RECENT ADVANCES IN THE SURGERY OF TYPHOID FEVER

Hunterian Lecture delivered at the Royal College of Surgeons of England

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by

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" *One man in his time plays many parts* "

THIS QUOTATION FROM Shakespeare's " Seven Ages of Man " can aptly be used to describe the diverse and varied ways in which typhoid fever, the King of Actors on the Stage of Disease, can present and progress. There are very few conditions which cannot be mimicked in this, the most lethal of all enteric diseases, and the surgical complications are as varied and as numerous as the medical. A case of typhoid may present as a case of apparent appendicitis, progress to an acute intestinal haemorrhage, simulate an acute meningitis, cause an " acute abdomen " with perforation, and finally in convalescence, with its evil spent, linger on as an orchitis, a chronic cholecystitis, or an osteomyelitis.

Typhoid has been recognized for many centuries. Hippocrates described a fever which was probably typhoid. It is said that Antonius Musa, a Roman physician, became famous by treating the Emperor Augustus with cold baths when he fell ill with typhoid. In 1684, Thomas Willis gave a fairly accurate description of typhoid in his famous *Practice of Physick*, but the standard triad of treatment in those days of " let blood, vomit and purge " might leave much to be desired! In the days of John Hunter (Fig. 1) in the eighteenth century, typhoid was a very real and lethal disease in this country. In the Hunterian Museum there are no fewer than 13 of John Hunter's specimens showing typhoid involvement of gut.

Typhoid is no respecter of classes, and both Prince and Commoner are susceptible to its virulence. Prince Albert, the Prince Consort, died of it in 1862, and it has been said that there were 50,000 cases a year in England alone at about this time. This has certainly changed for the better, but the number of typhoid cases has never fallen, even in recent years, below a hundred a year in England, with sporadic larger outbreaks, and in the 10 years between 1947 and 1957 there were 2,099 notified cases in England and Wales.

In many countries, however, typhoid is still an everyday problem. For instance, 19,551 cases were notified in Italy in 1955 (Table I), and well over 40,000 in the North and South American Continents. In 1951, 81,575 cases were notified in South Korea with 14,051 deaths, an indication

of the vast typhoid epidemics still occurring, particularly among the countless millions of the East. The reasons for this are not far to seek. Sanitation and hygiene are still abysmally poor in many of the lesser educated communities, and carriers are still numerous in many parts of the world. There were no less than 542 registered carriers in West Berlin alone in 1955.

War produces conditions ideal for typhoid outbreaks, as was shown in Korea; but in peace time English people are increasingly travelling by air to and from the more distant endemic areas of Africa and the East, and

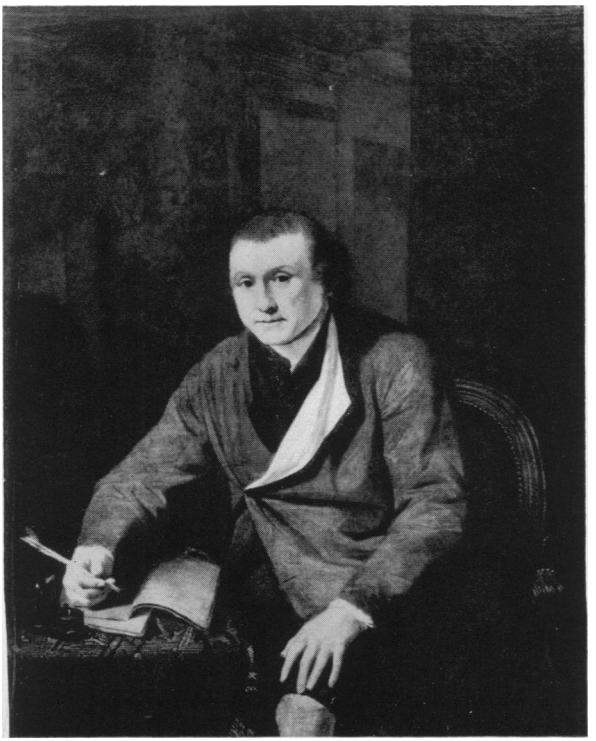

Fig. 1. John Hunter—as a young man—by his brother-in-law Home.

are taking holidays in nearer places such as Spain and Italy. An appreciable number are returning with undiagnosed salmonellae infections including typhoid (Macrae, 1959).

The last Hunterian lecture on typhoid fever was delivered by Lord Webb-Johnson (Fig. 2) in 1917. This was a brilliant review of the cases dealt with in a military hospital in France, and described the advances in treatment known in the First World War. During the last decade, however, more progress has been made in the treatment of typhoid than

since John Hunter's day; firstly with the introduction of chloromycetin in 1948 (and its synthesis as chloramphenicol), and secondly a greater realization of the importance of the fluid and electrolyte balance as emphasized by H. L. Marriott in 1947. In addition, there have been many advances in diagnosis, prophylaxis and treatment. For these reasons, a restatement of the surgical diagnosis and treatment of typhoid fever from the surgical point of view would appear to be timely.

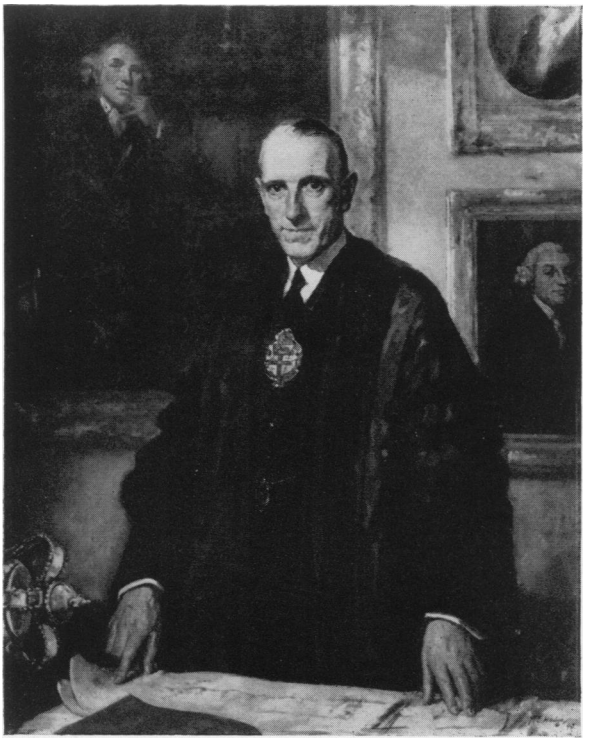

Fig. 2. Lord Webb-Johnson.

