# Study of One Hundred Cases of Typhoid Fever in University Hospital Kuala Lumpur (October 1967 to July 1972)

*by* *Dr. Tan Eng Kong*
**M.B., B.S.(Mal.) M.P.M.(Mal.)**
Department of Medicine
University of Malaya

(Presently, Lecturer in the Department of Psychological Medicine, Medical Faculty, University of Malaya).

## Historical Background

THE FIRST STUDY OF typhoid fever in West Malaysia, was reported in a bulletin from the Institure of Medical Research by William Fletcher[1] in 1927. This report was made to determine if enteric fevers were common in the country as there was an increase in the number of positive Widal tests. There was no epidemic reported; the carrier rate determined from faecal smears was less than 0.08 per cent and the author concluded that enteric fever was not common. The probable reasons postulated were the "evenly distributed heavy rainfall, the excellent water supply of the towns, the scarcity of flies, the absence of large milk-distributing companies and the presence of colloidal clay in the rivers." During 1925-1926 one hundred and eighty-two cases of typhoid fever were diagnosed either by examining the excreta bacteriologically or by three successive Widal tests.

Green and Mankikar[2] (1949) reported an epidemic of typhoid fever due to ice-cream. The infection first showed itself in epidemic form mainly among school children in a town with a population of 5,000. The ice-cream manufacturer was found to be "a fairly constant excretor of virulent typhoid bacilli" but was a "particularly healthy looking and active individual."

## Introduction

The clinical features of epidemic typhoid differs from endemic typhoid in various aspects. Textbook descriptions refer to epidemic typhoid, hence the admitting medical officer at the emergency room or medical clinic for the first time experience special difficulty in making an accurate and prompt diagnosis of endemic typhoid fever. (Wicks, Holmes, Lindsay, 1971)[3].

In 1962 Huckstep[4] described typhoid fever in East Africa as "the king of actors on the stage of disease." He noted that "a case of typhoid fever may present as a disease clinically indistinguishable from malaria, progress to a bacillary dysentry, mimic a case of acute bronchitis, simulate a full-fledged lobar pneumonia, cause an acute abdomen with perforation and then finally in convalescence, with its evil spent, linger on as an orchitis, a myocarditis or a peripheral neuritis."

This paper examines the clinical manifestations and the diagnostic difficulties of the disease as encountered in a teaching hospital.

## Material and Methods

The cases were studied retrospectively. The first one hundred cases where the diagnosis was made by isolation of S. typhi either in the faeces, urine or blood were analysed. There were 62 males and 38 females. The ethnic distribution is as seen in Table I. The youngest patient was aged one year and the oldest was 80 years of age. Mean age was 23 years (See Table II).

Information like history of T.A.B. vaccination, contacts or possible sources of infection were not available. The average duration of hospitalization was 24 days, the shortest stay being 4 days and the longest 67 days. 86 cases were admitted into medical, 11 into paediatric and 2 cases into surgical

**Table I**
**Ethnic group distribution of typhoid cases**

| Ethnic Group | No. of cases of typhoid fever |
|---|---|
| Malays | 27 |
| Chinese | 31 |
| Indians/Ceylonese/ Pakistanis | 41 |
| Others | 1 |
| Total | 100 |

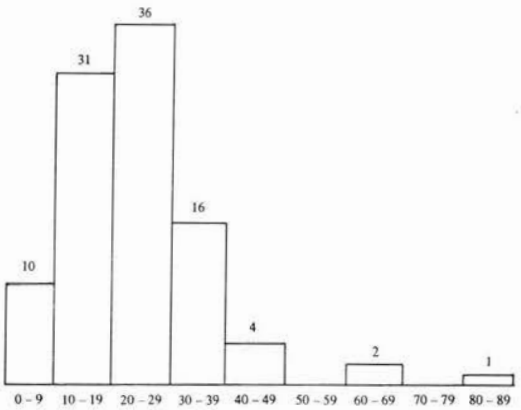


**Table II: Age distribution of typhoid cases**

wards. There was no statistical difference in the number of admissions by months in a year (See Table III).

