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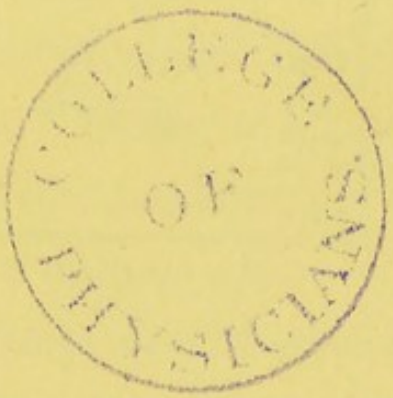

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PREFACE

In the past decade good progress has been made in the differentiation of the dysenteries. During this time the writer has had exceptionally favourable opportunities for investigating the subject in Calcutta, and has long been engaged in collecting material for the present work, which aims more especially at describing and differentiating the two great classes of amœbic and bacillary dysentery in their pathological and clinical aspects, and at giving indications for their treatment. During the progress of his investigations the author has been fortunate enough to discover the rapid specific action of hypodermic injections of the soluble salts of emetine in amœbic dysentery, a discovery which enhances the importance of distinguishing this variety of the disease from that caused by bacilli, and in his opinion makes the present an opportune moment for the appearance of this book.

The article on tropical or amœbic abscess of the liver, which appeared in the second edition of the writer's book on *Fevers in the Tropics*, has been

revised and included; as this condition is a complication of amœbic dysentery its description will be omitted from any future issue of the former work. A chapter on sprue is also included.

I desire to acknowledge my indebtedness to my colleagues in Calcutta for numerous opportunities for clinical and pathological research.

CALCUTTA, *January* 14, 1913.

CONTENTS

LIST OF ILLUSTRATIONS

CHAPTER I

HISTORY OF THE EVOLUTION OF OUR KNOWLEDGE OF DYSENTERIES

Perhaps the most remarkable fact in the history of dysentery is the rarity of the disease in temperate climates at the present day as compared with the frequency of its occurrence and great accompanying death-rate two or three hundred years ago. Thus in the seventeenth century dysentery held a very prominent place in the bills of mortality for Europe, but the disease is now rarely seen in England except in asylums, and has become mainly an affection of tropical and subtropical countries. That this great change is largely due to improvements in the conditions of life and progress in sanitation is clear from the fact that during the enforced absence of these favourable conditions in times of war, dysentery again makes its appearance. Indeed, this class of disease has ever been closely associated with military movements. Sir John Pringle has left us a graphic description of dysentery as seen by him in the Army in Flanders in 1752; Lyons in 1856 recorded its ravages in the Crimea; Woodward's account of the disease in the American Civil War is classical; while much sickness and invaliding was caused by it in the recent South African War, especially in besieged Ladysmith. Overcrowded jails have also often suffered severely. Epidemic dysentery in the

Millbank jail furnished Baly with material for his Goulstonian lectures in 1847, while Mackinnon in 1842 described it as a source of great mortality in Indian jails, in which it still produces much sickness and many deaths. In temperate climates dysentery is now mainly a disease of institutions, whilst in warm climates it occurs as an institutional disease and is also widely prevalent among the general population, but the incidence among the latter is largely due to the amœbic variety, which is very rarely met with as an indigenous disease in temperate countries. On account of this distribution of the disease much of the literature on dysentery during the last century of unexampled progress emanates from workers in warm climates; whilst it is now firmly established that at least two totally different diseases, etiologically considered, have up till quite recently been included under the term dysentery. In considering the history of our knowledge of dysenteries it will therefore be necessary to divide the subject into two periods, the first, antecedent to the differentiation of the great groups of amœbic and bacillary disease; the second, including the time during which modern research has led to the discovery of the causative agents of the two common varieties of dysentery.

HISTORY OF DYSENTERY BEFORE THE ETIOLOGICAL DIFFERENTIATION OF THE TYPES OF THE DISEASE

The term dysentery was used by ancient authors to denote a group of diseases of the large bowel characterized by the frequent passage of stools containing blood and mucus, accompanied by straining

and tenesmus. In view of the fact that even at the present day it is usually impossible by clinical symptoms alone to distinguish between the two main varieties of dysentery, it is not surprising that the descriptions of the older writers cannot enable the types to be differentiated except when the post-mortem appearances are fully described or illustrated by coloured plates, as in the great works of Annesley and Woodward. There is, however, a simple way in which a fairly accurate division of dysenteries into the two main groups can be effected from the recorded descriptions. It is now clearly established that large single abscesses of the liver complicate only the amœbic form of the disease, while even multiple small pyæmic abscesses are rare in bacillary dysentery, so that whenever clinically evident liver abscesses are reported to be common complications it may safely be concluded that the amœbic disease is present, while on the contrary, if in a large series of cases of dysentery hepatic complications are absent we may be practically certain that the majority are not amœbic, but are probably bacillary in nature. Epidemic dysentery, especially if it occurs in an asylum or jail, or in long occupied and insanitary military camps during war, is nearly certain to be bacillary, while sporadic cases in a warm climate are more frequently amœbic in nature. These various points will be repeatedly illustrated in the following brief epitome of some of the more important writings on dysenteries as a whole.

Sir John Pringle in 1752 published one of the earliest modern descriptions of dysentery, with its

post-mortem appearances, in his work *Observations on the Diseases of the Army*, based on his experience in Flanders. The disease was worse in fixed camps at the end of the close hot summer and in the autumn, when it was epidemic and contagious for about six weeks to two months before it ceased. Gangrenous cases were seen, whilst relapses were frequent. He looked upon heat and moisture of the air as the remote causes, and a putrefying state of the blood and scurvy as predisposing ones. Fifty got ill from contagion for one from any other cause. Pringle adds the following interesting remark: 'But having since perused the curious dissertation by Linnæus, in favour of Kercher's suggestion of contagion by animalculæ, it seems reasonable to suspend all hypothesis till that matter is further inquired into.' Over a century elapsed before this prophetic writing was fulfilled. Pringle does not record the occurrence of liver abscess, which, taken with the epidemic prevalence of the disease in fixed army camps in a temperate climate, leaves little or no doubt that he was dealing with bacillary dysentery.

John Hunter (1788) in his *Observations on Diseases of the Army in Jamaica* considered the disease to be the same as that described by Sydenham and others, and that so prevalent in London in 1779–80. Confluent ulcers and slight affection of the ileum were found after death, while liver abscess is not mentioned, so the disease was probably mainly bacillary in nature.

Annesley in 1828 published his beautifully illustrated *Researches on the Diseases of India*, con-

taining a very full description of dysentery and abscess of the liver as seen in the Madras Presidency. This account is especially noteworthy for his division of the cases into (1) Acute uncomplicated and (2) Hepatic dysentery, thus foreshadowing the much later differentiation of the amœbic variety, which is so often followed by hepatitis and tropical abscess of the liver. Annesley records having found liver abscess post-mortem in no less than 26 out of 51 cases, so that, after making liberal allowance for possible selection of those with complications, it is quite certain that he was chiefly dealing with the amœbic variety of the disease. Moreover, his description agrees very closely with that of amœbic dysentery, which forms such a large proportion of the cases now seen in the hospitals in Madras, as well as in the similar climate of Calcutta. Thus, he notes that the disease often begins in the cæcum, yet rarely involves the small bowel; sloughs of membranous lymph and of the mucous membrane are frequently passed; the stools at first are watery and then reddish-brown, like raw meat washings; the disease is most prevalent in the rainy season, while he never saw it contagious in India, although it might arise from overcrowding in hospitals. The post-mortem appearances strikingly confirm this impression, for he writes of the frequency of peritonitis; the presence of raised ulcers chiefly in the cæcum, and extensive effusion into the submucous coat exposing the muscular layers after separation. Lastly, several of the beautiful coloured plates illustrating the lesions found in the large bowel are typical of amœbic dysentery, the raised circular and

oval tawny yellow ulcers in Plate 28 being absolutely characteristic of the disease, although it happens that there were no hepatic complications recorded in this particular case, showing that some of those he classes as uncomplicated dysentery were also amœbic in nature. In short, Annesley's classical description is by far the best account of amœbic dysentery to be found in the older writings, if indeed it has ever been surpassed.

Twining in 1835 dealt fully with Dysentery in his *Clinical Illustrations of the more important Diseases of Bengal.* He also describes the disease as most prevalent in the rainy season, but rare in the hot one, and as affecting chiefly the cæcum and ascending colon, while his account of the pathological lesions is also that of amœbic disease, which is not surprising, as he mainly worked in the Calcutta European General Hospital, where this form is the common one to the present day. He regarded the hepatic complications as secondary to the dysentery, and correctly states that the bowel discharges may cease abruptly with the onset of the liver symptoms. He remarks on the frequency of hepatic disease in Europeans and its rarity in natives of Bengal: a statement which is still copied from one text-book to another, although it has long ceased to be true; a change which is associated with the decreased consumption of alcohol by Europeans since Twining's time, and the increased consumption by natives of large towns in India.

Edmund A. Parkes, 1846, in his *Remarks on Dysentery and Hepatitis in India*, gives a careful description of the lesions in the large bowel, which is

evidently mainly based on an experience of the amœbic variety as seen by him in the Madras Presidency. This view is confirmed by the fact that he met with liver abscess in 21 per cent. of cases among British soldiers. He also noted the rarity of liver abscess complicating dysentery in natives, among whom he had never seen one in a great number of post-mortems. He considered dysentery to be caused by bad food and water, chills, epidemic states, and alterations in the blood as in scurvy.

Kenneth Mackinnon in 1848, in his treatise on *The prevailing Diseases of Bengal and the North-West Provinces* (now known as the United Provinces), refers to the great prevalence in the jails of fatal dysentery often running a chronic course. He stated that pure air, moderate work, and good food and clothing will abolish it, as has largely been the case since his day, at least as far as the epidemic form is concerned. He does not mention having met with liver abscess as a complication, so that it is probable that the jail dysentery of his time may have been largely of the bacillary type, as it is thought to be by some at the present day.

William Baly, in his Goulstonian lectures of 1847, gave a good description of dysentery in the Millbank prison in London. The post-mortem appearances are carefully described, and his second stage with scanty superficial sloughing of the rugæ coalescing to form irregular worm-eaten ulcers not much affecting the submucous coat, clearly refers to bacillary dysentery, and he remarks that the same changes were found by Pringle in Walcheren

dysentery. This diagnosis is confirmed by the fact that liver abscess was never met with in several hundred cases at Milbank during his seven years' experience there, nor in the records dating back to 1823 and comprising twenty-three years. He considered that the disease was due to a local influence, malarial in nature, arising from the soil, and that it was not due to bad water, inadequate ventilation, or sewage defects. The disease was most prevalent during the autumn and spring, and especially so during a wet autumn after a hot summer. He discussed the question whether there is a special form of tropical dysentery, but concluded that there was only one disease.

Haspel in 1847 wrote an excellent account of dysentery in Algeria, where abscess of the liver was so frequent a complication that it is not surprising that his account of the pathological lesions is clearly that of the amœbic disease. It was most prevalent from August to November, while few but relapses or chronic cases were seen during the winter months. He noted that in the early stage the ulcers were small, round, and raised, with thickening of the submucous coat, and later became large and sloughing, but limited by the ileo-cæcal valve; he also described the gangrenous form, the common absence of fever, unless hepatitis or liver abscess ensued, and he recognized the amenability of the disease to ipecacuanha.

Bleker in 1849 recorded a minute description of dysentery in Batavia, which is a remarkably clear account of the amœbic disease, with the deposition of solid yellowish-white fibrinous

masses between the mucous and muscular coats of the large bowel, and with subsequent shedding of the superjacent mucous membrane in the form of larger or smaller green-brown or blackish sloughs, flakes, and shreds, sometimes going on to gangrene and perforative peritonitis.

James Morehead, in his *Diseases of India* (1860), deals with dysentery as seen in Bombay. He described yellow or grey sand-like granulations in transverse patches adherent to the mucous membrane, affecting the large bowel and the lowest part of the ileum, and occurring chiefly in cachectic conditions. This is clearly a terminal complication of bacillary dysentery, such as is also seen in Calcutta at the present day. He also mentioned circular ulcers generally in chronic cases, which may arise from circumscribed submucous suppuration of uncertain causation, and doubtless amœbic in nature. These lesions were most frequently distributed uniformly throughout the large intestine, next so in the cæcum and ascending colon, and much less so in the lower bowel. The greatest prevalence of the disease was in the damp hot monsoon months from June to August, so he attributed it to moist heat. Bad food and water might also cause it, but fæcal accumulations rarely did so, while malaria was not an exciting cause. Among the predisposing causes he enumerated high temperature, chills, cachectic states, malaria, bad atmosphere, and overcrowding.

Woodward, in his *Medical and Surgical History of the War of the Rebellion* (United States), Medical, vol. ii, published in 1880, gives a very exhaustive

account of diarrhœa and dysentery, with short notes of 878 post-mortems, and some illustrations of the lesions in the large intestines. Most of the cases were probably bacillary as in other wars, but there is clear evidence that some of them were amœbic, as the coloured plates opposite pages 452 and 454 are certainly from cases of this variety, one of them being also accompanied by liver abscess. This complication, however, although more frequently met with than in European dysentery, was much rarer than in India and other tropical climates, having been found in only 23 out of 511 cases in which dysenteric ulceration was present post-mortem. It was most common in chronic cases, of which 4 per cent. were complicated by suppurative hepatitis. As amœbic dysentery has recently been found to be widely prevalent in the United States, especially in the Southern portion, the occurrence of the two forms during the American Civil War is easily understood. The disease was most prevalent in the summer and autumn as in Europe.

Fayrer dealt with dysenteries and diarrhœas in his Lettsomian lectures of 1881, and quoted largely from the writings of his predecessors and contemporaries without adding much original material. He agreed with the general opinion in India in favour of the ipecacuanha treatment, his experience in Calcutta having doubtless been mainly concerned with the amœbic disease.

Maclean, in his *Diseases of Tropical Climates* (1886), deals mainly with dysentery as he saw it in the Madras Presidency, the disease being in the main amœbic in nature, as no less than 60 per cent.

of the cases were complicated with liver abscess. He considered it to be caused by bad water, and refers to the reduction of the disease in Calcutta on ships provided with a filtered supply.

Norman Chevers, in his *Commentary on the Diseases of India* (1886), based mainly on his Calcutta experience, looked on the early stages as a simple catarrh of the large bowel produced by chills, and rapidly curable at first by ipecacuanha or castor oil and opium, but if neglected going on quickly to intractable ulceration, so that after the fifth or sixth day only slow recovery can be hoped for. By means of Goodeve's method of washing the stools the progress could be accurately determined and a correct prognosis given (see page 78). He regarded the disease as beginning in the follicles, and had never seen diphtheritic-like membrane. He looked on chronic cases as repeated relapses of a subacute nature. Gangrenous cases should be segregated, and severe dysenteries should not be collected together.

Kelsch and Kiener, in their *Traité des Maladies des Pays Chauds* (1889), accurately described the appearances of amœbic dysentery in Algiers, including illustrations of the microscopic changes in the wall of the large bowel.

The above extracts will suffice to show that bacillary dysentery has always been the prevalent type of the disease in temperate climates, and especially in institutions and in military camps during war; whilst in warm climates the amœbic variety is the common one, although bacillary cases are also met with. As the experience of most of the writers was

based mainly if not entirely on one or other of the two forms of dysentery, it is not surprising that in the absence of accurate knowledge of the causative organisms the two diseases were not earlier differentiated from each other, as their clinical symptoms are so often indistinguishable. We may now proceed to describe the manner in which the separation of amœbic and bacillary dysentery has been brought about through recent scientific research.

THE DIFFERENTIATION OF AMŒBIC DYSENTERY

The history of the differentiation of the amœbic variety of dysentery is of great interest, for from the first discovery by Lambl of this class of organisms in the human intestine in 1859, up to quite recent years a great controversy continued as to whether the organisms were the active causative agents in the production of the disease or merely accidental or secondary concomitants. The problem was complicated by the fact that amœbæ might often be present without any symptoms of bowel disease, while many good observers failed to find amœbæ in a large series of dysentery cases. Although several workers had suggested the existence of more than one kind of dysentery, of which one type only was caused by amœbæ, and further that there might be saphrophytic as well as pathogenic varieties of this class of organism, yet it was not until Shiga discovered the *Bacillus dysenteriæ* in 1898, and this and other closely allied strains of the coli group were proved to be the cause of the forms of dysentery which prevail in temperate climates as well as of

a proportion of tropical cases, that the *Amœba dysenteriæ* has been generally recognized as the agent in producing a large proportion of cases of dysentery in the tropics as well as in subtropical and rarely in temperate climates, and the discordant facts recorded by research workers in all parts of the world became reconcilable. Only a brief account of the earlier work need be recorded here.