This paper is based on well over 1,000 cases of typhoid fever seen and treated personally in Kenya during the period February 1954 to May 1955. Of these 975 have been documented (Table II), 240 being investigated in considerable detail under clinical research conditions. The main findings will be based on these 240 " research " cases, amplified in places by experience with the other 735 patients. The material formed the basis of a Thesis in 1957 (Huckstep).

TABLE I

EPIDEMIOLOGY OF TYPHOID FEVER
Number of notified cases in 1955

Great Britain 221

Europe	Italy	19,551	*Asia*	Turkey	7,629
	Spain	14,394		Indonesia	6,081
America	United States	1,704	*Africa*	South Africa	3,997
	Colombia	14,561		Egypt	14,835

Carriers
(Registered in 1955)
West Berlin 542 chronic carriers

Epidemics in War
(Notified cases in 1951)
South Korea 81,575 cases with 14,051 deaths

TABLE II

TYPHOID FEVER — DIAGNOSTIC CRITERIA
Personal Series of 1,300 patients (approx.)

975 Documented

240 Patients (Clinical Research Series)		735 Patients (Subsidiary Series)
Strong Clinical Evidence		Laboratory, Circumstantial, or Clinical Evidence in all 735
Plus		*Plus*
Blood Culture ..	132	
Stool Culture ..	46	
Abscess Culture ..	2	Positive Bacteriological Evidence in a cross-section of 216 out of 735 Patients
Post Mortem Culture	2	
Widal T.O. over 1/480	58	
TOTAL	240 Pts.	

TABLE III

MAIN SYMPTOMS ON ADMISSION
(975 Patients)

	Research (240 Pts.)	Subsidiary (735 Pts.)	Total (975 Pts.)
Headache	179	552	731 (74.9%)
Abdominal Pain ..	168	424	592 (60.7%)
Joint Pains	105	422	527 (54.0%)
Diarrhoea *without* blood	88	201	289 (29.6%)
Severe Sore Throat ..	15	52	67 (6.9%)

SURGICAL DIAGNOSIS

The surgeon who is called upon to assess and treat an abdominal catastrophe in a patient who may be suffering from typhoid is confronted by a diagnostic necessity of major importance. The classical diagnostic tests, the Widal and blood culture, are of limited value because:

(1) They take too long.

(2) The Widal may be negative and the patient still have typhoid. Conversely, with large-scale T.A.B. inoculations a small rise in the Widal may occur in non-typhoid cases.

(3) Within 2 hours of chloramphenicol administration the blood is usually sterilized so that a newer method of treatment may invalidate an established diagnostic test.

(4) Stool culture has the disadvantage that it is usually not positive until the third week of illness, if then.

The surgeon must, therefore, have recourse to other diagnostic criteria:

(*a*) *History*

The history of contact together with an onset of low-grade fever are of special importance. The important symptoms on admission are shown in Table III.

(*b*) *Examination*

Abdominal tenderness (usually slight and lower), bronchitis, toxicity and mental confusion were found to be signs of especial diagnostic value (Table IV).

TABLE IV

MAIN SIGNS ON ADMISSION

(240 Patients)

Abdominal Tenderness (Mainly Slight) ..	60.8%
Bronchitis	55.8%
Toxicity	54.2%
Coated Tongue	39.2%
Abdominal Guarding (Mainly Slight) ..	25.0%
Palpable *and* Tender Spleen	13.9%

Two other signs of importance are a strange musty odour and an apathetic expression, the latter being helpful in differentiating the typhoid patient from one suffering from lobar pneumonia, malaria or bacillary dysentery. Nelson and Pijper (1951), among others, state that the rose spot of typhoid cannot be seen in a black skin, but it is in fact often visible and made more obvious by the application of a little oil to the skin. Figure 3 shows a biopsy of a rose spot, from a black patient.

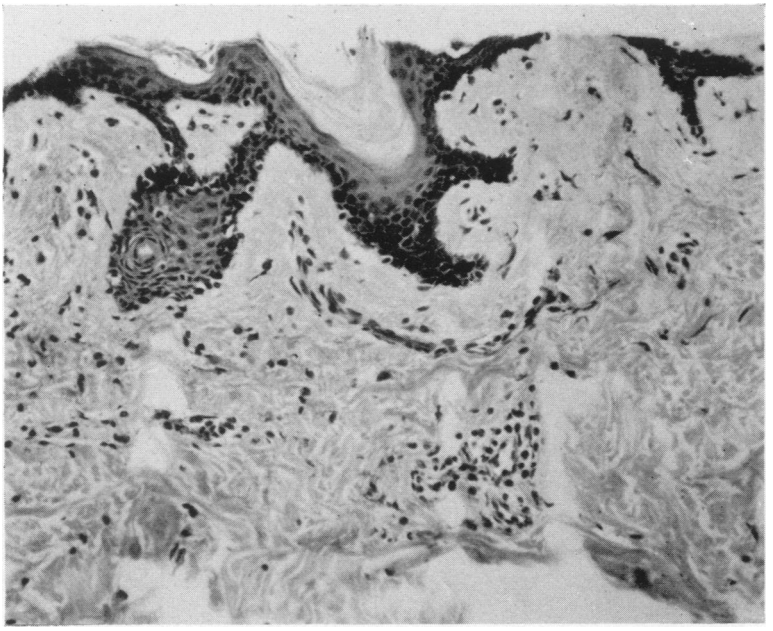

Fig. 3. Biopsy of a " Rose Spot " from a black patient (showing heavy melanin pigmentation, round cell infiltration and large vascular spaces).

(*c*) *Diazo reaction of urine*

This I believe to be the greatest single surgical diagnostic aid, and it can be done in 30 seconds under any conditions. Ehrlich described the test in 1883, and others at that time found it of great value. Few, however, in the last 40 years appear to have used it. With slight modifications it was used in 638 cases of typhoid and 2,115 controls. Others working in East Africa have confirmed its great usefulness (Manson-Bahr, 1958).