## Clinical Features

The symptoms and signs are summarized in Tables IV and V respectively. In the majority of cases (91%) the onset of illness was insidious. The most common symptoms were a triad of fever, chills/rigors and sweats. Headaches were described as generalized, constant and worsened as the fever rose. The step ladder type of fever described in textbooks as typical of typhoid was seen in only five cases. The patients had either intermittent, remittent or continued fevers. In fifty-one patients the spleens were palpable and in four the spleen was tender. Sixty-one patients had enlarged palpable livers of which fourteen had tenderness on palpation. Mental confusion were present in eight patients of whom four were severely toxic.

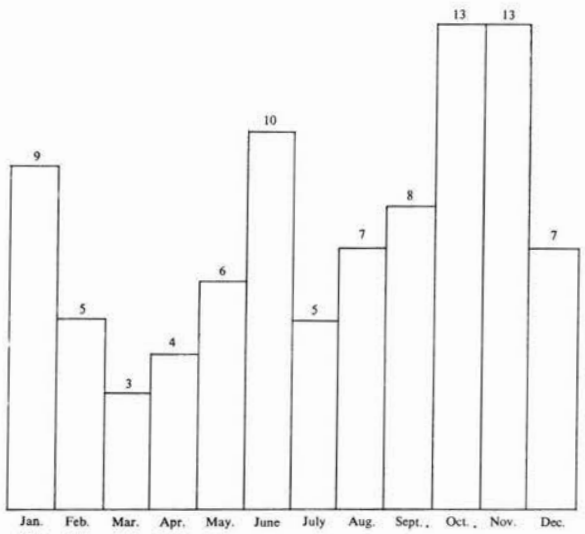


**Table III: No. of typhoid cases distributed monthly.**

**Table VI**
**Diagnoses on admission**

| Diagnoses | Percentage of Cases |
|---|---|
| Typhoid | 61% |
| Possible typhoid | 22% |
| Urinary tract infection (all female patients) | 5% |
| Malaria | 3% |
| Amebiasis | 2% |
| Infective hepatitis | 2% |
| Pneumonia | 2% |
| Pulmonary tuberculosis | 2% |
| Meningitis | 1% |
| Total | 100% |

## Diagnosis on Admission

As seen in Table VI the initial diagnosis of typhoid was correctly made in sixty-one and the disease was suspected in another twenty-two cases. Of the other 17% a variety of diagnoses were made.

## Investigations

In only half the number of cases was there any change in the nature of the stools. Microscopic

**Table V**

**Signs on admission – comparing with studies in Africa**

| Signs on admission | Percent of Cases | | |
|---|---|---|---|
| | A | B | C |
| *General* | | | |
| Fever | 100% | 98% | No data |
| Fever and Rigors | 74% | No data | No data |
| Relative bradycardia | 93% | 33% | No data |
| Jaundice | 6% | No data | No data |
| Rash (Rose spots) | 8% | 0% | 5% |
| Toxaemia | 4% | No data | 54% |
| *C I T* | | | |
| Abdominal tenderness | No data | 33% | 61% |
| Palpable spleen | 51% | No data | No data |
| Palpable spleen with change in size | 9% | No data | No data |
| Tenderness in spleen | 4% | No data | 14% |
| Enlarged liver | 61% | No data | No data |
| Tenderness in liver | 14% | No data | No data |
| *R.S.* | | | |
| Bronchitis | 11% | 33% | 56% |
| Lobar consolidation | No data | 3.5% | No data |
| *C.N.S.* | | | |
| Mental confusion | 8% | 33% | 29% |
| Meningism | No data | 8% | No data |
| *R.E.S.* | | | |
| Tender Lymphadenopathy | 1% | No data | No data |

A = present study of 100 cases
B = study of 243 cases in Rhodesia, 1966-1969 (Wicks, Holms, Lindsay)
C = study of 975 cases in Kenya and Uganda, 1954-1961 (Huckstep)

examinations of urine revealed three cases of haematuria and twenty-eight with albuminuria. The mean haemoglobin value on admission was 12.2 g % (PCV 37.4%). There was a range of 2,300 to 14,300 WBC/cmm. Leucopenia (<5,000 WBC/cmm.) was present in 37% of cases, while a leucocytosis (<10,000 WBC/cmm.) was found in 6% of cases.

The Widal test was not done in twelve cases and in sixty-six a repeat titre was not obtained. Of the eighty-eight cases where the first three was performed, thirty-six (41%) had H or O titre 1/250 dilution. In sixty-four the H and O titre were the same, twelve where the H antigen titre was greater than the O titre and another twelve where the reverse was noted. In only thirty-four was a repeat test performed.

