A chronic typhoid carrier is a person who is excreting typhoid bacilli in stools or urine for more than a period of one year.

a) **Faecal carriers:** In general 2-5% of all persons who develop clinical or subclinical infection with S. typhi become chronic gall bladder carriers and thereby serve to maintain endemicity of the disease. The propensity to become chronic carriers after acute infection increases with age and is greater in women, observations which are in keeping with the epidemiology of cholelithiasis. A study on the prevalence of chronic typhoid carriers in Santiago city estimated 25,019 female and 4,575 male carriers, yielding a crude rate of 694 per 100,000 population. The frequency of chronic carriers in the West European countries is of the order of 1 per 200,000 or less.

b) **Urinary carriers:** Chronic urinary carriers are 32 times less common than faecal carriers. They do assume importance in African situations where urinary schistosomiasis is common. Urinary carriage develops in 10% of patients with chronic Schistosoma haematobium infection.

(IV) **Diagnosis and bacteriology**

In endemic areas typhoid is often diagnosed and treated on clinical grounds due to lack of laboratory facilities. This contributes to inaccurate reporting of the number of cases. In the past reliance was placed primarily on serologic methods of diagnosis—widal reaction. These tests are more useful in determining the prevalence of exposure to S. typhi by measuring antibody titre to flagellar H antigen. This antibody resides in the IgG class and is long lived. Since vaccination with parenteral killed whole cell typhoid vaccine also stimulates the appearance of flagellar antibodies, this serological test is not useful where vaccine is commonly used. Blood culture is the most useful test for the diagnosis of typhoid fever, however a recent study has shown that bone marrow aspirate culture is more sensitive and chloramphenicol does not interfere with the recovery of organism. The detection of chronic typhoid carriers requires collection of a series of daily stool cultures, is expensive and only intermittently positive. Serological methods have been widely employed to detect typhoid carriers. The VI assay has been found to be useful for screening of chronic carriers and has 75% sensitivity and specificity. By following the contaminated sewage from the main sewers to the tributary sewers and then to the household drains Moore's sewer swab technique has been used as a public health tool to detect carriers in the past.
Control strategies in typhoid fever

The control of typhoid fever depends primarily upon the universal availability of adequate water and sewer systems. Endemic regions of the world exist primarily because the poorer segments of the population remain in areas under served in terms of adequate water and sewage systems. In addition the detection of typhoid carriers and the restriction of their occupations are inadequate. Until these measures for disease control are enacted, perhaps the only worthwhile option is to utilise vaccines to prevent disease.

1) Improvement in epidemiologic information:
Morbidity statistics grossly underestimate the magnitude of typhoid disease. There is no agreed definition of a case. Frequently typhoid is lumped with other conditions such as salmonella-shigella infections and gastroenteritis. This situation poses difficulties in interpreting available data and emphasises the need for uniform reporting criteria and improved surveillance.

2) Provision of adequate water supply and effective sewage disposal system:
This has been one of the prime goals of the WHO during 1981-90. The International Drinking Water-supply and Sanitation Decade. The magnitude of the task is exemplified by the situation in Latin America, where it is estimated that these basic services are needed for some 485 million people. Most countries do not have the capital to fund such undertakings. Little work has been done in the past in estimating the effect of water supply and sanitation on the incidence of typhoid fever and it has been lumped with other diarrhoeal diseases. A review of 67 studies from 28 countries to evaluate the impact of water supply and sanitation on diarrhoea and related infections suggested that substantial reduction in diarrhoea morbidity and mortality rates can be expected from investments in these control measures. That the incidence of typhoid fever decreases dramatically with chlorination and filtration of water was repeatedly shown in the United States in the 1920s. Such benefits will not be confined to typhoid alone but to all faecal-oral infections.

3) Detection and control of carriers:
VI antibody assay is now a feasible test for screening typhoid carriers. Once these individuals have been identified, the problem is how to prevent them disseminating Stphi. Cholecystectomy and I/V antibiotics are impractical. What seems most worthwhile at present is a 4 week course of oral amoxicillin with probenicid alongwith intensive health education of carriers and their restriction from occupations entailing food handling.