The diazo reagent is made up from 2 solutions, A and B (Fig. 4).

Solution A: Sulphanilic acid 0.5 G., concentrated hydrochloric acid 5.0 ml., distilled water 100 ml.

Solution B: Sodium nitrite 0.5 G., distilled water 100 ml.

40 parts of solution A are mixed with 1 part of solution B to make the diazo reagent, which will keep fresh in a refrigerator for 3 days. 5 ml. of diazo reagent are added to an equal quantity of the urine, a few drops of 30 per cent. ammonia are added, and the whole shaken up in a test tube. The colour of the froth alone is noted, a pink or red coloration being a positive reaction, and all other coloration considered negative.

The reaction is positive in many typhoid cases at some period between the 5th and 14th day of the illness, in relapses, and often at other times as well. It is occasionally positive in advanced tuberculosis, bacillary dysentery, and lobar pneumonia, but usually only weakly so. It is rarely positive in other conditions.

An early morning specimen of urine should be tested where possible because of its higher concentration. If the test is negative on one specimen it should be repeated on further specimens. Although the diazo solution should be made up fresh, typhoid urine weeks old will still give a positive reaction.

The results of the diazo reaction are shown in Table V. The salient points are:

(1) 79.4 per cent. of the typhoid patients in the research series had positive diazo reactions on admission.

(2) Out of a total of 638 typhoid patients tested, 82.9 per cent. had positive diazo reactions, and if only those tested between the 5th to the 14th day are included the percentage with a positive reaction is 90.6 per cent.

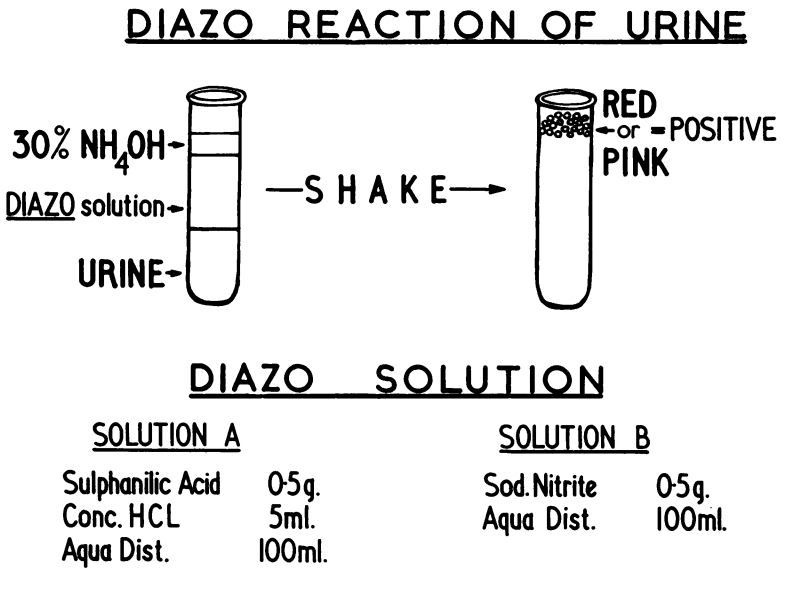

Fig. 4. Diazo reaction of urine.

TABLE V

RESULTS OF DIAZO TEST OF URINE

638 Typhoid Patients

	Positives
1. On Admission	79.4%
2. Irrespective when tested	82.9%
3. 5th to 14th days of illness only ..	90.6%

2,115 Control Patients
(107 different Medical and Surgical Conditions)

Mainly *Weakly* Positive	5.7%

In contrast to this only 5.7 per cent of the 2,115 patients in a control series had positive diazo reactions and these usually only weakly so. The control series included 107 different medical and surgical conditions.

Considerable research was done on the nature of the substance causing the positive diazo reaction and this has been published elsewhere (Huckstep, 1957).

Suffice it to say that, used correctly, and with due respect to its limitations, the diazo reaction of urine should be a major asset to the surgeon, especially where a complication such as intestinal perforation may obscure the diagnosis.

(*d*) *Other diagnostic tests*

The bone marrow, unlike the blood, is not sterilized within 2 hours by chloramphenicol, but one still has to wait 2 days for the result of culture.

A Widal in the value of O. antigen agglutination of 1/240 or over is practically diagnostic of typhoid, especially in the presence of other evidence. The H. antigen agglutination is much less specific.

The white blood count is of value in the differential diagnosis in so far as a count of over 10,000 is strong evidence against the diagnosis of typhoid. It should be made a routine test in all cases.

VALUE OF T.A.B.

In one epidemic in an isolated community of 17,000 in Kenya, there were 870 probable cases of typhoid with a high mortality and complication rate. Over 90 per cent. of these had received inoculations with alcoholized T.A.B. 3 or 4 months previously.

Marmion (1952, 1953) described two epidemics in Egypt involving 535 Royal Air Force personnel. Practically every one of these had had T.A.B. in recognized doses, and yet there was an appreciable morbidity, mortality and complication rate.

Anderson and Richards (1948) described a similar state of affairs in the Middle East with 110 cases of typhoid, 91 per cent. of whom had had T.A.B.

These findings are in contradiction to those of earlier workers. I feel, therefore, that improved sanitation and hygiene are more important factors in prophylaxis than T.A.B. itself. The answer to this important question may be to give a living attenuated vaccine of several phage types, but more research requires to be done on the subject.

GENERAL TREATMENT OF TYPHOID

Chloramphenicol is the drug of choice, and should always be given to all but the mildest cases. In this series it reduced the average duration of pyrexia from 14.6 to 4.1 days (Table VI).

TABLE VI

AVERAGE DURATION OF PYREXIA

Without Specific Chemotherapy	14.6 days
With Chloramphenicol and Aureomycin ..	4.6 days
With Chloramphenicol alone	4.1 days

The optimum chemotherapeutic treatment of typhoid fever is shown (Table VII). Salient points are:

(1) It must be given in adequate doses to the toxic patient despite the risk of aplastic anaemia and the toxic crisis. Both of these in my opinion have been over-rated.

(2) Dosage must be continued for at least 14 days, otherwise the relapse rate is markedly increased. T.A.B. may decrease the likelihood of a relapse.

(3) Cortisone is said to have an effect in the very toxic case, although I have not had personal experience of this in typhoid. There is an increased likelihood of perforation and haemorrhage with its use.