In 1859, at Prague, Lambl, in a case of infantile diarrhœa, found a living amœba, which he subsequently demonstrated in other cases of dysenteric diarrhœa, but he was doubtful if it was pathogenic in nature, although he appears to have thought it might be so.

In 1870 D. D. Cunningham and Lewis met with amœbæ in cholera stools, but did not consider them to be of pathogenic significance.

In 1875 Loesch, at St. Petersburgh, found amœbæ repeatedly in the stools of a case of chronic dysentery, and after death he demonstrated them in large numbers in the ulcers in the large intestine. He also injected mucus containing amœbæ into the rectum of dogs, and produced dysenteric symptoms and lesions accompanied by the presence of the organisms in one of them. His paper was well illustrated, and he named the organism *amœba coli.*

Between 1876 and 1881 Sonsino, Grassi, and Perroncito found amœbæ in dysenteric stools, while Grassi and Leuckart also discovered them in healthy subjects, and so the etiological importance of amœbæ in dysentery remained very doubtful.

In 1883 Koch discovered amœbæ in sections of

the intestines in cholera cases in Egypt, and got Kartulis to investigate their relation to dysentery in that country.

In 1885 and 1887 Kartulis published very important results, which placed the rôle of the amœbæ in an entirely new position. In the first place, he found the amœbæ invariably present in the large intestine in 150 consecutive post-mortems, but never met with them in patients who had died of other diseases. He also found the organisms in sections of the intestines of dysentery subjects only, but he failed to reproduce the disease in rabbits or guinea-pigs. Moreover, in 1887, he discovered for the first time similar amœbæ in liver abscesses secondary to dysentery.

In 1887 Hlava, at Prague, confirmed Kartulis's work on the presence of amœbæ in dysentery cases, and thought them to be the cause of the disease.

In 1889 Massioutine, a former pupil of Loesch, found amœbæ at Kiev in the stools of cases of dysentery, chronic diarrhœa, and typhoid fever, but thought they flourished in pre-existing ulcers, and did not look on them as the specific organisms of dysentery.

In 1890 Osler, in the United States of America, found large numbers of amœbæ in the stools of a case of chronic dysentery from Panama. He got Councilman and Lafleur to investigate the cases in his wards, and in the following year they published their classical description of the disease, together with a full review of earlier literature on dysentery. The amœbæ agreed with the descriptions by Loesch, and they were most numerous in acute cases

with extensive lesions, but were not found in catarrhal or diphtheritic dysentery. The cases varied much in character, but had a tendency to be chronic. Fever was absent in the great majority unless hepatitis ensued. They distinguished between the harmless *Amœba coli* and the organism of amœbic dysentery, which they called the *Amœba dysenteriæ*.

In 1891 appeared a valuable paper by Lutz, who independently came to conclusions very similar to those of Councilman and Lafleur. Lutz considered the amœbæ he found in three dysentery cases to be the cause of a chronic form of the disease, often followed by liver abscess, which was quite distinct from epidemic dysentery with diphtheritic lesions of the large bowel. These two last-mentioned papers led to renewed investigations by a number of workers.

Dock had already in 1891 reported finding amœbæ in twelve cases of dysentery in Texas in the Southern States, and by 1892 similar observations had also been made in Italy, Austria, Germany, and Batavia.

In 1893 Kruse and Pasquale reinvestigated the question in Egypt, and in this and the following year published important communications corroborating the work of Councilman and Lafleur and of Lutz, and described a pathogenic and a harmless variety of amœba, the description agreeing in many particulars with the later observations of Schaudinn. They also produced dysenteric symptoms and lesions in cats by injecting per rectum amœbæ contained in dysenteric stools or in liver abscess pus, thus

completing the chain of evidence as to the pathogenicity of the organism.

In 1893 Quincke and Roos also fully described the dysentery amœba and distinguished between it and the harmless form. This view, however, continued to meet with much opposition, especially from biologists.

In 1895 Celli and Fiocca opposed their view and maintained that all dysentery was bacterial in origin, the amœba being harmless. Janowski in 1897 thought that amœbic dysentery was caused by a combination of bacteria and a specific amœba. In the same year Casagrandi and Barbagallo of Catania dealt fully with the subject from the biological point of view and concluded that no amœba was pathogenic.

In 1898 Harris, in the Southern States of America, studied clinically and pathologically 35 cases of amœbic dysentery, and confirmed and added to Councilman and Lafleur's observations.

In 1889 Marchoux demonstrated the amœba in 47 dysentery cases in Senegal, but found them absent in mild forms of diarrhœa. He also succeeded in infecting cats with the parasite.

In 1901 Rogers recorded the occurrence of amœbic dysentery in India, and showed that the amœba is the sole organism constantly found in liver abscesses secondary to amœbic dysentery. Two years later he recorded further observations, with a coloured plate illustrating the lesions in the large bowel.

In 1901 Jaeger identified the disease in East Prussia. In the same year Jurgens had an oppor-

tunity of studying amœbic dysentery among troops returned from China and at the same time the epidemic form of temperate climates in a camp, and clearly distinguished between the two varieties of the disease.

In 1903 Schaudinn published his important observations on the life-history of the pathogenic and saphrophytic forms of amœba met with in the human intestine, and named the harmless one *Entamœba coli* and the dysenteric one *Entamœba histolytica.* This work went far towards removing any remaining doubts as to the pathogenic powers of the amœba of tropical dysentery, although some of Schaudinn's statements appear to require some modification in the light of more recent researches.

Between 1900 and 1905 an important series of papers on amœbic dysentery in the Philippine Islands were published by Strong, Musgrave, Clegg, Craig, and Wooley, which added much to our knowledge of the disease and also contributed an important advance by cultures of certain amœbæ obtained by Musgrave and Clegg, which opened up opportunities for further study of these organisms.

During the last few years attention has mainly been directed to work on the life-history of dysenteric amœbæ, several varieties of which have been described, which will be dealt with in another section of this work. (See Chapter III.) The occurrence of a definite form of dysentery most prevalent in warm climates caused by amœbæ is no longer in doubt. The final acceptance of this conclusion was materially hastened by the discovery that the bacilli, which in the meantime had been proved to be the

cause of the dysentery of temperate climates in the manner now to be described, were absent from amœbic cases.

THE DIFFERENTIATION OF BACILLARY DYSENTERY.

The possibility of dysentery being caused by a specific bacterium naturally led to investigations by numerous bacteriologists, who were long baffled by the difficulties in isolating such an organism from the very varied flora of the intestinal canal. As early as 1869 Basch described leptothrix filaments which he had found in sections of the walls of a dysenteric bowel, and he was followed by a long procession of workers, most of whom attributed the disease to more than one organism isolated by them, thus considering the disease to be polymicrobic in nature. Among those who described a single bacillus as the cause of dysentery are Klebs in 1887, Chantemesse and Widal in 1888, Grigorieff and Ogata in 1892. Of these, that found by Chantemesse and Widal and confirmed by Grigorieff alone resemble Shiga's dysentery bacillus, although in their day all the tests by which the latter is identified were not known, and the claims of the French authors to have been the first discoverers of the dysentery bacillus have been disputed by some authorities. *Bacillus coli*, of exalted virulence, was said to be the cause of dysentery by Maggiora in 1892 and by Arnaud in 1894; the *Bacillus pyocyaneus* was incriminated by Calmette in Cochin China in 1893, Bertrand in 1897, and by other writers, as one of a number of causative organisms; and streptococci were thought to be the true organism by Durham

and Mott in 1896, by Ciechanowski and Nowack in 1898, by Petrides at Alexandria in 1898, and by Ascher in 1899. In addition, numerous observers have accused the *Bacillus coli* in addition to other organisms, including *B. proteus vulgaris*, *B. subtilis*, and micrococci.

It was not until 1898 that Shiga's classical work on epidemic dysentery in Japan threw clear light on the subject by his discovery of the bacillus which bears his name as a distinct species of the great typho-coli group of organisms, and the demonstration that the serum of patients suffering from dysentery agglutinated his bacillus. Confirmation of these important results was not long in coming.

In 1900 Kruse isolated Shiga's bacillus in Westphalia and also obtained another type in cases of asylum dysentery, which he called pseudo-dysentery bacillus, but which was later proved to belong to the Flexner type of dysentery bacillus.

In 1900 Flexner obtained bacilli of the Shiga type, and also found at Manila a species differing from the former in its power of fermenting mannite and with distinct agglutinating properties as first shown by Martini and Lentz in 1902. A little later, Strong in Manila obtained another variety, which he proved to be able to produce dysentery in a condemned prisoner who swallowed the cultures. Subsequently Hiss isolated the Y-bacillus, which is a sub-variety of the Flexner type, whilst Ruffer, Morgan, and others have described yet other varieties with slightly varying sugar fermenting powers. Since then confirmatory discoveries of the dysentery bacilli have been made in various places in Europe

and America by a number of observers, in India by Rogers in 1902, by Castellani in Ceylon in 1904, Morgenroth in China in 1904, and by Nicolle and Cathoire in Tunis in 1905. In the United States, Flexner and his colleagues isolated dysentery bacilli from many cases of infantile diarrhœa.

Thus bacillary dysentery has become established as a distinct disease with an etiology different from that of the amœbic variety; the former produce both epidemic and sporadic cases, more especially in temperate climates, although also widely prevalent in tropical countries, especially in such institutions as jails and asylums; whilst the amœbic form is very common in warm countries, as an acute, but more especially in a chronic relapsing form, but only very rarely occurring in those who have never been out of a temperate climate. We shall see later that the two diseases also require very different treatment in many respects, and so require to be most carefully differentiated from each other: a difficult task which will be attempted in the subsequent descriptions of the dysenteries, using that term in the plural as has now become necessary.

HISTORICAL REVIEW OF THE TREATMENT OF DYSENTERIES.

There are few diseases in which such a great variety of remedies have been used as in dysentery, and regarding which there is still so much difference of opinion. Nor is this surprising seeing that at least two totally distinct affections are included under the term, whilst in addition there is an immense range of clinical variation, extending from

the mildest to the most severe constitutional disturbance, and from short, sharp attacks to the most lingering of chronic affections demanding the utmost patience in meeting the changing therapeutic indications. A brief account of the treatment advocated by the most experienced writers on dysentery of the past century, permitting of some insight into the gradual evolution leading up to our present knowledge on the subject, will, therefore, be of some practical as well as historical interest. I propose to record in chronological order the views of leading authorities in different countries, and then to trace the history of the most important drugs which still hold the field.

Pringle (1774), who had to deal with epidemic bacillary dysentery during the ill-fated Walcheren expedition, recommended moderate bleeding in recent cases in sthenic subjects, and repeated it if fever persisted. He gave 20 grains of ipecacuanha with 2 of tartar emetic to produce vomiting, but notes that the best results were obtained if a stool followed hourly doses of 5 grains of ipecacuanha. He next gave a purge of calomel and rhubarb, followed by opium and ipecacuanha for several nights. He considered astringents never to be of use in recent dysentery, but in chronic cases he gave opium enemata and astringents, together with salines to keep the bowels open.

Annesley (1828) also advocated bleeding and leeches, warm baths to relieve spasms, and fomentations. He then gave 30 grains of calomel with 2 grains of opium at night, and on the following morning a purge of jalap, castor oil, and tartrate

of soda. Purgative salines he found seldom to do good, whilst they might do harm by reducing the strength through the watery motions; he also avoided colocynth and aloes. Dover's powders were useful, and camphor might be given instead of opium. Anodyne enemata were useful for tenesmus, and oil of turpentine should be added for flatulence. He appears only to have given ipecacuanha in small doses of 1 to 3 grains two or three times daily, although he thought that the 20 to 30 grain doses used by some doctors were good in early cases. In chronic dysentery he continued calomel and opium at night, mercury frictions and mild purges, to which he added tonics, nitromuriatic acid, massage, and abdominal bandages.

Twining (1835) also bled copiously, and gave strong purges. He only used opium in enemata, and considered it to be harmful by the mouth owing to its masking symptoms. Ipecacuanha he gave in 6 grain doses twice a day with 4 grains of extract of gentian to prevent vomiting and 5 grains of blue pill, and he considered ipecacuanha the best remedy in dysentery. He advised cold water enemata if there is anuria (as in the choleraic form of bacillary dysentery) or much blood in the stools, and he also gave injections by the bowel of 10 grains to the ounce of acetate of lead. He held that salivation should not be produced, and that mercury was particularly bad in cachectic subjects. With regard to the saline treatment he observed: 'Great caution is necessary in the administration of saline purgatives in all stages of dysentery; even the mildest saline solutions are sometimes apt to cause

irritation by carrying away the natural mucus of the intestines.'

Edmund Parkes (1848) agreed with Twining in the use of bleeding and leeches, but only gave mild purges, such as castor oil or 3 to 8 grains of calomel with opium, followed by blue pill, ipecacuanha and opium in small doses. He only used mercury inunctions in chronic cases, and never to salivation. He found 30 to 60 grains of ipecacuanha much more satisfactory than Annesley and Twining's small doses. He considered that astringents were rarely useful in acute dysentery and never in the chronic disease, but advocated one-eighth of a grain doses of perchloride of mercury with cinchona, and also gave injections by the bowel of silver nitrate and nitromuriatic acid in chronic cases.

As already pointed out, the three last mentioned Anglo-Indian writers had mainly to deal with the amœbic variety of dysentery.

William Baly (1847), in treating the bacillary dysentery of the Milbank prison in London, applied leeches if there was local tenderness or acute inflammation, and gave calomel and opium and gentle aperients, castor oil in 1 to 3 drachm doses being best. Small doses of salines were rarely necessary, and were harmful if violent in their action. He saw no good from the active purging recommended by some Anglo-Indian workers. Large doses of calomel might sometimes be necessary at first, but were injurious if given to salivation. Ipecacuanha, he considered, might be useful as a diaphoretic with others, and he adds: 'But ipecacuanha has wholly

failed in my hands as a specific, or in any way active remedy for the disease.' In chronic dysentery he used astringents, opium and chalk, and sulphate of iron; but not to produce constipation, and locally enemata of silver nitrate, or better, a few ounces of black wash with laudanum or zinc sulphate.

Morehead (1860) in Bombay in the early stages of dysentery used bleeding and leeches, mercury, purges, ipecacuanha and opium, but considered that these measures were harmful during repair, when astringents, alteratives, and opium were indicated. He remarks that large doses of calomel and the mercury treatment had been generally and justly abandoned in his day, but he gave calomel 10 grains, ipecacuanha 2 grains, and opium 2 grains in the evening, followed by an ounce of castor oil the next morning. He regarded ipecacuanha as the best remedy, but gave it in small doses according to Twining's formula. In chronic cases he added tonics and astringents, such as pernitrate of iron, gallic and tannic acid, and also used acetate of lead, bismuth, and sulphate of copper. Chloroform in 20 minim doses relieved severe tenesmus. He did not think that silver nitrate or bael fruit were of much service. Opium enemata were good for tenesmus, but large watery injections he considered to be too disturbing and probably dangerous.

Woodward (1880) records the following experience in the American Civil War. Salines, especially magnesium sulphate, and also castor oil were much used. Calomel was also given largely at first, but was condemned by some, and Woodward never prescribed it. At first he used opium much,

but later only cautiously for pain and sleeplessness. In diarrhœa he also thought opium might do harm, and advised $\frac{1}{4}$ of a grain of morphia with $\frac{1}{100}$ of a grain of atropine as an anodyne. Ipecacuanha was not much used during the war, and with variable success. Woodward limited its use to acute catarrhal dysentery in vigorous subjects, the preliminary stage of diphtheritic dysentery, and chronic cases only where little or no ulceration was present. With regard to astringents he thought tannic acid was of limited use, and might be harmful from its constipating effects. He condemned the administration by the mouth of strong iron salts, copper sulphate, silver nitrate, and acetate of lead, the latter being especially dangerous. He approved of bismuth, and if anæmia was present mild iron salts were useful. There was no evidence of antiseptics being of value. Concerning rectal injections opium was much used as an anodyne, but Woodward preferred morphia subcutaneously. Nitrate of silver injections, in strengths varying from $\frac{1}{2}$ to 15 grains to an ounce of water, were largely used during the American War with varying results. He refers to the good results obtained by Hare in India by the use of large simple enemata, and he recommends a further trial of normal saline solutions at blood heat.

Haspel gave 1 grain doses of calomel and ipecacuanha, but found it less effective in chronic cases than in acute ones.