*S. typhi* was isolated in forty-one cases in faeces alone, in thirty-one in blood alone and in twenty-five in both faeces and blood (See Table VII). In two cases *S. typhi* was isolated in the urine as well. The percentage of positive blood and/or stool cultures

**Table IV**

**Symptoms on Admission – comparing with studies in Africa**

| Symptoms | Percent of Cases | | |
|---|---|---|---|
| | A | B | C |
| Fever, chills/rigors and sweats | 76% | No data | No data |
| Diarrhoea without blood | 35% | 37% | 30% |
| Headaches | 32% | 75% | 75% |
| Cough | 23% | 53% | 22% |
| Abdominal pain/discomfort | 22% | 52% | 61% |
| Constipation | 15% | 17% | No data |
| Anorexia | 14% | No data | No data |
| Vomiting | 12% | 24% | 25% |
| Muscle or bone aches or joint pains | 7% | 18% | 54% |
| Jaundice | 5% | No data | No data |
| Fever | 19% | 39% | No data |
| Chest pain | No data | 27% | 20% |
| Dysuria | No data | 24% | No data |
| Sore throat | No data | 6% | 7% |
| Epistaxis | No data | 1% | No data |

A = present study of 100 cases
B = study of 243 cases in Rhodesia, 1966 to 1969 (Wicks, Holmes and Lindsay)
C = study of 975 cases in Kenya and Uganda, 1954 to 1961 (Huckstep)

**Table VII**

**Confirmation of diagnosis by Isolation of Salmonella typhi**

**Number of Cases where Salmonella Typhi was isolated**

| Week | Blood | Urine | Faeces | Bl + Fe | Fe + Ur. | Total |
|---|---|---|---|---|---|---|
| 1st | 1 | 0 | 2 | 1 | 0 | 4 |
| 2nd | II | 0 | 12 | 15 | 1 | 39 |
| 3rd | 10 | 0 | 13 | 2 | 0 | 25 |
| 4th | 9 | 2 | 14 | 7 | 0 | 32 |
| Total | 31 | 2 | 41 | 25 | 1 | 100 |

was evenly distributed amongst patients in the second, third or fourth week of illness.

In all cases *S. typhi* was sensitive to chloramphenicol in the antibiotic sensitivity test. Next highest in sensitivity was cephaloridin and ampicillin (45% in blood, 42% in stool). Only 22% were sensitive to kanamycin and less than 3% were sensitive to penicillin, streptomycin, tetracycline or erythromycin.

**Treatment and Response**

There was an average of twenty days delay after the onset of the patient's illness before specific drug therapy was commenced. This was largely due to the delay in patients coming for hospitalization.

After chloramphenicol was started it took an average of 5.3 days before the patients became afebrile for at least twenty-four hours.

The average dose of chloramphenicol given before clinical defervescence was achieved (i.e. afebrile for at least twenty-four hours) was 10.35 gms, – approximately 2 gms per day or 500 mgm four times a day for five to six days. The highest dose was 32 gms and lowest 1gm before clinical defervescence.

The average total dose of chloramphenicol used was 22.6 gms. In the majority of cases chloramphenicol was continued for ten days after clinical defervescence at an average of 1.25 gms/day i.e. 250 mgm five times a day.

Most cases convalesced in hospital for an average of five days after chloramphenicol medication was stopped. This was also the waiting period for at least two negative stool cultures before the patient was discharged. Only one case required surgical intervention for terminal ileal perforation. 67% of cases had three negative stool cultures before discharge.

**Recurrence of Symptoms**

There were 10% of cases with recurrence of symptoms in this series, half of which occurred before the patients were discharged from hospital. The other five cases had recurrence of fever at the follow-up clinic and were promptly readmitted. The relapse usually occurred nine days after cessation of chloramphenicol therapy.

Six cases with recurrence were treated with both chloramphenicol and amipicillin, two had only chloramphenicol whilst the other two had only ampicillin.

**Mortality**

Only one death occurred in the series. The patient was twenty-three years of age, had a prolonged fever with chills and rigors and after one month of severe illness was admitted in a state of confusion and dehydration. He was diagnosed as a case of septicemia due to typhoid. On admission he was treated with intramuscular chloramphenicol and subsequently intravenous hydrocortisone and ampicillin. On the fourth hospital day he was hypotensive and had haemetemesis which proved fatal. Postmortem findings showed generalized fulminating typhoid lesions. There was lymphoid hyperplasia and ulceration of the gut with congestion and hyperplasia of spleen and lymph nodes.