TABLE VII

GENERAL TREATMENT OF TYPHOID FEVER (CHEMOTHERAPY)

1. The Acute Fulminating or Severe Toxic Case
   1 G. Chloramphenicol 6 hourly for 3 days,
   then 0.5 G. Chloramphenicol 6 hourly for 12 days

2. The Ordinary Acute or Subacute Case
   0.5 G. Aureomycin } 6 hourly for 3 days,
   0.5 G. Chloramphenicol }
   then 0.25 G. Aureomycin } 6 hourly for 12 days
   0.25 G. Chloramphenicol }

3. Additional Treatment
   (a) Cortisone for the first 3 days in very severe toxicity, and in haemolytic anaemia, but *not* in abdominal complications.
   (b) Up to 4 G. stat. of chloramphenicol in extreme toxicity.
   (c) T.A.B. 0.5 ml. on the third afebrile day (uncomplicated cases).

Although treatment with a specific antibiotic has been mentioned first, the general care of the typhoid patient is still of foremost importance, although even this has changed recently. Strict confinement to bed is still important, because of the toxic effects on the myocardium. The absolute immobility which used to be advocated must, however, be tempered with physiotherapy in order to diminish the likelihood of complications such as bed sores, bronchopneumonia and venous thromboses. The patient's ambulation must be gradual, because myocardial damage may last for several weeks after the pyrexia has settled, quite apart from the risk of late complications and relapses.

The diet must be low in roughage because of the danger of intestinal perforation and haemorrhage. Except in cases of intestinal complications, however, there must be an adequate calorific intake, especially of protein, at all stages of the disease. The gastric diets I—IV are a good guide, using milk fortified with added protein and vitamins, especially ascorbic acid and iron.

Fluid and electrolyte balance is important as dehydration is common, and may occur rapidly. If an adequate fluid intake cannot be taken by mouth, the intravenous route is normally the method of choice in adults. In more primitive parts of the world, however, intravenous therapy may be impossible, and fluid may be given intraperitoneally. This will be discussed later.

Despite the optimum treatment of typhoid, however, complications are still common, relapses and carriers still occur, and there is an appreciable mortality. With a few exceptions, most reported mortality rates exceed 5 per cent. even with chloramphenicol. This is especially so abroad, where patients are likely to attend hospital much later, and the mild cases are usually never even seen by a doctor. Patients in Africa and the East also tend to be in a much poorer state of health, and are sometimes infected with massive doses of the typhoid bacillus. The overall mortality in the research series, i.e. mainly the more seriously ill patients and those with complications, was 5.4 per cent.

Two final points on general treatment should be considered:

Firstly, complications such as intestinal haemorrhage, perforation and orchitis may occur during convalescence, and a careful watch must, therefore, be kept.

Secondly, the carrier state, either urinary or faecal, is always a potential danger, and no patient should be sent home until six negative stool and urine cultures have been obtained.

SURGICAL COMPLICATIONS

Diagnosis of the acute abdomen in the typhoid patient

It is important not to subject typhoid patients to unnecessary operations for many reasons. They stand anaesthesia extremely badly, because of toxic effects on the liver and general poor state of myocardium and respiratory system; and although many abdominal catastrophes can be mimicked by typhoid fever, conditions such as cholecystitis and perforation are usually best treated conservatively.

The diagnosis of the acute abdomen in such patients is made difficult because:

(1) They are toxic and have a higher threshold to pain.

(2) The natural abdominal tenderness and sometimes guarding seen in these patients may mimic a true appendicitis.

(3) A toxic hepatitis and occasionally a haemolytic jaundice may occur in typhoid, and add to the difficulties in diagnosis of acute cholecystitis.

(4) Typhoid perforation of the intestine may be insidious, particularly when patients are on chloramphenicol, and often so if they are exhausted, toxic and delirious. Rapid deterioration in general condition, a rising pulse rate, paralytic ileus, and free fluid in the abdomen, may be the first indications of perforated gut.

THE TREATMENT OF TYPHOID PERFORATION

To appreciate the rationale of the treatment it is important to consider the pathology of perforations in some detail. In typhoid fever, the part of the gut to perforate is the lower ileum in most cases, because here there is an accumulation of Peyer's patches, and the disease selectively affects these lymphoid aggregations. John Hunter realized this, and 2 out of the 13 specimens in the Hunterian Museum are illustrated in Figures 5 and 6.

Figure 5 shows several enlarged and friable Peyer's patches in the lower ileum.

Figure 6 shows no obvious perforation, yet the gut in the lower ileum is paper thin in many places and liable at any moment to perforate at more than one spot. It can readily be appreciated that the repair of such a friable gut would be an almost impossible task, and attempts to suture it merely result in further tears. It may be likened to wet blotting paper, and on two occasions I have watched adherent lower bowel torn as the peritoneum was opened.

It may thus be seen that the danger lies in the perforation, not of one Peyer's patch, but of many; and that even where the gut does not perforate