Maclean (1886) used hot baths, 2 to 4 pint tepid enemata, and gave ipecacuanha as soon as possible in 30 grain doses after opium, repeated every 8 to

10 hours until the patient was better. Later he administered Dover's powder at night and vegetable astringents with bismuth.

Norman Chevers (1886) also gave 15 to 20 grains of ipecacuanha in Calcutta, and found it successful except in gangrenous cases. He never used large enemata as he had seen fatal perforation follow this measure.

HISTORY OF THE MOST IMPORTANT DRUGS USED IN THE TREATMENT OF DYSENTERY.

A brief account of the history of the most important drugs used in this disease will best complete this subject. I am indebted for much of the following information to Woodward's learned work.

Purgatives.—From very remote times various purgatives have been used in dysentery to expel the morbid secretions from the bowel. According to Woodward, **Calomel** was first used in the seventeenth century by Andreas Libovius and by Robert Boyle. In the eighteenth century Pringle and Hunter both advocated this drug in dysentery. Early in the nineteenth century it was given in Calcutta until salivation was produced, in spite of a very high mortality, a practice which was also adopted by Annesley if hepatic complications were present. His contemporary, Twining, however, gave blue pill, but avoided salivation, and their later successors in India used calomel only in comparatively small doses, excessive ones having been denounced by J. Macpherson in 1841. **Perchloride of Mercury** was used in dysentery as early as 1827,

and later was advocated by Parkes, but Woodward considered the evidence in its favour to be doubtful during the American Civil War. **Drastic purgatives,** such as jalap, were largely given as late as the early part of the nineteenth century by Annesley and Twining, but gradually fell out of use after their time.

Saline purgatives, such as magnesium and sodium sulphate, were given in the seventeenth century, but were later largely replaced by calomel, both Annesley and Twining condemning salines as harmful. During the American Civil War they were extensively employed, Woodward preferring the sodium salt on account of its cholagogue action. Baly preferred **Castor oil,** as did most Anglo-Indian writers up to quite recent times. Within the last few years the saline treatment of dysentery has once more come much into fashion, having been greatly used in the South African War and in Indian jails, and it is worthy of note that in both the American and Boer Wars bacillary dysentery was the prevailing type, as is also the case to a considerable extent in Indian jails as far as our present information goes. On the other hand, the Anglo-Indian writers of the last century, who found no use for salines in dysentery, had to deal mainly with the amœbic form of the disease.

Ipecacuanha, or Brazilian root, was first brought to Europe in 1658 by Piso and given in the form of an infusion or decoction. It appears to have been used in India as early as 1660, but to have again largely fallen out of use there. The same fate seems to have overtaken the drug in Europe, for

after having been sold to Louis XIV as a secret-remedy and looked on as a specific for dysentery, it gradually became neglected except as an emetic, for which purpose Pringle used it in the Walcheren disease. Early in the nineteenth century it was again extensively employed by Annesley and Twining in India, though chiefly in small doses, but in 1846 Parkes advocated it in doses of 30 to 60 grains at a time. Docker, however, is generally credited with having reintroduced large doses of ipecacuanha in 1858, using 20 to 30 grains after opium, and in bad cases as much as 90 grains, and he only lost one out of fifty cases among British troops at Mauritius; many years later he received a small special pension from the Government of India for his services in this connexion: a very practical form of recognition of life-saving work. Woodward found ipecacuanha of little or no service in the bacillary dysentery of the American Civil War, but in 1886 both Maclean and Norman Chevers advocated it in full doses in India, while they also recognized its influence in preventing serious hepatic complications ending in liver abscess. Maclean writes: 'How this remedy, almost deserving the name of a specific, came to be superseded by calomel and opium in the treatment of dysentery in the East is one of the most curious questions in the history of tropical medicine.' Yet after his day ipecacuanha was again largely supplanted by the saline treatment, mainly as a result of favourable reports by those who we now know were chiefly dealing with the bacillary disease. The pendulum has once more swung back and, chiefly due to the writings

of Sir Patrick Manson in England, some American workers in the United States and the Philippine Islands and the author in India, ipecacuanha is now taking its rightful place as a specific in the treatment of the recently differentiated amœbic form of dysentery, and as a preventative of secondary hepatitis and liver abscess. Further, the differentiation of the amœbic from the bacillary type of dysentery has furnished the solution of the difficulty which puzzled Maclean, for the facts recorded in the foregoing history make it abundantly clear that those who found ipecacuanha of little or no use, such as Baly, Woodward, and the Army Medical Officers in South Africa, had to deal with the bacterial form of dysentery; whilst on the contrary, the host of able Anglo-Indian workers who advocated ipecacuanha treatment, Annesley, Twining, Parkes, Morehead, Maclean, and Norman Chevers, all encountered the amœbic variety. Lastly, the recent researches of Vedder and the author have demonstrated that emetine, the active principle of ipecacuanha, has a most powerful destructive action against both saprophytic and pathogenic amœbæ, so that there can no longer remain any doubt that we possess in ipecacuanha and its principal alkaloid a specific against amœbic disease at least as powerful as quinine is against malaria, or indeed as any other known drug.

Emetine was isolated by Pelletier in 1817, the same year in which morphine was obtained in a pure state. In 1829 Bardsley of Manchester pointed out the value of emetine in dysentery and other diseases, while Tull-Walsh gave it by the mouth in Calcutta

in 1891 in dysentery, but concluded it did not give better results than other drugs. In 1912 the writer gave soluble salts of emetine hypodermically with the very favourable results recorded in Chapter VI.

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CHAPTER II

EPIDEMIOLOGY OF DYSENTERIES

THE SEASONAL INCIDENCE OF DYSENTERY IN RELATION TO RAINFALL AND TEMPERATURE.

It is well known that the prevalence of dysentery in India increases greatly during the rainy season and continues into the autumn months. The considerable variations in the rainfall of different provinces, together with the annual variations in the amounts in each area, furnish ample material for studying the relationship between the monthly incidence of the disease and the meteorological data. For this purpose I have worked out the curves shown in Diagram I (at the end of this work) for the five years 1906 to 1910 inclusive. The statistics are taken from the annual reports of the Sanitary Commissioner with the Government of India relating to the prevalence of dysentery among the jail populations of the several provinces dealt with, as they constitute the largest series of reliable data available, those relating to the general population being far too inaccurate for the purpose, as will be realized from the simple fact that during an inquiry into the true causes of death in the Dinajpore district of Bengal a few years ago, I found that only one death out of 70 due to dysentery or diarrhœa had been returned under that heading, and the remain-

ing 69 under the elastic term 'fevers'. The chart shows (1) in vertical columns at the bottom the monthly rainfall in inches; (2) as a broken line the monthly mean temperature; and (3) as a continued line the monthly admission rate per thousand for dysentery worked out from the figures given in the reports referred to. The rainfall and temperature data are those of a large town at about the centre of the area it relates to, a geographical group the data for which have fortunately been arranged for many years past, irrespective of the kaleidoscopic changes in the boundaries of the provinces, so marked a feature of recent Indian administration. Working from east to west, the following are the areas illustrated in Diagram I.

1. **Assam,** situated in the extreme north-west of India proper (excluding Burma), has a cold and dry winter, a short dry hot season with a very moderate temperature, the highest monthly mean figure being 83° F. The rains set in very early, namely in April or May, and are heavy and continuous up to the beginning of October, the average annual fall at Sibsagar being 95·9 inches.

Assam well illustrates the close relationship between the rainfall and the prevalence of dysentery in this very wet part of India. Thus, the curve of the disease falls to its minimum during the latter part of the cold, dry winter months, reaching the lowest point as a rule in February, but in 1910 it was in January following a very low incidence in the former rainy season. There is occasionally a slight rise in March with the increase in the mean temperature, this having been most marked in 1906 and

1909 after especially low minimal cold-weather rates. The main increase, however, occurs regularly with the onset of the rains in April and May. Thus, there was an early rise in April in 1908 and 1910, and in May in 1906, when the yearly maximum occurred in that month, which was never the case in any of the other areas dealt with in the diagram. Moreover, in the years of highest rainfall in 1906 and 1907 an exceptionally heavy monsoon was accompanied by a high dysentery curve, both being low in 1908. In the following year, however, a high total rainfall coincided with a low dysentery rate, but in this case the heaviest rain came unusually late for Assam, namely, in August, when it appears to have less effect on the dysentery curve than earlier excess.

2. **Lower Bengal and Orissa,** comprising the whole of Lower Bengal and the three east coast districts of Orissa, has a dry cold season when the mean monthly temperature only falls to about 60° F. In the dry hot season it rises to the moderate mean point of 88° F., and is tempered by occasional rainstorms. The monsoon rains begin in the latter half of June, and are heavy and continuous until early in October, with a mean temperature of about 82° F. The average annual rainfall at Calcutta is 64·2 inches.

In this area, again, the minimum dysentery prevalence occurs in the latter part of the cold weather in January, or more frequently February. This is followed by a slight rise in March with the increase of the mean temperature to about 80° F., sometimes succeeded by a slight fall as the temperature in-

creases to its highest mean monthly figure of about 86° F., as in the years 1907, 1909, and 1910, but this feature is less marked and constant than in the hotter more westerly parts, as will appear presently. The arrival of the monsoon late in June or early in July is rapidly followed by the main annual rise in the dysentery rates during the latter month, to reach its maximum usually about August. The exceptionally heavy monsoon rains of 1908 coincided with a high dysentery curve, and the low rains of 1910 with but little dysentery, but this relationship is not so definite in the other three years.

3. **The Deccan** comprises the Central Provinces and contiguous portion of the Bombay Presidency up to the eastern side of the Western Ghats. It includes the central plateau of India, and its climate differs from the last in that the mean monthly temperature only falls to about 76° F. in the winter season, but rises to about 96° in the hot weather, the average rainfall in Nagpur being 55·9 inches. The dysentery curve is also very similar to that of Bengal, only the minimum is longer on account of the absence of the slight hot weather rise, owing apparently to the comparatively high mean temperature in the colder months. On the other hand, the monsoon increase of dysentery is especially well marked, and reached an exceptionally high point in the two very wet years of 1906 and 1910 compared with the drier intermediate years.

4. **Behar and the Eastern United Provinces, including Chotta-Nagpur,** has a mean temperature falling to about 60° F. in the cold season, and rising to about 94° F. in the dry hot months, and an

averagely good monsoon, but with less abundant rain than in Assam and Lower Bengal, the average annual rainfall at Allahabad being 33·9 inches. In this area the main features already pointed out are well displayed, the early hot weather rise in March from the cold weather minimum being especially well marked, to be followed by a fall in the very hot months of April to May and June, which is in turn succeeded by the regular monsoon rise to the maximum point about August.

5. **The Upper Sub-Himalaya** region comprises the western part of the United Provinces and the eastern portion of the Punjab, and only differs from the preceding one in that the mean temperature falls to 58° and rises to 96°, whilst the monsoon is more variable and lighter, the average annual rainfall at Delhi being 30·6 inches. Here the early hot weather increase is but slightly marked, apparently owing to the very rapid rise of the mean monthly temperature from 58° F. in February to about 84° in April, so that it remains but a very short time at the more favourable point of about 76° F. Further, the monsoon dysentery rise is usually not well marked until September, this retardation being clearly connected with the lateness and comparative scantiness of the rain in this region, for in 1909, when heavy rain fell in June and July, the maximum incidence of dysentery took place in August. Moreover, the excessive prevalence of dysentery in 1908, and to a less extent in 1909, was evidently related to the exceptionally abundant rains of those years, while the lowest dysentery rates coincided with the feeble monsoons of 1907 and 1910, once more demon-

strating the very close connexion between the two events.

6. **North-west Frontier, Indus Valley, and North-western Rajputana.**—This is the driest portion of India, having a cold winter with some rain from the west, when the mean temperature falls to about 50° F., a rapid hot weather rise to 96° F., and extremely little rain in the monsoon months, during which the temperature remains high, but rapidly falls in the autumn. The average annual total rainfall at Peshawar is only 15·6 inches. In this dry area the general curve of the dysentery prevalence is much flatter, and varies but little from year to year as compared with those of the other parts already dealt with, owing to the absence of the usual monsoon rise, as the moisture-bearing current scarcely penetrates into this area. (The sudden decline in the dysentery curve in 1910 must have been due to some administrative change, possibly in the nomenclature of the returns.) In the absence of the monsoon rise the maximum tends to occur in the early hot season of March and April, as seen in 1908 and 1909, when the mean temperature was from 72° to 74° F., followed by the usual fall during the hottest months with a mean temperature of about 92°. A second rise very similar in degree ensues with the decline of the mean temperature once more to about 76° F., in the autumn months, as is well seen in 1907 and 1908, this increase being prolonged into the last quarter of the year and then succeeded by a rapid winter fall to the minimum point. This area, then, is of great interest in showing the close relationship of the temperature

variations to the prevalence of dysentery in a very dry part with no regular monsoon rains, and the importance of this factor in producing the early hot weather rise in some of the other areas, to which reference has been made, is thus confirmed.

General Conclusions.—The results of the above study may be summarized as follows. The minimum dysentery season occurs in the late cold weather months of January or February, in relationship to the minimum temperature of the year, and is commonly followed by a slight increase in the early hot weather month of March with the rise of the mean monthly temperature to between 72° and 78° F., succeeded by a slight fall during the very hot months of May and June, during which the mean temperature reaches from 94° to 96° F. The main increase in the prevalence of dysentery always closely follows the onset of the heavy monsoon rains late in June, and thus usually begins in July, when the mean temperature has again fallen to about 80° to 82° F., and reaches its maximum in August and September; this marked monsoon rise is only absent in the extreme North-West Frontier of India, owing to the rain-bearing currents not penetrating as far as this area. Lastly, the curve steadily declines with the cessation of the rains late in October and the fall of the temperature to its minimum. Further, in years of excessive rainfall the dysentery curve is also unusually high and vice versa. The above data relate to all forms of dysentery combined, no extensive separate figures being at present available regarding the incidence of the different types.

The Seasonal Incidence of Dysentery, Diarrhœa, and Hepatitis in Calcutta.—The fact that amœbic colitis often produces only symptoms of diarrhœa, and is also intimately related to hepatitis in the tropics, makes it of interest and importance to study the seasonal incidence of the three conditions in relationship to each other. For this purpose I have worked out the data shown in Diagram II (at the end of this work) illustrating (1) the monthly first attendances at the out-patient department of the Medical College Hospital for a complete year, and (2) the monthly admissions to the European General Hospital for the five years 1904–9. The quarterly incidence is also shown in the diagram as a double line, which serves to bring out more clearly the closely parallel nature of the curves of the three affections.

The seasonal incidence of both the Indian and the European cases of dysentery will be seen to be similar to that in the provinces of India already described, namely, the minimum in the late cold weather and the maximum in the rainy season and autumn months, the monsoon rise being earlier and more marked in the case of the Europeans, who come early to hospital, while the maximum among natives is later in November and December, as so many of them only come for treatment after the disease has become chronic, while relapses are greatly predisposed to in these thinly clad people by the cold nights of the early winter months.

On turning to the curves of the diarrhœa cases they will be seen to follow very closely those of the dysentery, only the maximum incidence is slightly earlier in the case of both classes of patients. In

the case of Europeans the incidence in the children and adults has been also separately plotted out, both proving to be practically identical, the maximum of each occurring in July with the establishment of the rainy season accompanied by a considerable fall of temperature. In the native out-patients, also, the diarrhœa cases do not materially increase until the height of the monsoon and reach their maximum in October. Thus, not even in the European children is there any marked increase in the incidence of diarrhœa in the dry hot season, as might at first sight have been expected in view of the well-known relationship of infantile diarrhœa in temperate climates to excess of heat. Cases of infantile diarrhœa do occur in the hot season in Calcutta, but much less frequently than one might expect, probably on account of the great care devoted to boiling all milk used for human food in the tropics, and possibly also to the extreme dry heat being unfavourable to the saphrophytic existence of the infective organisms.

The important question remains as to what is the nature of the monsoon diarrhœa in Calcutta and other parts of India. My recent observations clearly show that the great majority of the dysentery cases at this season are amœbic in nature, and as mild cases of this infection often only produce diarrhœal symptoms, it appears probable that much of the rainy season diarrhœa is also amœbic in origin, and consequently amenable to the specific remedy for this disease, but further work is required to test this suggestion.