**Comments**

Comparing the symptomatology of patients in this series with those of Wicks et al and Huckstep there were some notable differences. Headaches, abdominal pain, discomfort and muscle/bone/joint pains were much less common amongst this group of patients whereas chest pain and dysuria which occurred in about a quarter of the cases studied by Wicks et al was not noted.

It would appear that the cases of typhoid studied in Rhodesia, Kenya and Uganda were more fulminating in severity; 54% of Hucksteps cases had toxemia (compared to 4% in this series) and 33% of Wick's cases had mental confusion (compared to 8% in this series). Also, bronchitis as a complication occurred more frequently in the African patients (33% and 56% of cases in the two studies) whereas it was detected as a clinical sign in only 11% of this series.

A relative bradycardia was recorded in 93% of the patients under study whilst this was found in only 33% in Wick's group. No data were available with regards to splenic and hepatic enlargements in the other two studies but 51% and 61% of our patients had enlarged spleens and livers respectively.

The results of the Widal tests will depend on the stage of illness when the blood sample was taken. The Widal tests performed in this series showed that a single Widal test had little diagnostic value (Christie 1969). Where a repeat test was performed, less than a third showed a significant rise in titre to confirm the clinician's suspicions in doubtful cases. Three-quarters of the cases were treated with chloramphenicol based on clinical diagnosis before the Widal reaction results were known and only a quarter had therapy withheld until the Widal tests results were available.

With regards to isolation of salmonella typhi, this study showed the importance of culturing blood and stool samples. These samples should be taken regardless of the stage of the illness because results from this series demonstrated the even distribution of the number of positive cultures during the second, third or fourth week of illness. The belief that the organism is present only in the first week in the blood stream and thereafter disappears is not borne out in this study. With current bacteriological methods positive cultures of faeces and urine occur earlier than the third week of the disease.

There were ten percent of cases with recurrence of symptoms in this series, half of which occurred before the patients were discharged and the other half had recurrence of fever when seen at the follow-up clinic. Osler[6] found that the relapse rates varied in different clinics and in spite of application of various antibiotic regimes, relapses occurred in twenty percent of cases. However it must be pointed out here that it is difficult to determine whether a case has relapsed, has a re-infection or a recurrence of symptoms. In all the ten cases with recurrence of symptoms, antibiotic treatment with chloramphenicol and/or ampicillin was effective.


## Summary

This is a retrospective study of the clinical presentation, physical findings, differential diagnosis, investigations, treatment and response of 100 cases of bacteriologically proven typhoid cases. The symptomatology and clinical signs are compared with two other studies and reference is made to the problem of diagnosis. The value of the Widal test and culture for isolation of the bacteria is examined and emphasis is placed on the importance of blood and stool culture. All cases responded to chloramphenicol therapy.



## Acknowledgements

The author would like to thank Dr. M. Somasundram (formerly Senior Lecturer, Department of Medicine) and Professor H.O. Wong, the Head of the Department of Medicine for their invaluable guidance in the preparation of this paper. Gratitude also goes to Mr. Lai and Mrs. Phung of the Medical Records Department for their kind assistance in data collection.


## References


1. Christie, 1969; "Infectious Disease, Epidemiology and Clinical Practice", E & S Livingstone Ltd
2. Fletcher, William, (1927); "Typhoid Fever in Malaya", Notes on Epidemiology of Enteric Fevers in the F.M.S.
3. Green, R. and Mankikar, D.S. (1949); "Epidemic due to Ice-Cream", Bulletin from I.M.R., Fed. of Mal., No. 3.
4. Harvey, A.M. and McKinsick, V.A., 1967, Osler's Textbook Revised, Appleton-Century Crofts, New York pp. 19-74.
5. Huckstep, R.C. (1962) "Typhoid Fever and other Salmonella Infections", E & S Livingstone Ltd , Edin. and London.
6. Wicks, A.C.B., Holms, G.S., Lindsay, D. (1971) "Epidemic Typhoid Fever – A Diagnostic Pitfall", Quarterly Journal of Medicine, July.