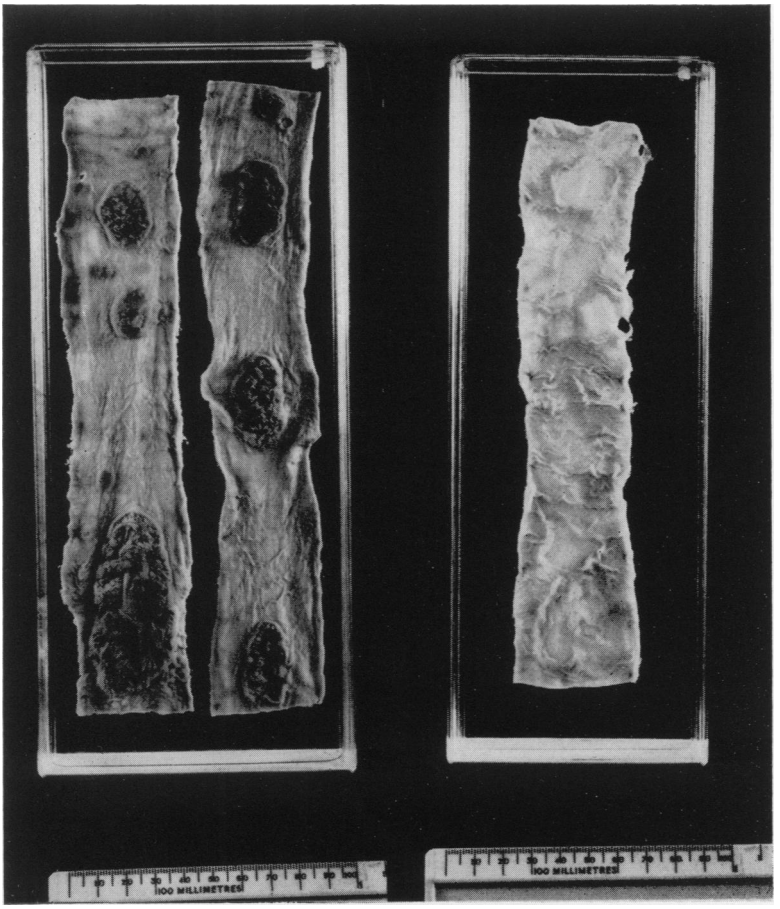

Fig. 5 (left). Hunterian specimen—showing several enlarged and friable Peyer's patches in the lower ileum.

Fig. 6 (right). Hunterian specimen—showing several large paper thin areas in the lower ileum, which are liable to perforation at more than one spot.

it tends to be friable. Such diffuse inflammation will also tend to make adjacent loops become adherent. One has the impression that this happens more often after chloramphenicol, because of a virtually sterile and presumably lower grade of perforation.

Despite the many dangers practically all authorities have hitherto advocated operative treatment. The results usually have been disastrous and reported mortalities very high (Table VIII). Webb-Johnson reported

TABLE VIII

TYPHOID PERFORATION—OPERATIVE AND CONSERVATIVE TREATMENT

Operative Treatment

	Mortality
Webb-Johnson (1917)	100%
Hamilton Bailey (1958)	Over 80%

Conservative Treatment

		Mortality	
Present Series (1954/45)	13 Pts. with Perforation	30%	20%
	7 Pts. with Peritonitis	0%	

a mortality of 100 per cent. in 1917, and Hamilton Bailey in 1958 (10 years after the introduction of chloramphenicol) well over 80 per cent. of deaths following operative intervention.

One case I operated on required a transverse colostomy because of pelvic obstruction, and after a stormy convalescence eventually recovered. The post mortem appearances in fatal cases of perforation, and loss of patients after operation, make me feel that an adequate operation is often impossible. I, therefore, decided to treat a series of patients by conservative measures only.

In my series treated conservatively there were 20 cases. 13 of these were diagnosed as intestinal perforation on several criteria, and this diagnosis was confirmed at post-mortem on those who died. A further 7 who had free fluid and other signs of peritonitis were labelled merely as " peritonitis ", although they were almost certainly cases of true, though atypical, perforation. 4 out of 13 of the cases of intestinal perforation died, and none out of 7 of the cases of " peritonitis ". This gave a mortality of 30 per cent. or of 20 per cent. if all 20 cases are included.

The method of treatment was by general methods similar to the Ochsner-Sherren regime plus large doses of chloramphenicol. Phenobarbitone gr. $\frac{1}{2}$ t.d.s. after gastric aspiration was found useful in allaying vomiting. Very careful fluid and electrolyte replacement by intravenous routes was important, as there was on the one hand a toxic myocardium and on the other a dehydrated patient. Chloramphenicol was given in a dosage of 2 Grams 4-hourly in an adult for 2-3 doses, and then reduced to 1 Gram 4-hourly, gradually reducing the dose to 0.5 Gram 6-hourly as the patient improved. The danger of the so-called toxic crisis after large doses of chloramphenicol in typhoid is much over-rated. Oral administration of chloramphenicol is usually satisfactory, but the intravenous route may be better suited in some cases. Even if this route is preferred, some of the drug should be continued by mouth to make sure of the sterility of the bowel.

The exceptions to the rule of conservative treatment of perforation are:

(1) Sudden perforation in the otherwise convalescent patient. If this case is seen within 6 hours, I feel operation is the treatment of choice.

(2) The perforation leading to complications such as adhesions causing obstruction. One case of obstruction due to a pelvic abscess following perforation, and necessitating a transverse colostomy and drainage of the peritoneum, has been already mentioned.

Summarizing then, all perforations in typhoid fever, with these exceptions, should be treated conservatively, with large doses of chloramphenicol, and an Ochsner-Sherren regime. The high mortality of operative measures should, therefore, be drastically reduced, although not eliminated.

INTESTINAL HAEMORRHAGE

This is still a severe complication of typhoid fever (Table IX), and may occur despite chloramphenicol therapy. Its mortality rate has been greatly diminished by adequate and early blood transfusion. This complication, however, may sometimes be " silent ", and the first evidence of haemorrhage a collapsed patient with extreme pallor of the conjunctivae.

TABLE IX

ABDOMINAL COMPLICATIONS OF TYPHOID FEVER

	No. of Patients	*Mortality*
Intestinal Perforation ..	13 + 7	20%
Intestinal Haemorrhage ..	8	38%
Acute Cholecystitis	5	—

It is important, therefore, to keep a careful watch on all typhoid cases. It may be difficult to diagnose if concomitant diseases such as bacillary dysentery are present, especially during the third week, which is the common time for haemorrhage to occur. It is wise to have an initial haemoglobin estimation done on all patients, and to group their blood, as some degree of anaemia is normally present in typhoid. The anaemia is probably due in the main to a toxic effect on the bone marrow, although a mild haemolytic anaemia is also common. Care must be taken not to give blood too rapidly or in too great a quantity because of the poor state of the myocardium and lungs. There is no indication for operation as the sites of haemorrhage are usually multiple, and it would be virtually impossible to deal with them.

There were eight cases of true haemorrhage in the series with three deaths.

ACUTE CHOLECYSTITIS

This complication occurs more frequently than is generally recognized, and I have found mild right epigastric pain, associated with slight jaundice, particularly common in the acute and convalescent carrier. 13 out of 17 patients with persistent positive stool cultures were found to have more marked and more localized right epigastric tenderness than in the average case which was not excreting the bacillus. A marked degree of jaundice was seen in four such cases.