Lastly, on coming to the incidence curves of

hepatitis we see that they follow very closely those of dysentery and diarrhœa in both series of cases. In the European patients the maximum of the hepatitis cases occurs two months after that of the dysentery and three months later than the milder diarrhœa, just as might be expected if the disease of the liver is secondary to that of the bowel. The great increase of hepatitis among Europeans in October is very probably due to the prevailing custom of going to the hills during the short holiday at the end of September and beginning of October, as it is well known that the liability to chills inseparable from such a change from the damp hot plains to the cold of an elevation of about 8,000 feet above sea-level greatly predisposes to congestion of the liver, especially in those who have previously suffered from any bowel complaint.

All the facts, then, point to the great majority of hepatitis attacks in Calcutta being secondary to amœbic dysentery, as indeed has now been amply proved to be the case by their amenability to ipecacuanha, provided the hepatitis has not been allowed to run on into abscess formation before being detected and adequately treated, as should now very rarely be the case with our present knowledge of the disease.

The Relative Prevalence of Amœbic and Bacillary Dysentery in Warm Climates. — Accurate information on this point is still very scanty. The most reliable data are those of American workers in the Philippine Islands and the Panama Canal zone, in each of which the amœbic type has been found greatly to predominate. In Fiji, Bahr has

recently also met with this variety, but most of his cases were bacillary. In India, Greig and Wells found the amœbic variety by far the more common in Bombay, and Robertson's experience was similar in Madras, whilst I have shown that the incidence is the same in Calcutta, where during the past year two-thirds of the cases in my wards were demonstrated to be amœbic. In Indian jails dysentery is very prevalent, but recent researches have furnished somewhat contradictory results regarding its nature, for while Forster found a majority of the cases to be bacillary in nature, Wells has recently discovered pathogenic amœbæ in 19·5 per cent. and only succeeded in isolating dysentery bacilli in 4·9 per cent., but as in no less than 75·6 per cent. he failed to find the cause of the disease during life, the proportion of bacillary cases is probably much under-estimated owing to the difficulty in isolating this organism, especially in the chronic cases which so frequently occur in Indian jails. Much further work is required on this subject. Recently at Keiv, in Southern Russia, 90·2 per cent. of dysentery cases were found to be bacillary. In Morocco, out of 374 cases investigated, 79 per cent. were bacillary and 21 per cent. amœbic. In Cochin-China 53 per cent. were amœbic, while in only 8 per cent. were dysentery bacilli isolated. These figures will show the steady decrease in the proportion of bacillary and increase in amœbic dysentery as the equator is approached. Now that the emetine treatment allows of the early cure and elimination of the amœbic cases, it is to be hoped that more rapid progress will be made in ascertaining the relative prevalence

of the two types of dysentery in different parts of India and in other warm climates.

The Ratio between the Admission Rates for Liver Abscess and Dysentery as an indication of the Prevalence of Amœbic Disease.—It will be shown in a later section of this work that large tropical abscesses of the liver are always secondary to amœbic dysentery and never to the bacillary form. We may therefore safely conclude that where there is a considerable admission rate for liver abscess in proportion to that for dysentery, there amœbic disease will certainly be widely prevalent, and will probably constitute the majority of cases of the bowel complaint. I have therefore worked out the relative proportion of admissions in the British Army hospitals in different areas of India both for dysentery and liver abscess during the ten years 1901–10, with the following results. In the first place the figure for the whole of India gave the very high proportion of one admission for liver abscess for each seven for dysentery, which clearly indicates an extensive prevalence of amœbic dysentery in the country as a whole. Secondly, there was a remarkable uniformity in the proportion between the two diseases in different areas, for in the whole of the central and northern parts of India, of which the meteorological data are given in Diagram I, and which include the great bulk of the entire country, the ratio was practically uniform, namely, one liver abscess to six or seven dysentery admissions, although the climatic conditions vary extremely from steamy Lower Bengal to the very dry hot North-West Frontier.

The only possible conclusion from these data is that amœbic dysenteric disease is common all over the country, and probably constitutes a large proportion of the dysentery in the British Army in India at the present time: a conclusion of great practical importance now that the disease is so easily and rapidly cured by the emetine treatment described later (see p. 121).

CHAPTER III

DYSENTERIC AMŒBÆ AND THEIR DIFFERENTIATION FROM HARMLESS INTESTINAL FORMS

The long controversy regarding the pathogenicity or otherwise of the amœbæ so frequently found associated with dysentery in warm climates has already been dealt with in the opening historical section. It remains to describe the forms now generally admitted to be the cause of the disease, together with their differentiation from the non-pathogenic variety met with in the intestinal canals of healthy persons. During the last few years some further confusion has been caused by several observers describing what they considered to be new varieties of amœbæ, often on very slender grounds. The only reliable classification is based upon constant differences in the life-history of the organisms, and especially in their reproductive processes, which require to be worked out by competent zoologists. Although Strong and Musgrave in 1900, and Jurgens in 1902, described many details concerning the dysentery amœba, yet it was not until Schaudinn's classical account of the complete life-histories of the *Entamœba histolytica* and *Entamœba coli* was published in 1903 that these two forms were clearly defined. To these a third variety with an established life-history has been added by the studies of Viereck and of Hartmann and Prowazek

in 1907, namely, the *Entamœba tetragena*, which was first met with in dysentery cases from Africa. Fantham, in a recent critical review of the literature of the subject from the zoological aspect, arrived at the conclusion that none of the other described forms of human intestinal amœbæ are entitled on the present evidence to rank as definite species. Thus, he considers that *E. tropicalis* of Lesage, and possibly *E. hominis* of Walker, are varieties of *E. coli*, and that *E. nipponica* of Koidzumi belongs either to the same species or to *E. tetragena*, while *E. minuta* of Ilmassian is only a variety of *E. tetragena*. Further, the entamœba obtained by Noc in Cochin-China in 1909 and *E. phagocytoides* of Gauducheau show close affinities with Schaudinn's *E. histolytica*. Craig has also come to a very similar conclusion in his work on the parasitic amœbæ of man, to which I am indebted for many of the details of the life-histories of the recognized species.

Methods of detecting Amœbæ in Stools.—In warm climates intestinal amœbæ retain their vitality for some hours, and may usually be detected in stools by their movement. In examining for them it is advisable to make two or more preparations from different pieces of mucus, especially from the blood-stained portions, as the organisms are often very irregularly distributed, none being seen in one piece, but a number in a second specimen. The selected portions are placed on slides under cover-glasses, and gentle pressure applied so as to spread out the viscid mucus without damaging the organisms, a ring of vaseline placed round the edge of the cover-glass to prevent drying of the specimen, and

examined with a one-sixth inch lens with a low eyepiece and the iris diaphragm partly closed. If the amœbæ are motionless they are somewhat difficult to detect without a good deal of experience, but if the air temperature is anywhere near 80° F., as is so often the case in the tropics, there will nearly always be some parasites showing activity. If the temperature is lower the slide should be warmed, and the material to be examined placed in an incubator at about blood heat for a short time before the examination is made. In the majority of cases of amœbic dysentery the organisms are sufficiently numerous to allow of their being readily detected within a few minutes by such a simple microscopical examination, but when scanty great assistance may be obtained in the search for them by one of the following methods.

As advised by Vincent, a drop of 1 per cent. solution of methylene-blue in normal saline is added to a little mucus on a slide, well mixed with it, and a cover-glass applied as before. The leucocytes and epithelial cells are rapidly stained blue, in contrast to which the unstained amœbæ show up very clearly, while they continue in motion for some time before the endoplasm gradually takes up the stain and their activity ceases. I have recently found that with a little practice the amœbæ can easily and very rapidly be detected in such a preparation with a half-inch lens and a No. 2 eyepiece, a higher power being then turned on to verify the find. With experience the same magnification suffices for finding amœbæ in dysenteric stools even in unstained mucus, and by this means a cover-

glass preparation can be completely searched within a very few minutes, and much time be thereby saved when the organisms are present in only small numbers. If the parasites are fairly numerous, from a half to two minutes suffices for recognizing their presence, and if scarce several specimens can be thus examined without consumption of an undue amount of time, and I have repeatedly found amœbæ in this way when I had failed to detect them by using a higher magnification.

Another useful staining method is the addition of a drop or two of a 1 in 10,000 normal saline solution of neutral red, which serves to colour both living and dead amœbæ a rose pink without interfering with the motion of the former, whilst the leucocytes and other cells do not stain with this strength, so that the amœbæ stand out clearly. This method is especially useful in distinguishing inactive organisms.

The Appearances of the different fresh Amœbæ seen in Human Stools.—As a study of the distinguishing reproductive characters of the different intestinal amœbæ is a very difficult and lengthy process, it is of greatest practical importance to know how to differentiate between the harmless and pathogenic forms by the appearances of the living organisms in fresh specimens, as can be done with a little care. The distinguishing points can be best made clear by dealing with each in turn as it concerns the three recognized species, while they will also be found briefly summarized in the Table on page 63. Fortunately the *E. coli* differs from the two pathogenic varieties in a number of parti-

culars, while the exact distinction between the *E. histolytica* and *E. tetragena*, although more difficult, is not nearly so essential, since both give rise to identical symptoms and pathological changes and, as far as we know at present, are amenable to the same treatment.

Size is of comparatively little importance in the differentiation of the amœbæ, as each species may vary so widely in this feature during different stages in its development. The *E. coli* is on the average smaller than the other two, varying, according to Craig, from 10 to 30 micromillimetres in diameter, against 10 to 50 or even 70 in the case of the two pathogenic species. Thus, if a number of organisms of well over 30 micromillimetres diameter are present they will be pathogenic ones, but in this case other better marked features will also be available for their differentiation. On the other hand, the fact that all the visible amœbæ are small in no way excludes their being pathogenic, as it is not uncommon for a number of them to have been recently developed from spores and not yet to have attained any large size.

Shape is also of little value, as all are round when quiescent and very irregular when in motion.

The **Protoplasm** in the case of the *E. coli* is not clearly differentiated into endo- and ectoplasm, the parasite being uniformly granular, although when moving the ectoplasm is more finely granular than the endoplasm, but it never presents the clear appearance of the pseudopodia, which is so characteristic of the pathogenic species. In the endoplasm of all species may be seen coarser granules and

crystals of phagocytosed substances, but red corpuscles are very rarely found in *E. coli*, and never more than one or two, while it is an especially noteworthy and important diagnostic feature that the two pathogenic forms commonly contain numerous red cells, some of which they have digested.

Vacuoles are never of the contractile variety in intestinal amœbæ, but a few non-contractile ones are often seen in *E. coli* and more numerous ones in the other two species.

The **Nucleus** in *E. coli* is clearly defined in unstained fresh specimens, and situated about the centre of the organism. In *E. histolytica* it is commonly invisible in unstained specimens, and never as distinct a structure as in *E. coli*, while when seen it is situated eccentrically at about the junction of the endo- and ectoplasm. In *E. tetragena*, however, the nucleus is much more distinct, in which respect it resembles the *E. coli*.

The **Colour** of *E. coli* is always grey, but that of the pathogenic forms often is of a greenish tinge, due, according to Craig, to the digestion of red corpuscles, as he has observed the appearance of the green colour develop with the dissolution of red cells within the parasite.

The **Pseudopodia** are of the greatest diagnostic importance, for in the case of *E. coli* they are always granular and scarcely to be distinguished from the endoplasm, while they are small and blunt, and consequently their motion is sluggish. In marked contrast to this in both the pathogenic forms the pseudopodia are very clear and refractile, so as to be well differentiated from the granular endoplasm,

and either large blunt, or longer finger-like transparent processes are protruded, sometimes more than one at the same time. During the greatest activity a large clear pseudopodium is pushed out, and the endoplasm soon flows into its centre; the whole organism, becoming much elongated, flows steadily across the field of the microscope to pass out of sight at the edge of the field, a degree of motility rarely if ever seen in *E. coli*. The clear ectoplasm is not so extensive in *E. tetragena* as in *E. histolytica*, but it is still quite distinct during movement, and suffices to distinguish the organism from *E. coli*.

The **Cystic** forms are much less often seen in fresh stools than the active organisms, being most numerous when the conditions are becoming unfavourable for the parasitic forms, as during recovery from amœbic dysentery. They have a double contour due to thickening of the wall. In *E. coli* eight young amœbæ develop in each cyst and in *E. tetragena* only four; while *E. histolytica* multiplies by a form of budding which will be described later, as it cannot well be studied except in stained specimens.

Methods of Fixing and Staining Amœbæ.—As the details of the life-history of amœbæ can only be worked out by the aid of stained specimens, the preparation of these is of great importance in studying the reproductive processes in particular, on which the establishment of new species depends. Such work, however, can only be carried out in a well-equipped laboratory by experienced investigators, so need only briefly be dealt with here.

Fixing is best performed while the smear is still wet by quickly spreading the mucus or other material

in a thin film on a glass slide and plunging into the fixing solution before it has had time to dry. The best fixing medium is an alcoholic solution of perchloride of mercury, which is made by adding one part of absolute alcohol to two parts of a saturated solution of perchloride of mercury in normal saline. Craig also recommends two parts of osmic acid in 100 parts of a 1 per cent. solution of chromic acid, or the film may be briefly exposed while wet to the vapour of this solution, a few minutes being sufficient in the case of either solution, and one or two for the action of the osmic acid vapour.

Staining is best accomplished by means of the iron hæmatoxylin method of Heidenhain. After washing the fixed specimen in distilled water, it should be placed for some hours, preferably overnight, in a 2·5 per cent. watery solution of ferrous ammonium sulphate, and then immersed for from 6 to 24 hours, or in the case of sections up to 36 hours, in a 1 per cent. old watery solution of hæmatoxylin. After again washing in distilled water they are partially decolorised in the iron solution, the advance of the process being watched from time to time under the microscope until the nucleus is seen to be deeply stained, while the cytoplasm has a light grey colour. After washing and drying the slides may be examined directly with an oil immersion lens, or after passing through alcohol of different strengths up to absolute and clearing in xylol, they may be mounted in Canada balsam if sections are being dealt with.

Wright's method is also of importance, as when successful it helps in differentiating the species of

intestinal amœbæ. Add a few drops of Wright's stain to either a wet unfixed specimen or one which has been fixed with osmic acid vapour followed by alcohol, and let it stand for five minutes before adding a few drops of distilled water, and then stain for from ten minutes to an hour, and if too deeply stained wash in alcohol and xylol. Repeated trials may be necessary to ensure a good differentiation with this stain.

Giemsa's stain will also give very good results. 10 drops of the stock solution in 10 c.c. of distilled water, to which one or two drops of a 1 per cent. solution of potassium carbonate has been added, is allowed to act for from one-half to six hours on a previously fixed specimen, any excess of stain being removed with alcohol.

The Appearances of Stained Intestinal Amœbæ.—The characteristic changes in the protoplasm are best brought out by Wright's stain, with which in the case of the *E. coli* the endoplasm becomes a dark blue, while the ectoplasm is light blue. In the case of the *E. histolytica* this staining is reversed, the endoplasm being light and the ectoplasm a dark blue. The *E. tetragena*, on the other hand, does not stain well with Wright's method. In each case the chromatin of the nucleus stains red, the tint being lighter in the *E. histolytica* than with *E. coli* or *tetragena*.

With the hæmatoxylin method the chromatin stains a very dark black, while the protoplasm takes a light grey coloration, and this method is most valuable for studying the characters of the nuclei and their changes during the reproductive

processes. In the first place, in the active vegetative stages of the organisms the following differences are found in the nuclei of the three human species. In *E. coli* the chromatin is abundant, forming a well-defined nuclear membrane with marked thickened portions projecting from its inner surface, while in the centre is a large mass of chromatin, the karyosome. In contrast with the *E. coli*, in the case of the *E. histolytica* the nucleus is a much less prominent body with comparatively little chromatin, without a well-developed nuclear membrane, and with a much smaller central karyosome. The nucleus of the *E. tetragena* closely resembles that of *E. coli* in having a well-developed chromatin nuclear membrane and a large karyosome.

The Reproductive Processes of Human Intestinal Amœbæ.—During the vegetative stage each of the human intestinal amœbæ multiplies by repeated simple division, beginning with the nucleus, followed by that of the body. On the other hand, the sexual reproduction is different in each and constitutes the essential feature of their differentiation into separate species. Briefly, the processes are as follows.

In *E. coli* reproduction by schizogony takes place with the formation of eight daughter cells. The organism first ceases its active motion and extrudes all foreign particles from its protoplasm. The nucleus becomes enlarged, and eight thickenings projecting from the inner surface of the nuclear membrane separate to form eight daughter nuclei, which then become free in the cell protoplasm by rupture of the nuclear membrane, and finally the

cytoplasm collects around them and also divides to form eight young amœbæ. Under unfavourable conditions, such as keeping a stool with the organisms in it for a time, encystment takes place with the formation of a thick double contoured external membrane, resisting staining processes, and measuring from 10 to 15 mm. in diameter. The nucleus eventually divides into eight daughter nuclei by a complicated process, and an equal number of young amœbæ are formed, which, when the cyst again finds itself under favourable conditions, escape and develop into full-grown individuals.