4) Current state of typhoid vaccine:
The first typhoid vaccines to be used extensively were the parenterally inoculated S.typhi, inactivated by heat and phenol or by acetone. They provided reasonable protection against typhoid fever (heat. phenolised vaccine 5 1-67% and acetone inactivated vaccine 56-88% efficacy). These vaccines are generally considered to be unsatisfactory public health tools for routine immunisation of children since they elicit adverse reactions at high frequency. Fever occurs in approximately 20-25% and local reactions in 40-50% of recipients. In approximately 15% of the vaccinees the systemic reaction results in absenteeism.

Two new typhoid vaccines have been shown to be safe immunogenic and protective in clinical trials. These include:

a) an attenuated strain of S.typhi ty21a used as live oral vaccine;
b) the purified polysaccharide capsular antigen of S.typhi Vi, administered as a parenteral vaccine. Randomised controlled field trials of both vaccines have been conducted and are summarised in the Tabel II. If typhoid vaccine is to be considered for incorporation in national immunisation programmes, its present use would be based on vaccination of school children. This is rational Since:

a) for most part school age children are reported to have the highest incidence of clinical typhoid fever;
b) school children are relatively “captive” population amenable to school based immunisation programmes; and,
c) both vaccines are protective in this age group. So far it is clear that the duration of protection offered by ty21a vaccine is 5 years, whereas the experience with VI vaccine is much less. The former has an additional public health benefit of offering herd immunity and is recommended presently.

5) Typhoid fever epidemics:
Epidemics of typhoid fever are not uncommon in most endemic areas. In such situations the following measures be implemented:
a) Provision of plenty of clean water and proper chlorination depending on the source of water,
b) Provision of facilities for disposal of human excreta. In areas without adequate facilities for human waste disposal, digging of pit or bore-hole latrines constitute a practical solution.
c) Health education: It is imperative that the public be informed about the mode of spread of typhoid fever, through all available channels. Messages must be carefully prepared taking the local culture, traditions and beliefs into consideration. Measures such as proper hand washing, food and domestic hygiene, prevention of fly breeding and maintenance of latrines be stressed.
d) Post-epidemic follow-up: Careful surveillance should be continued to ensure that sporadic cases of typhoid fever are promptly detected. An intensive search be made to identify and treat chronic carriers in the community.

VI. Epidemiologic model for typhoid fever:
An epidemiologic model for typhoid fever was proposed in order to study the transmission of infection at different levels of endemicity. This model is readily applicable in planning and evaluating anti-typhoid immunisation and sanitation programmes like mass vaccination and privy construction. It suggests that although vaccination in the short run may be more effective for the control of typhoid, privy construction would give a more lasting effect than immunisation alone. Evaluation of cost-effectiveness and benefits of control measures in typhoid fever suggests that with privy construction although the cost-benefit ratio becomes favourable only after a period of 20 years, it would ultimately lead to eradication of the disease. This analysis does not consider the beneficial effect of privies on other intestinal infections and the savings in lives and wages.

VII. Summary and Conclusions:
1) Typhoid fever is a major public health problem in many areas of the developing world, with an incidence of 540 /100,000 people.
2) School age children and young adults constitute the high risk group in endemic areas.
3) There is a worldwide difference in case fatality ratio and in severity of the disease in different geographic areas.
4) Detection of typhoid carriers has been made easier by performing Vi antibody titres. Flagellar H-antibody provides means for estimating the prevalence of typhoid fever.
5) Control strategies for typhoid fever include a)improvement of epidemiologic information; b)adequate water supply and effective sewage disposal; c)typhoid carrier detection and treatment; d)typhoid vaccine.
6) Newer typhoid vaccines are safe and efficacious and can be considered for incorporation into national immunisation programmes for school age children.
7) Vaccines are much more useful on a short term basis. Long term control of typhoid fever depends on improvement in water supply and sanitation. Do most countries have the capital for such undertakings? is the crucial question.

REFERENCES