The treatment of acute typhoid cholecystitis should be conservative unless an empyema of the gall bladder makes surgical intervention imperative. The treatment of chronic cholecystitis will be discussed later, together with the problem of the carrier.

Owing to the difficulty of diagnosis of acute typhoid cholecystitis, only five undoubted cases could be included in this series.

OTHER ABDOMINAL COMPLICATIONS

On several occasions, paralytic ileus was present in very toxic patients, quite apart from those cases in which it followed a perforation.

Typhoid simulating acute appendicitis was seen on more than one occasion, but no proved case of typhoid appendicitis occurred.

It is said that peritonitis may be caused by rupture of a typhoid abscess in a mesenteric gland, but I consider that it is usually due to a small undiagnosed intestinal perforation.

GENERAL SURGICAL COMPLICATIONS OF TYPHOID FEVER

TABLE X

GENERAL SURGICAL COMPLICATIONS OF TYPHOID FEVER

	No. of Patients	*Deaths*
Typhoid Abscesses	7	—
Typhoid Arthritis	2	—
Osteomyelitis	1	—
Typhoid Spine	? 1	—
Typhoid Orchitis	2	—
Parotitis	2	1
Otitis Media	4	—
Zenker's Degeneration (Biceps)	1	—
Bed Sores	2	—
Venous Thromboses (Severe)	2	1

1. Typhoid abscess

This is a complication which is often mistaken for a boil and vice versa. The danger of it is not so much to the patient, but to those who surround

him, as a virtually pure culture of typhoid bacilli is present. Differences noted between a typhoid abscess and an ordinary boil were that the typhoid abscess was usually on a deeper plane, and usually, although not invariably, less acute. Most of the typhoid abscesses were situated in and around the buttocks, but this was not invariable, and one abscess was in the axilla and presented exactly like a boil. I would like to stress that all boils in typhoid must be regarded as typhoid abscesses until proved otherwise. On the other hand, staphylococcal boils are a fairly common complication, for in the research series 5 per cent. had moderate or severe boils.

The danger attending incision, apart from infection to the surroundings, is the poor tolerance of the patient to general anaesthesia already mentioned. The indication for incision is when the abscess is pointing; but the majority, being deep, clear up by conservative measures.

Seven cases of typhoid abscess, proved by culture, were seen among 240 cases. All seven patients were treated by repeated aspiration and systemic chloramphenicol. Five cleared up in a few days, but in two the convalescence was prolonged.

2. Arthritis

Although painful joints are a very common presenting symptom in typhoid a true arthritis is rare, and only two definite cases occurred in the series. In one patient the right sternoclavicular joint was involved, and in the other the right hip. Both these patients were treated conservatively with rest and chloramphenicol. Resolution was complete, but took many weeks to achieve.

3. Osteomyelitis

Typhoid osteomyelitis is now less common, probably because the disease is treated early with chloramphenicol. I only diagnosed one case of osteomyelitis among a total of over 1,000 cases of typhoid. This was in a convalescent patient aged 20 who presented with pain and swelling over the midshaft of his left tibia. X-ray showed an area of osteoporosis. He was treated conservatively and slowly improved over a period of weeks.

4. Typhoid spine

There have undoubtedly been true cases of typhoid spine in the past, but this is a condition which almost certainly has been misdiagnosed. It is probable that the advent of chloramphenicol has made this a very uncommon complication; but marked wasting is common in typhoid and low back strain occurs as a result. In the series 7.1 per cent. of the patients complained of backache on admission.

Only one suggestive case occurred in this series. This was in a patient aged 28, who had pain in the lower thoracic region. The X-rays were equivocal and the case is therefore unproven.

5. Typhoid orchitis

This condition is said to be rare, and only two cases were seen. Both occurred unilaterally during convalescence in patients aged 25 and 26 years respectively, who had not been treated with chloramphenicol. There was no urethral discharge. The treatment was conservative and recovery was slow, much as would be the case in a non-specific orchitis.

6. Parotitis

This occurs in any feverish illness where inadequate attention has been paid to the hygiene of the mouth, or where cachexia is common. When it occurs in typhoid it is almost certainly due to an infection by a non-specific organism, and not to the typhoid bacillus. It is a very lethal condition and often terminal, and was seen in two patients, one of whom died and the other recovered. Both were treated conservatively, but in retrospect I feel that incision under local anaesthesia should have been carried out.

OTHER SURGICAL COMPLICATIONS

Many other surgical complications of typhoid may occur, due to concomitant infection and not the typhoid bacillus, and usually associated with the poor general state and toxicity of the patient. They are, however, classical and well recognized complications of typhoid fever, and therefore will be included.

1. Otitis media

This occurred in four patients with typhoid. The pus was cultured on all occasions, and no typhoid bacilli were isolated. All were treated satisfactorily with penicillin.

2. Zenker's degeneration of muscle

No case of this was seen in the classical site of the rectus abdominis. One patient, however, was seen with marked swelling of the biceps. This was in a boy of 17 with a severe attack of typhoid. The swelling, on aspiration, yielded pure blood, and was almost certainly a tear in a partly degenerated biceps.

3. Bed sores

These are common in typhoid despite the best nursing care. In the series two severe bed sores occurred, both in patients with intestinal

perforation associated with a toxic myocarditis. This complication is mentioned merely to stress that skin grafting should be deferred until well into convalescence, because of the poor tolerance to general anaesthetics, even weeks after an acute attack of typhoid fever.

4. Venous thrombosis

Minor thromboses in the veins of the calf may be difficult to detect in a toxic patient. Major thromboses, however, may occur in large veins. Anticoagulants, though indicated in other conditions, should be used cautiously in typhoid because of the possibility of haemorrhage from the gut which may be potentially lethal. I think they should be given to the severe cases only. Major venous thromboses should be minimized by adequate hydration, general treatment including antibiotics and gentle mobilisation of the limbs. There were only two unequivocal examples of major vein thrombosis in the series. One occurred in the left femoral vein, and the patient recovered; one in the left subclavian and the patient died.