In *E. histolytica* reproduction occurs by means of a very different process, namely budding or gemmation, which was first described by Schaudinn. In this case the nucleus gives off particles of chromatin, or chromidia, into the cytoplasm, throughout which they become distributed. These particles next become collected into groups in the ectoplasm of the organism, and a stain-resisting sheath is formed around them. Then they bulge from the surface of the organisms as bud-like processes, and finally separate as young spores. In fresh fæces these spores appear as rounded bodies with a refractile membrane, and measure from 3 to 7 mm. in diameter.

In the *E. tetragena* the process is simpler, for after the extrusion of foreign matter the nucleus enlarges and divides into two, and at the same time a cyst wall develops around the organism. The two daughter nuclei both divide into four, around which the protoplasm becomes grouped to form four young amœbæ within the cyst.

According to Craig conjugation of two vegetative forms may be occasionally seen in all the human intestinal amœbæ, although not much is known about the process. I have once seen what I believe to be this condition in *E. histolytica.*

The Cultivation of Amœbæ.—There is no part of the subject regarding which there is still greater differences of opinion than over the cultivation of amœbæ. Many observers have cultivated amœbæ from human fæces, from D. D. Cunningham in 1879 up to the extensive work of Musgrave and Clegg in 1904, when the latter investigators reported that they had cultivated dysenteric amœbæ in symbiosis with pure cultures of bacteria, especially intestinal pathogenic ones, such as *B. coli, typhosus,* and the vibrio of cholera, and had produced typical dysentery in monkeys with such cultures; while Walker in 1908 supported much of their work. Musgrave and Clegg used the following culture medium: Agar 20 grm., sodium chloride 0·4 grm., extract of beef 0·4 grm., in 1,000 c.c. distilled water, prepared as ordinary nutrient agar and made 1 per cent. alkaline. The surface of agar plates in Petri's dishes are smeared in streaks with the stool to be examined, a culture of *B. coli* being first spread over its surface if isolated amœbæ are to be grown. The amœbæ grow well at room temperature, and can easily be seen with the microscope spreading out from the inoculated lines.

The question in dispute is whether the amœbæ which can thus be grown are those which flourish and develop in the human intestine, or whether they are only the offspring of encysted saprophytic

forms, so numerous in water and other articles of food, which have passed unchanged through the gastro-intestinal tract and develop on the plates. Braun and Luhe, in their work on parasitology (1910), state their opinion that the amœbæ which are parasitic in mammals have never been successfully grown outside the tissues of their host, and Craig, who has minutely studied the whole question of amœbæ in man, most strongly supports this view, mentioning that Major Whitmore of the U.S. Army Medical Corps recently worked with Hartmann in Hamburg, and concluded that all the cultures of amœbæ he obtained in Manila from dysenteric patients, both from their stools and from liver abscess pus as well as cultures from water, were found on close study to be free-living amœbæ and of no etiological significance in dysentery. Wells, in India, has recently cultivated amœbæ on agar plates exposed to the air, and thinks that unless special precautions are taken stools may thus be contaminated with culturable amœbæ. In my own laboratory I have been struck by the fact that stools swarming with active *E. histolytica* often fail to produce any amœbæ on Musgrave and Clegg's media. We may, therefore, conclude that it is not yet conclusively demonstrated that either of the pathogenic amœbæ or the *E. coli* have yet been cultivated outside the human body.

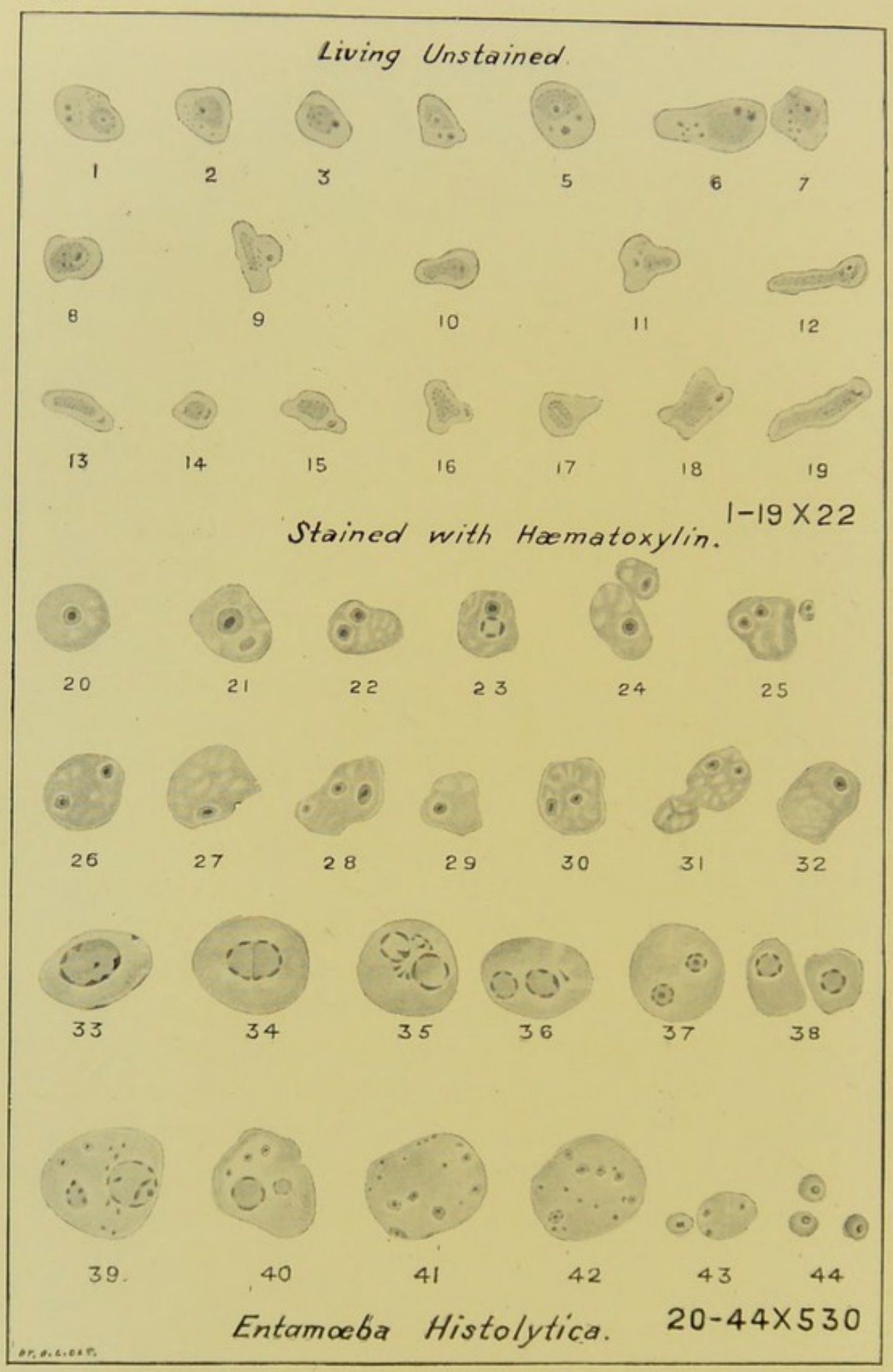
The Pathogenicity of Human Intestinal Amœbæ.—Here we have to rely on the effects produced in susceptible animals, chiefly cats, or preferably half-grown kittens, by either feeding with, or injecting per rectum, human stools containing amœbæ; for

we have just seen that there are good reasons for rejecting as open to doubt the evidence derived from the use of cultural material for such experiments. The above methods involve the possible fallacy that pathogenic bacteria may have been introduced at the same time, but attempts have been made with a considerable degree of success, more especially by Harris and by Craig, to eliminate this factor by separating all possible pathogenic organisms from the amœba-containing stools, and separately proving by experiments that they were not capable of producing dysenteric symptoms or lesions in cats. Even more conclusive is the experimental production in the large intestine of cats of dysenteric lesions presenting the typical naked eye and microscopic changes of human amœbic disease, including secondary liver abscesses containing the pathogenic amœbæ without any bacteria whatever. Such conclusive positive results, however, have only been obtained with *E. histolytica* and *E. tetragena*, but never with *E. coli*, proving that the latter is a harmless inhabitant of the human intestine. Schaudinn explained this by the fact that *E. coli* has soft pseudopodia, which are unable to penetrate through the intestinal mucous membrane, while *E. histolytica*, on the contrary, possesses a very firm ectoplasm and is able to force its way between living cells of the tissues of its host, and the same is true of the *E. tetragena*. Feeding experiments are most successful if the stool containing the amœbæ is kept for some hours before being used, as this causes the amœbæ to become encysted and thus more resisting to the digestive processes.

The Frequency of the presence of harmless Entamœbæ coli in Human Stools.—In view of the necessity of differentiating between *E. coli* and the pathogenic varieties it is of importance to know how frequently the former is likely to be met with in examinations of human stools. As far back as 1881 D. D. Cunningham found amœbæ both in healthy and in choleraic stools. In the Philippine Islands Strong and Musgrave found amœbæ in only 4 per cent. of healthy persons, while they were not pathogenic for animals. Dock, in the United States, found them in only 2 per cent., but Schaudinn, in 1903, met with them in 50 per cent. of healthy men in West Prussia, in only 20 per cent. in Berlin, but in as many as 66 per cent. on the Adriatic shores. Craig, in 1905, showed that in healthy American soldiers at San Francisco, after the administration of ounce doses of magnesium sulphate, the *E. coli* was found in 65 per cent., at least eight specimens being examined before a negative result was recorded. Anderson (1907), in the Andaman Islands, found amœbæ in 53 per cent. of dysentery cases, and in 29 per cent. of other diseases, but did not distinguish between the species, and thought them to be harmless commensals. Ashburn, in the Philippine Islands, found 71 per cent. of 107 healthy American soldiers to harbour the *E. coli*, while in two the *E. histolytica* was found, the last two only suffering from diarrhœa or dysentery. Craig has also investigated the occurrence of the harmless amœbæ in various unselected diseases, and out of 250 subjects he obtained a positive result in 49 per cent., and he states that he has repeatedly seen patients with this

form of amœba alone present submitted to prolonged treatment for amœbic dysentery.

In most of the above cases in which *E. coli* has been found in a higher percentage of healthy individuals a preliminary saline purge has been administered, which makes the organism much easier to find. In Calcutta, in dysentery patients who have received only a dose of castor oil before their stools were examined, I have rarely met with *E. coli*, so have not found it to be a serious source of confusion, but if salines are first given it would probably be encountered more frequently. It is clear, however, that it is of the utmost importance to be able to distinguish between the harmless and the pathogenic varieties, and this can fortunately easily be done by means of the appearances of the amœbæ in fresh unstained specimens, especially when in active movement, as they nearly always are in stools examined with the precautions already detailed within an hour or two of being passed. This section may, therefore, be suitably concluded with the following table of the differences between the three well recognized species of human intestinal amœbæ, the first half of it containing the points to be relied on by practitioners in examining fresh specimens, whilst in the second part will be found the morphological characters on which experts and zoologists depend for establishing new species.



VARIOUS FORMS OF *ENTAMŒBA HISTOLYTICA*.

1–7. Living unstained amœbæ, some containing red corpuscles. 8–19. Shapes successively assumed by an amœba during its movements. 20–32. Amœbæ fixed in alcohol and perchloride of mercury and stained with hæmatoxylin. 33–8. The same showing simple division. 39–44. The reproduction of *Entamœba histolytica* by budding off of young forms.

1 to 19 under Zeiss D, Oc. 2 × 220. 20 to 44 under $\frac{1}{12}$ inch, Oc. 2 × 530.

TABLE OF DIFFERENCES BETWEEN THE HUMAN INTESTINAL AMŒBÆ.

	E. Coli.	*E. Histolytica.*	*E. Tetragena.*
I. *Morphological characters in unstained specimens.*			
Size	10–30 micromillimetres	10–70 micromillimetres	10–50 micromillimetres
Nucleus	Well defined, in centre of endoplasm	Not well defined, at junction of endo-ectoplasm	Well defined
Protoplasm	Granular throughout and not clearly differentiated into endo- and ecto-plasm	Endoplasm granular, ectoplasm clear and well differentiated from endoplasm	Like *E. histolytica*, but clear ectoplasm less well developed
Colour	Always grey	Often of a greenish tinge	Often of a greenish tinge
Vacuoles	Few, non-contractile	More numerous, non-contractile	Like *E. histolytica*
Pseudopodia	Small, finely granular, and not well differentiated from endoplasm	Large, clear, and well differentiated from endoplasm	Clear and well defined, but smaller than in *E. histolytica*
Movement	Very sluggish	Very active	Very active
Contents	Very few or no red corpuscles	Often with numerous red corpuscles	Often with numerous red corpuscles
II. *Morphological characters in stained specimens.*			
Nucleus	Large amount of chromogen, well developed nuclear membrane	Small amount of chromogen, badly developed nuclear membrane	Large amount of chromogen, well developed nuclear membrane
Protoplasm with Wright's stain	Endoplasm dark blue Ectoplasm light blue	Endoplasm light blue Ectoplasm dark blue	Not well differentiated
Reproduction	Nucleus first divided into 8, and afterwards the protoplasm divided to form an equal number of young amœbæ	Nuclear chromogen dispersed in protoplasm, and young forms containing parts of it bud off	Nucleus divided into 4, and an equal number of young amœbæ formed
Multiplication	By simple division	By simple division	By simple division

CHAPTER IV

PATHOLOGICAL ANATOMY OF AMŒBIC DYSENTERY

A PERUSAL of the accounts of the morbid anatomy of dysentery in the writings of competent observers in various countries show the most striking differences and often diametrically opposed statements on nearly every conceivable point. Thus, some regard primary lesions as affecting the mucous membrane, while others locate the disease in the submucous coat, the surface membrane being only secondarily affected. Similarly, with regard to the involvement of the lower part of the ileum and numerous other features of the disease the experience of different authorities is equally at variance. The diphtheritic membrane of the fibrinous form is recorded by some writers as being the rule and others as very exceptional or never seen. In short, only the most confused idea of the pathological anatomy of dysentery can be gathered from a study of the older literature, as can be seen by reading the quotations in Sir Joseph Fayrer's Lettsomian Lectures of 1881, and from the historical review in the first chapter of this work. The explanation of these discrepancies is simple now that the two great groups of amœbic and bacillary dysentery have been recognized; for the former is a sporadic disease mainly of tropical and subtropical countries, producing primarily an exudation into the submucous

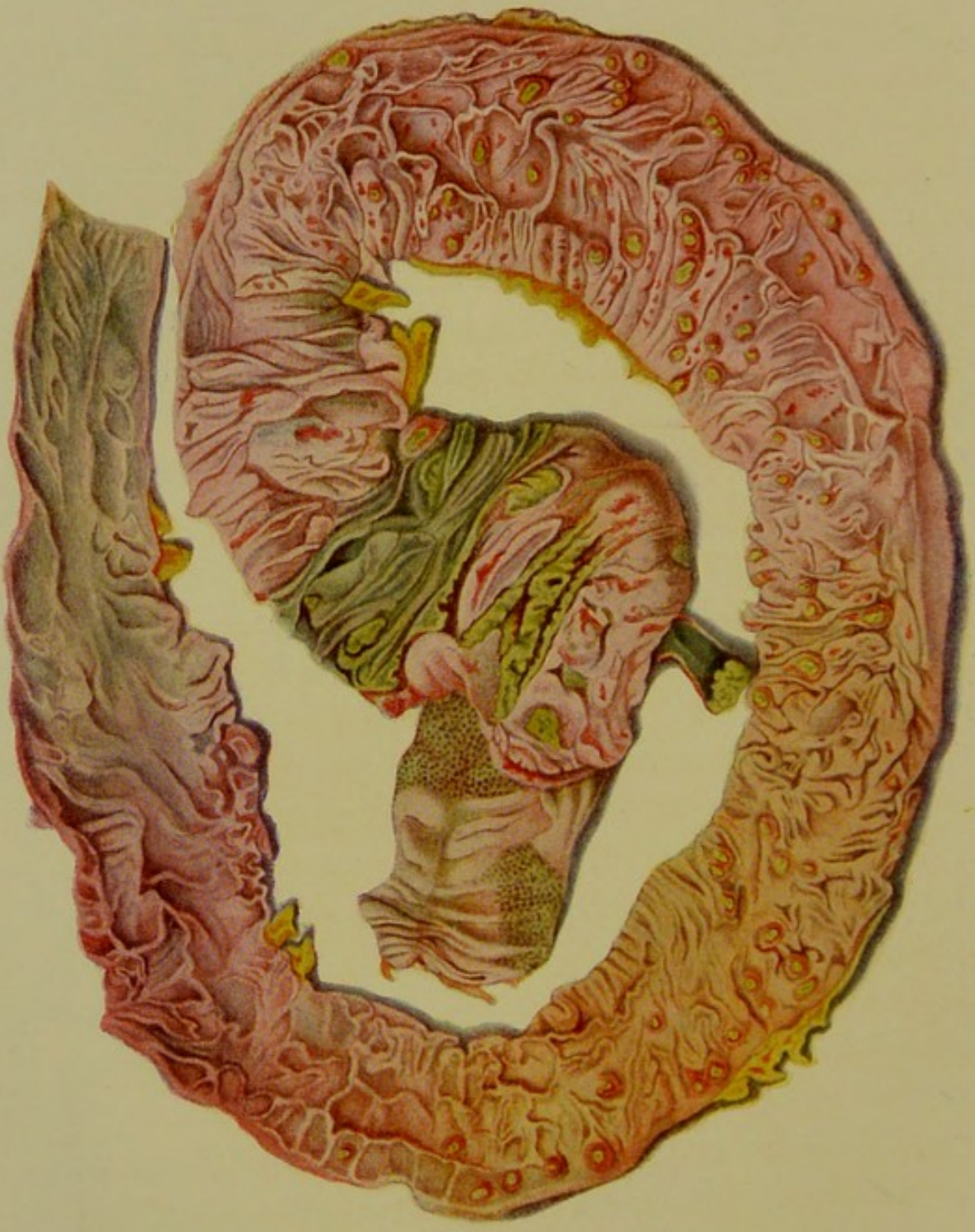


PLATE II.—EARLY AMŒBIC DYSENTERY.