MEDICAL COMPLICATIONS

TABLE XI

MEDICAL COMPLICATIONS OF TYPHOID FEVER

	No. of Patients	*Deaths*
Typhoid Lobar Pneumonia	3	1
Typhoid Meningitis	3	1
Typhoid Nephritis	3	1
Haemolytic Anaemia ..	5	3

1. Typhoid lobar pneumonia

Seven undoubted cases occurred, and great care was taken to confirm the diagnosis. Points of interest are that the white blood count was found to be below 10,000, herpes labialis did not occur, and the patients did not respond to penicillin. Although two of these developed a pleurisy in convalescence, the complications of interest to a surgeon, namely lung abscess and empyema, were not seen.

2. Typhoid meningitis

Meningeal irritation is common in typhoid, especially in children, so care must be taken with the diagnosis. Three cases, however, of true meningitis occurred among the research series. One of the three patients died, and it is of interest that at post mortem a pure culture of salmonellae typhi was obtained from the meninges. Surgical complications such as brain abscess were not seen in the two cases that recovered.

3. Typhoid nephritis

This condition is not really of surgical interest. It must not be mistaken diagnostically for the commonly occurring small amount of albumen in the urine of toxic cases of typhoid fever. Three cases of nephritis were seen in the research series. All three patients had the typical distribution of oedema, together with albumen, blood and casts in the urine. The treatment was along the general lines of both typhoid and acute nephritis.

4. Haemolytic anaemia

A mild degree of haemolytic anaemia was not uncommon in the very toxic cases, and was presumably due to some haemolysis, in organs such as the spleen. A moderate or marked degree with jaundice was not common, however, and was seen unequivocally in only five patients, an incidence of 2 per cent. There were three deaths, thus indicating the seriousness of this complication. In only one patient was the haemolysis sufficiently large to cause haemoglobinuria. The surgical interest of this condition is that it must be considered first in the differential diagnosis of an obstructive jaundice. Pigment gall stones may also occur, although this latter complication was not seen in this series.

TYPHOID FEVER IN PRIMITIVE CONDITIONS

Typhoid fever is usually the scourge of poorly educated communities with poor hygienic habits. Hospital, laboratory, and medical personnel are often in short supply, and methods of diagnosis and treatment as advocated by most standard textbooks totally impracticable. The medical officer needs a rapid simple diagnosis, and a simple reliable treatment, supervised often by lay personnel. A number of the patients in the series were seen in primitive circumstances, and therefore the methods of diagnosis and treatment advocated are tempered by practical experience.

Diagnosis

A clinical history and examination plus a diazo test of urine will do much to clarify the position. A single specimen of blood in suitable culture media can be used for both culture and Widal reaction. Stool culture, blood for malarial parasites, and a white blood count are also useful.

Therapeutic test

As a preliminary measure in primitive circumstances only, suspected bacillary dysentery, malaria, and pneumonia may be rapidly differentiated from typhoid by their response to sulphaguanidine, mepacrine and

penicillin respectively. This should not be the routine where modern facilities are available.

Antibiotics

In primitive conditions chloramphenicol could be given in a dosage of 0.5 G. t.d.s. instead of 6-hourly.

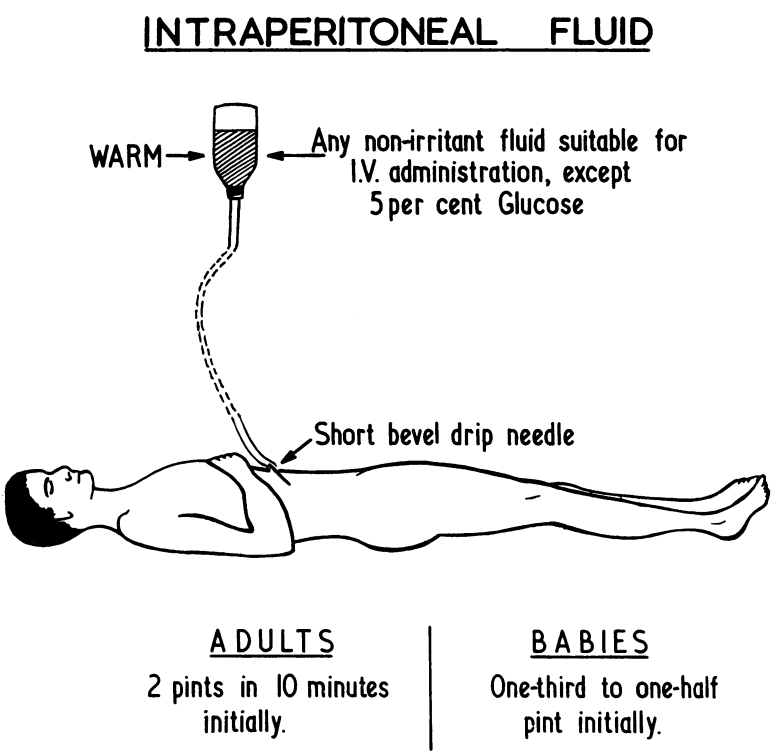

Fig. 7. Intraperitoneal fluid.

Intraperitoneal fluid (Fig. 7)

The administration of intravenous fluids, although the treatment of choice in this country in adults, is often impracticable in an epidemic in primitive surroundings. Many patients have to be treated in poorly lit mud huts by overworked surgeons and physicians, who have neither the time nor the staff to supervise an intravenous drip, and it is in these circumstances that the intraperitoneal drip comes to the fore. It is also invaluable for the treatment of dehydration in young children where adequate nursing is not available or when the veins are collapsed.

The rationale behind the use of intraperitoneal fluid is that the large peritoneal area in the abdomen will absorb as much fluid and other constituents as it requires. The effect is often dramatic although less so than by intravenous administration. I have given intraperitoneal fluid in over 200 patients, and have not experienced any complications from its use. Contraindications to this method are abdominal complications of typhoid such as intestinal perforation, peritonitis and paralytic ileus.

The great advantage of the intraperitoneal drip is the great speed at which it can be given with absolute safety, and with no danger of overloading the circulation (2 pints of fluid in 10 minutes in an adult). It also requires little technical skill, and a nurse can easily master the method. Boiled tap water can even be given in an emergency if nothing better is available. There is no worry about confused patients pulling out a drip needle or of veins thrombosing.

The method of administration is by an ordinary short bevel drip needle inserted obliquely in the midline of the upper abdomen. It should be nearer the xiphisternum than the umbilicus to minimize the risk of injuring the bowel although this must be rare. No anaesthetic is required for the ordinary toxic case or baby, although a little 2 per cent. Xylocaine is kinder for other patients. The needle should be inserted with fluid running slowly out of it. Once inserted, if the fluid does not run continuously on turning up the drip, the usual cause is that the needle is still in the abdominal wall. The fluid should preferably be warmed to the temperature of the body before administration and run in with the clamp fully open. Depending on the head of pressure and size of needle the administration of 2 pints requires about 10 minutes. The needle is then pulled out and the procedure is repeated as required.

The amount of fluid is gauged by the amount of dehydration, and the size of the patient. One-third to one-half pint for a small baby, 2-3 pints for an adult, given fast, is a safe initial amount. 0.45 per cent. saline is the best fluid for routine administration, but normal saline, 2.5 Glucose, Hartmann's solution and plain sterile water can all be used; even ordinary tap water was used on one case in an emergency, with no harmful effects. 5 per cent. Glucose in water (isotonic) should not be used for prolonged administration because electrolyte loss may occur into this from a plasma already deficient in these essential constituents. For repeated administration as in the case of intravenous fluid, care must be taken to assess the relative fluid and electrolyte state of the patient.

With due regard to its occasional limitations, intraperitoneal fluid should prove of considerable value, especially in adults in more primitive conditions, and in children everywhere, and with the exceptions mentioned, irrespective of the disease responsible for the dehydration.

TYPHOID IN CHILDREN

The clinical diagnosis differs from the adult in that the onset is much more acute, and an enlarged tender spleen very commonly found. 56 children under the age of 16 were seen with typhoid, but only six of these were under five. The diazo reaction of urine proved of great value and, from a practical aspect, the stool culture better than the blood culture. Dehydration often necessitated urgent treatment, and the intraperitoneal drip proved of inestimable value. A liquid preparation of chloramphenicol, " chloromycetin palmitate ", was found well tolerated, even by small children. The complication rate was found to be no higher than in adults, but in view of the speed of progress, treatment, to be effective, had to be adequate and early.

THE CARRIER

Urinary carrier

The chronic urinary carrier can usually be cleared by chloramphenicol (Miller and Floyd, 1954, Lewin *et al.*, 1951, McLintock, 1950), and is not much of a problem. The occasional refractory case with renal damage may require a pyelolithotomy or nephrectomy (El Sadr, 1953).

Faecal carrier

The faecal carrier is a much more difficult problem, and has in the past often been thought to necessitate a cholecystectomy. This has been far from the complete answer, however, and in a definite percentage it fails completely. Chloramphenicol on its own has very little effect (Manson-Bahr, 1958), and even cholecystectomy with chloramphenicol cover may sometimes fail (Carnes *et al.*, 1954/1955). The problem was, therefore, investigated with two series of cases (Table XII).

TABLE XII

CONSERVATIVE TREATMENT OF THE FAECAL CARRIER

Aureomycin and Chloramphenicol

		No. of Patients	*No. Cured*
Series I	Acute Disease	11	8
Series II	Convalescent Carriers	9	6

Series I consisted of a trial to prevent the carrier state from occurring in the first place. 11 patients with acute typhoid fever, all of whom were excreting the bacillus, were treated with a combination of 0.5 G. each of aureomycin and chloramphenicol for 7 days. Eight out of 11 of these ceased to excrete the bacillus.

Series II consisted in treating nine persistent convalescent carriers with combined aureomycin and chloramphenicol, and six out of nine were cleared.

It was felt that a longer course than seven days might have cleared both series completely.

It is concluded that in a chronic carrier, a course of combined aureomycin and chloramphenicol should be tried for 2-3 weeks before surgery is contemplated. If this fails, cholecystectomy should be carried out, the operation being covered by a combination of aureomycin and chloramphenicol. In the case of stones or other definite pathology in the gall bladder, early cholecystectomy should be done, again covered by the above two chemotherapeutic agents.

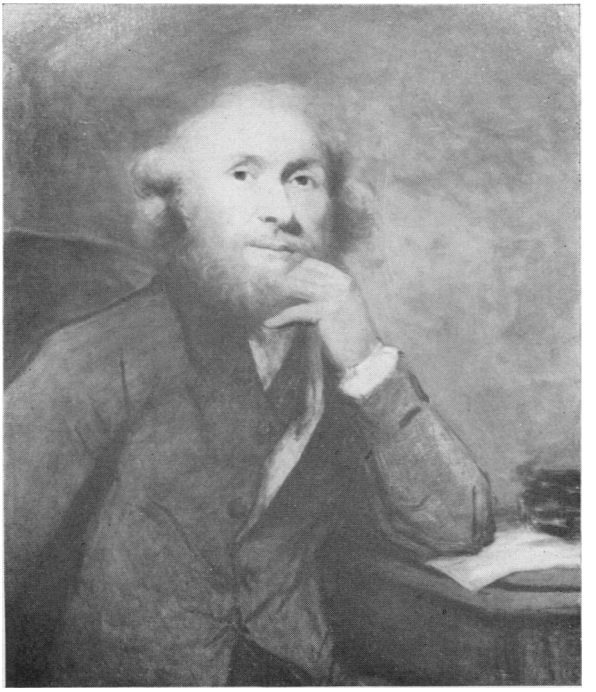

Fig. 8. John Hunter—in his later years—by Reynolds.

CONCLUSION

It may be thought that one has spared the knife too much from these patients, and tended to advocate conservative treatment where operation hitherto has been the more accepted treatment. Acceptance of a method, however, does not necessarily mean that it is either good or immutable,

and the results of operations based on analogy with other abdominal emergencies have been anything but encouraging.

Typhoid fever differs in many aspects from the diseases and surgical conditions which it may mimic, as John Hunter recognized (Fig. 8). The friable lower ileum, multiple-perforated and chloramphenicol sterilized, is a completely different entity from the peptic perforation of stomach or duodenum.

The simpler methods of treatment such as intraperitoneal fluid have been stressed for those of us who have worked, or will work, in countries where typhoid is endemic and occasionally epidemic. The necessity is for speed and simplicity, with safety.

The most important thing that I have gained from my experience in this investigation has been an appreciation of the value of conservatism in the management of the surgical complications of typhoid fever. Otherwise our patients might echo those famous words of Mark Antony:

"*This was the most unkindest cut of all*".

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