[*To face p.* 65.

coat of the large bowel, whilst the latter is much the more common form in temperate climates, although by no means rare in warm countries; often occurring in epidemic form in armies on service and in such institutions as asylums and jails, and is essentially an inflammatory affection of the mucous coat with a fibrinous or granular exudation on the surface of the membrane. These differences will best be brought out by a separate description of the two diseases illustrated by coloured plates prepared from fresh specimens, and made under my immediate supervision. They have been selected from among a number made by the Calcutta Medical College artist, to whom I am much indebted for his beautiful and accurate pictures. The amœbic form will be dealt with here, and the bacillary variety in Chapter IX.

Although the primary lesion in amœbic dysentery is essentially an exudation into the submucous coat of the large bowel, leading to secondary necrosis of the overlying mucous membrane, the naked eye appearances vary widely according to the stage and degree of severity of the disease. Yet the essential unity of the pathological changes is demonstrated by the occasional presence of all the stages in a single specimen, from the earliest minute lesions up to greatly thickened yellowish-white exudations several square inches in extent, as shown in the coloured plate illustrating the first description of amœbic dysentery in India in my paper in the *British Medical Journal* of June 6, 1903, and Plate II facing this page. It will, therefore, be necessary

to trace the progress of the disease from the earliest to the most advanced stages.

Early Stages of Amœbic Dysentery.—These are not often seen in patients dying directly of the bowel disease, but I have repeatedly encountered them in those who have succumbed to that commonly fatal complication, amœbic abscess of the liver, during which the primary dysenteric disease is frequently completely latent in character and gives rise to no symptoms, as I pointed out in 1902. Plate II is a remarkably good illustration of this condition, the patient having died of liver abscess without having suffered from dysenteric symptoms while in hospital. The transverse and descending colon show the earlier lesions very well, while in the cæcum the disease is passing into a more advanced stage.

The earliest lesions are small red raised dots, which may be little larger than a pin's head. They are produced by congestion or even hæmorrhage into the mucous membrane over the early exudation into the submucous coat beneath. They are well seen in the ascending and transverse colon in Plate II. As soon as a slightly larger size is reached a light yellow spot appears in the centre of the darkly congested area, due to loss of the epithelial portion of the mucous membrane allowing the gelatinous citron-yellow coloured infiltration of the submucous coat to appear on the surface, thus producing the earliest stage of ulceration. At this period the most marked feature is the elevation of the affected patches, causing them to stand up like small buttons from the healthy mucous membrane, while the surround-

ing ring of congestion throws up in relief the central yellow exudation in specimens obtained within a short time after death, as in Plate II. Even in this early stage some of the lesions will present an oval form, with the long axis across that of the bowel, especially when situated on the summit of a fold of the membrane. In the latent cases presenting these early lesions the ulcers are commonly limited to the upper parts of the large bowel, the sigmoid and rectum remaining free as in Plate II, and this accounts for the absence of active dysenteric symptoms and tenesmus, although a history of irregular diarrhœa, often alternating with constipation, may sometimes be obtained.

The next stage is an extension of the lesions across the long axis of the bowel, the invading amœbæ meeting with the least resistance along the course of the blood-vessels encircling the gut in the submucous membrane. The cæcum in Plate II furnishes typical examples of this form of lesion, the rugæ being especially affected, while it will also be noticed that the tip of the vermiform process presents a similar lesion, although the lowest part of the ileum is perfectly healthy, as is almost invariably the case in amœbic dysentery, which differs widely from the acute bacillary form in this respect. Once the ulcers have extended round the greater part of the bowel in this manner, through extension of the exudation into the submucous coat leading to necrosis of the overlying mucous membrane by cutting off its blood-supply and by pressure, the production of the most advanced lesions is only a matter of degree. When we come to deal with the

microscopical changes it will be shown that in the early stages the tube glands of the mucous membrane are practically healthy right up to the congested margin around the yellow infiltration of the submucosa, clearly showing that the surface layer is not primarily involved in the disease, as we shall see later is the case in bacillary dysentery.

Advanced Lesions of Acute Amœbic Dysentery.—In a patient dying of an acute attack of amœbic dysentery much more extensive and advanced lesions than those above described are found in the large gut, with or without those typical of the earlier stages in some part of the bowel. Plate III (facing this page) illustrates the most important features of this condition, the patient having been admitted to my ward in a very bad condition, the greatly thickened bowel wall being easily felt through the abdominal wall as sausage-shaped masses, and evincing tenderness due to commencing local peritonitis; death ensued within two days, even ipecacuanha being unavailing at such an advanced period of the disease. The first point to be noticed is that the lesions are not continuous throughout the large bowel, even in such an acute gangrenous case as this, for there still remain extensive areas of quite healthy mucous membrane between the enormously thickened and raised patches of tawny yellow ulceration. This is a very common and characteristic feature of amœbic dysentery, although the unaffected parts are not often so extensive as in this example, while it is one which I have never seen in bacillary dysentery, in which such extents of bowel as are involved are uniformly affected, as in Plate VII (opposite page 172).

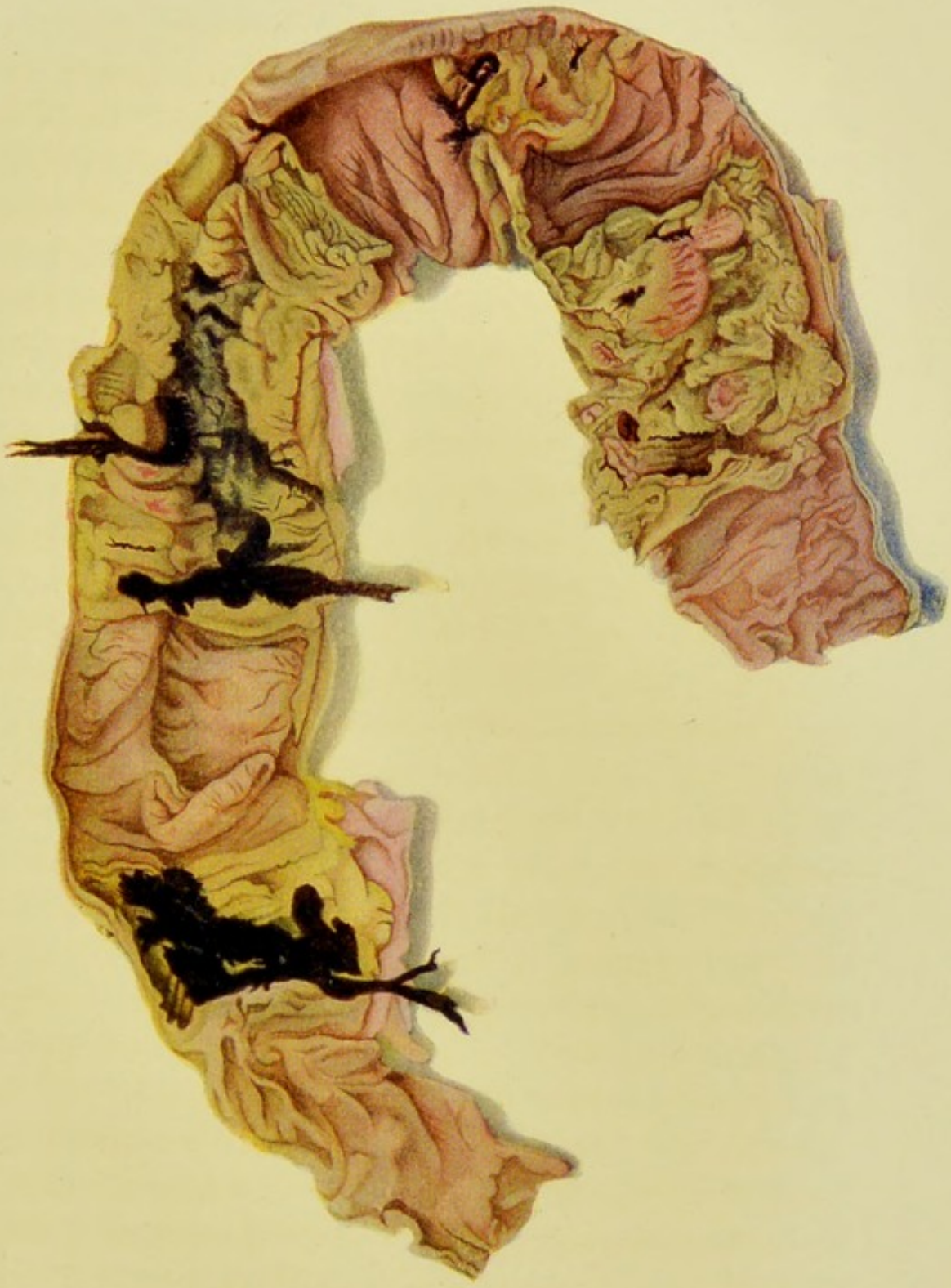


PLATE III.—ACUTE AMŒBIC DYSENTERY.

[*To face p.* 68.

Again, the ulcerated portions in Plate III stand up abruptly from the relatively depressed healthy portions, in complete contrast to what takes place in the bacillary variety of dysentery, in which the ulcers are depressed areas in a generally thickened mucous membrane. This feature of acute amœbic dysentery is very well brought out in Plate III, the extensive lesion in the sigmoid being raised fully a quarter of an inch above the healthy portions of the mucosa above and below it, and similarly with the other ulcers. The lowest lesions present the same tawny yellow appearance as the smaller ulcers in the cæcum in Plate II, only differing in their greater thickness and extent, which are but matters of degree. Once more, although the cæcum shows an extensive gangrenous ulceration involving the under surface of the ileo-cæcal valve, yet the contiguous lowest part of the ileum is quite healthy; another characteristic point of differentiation from acute bacillary dysentery, as will be evident from a glance at Plate VII. Lastly, the upper two ulcerated patches in Plate III show the pathognomonic black cobweb-like sloughs of the mucous membrane of amœbic disease, produced by the rapid extension of the exudation into the submucous coat, destroying the vitality of large areas of the undermined epithelial layers and causing them to be cast off as necrosed portions. I have frequently seen such sloughs, several square inches in extent, hanging by a narrow margin to the edge of a large raised ulcerated patch, while Goodeve, Norman Chevers, and other Anglo-Indian writers correctly describe them as being passed with the stools or hanging

from the anus, being in their experience a sure presage of the early death of the patient, who has come too late to be saved by even that remarkably active drug ipecacuanha; although I have recently cured several such cases by my new method of hypodermic injection of the soluble salts of its active principle.

In most cases of acute amœbic dysentery the ulcers will be less widely separated from each other than in Plate III, but although either the upper or the lower part of the large bowel may be nearly continuously involved, yet in some part healthy mucous membrane nearly invariably remains, in my experience most frequently in the lower half of the great intestine.

Peritonitis complicating Acute Amœbic Dysentery.—In the gangrenous form of the disease the lesions are no longer confined to the mucous and submucous coats, but the gelatinous infiltration extends to the muscular layers, separating the bands of fibres and causing softening of the tissues to such an extent that the bowel wall may attain a consistence not far removed from damp blotting-paper, so that after death, unless great care is taken during its removal, it may easily be torn completely across. In such cases the peritoneal coat will also be involved and extensive patches of purulent lymph will be found adherent to its external surface over the situation of the sloughing ulcers within, although no actual perforation of the bowel wall has taken place. Occasionally rupture with general perforative peritonitis may have taken place before death, most frequently involving the descending colon or sig-

moid, but this is exceptional, and very careful handling is necessary to avoid tearing through the peritoneal coat, where it alone remains intact, and thus mistaking the post-mortem rupture for one which has taken place during life.

Extra-peritoneal perforation may also take place, most commonly of the cæcum or ascending colon, giving rise to a post-peri-colic abscess in the right iliac or lumbar regions, easily mistaken for appendicitis, while I have once met with a perforation of an amœbic abscess in the vermiform process itself. Occasionally a more chronic form of peritonitis may result from amœbic dysentery, with the formation of fibrous bands, which in one case gave rise to fatal strangulation of the small intestine, while in addition a liver abscess had opened into the stomach ; a series of complications which might well baffle the most experienced physician.

Chronic and Healing Amœbic Dysentery.—Lastly, there remain to be described the more chronic lesions and the process of healing in amœbic dysentery, which are well illustrated in Plate IV (facing page 72), together with both early and acute gangrenous lesions, being the most complete picture of all the various phases of the disease that I have ever met with. The ileum as usual is healthy, while the cæcum shows a large, shaggy, yellow ulcerated patch of the acute disease. In the ascending colon is an area in which the mucous membrane is studded with the early small yellow patches of exudation into the submucous coat with a narrow congested ring around each, having evidently been only quite recently affected. Just beyond this, in the hepatic flexure, is a large

gangrenous ulcer with a cobweb-like black slough attached to its surface. On the other hand, the whole of the transverse and descending colon shows the characteristic changes of chronic amœbic disease. Here we see slightly depressed but smooth-floored ulcers, nearly free from the yellow gelatinous infiltration of the earlier stages, separated from each other by fairly healthy mucous membrane, and more or less rounded or oval in shape, being thus quite different in appearance from the serpiginous narrow ulcers running into each other of bacillary dysentery. Another characteristic feature is the extensive patchily distributed pigmentation of the mucous membrane, partly surrounding half-healed chronic ulcers, partly as distinct, more or less circular, dark areas resulting from final complete scarring of the destroyed mucous membrane. In the sigmoid we once more meet with recent sloughing ulcers, succeeded by two or three inches of absolutely healthy mucosa, the lower part of which once more illustrates the chronic lesions, and finally in the rectum a number of recent acute ulcers are seen: the whole constituting a kaleidoscopic picture of all the stages of the protean lesions of this remarkable disease. As in museum specimens it is quite impossible to preserve the characteristic appearances, and especially the striking coloration, of amœbic bowel disease, such an illustration as Plate IV furnishes a better idea of the pathognomonic lesions than any amount of verbal descriptions, and when compared with the totally different appearances of bacillary disease, as depicted in Plate VIII (opposite page 259), can leave little or no doubt in any

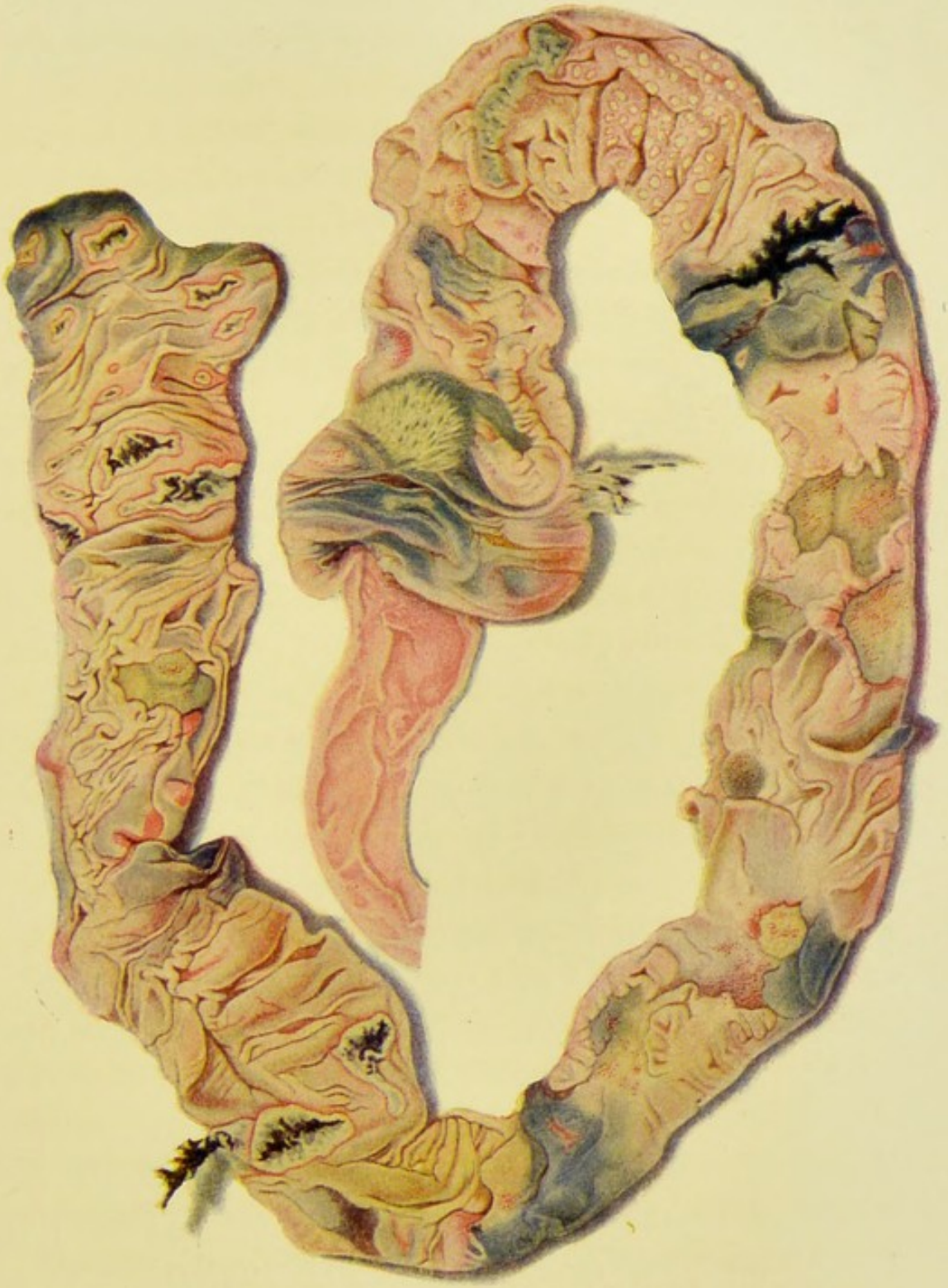


PLATE IV.—CHRONIC AMŒBIC DYSENTERY.

[*To face p.* 72.

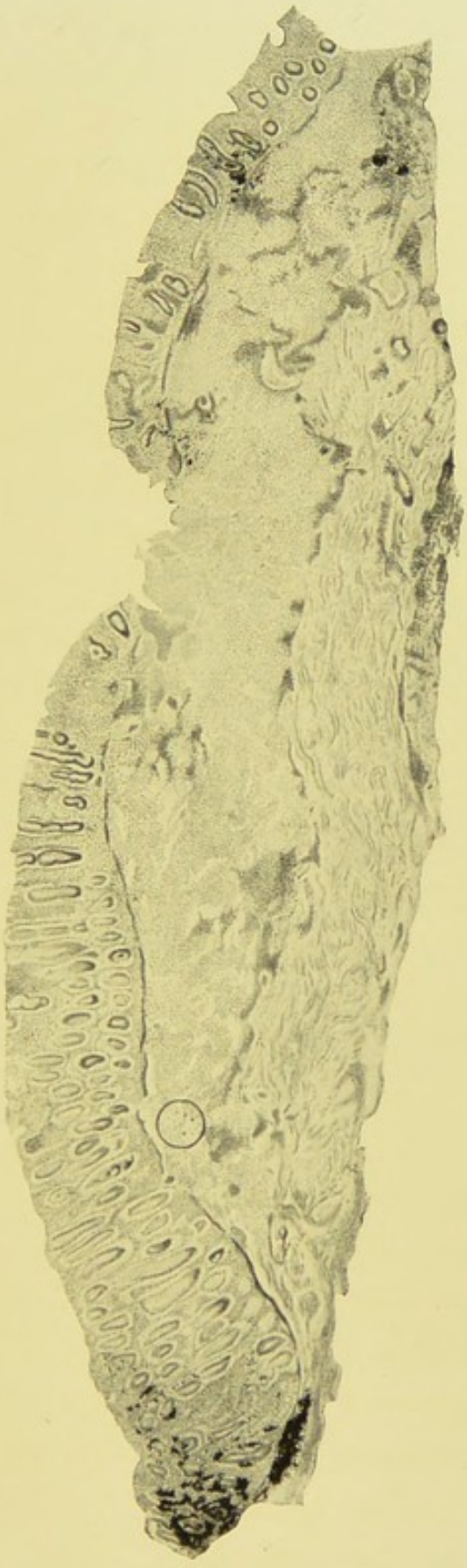
unbiased mind regarding the totally distinct nature of the two types of dysentery.

In addition to the above-described changes in chronic amœbic disease, the bowel wall may show fibrous thickening in places, or actual puckering of the mucous membrane around large chronic ulcers or the site of their completely healed scars. In these cases secondary cirrhosis of the liver may also not rarely be met with, as I have elsewhere described (*Ind. Med. Gaz.*, 1911, Feb.), and a careful study of this subject has convinced me that much of the excessive prevalence of hepatic cirrhosis in Calcutta is directly the result of a chronic amœbic infection of the liver derived from a long-existing ulceration of the bowel.

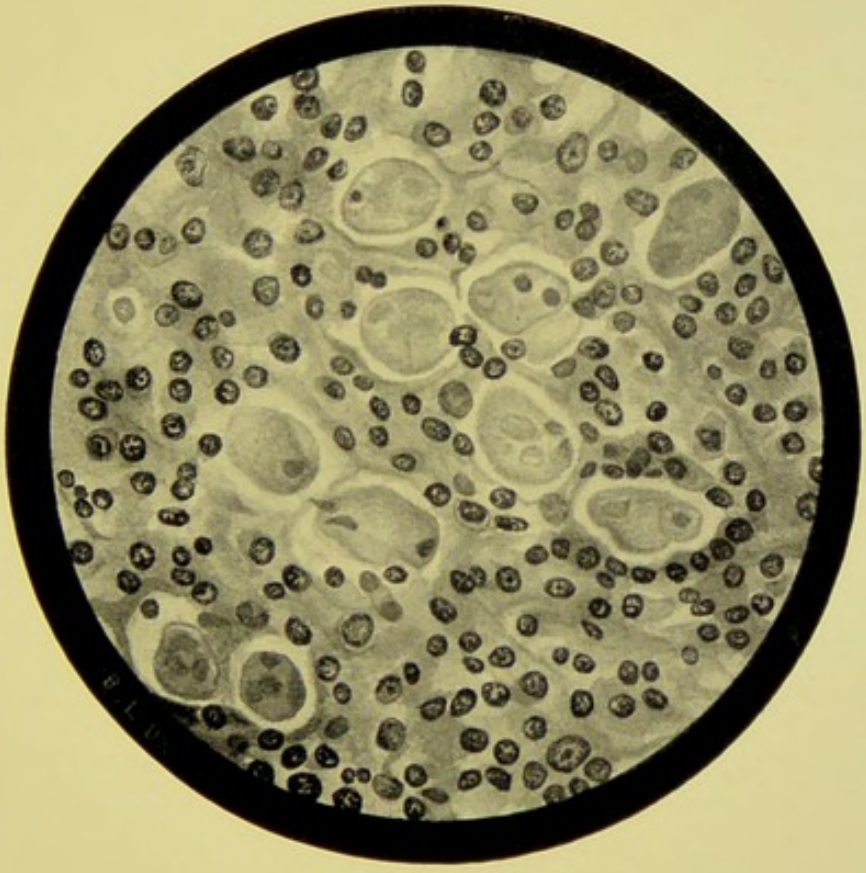
In patients dying of liver abscess chronic dysenteric lesions are often met with, which throw some light on the process of healing of the ulcers. In the not infrequent cases in which there was no history of dysentery during life the amœbic disease will generally be limited to the upper third of the large bowel. There may then be shallow oval or slit-like depressions with thickened edges in the mucous membrane, often still showing the characteristic light yellow bases, while active amœbæ can be found in scrapings of their floors. If small, there may be no puckering or pigmentation around them, so that it is easy to see that they might heal without leaving any lesions which would be obvious at a rapid post-mortem inspection of the gut, although close examination, more especially of the cæcum, might lead to the detection of slight scarring, with or without some pigmentation. Since I have been

on the look-out for such lesions I have found evidence of active or previous dysenteric disease in 98 per cent. of fifty post-mortems in cases of amœbic liver abscesses, whilst the single exceptional case may easily have been due to slight earlier amœbic ulceration, which had left no obvious scarring. In one instance of multiple amœbic hepatic suppuration only two small, shallow, nearly healed ulcers were detected on turning the cæcum inside out, which would probably have left no very definite scarring if the patient had lived a little longer, ipecacuanha having been given during life.

Such are the naked-eye lesions of amœbic dysentery, which are all readily explained as an outcome of an invasion of the submucous coat by the parasites setting up an inflammatory effusion of varying extent and acuteness, yet, when considered as a whole, presenting easily distinguishable characters, and so widely differing from those of bacillary dysentery that it seems at first sight surprising that the two forms were so long confused together as one disease. The most obvious explanation would appear to be that observers in different countries regarded the lesions of the particular form they most commonly met with as the typical ones, and the few exceptional cases as only variations from the common type. Having had the good fortune to have had twelve years' experience of post-mortems in dysentery cases in Calcutta from about the time the two groups were beginning to be recognized, I have been able to accumulate material for their description and illustration.



Section through an early Amœbic Ulcer of the Colon.



The Submucous Coat of the Colon shown in the previous plate.

THE MICROSCOPICAL CHANGES IN AMŒBIC DYSENTERY

A microscopical study of the early lesions of amœbic dysentery brings out very clearly its essential characteristics. These are well shown in the drawings of Plate V, which represents the appearances of a section through a small, raised, early amœbic ulcer with the typical tawny yellow centre, under a low power (Zeiss A lens, ocular, No. 2), together with the small portion of the submucous coat enclosed in a circle shown under a Zeiss D lens (on Plate VI). The drawing under the low power includes the ulcer and its edge, and shows that the change is an extensive small-celled infiltration of the submucous coat, which raises the mucous membrane to form the button-like elevation on the inner surface of the bowel wall, and separates the muscular from the mucous layer. The mucous membrane itself is comparatively little damaged as compared with the lesions in bacillary dysentery depicted in Plates V and VI. The tube glands are clearly seen nearly up to the central ulcerated area, although the mucous membrane shows a considerable amount of small-celled inflammatory infiltration between the epithelial columns, which increases in degree as the centre of the patch is approached, to merge into the denuded portion, where the necrosed mucous membrane has been thrown off and reveals the small-celled submucous accumulation constituting the characteristic light yellow centre of the ulcer. In this early stage the muscular coat is but slightly involved, although in places the inflammatory effusion will be seen to be spreading between the layers of

fibres, especially to the right of the drawing, where small-celled masses are even seen just beneath the peritoneal coat. This shows the tendency of the process to extend deeply through the wall of the gut, which is so marked a feature of the more acute and advanced lesions of amœbic colitis, when it may cause localized peritonitis without any actual perforation, as has been already described under the naked-eye changes.

The nature of the submucous infiltration is well shown in the circular drawing of Plate VI. The great majority of the cells consist of leucocytes, among which may be seen several very large faintly staining bodies, which are the amœbæ present in unusual numbers, as is often the case in the earlier lesions. These organisms may occasionally be seen within the tube glands, and probably obtain access to the deeper layers by perforating the basement membrane surrounding the epithelial cells, while they certainly burrow between the muscular fibres to reach the subserous coat. Further, these active organisms find their way into the smaller veins, especially in the submucous layer, and may thus be carried throughout the portal system and excite the common hepatic and rarer splenic inflammatory complications.

The more advanced lesions only differ in degree from those of the earlier ones above described. The inflammatory infiltration of the submucous coat extends widely, and the superjacent mucous membrane necroses in smaller or larger pieces, as a result of its blood-supply being cut off, and when the process is exceptionally acute large areas may

be shed in the form of the typical black or grey sloughs already described. The muscular layers are also more extensively invaded until the peritoneal coat is reached, and in extreme cases all the layers may necrose in a number of places with fatal results. Large vessels may also be involved in the ulcerative process and severe and even fatal hæmorrhage ensue.

Distribution of the Lesions in the Bowel.—The principal points of difference in the naked-eye appearances of the large intestine in amœbic and bacillary dysentery respectively are pointed out in the descriptions of the coloured plates illustrating this work. Further important information has been obtained from an analysis of over one hundred post-mortems on dysentery cases made by me during twelve years at the Calcutta Medical College Hospital. In order best to bring out the results of this inquiry I have prepared the Diagram 3 shown at the end of this work, in which the distribution of the lesions in the different parts of the large intestine and lower part of the ileum is shown, the cases being classified according to the acuteness of the disease, and also in the case of amœbic dysentery in relationship to its complication by liver abscess, &c. The results are highly instructive and well serve to emphasize the marked distinctions between the two great classes of dysentery both in their acute and chronic stages. The parts of the bowel in each case affected by the dysenteric process are in the diagram shaded continuously when the mucous membrane was uniformly involved over a large part of the intestine, as is usual in bacillary disease, and in an interrupted manner

when there were healthy portions of the mucous membrane remaining between the ulcers, as is almost invariably the case in the amœbic form. Transverse dark lines represent ulcers extending across the axis of the bowel with healthy mucous membrane between them; a dot stands for smaller round or oval separate ulcers on an otherwise normal mucous membrane of less advanced amœbic disease; while the separate square or oblong shaded parts represent the large thickened patches of ulcerated bowel in acute amœbic dysentery, No. 7 of line 2, for example, being the diagrammatic representation of Plate II, the unshaded portions of the vertical line standing for the healthy mucous membrane between the large ulcers. An X indicates scarring of healed ulcers, and a dot within a small circle represents perforation of the large bowel at the point indicated. In the second line of the diagram is shown the distribution of the bowel lesions in twenty-five cases of death primarily due to amœbic dysentery, while in the third and fourth lines are represented those of forty-four deaths from liver abscess or post-colic suppuration secondary to amœbic ulceration.

Acute and Gangrenous Amœbic Dysentery is illustrated by the first fifteen cases in line 2, from which it will be seen that as a rule the whole, or nearly the whole, of the large bowel is involved in the process, although the lesions are usually most advanced and extensive in the upper half or two-thirds of the great gut, the lower portions often presenting only the earlier small round or oval ulcers, as in Nos. 1 to 5, 10 and 12, or being entirely

free, as in 10 and 11. Occasionally the patches may be more extensive in the sigmoid than in the higher parts, as in 15. Another important feature is that although the cæcum commonly presents the most advanced lesions, yet the adjacent lowest part of the ileum almost invariably entirely escapes, and when it is infected the roughened appearance of the mucous membrane is limited to two or three inches of the small gut only, instead of involving several feet as is so frequently the case in acute bacillary dysentery (see Plate VIII, page 259). Again, it will be observed that in no case even of acute amœbic dysentery are the lesions continuous throughout any great length of the large intestine, healthy portions of mucous membrane persisting between the patches of ulceration, a characteristic feature wherein the amœbic disease differs widely from the bacillary form, as will be evident from a glance at the representations of the lesions of the latter in line 1 of the diagram.

Of the acute amœbic dysentery cases in the second line the first seven represented fatal attacks of the uncomplicated disease; No. 8 was a gangrenous amœbic dysentery with general peritonitis secondary to perforation high up in the rectum; No. 9 was another gangrenous case with extensive peritonitis, in which the gut was so rotten that it could not be removed after death without tearing it; whilst No. 10 was also a very acute case with local peritonitis in the course of the large bowel due to spread of the inflammatory process through the whole thickness of the gut without any actual perforation. Nos. 11 to 13 and No. 15 were very

acute cases complicated by small multiple liver abscesses unsuspected during life, and were clinically severe dysenteries, while No. 14 showed extensive acute lesions in the cæcum and ascending colon, but only scars of widespread former ulceration in the lower two-thirds of the large bowel, and was also complicated by a small liver abscess. In all these last cases the small multiple amœbic liver abscesses were only found post-mortem, and had not been clinically in evidence, the bowel disease having been too rapidly fatal to allow of the symptoms of hepatic suppuration becoming clear during life.

The duration of the disease in these acute cases is of great importance. Thus no less than 7 of the 15 were admitted in such a desperate condition that death took place within two days of their coming into hospital. Nevertheless, of those in which a clinical history is also available the shortest total duration of the dysenteric disease was fifteen days, the fatal exacerbation often coming on very suddenly. As we now possess an effective specific treatment for amœbic dysentery, the importance of the early diagnosis of the nature of the disease before gangrene of the bowel, peritonitis, or multiple liver abscesses have ensued, is very evident.

Chronic Amœbic Dysentery uncomplicated by Liver Abscess is illustrated in the diagram by Cases 16 to 25 of line 2, which include all such cases proving fatal in the medical wards without hepatic complications. Nos. 16 to 20 show the distribution of the bowel lesions in cases dying directly of the dysenteric process apart from perforation of the large intestine,

which was the immediate cause of death in Nos. 21 to 25. It will be seen that the lesions are fairly uniformly distributed throughout the large bowel, but the ulceration is much less extensive as a rule than in the acute type already described. The rectum may occasionally show more marked ulceration than the rest of the gut, as in Nos. 18 and 19 of line 2, whilst the sigmoid was most affected in No. 20. Scars of former healed ulcers may be present side by side with recent ones, the relapsing nature of the disease being thus accounted for by the appearance of fresh lesions from time to time; the disease continuing in this manner until the patient dies exhausted, or succumbs to one of the frequent serious complications of the disease, of which liver abscess is by far the most common.

Among the complications other than hepatic in nature, in No. 21 an abscess in and around the spleen was the immediate cause of death, while in the remaining four, Nos. 22 to 25, it was due to general peritonitis secondary to perforation of the rectum in two, and of the transverse and descending colon respectively in one each.

Post-colic Abscess also proved fatal in Cases 18 to 20 of line 3, in each of which the perforation took place in the ascending colon, usually close to the cæcum, where the condition is likely to be mistaken for appendicitis.

The Distribution of the Bowel Lesions in fatal Liver Abscess secondary to Amœbic Dysentery is shown in the third and fourth lines of the diagram for the same period of time as the cases dying directly of acute or chronic amœbic dysentery already

dealt with. It will be observed that they amount to 43, or a much larger number than the deaths due to the bowel lesions alone, showing their great importance. They have been classified in accordance with the number of liver abscesses present.

Multiple Small Liver Abscesses were found in Nos. 1 to 5 of line 3. The first two cases presented a large liver abscess which had been opened during life, and after death a number of small ones were also found throughout the liver. Nos. 3 and 4 were admitted to the surgical wards for peri-urethral abscess and for gangrene of the rectum respectively, the post-mortems revealing acute gangrenous amœbic dysentery and multiple liver abscesses containing amœbæ, just as in Nos. 11 to 13 of line 2 already described. It will be observed that in each of these four cases there were the usual extensive ulcers throughout the greater part of the large gut as in other acute sloughing amœbic dysenteries. No. 5 of line 3 was a remarkable case in which a tenotomy of the tendo Achillis had been performed for fractured femur; the wound became septic, and the boy died very suddenly and unexpectedly. Four large and numerous small liver abscesses were found after death, and streptococci were cultivated both from the ankle wound and the liver pus, amœbæ being also found in the latter, and a few small amœbic ulcers confined to the descending colon. There had been no dysenteric symptoms while the boy was in hospital, and I attribute the very exceptional occurrence of small multiple liver abscesses associated with such limited ulceration of the bowel to the streptococcal complication. The sigmoid showed

scars of healed ulcers, so that the dysentery was chronic in nature.

More than one large Liver Abscess was present in Nos. 6 to 17*a*, most frequently either two or three being found, but occasionally from four to six, as shown in the figures at the top of the columns in the third line. In these cases we find a very different distribution of the bowel lesions to that in the acute dysenteries, with or without multiple abscesses, so far considered. The most noteworthy feature is the comparative paucity of ulcers and the marked tendency to their limitation in the upper third of the large intestine, and especially in the cæcum alone. In only three of thirteen cases were fairly numerous ulcers present through the greater part of the large bowel, and in none of these were they anything like so extensive or of such a sloughing character as in the cases showing multiple small liver abscesses. In five of the cases scars of old ulcers were recorded, proving the chronic nature of the bowel disease.

A single large Liver Abscess was present in Cases 21 to 43 of the fourth line of the diagram, and it will be observed that the bowel lesions are similar in nature to those just described as associated with two or more large abscesses, only the limitation of the disease to the first part of the large intestine is even more marked in a considerable majority of them. Thus, out of the twenty-three cases, the ulceration was absolutely limited to the cæcum in no less than nine, while in four more it only extended to the ascending colon and in a fifth to the transverse. In the last six cases only scarring of

old ulcers (represented by x) was found after death from a large single liver abscess, being also generally limited to the upper third of the great bowel. In some of these there was a previous history of dysentery, but it is by no means uncommon for no record of bowel disease to have been obtainable during life.

This very frequent limitation of amœbic ulcers or their scars to the upper part of the great intestine in patients dying of large tropical liver abscesses, where they may give rise to no definite symptoms of dysentery during life, fully accounts for the old doubts regarding the causal relationship between tropical liver abscess and antecedent dysentery, which have now been set at rest by the differentiation of the amœbic from the bacillary disease, and the proof that hepatic suppuration is only associated with the amœbic disease, which I have shown may often be latent in nature, and give rise to no definite signs during life.

In No. 44 of the last line amœbic ulcers and scars limited to the upper third of the large bowel were found in a patient who died of cirrhosis of the liver, the close association of which with antecedent amœbic dysentery is referred to on page 73.

The above facts may be summarized as follows :

1. Acute amœbic dysentery produces extensive ulceration and even gangrene, distributed through the greater part of the large bowel, but with some healthy portions of mucous membrane remaining between the lesions. It proves fatal either directly or by causing perforative or local peritonitis and occasionally multiple small liver abscesses.

2. Chronic amœbic dysentery, if it affects the greater part of the large gut, is likely to prove fatal by exhaustion or by perforation of the bowel leading either to general peritonitis or post-colic abscess. If the ulcers are more limited and found mainly or entirely in the upper third of the large intestine, death is commonly produced by secondary large liver abscess, often without any dysenteric symptoms being present.

3. If active dysentery complicates liver abscess the prognosis is more grave, as the hepatic suppuration is likely to be multiple.

CHAPTER V

CLINICAL DESCRIPTION OF AMŒBIC DESENTERY OR COLITIS

Amœbic disease of the large bowel by no means always produces typical dysenteric symptoms, but may only cause irregular diarrhœa, often alternating with constipation, while occasionally a few latent amœbic ulcers of the cæcum and ascending colon may be present without producing any bowel symptoms, yet give rise to serious complications, such as hepatitis leading to abscess formation. For these reasons the term amœbic colitis is more correct than amœbic dysentery, although a large proportion of cases do at some time present typical dysenteric stools. The extreme variation in the symptoms and degree of severity of amœbic colitis necessitates its subdivision into different clinical types for purposes of description; in dealing with these it must always be borne in mind that they are very far from being sharply defined, but shade imperceptibly into each other. Moreover, a mild or chronic type is liable at any time to be rapidly converted into a very acute one by a sudden exacerbation of the symptoms. In the first place it is necessary to distinguish between recent, more or less acute attacks and the hitherto very intractable chronic disease, brought about by repeated recurrences of amœbic ulceration of the large intestine with extensive organic changes

in the bowel wall. Further, recent cases may be conveniently subdivided in accordance with the severity of the symptoms into the three following classes :

1. The average—moderately acute attacks presenting typical dysenteric symptoms, which form a considerable majority of the whole, and occasion comparatively little difficulty in their recognition and treatment.

2. Very acute fulminant cases—frequently with gangrene of the bowel, which sometimes simulate other diseases and require very prompt recognition and active treatment if a fatal issue is to be averted.

3. Very mild or even latent cases—not presenting typical dysenteric signs, and consequently likely to be overlooked.

MODERATELY ACUTE AMŒBIC COLITIS WITH TYPICAL DYSENTERIC SYMPTOMS

It will be well at the outset to emphasize the fact that in the average case of amœbic colitis the clinical symptoms present no definite and constant points which will enable the disease to be distinguished from one totally different as regards the pathological and therapeutic points of view, namely, bacillary dysentery. In fact, the amœbic affection can only be recognized with certainty by the discovery of a pathogenic form of amœba in the evacuations or from the striking results of specific treatment. The routine use of the microscope is even more necessary as a guide to proper treatment in dysenteries than is the case in fevers of the tropics, for in the latter four-hour temperature charts, as shown in my book

on the subject, will enable most of the different varieties of malaria and some other fevers to be easily recognized clinically. Moreover, by the methods described in Chapter III of this work (pp. 48–50) the examination for amœbæ is a much easier and more rapid one than that for malarial parasites, provided large doses of ipecacuanha or emetine have not already been given. Nevertheless, there are a number of clinical features which may help in coming to a conclusion as to whether a given case is of amœbic or bacillary origin; these will be pointed out in their proper places, but it must be remembered that they are only of relative value and liable at times to mislead if too implicitly relied upon.

Onset.—An analysis of sixty cases in my ward shows that in the majority of amœbic dysentery attacks the onset is sudden, as in the bacillary form, but in a considerable minority the disease began gradually with diarrhœa, and only after several days did the stools assume a dysenteric character. Nor was this insidious onset by any means confined to the milder types of the disease, for it ushered in several of the most severe and rapidly fatal cases. A history of fever was not infrequently absent, but was noted in a fair proportion, especially in the severer cases. Most of the chronic cases also gave a history of a sudden commencement of the symptoms of the relapse which brought the patients to hospital, but here also the attack may begin with simple diarrhœa. Moreover, even in fatal cases of amœbic dysentery, as seen post-mortem at the Calcutta Medical College Hospital, over one-sixth had

been diagnosed during life as either tubercular or simple diarrhœa, and their dysenteric character had not been recognized nor anti-dysenteric treatment adopted. It is only by finding amœbæ in the stools that such cases can be detected and adequately treated, and the danger of serious subsequent hepatic complications thus prevented. It is surprising what a considerable proportion of amœbic hepatitis patients give a history of irregular diarrhœa, without actual dysenteric symptoms, the lesions being probably limited to the upper part of the great intestine, and the typical signs of dysentery thus largely masked. A gradual onset of the symptoms with loose fæculent stools containing little or no obvious mucus and blood, or such diarrhœal evacuations alternating with truly dysenteric ones, is much more frequently met with in amœbic than in bacillary dysentery.

Fever and Constitutional Symptoms.—These are much less marked in uncomplicated cases of amœbic than in bacillary dysentery. Indeed, it is remarkable what serious lesions may be produced by the protozoal parasite without any fever and with very little constitutional disturbance, and the physician may thus be easily deceived into thinking a patient to be only suffering from a mild attack of the disease, to find at his next visit that he has rapidly drifted into a hopeless condition. For example, I have seen a patient walk into my ward one morning with a history of having suffered from dysenteric symptoms for several weeks but presenting no obvious serious signs, and on coming round the next morning was astonished to find him at the point of death

with gangrenous amœbic colitis. Such cases are fortunately rare, for as a rule some of the signs to be described under the head of the fulminant type of the disease will be present and warn the physician of the impending danger. The degree of fever present in a series of cases under my care is shown in the following Table:

TABLE OF DEGREES OF PYREXIA IN AMŒBIC DYSENTERY

	Acute Cases.		Chronic Cases.		Total.	
	Died.	Recovered.	Died.	Recovered.	Died.	Recovered.
Remittent fever	4	2	—	—	4	2
Intermittent to over 100° F.	—	2	1	6	1	8
Intermittent to 100° F. or below	3	8	—	4	3	12
No fever	2	13	3	9	5	22
Total	9	25	4	19	13	44

It will be seen from the figures of the above Table that in about half of both the acute and chronic cases (one month or over in duration) of amœbic dysentery there was no fever during their stay in hospital, while when present it was usually of a slight intermittent type only, and seldom lasted more than two or three days under treatment. The few cases in which well-marked fever of the remittent type was present were very severe and frequently fatal, usually from some complication such as peritonitis or liver abscess. In chronic cases fever is only occasionally met with, and may not rarely be absent even in those proving fatal.

Apart from complications, then, pyrexia is not a marked feature of amœbic dysentery; less so than in the early and acute forms of the bacillary disease. If fever persists more than a very few days in amœbic colitis complications should be looked for, especially because those involving the liver, such as hepatitis, even going on to suppuration, are often insidious in their onset, and very liable to be overlooked until they have reached an advanced stage, when it is too late to cut them short by specific anti-amœbic treatment. If the spleen is enlarged fever may be due to complicating malaria or kala-azar, and only a blood examination will enable the case to be correctly diagnosed.

The Number of the Stools.—In primary acute attacks the number of the stools is nearly always very considerable, being most commonly between ten and twenty in the twenty-four hours, and by no means infrequently exceeding the larger number, in which case they generally belong to the severe type of cases. In chronic amœbic dysentery the stools often do not exceed fifteen, and rarely exceed twenty daily, the larger number being usually seen in fatal cases. In the amœbic disease full doses of ipecacuanha produce a considerable diminution in the stools within a few days, although the complete subsidence of the symptoms may take some time. Emetine rapidly reduces the number, and produces healthy stools in three or four days.

Character of the Stools.—Before describing the characters of the stools it will be advisable to state once for all that there is no single and constant feature whereby the evacuations of amœbic dysen-

tery can be distinguished from those due to other inflammatory conditions of the large gut, or even from those met with in such diseases as cancer or syphilis. The only way of being certain of the presence of the variety of dysentery under consideration is to find amœbæ with the characteristics of pathogenic varieties in the recent evacuations by means of a simple microscopic examination, without which the treatment of any disease with blood and mucus, or either of them, in the stools cannot be satisfactorily undertaken. Moreover, the discharges from the bowel are not only extremely variable in different cases and stages of the disease, but vary very greatly from day to day, presenting the appearances of simple diarrhœa without amœbæ one day, and on the very next consisting of nearly pure blood and mucus swarming with active amœbæ. This important fact necessitates the repeated microscopic examination of the stools for the parasites before amœbic disease is excluded, for I have met with two chronic cases in which three negative examinations were followed by the discovery of extensive amœbic ulceration of the large bowel after death. Even several negative examinations, then, will not allow of the exclusion of amœbic disease with absolute certainty. Such cases, however, are fortunately rare, especially when some experience in searching for amœbæ has been obtained.

In cases of fairly acute amœbic dysentery, which have not been actively treated with ipecacuanha or its active principle emetine, both blood and mucus are nearly always present in the stools, but their naked-eye characters do not differ essentially from

those of many cases of bacillary disease, although experience will often allow of a very shrewd guess being made. As a general rule, but one with many exceptions, numerous separate large pieces of rosy blood-stained mucus are suggestive of the protozoal disease, whilst either large white fibrinous masses or small glairy, raw white-of-egg-like pieces of mucus, intimately mixed with loose fæcal matter, and best seen on pouring out some of the stool in a thin layer in a glass Petri's dish, are more commonly met with in the bacillary form, especially if not very acute. If the blood-stained mucus has a red, opaque, pus-like appearance, or presents a light red purulent aspect, very like the contents of a recent amœbic abscess of the liver, numerous amœbæ will usually be found. These are the most characteristic appearances of the stools in amœbic dysentery, but the organism may also be met with in pure mucus without visible blood, or in watery fæcal stools without evident mucus, so that there is no common form of intestinal evacuation in which it may not be found, and consequently it may be repeated that the use of the microscope is the only sure method of diagnosis.

Microscopical Characters of the Stools.—These will vary as widely as the naked-eye appearances. The most common conditions are very numerous pus cells mixed with a variable but usually large number of red corpuscles, scattered among which will be found active amœbæ. Epithelial cells will also be present, but commonly in much fewer numbers than in bacillary dysentery, whilst extensive bands of fibrin are much more frequently seen

in the latter form than in amœbic dysentery, although I have very occasionally seen streaks of fibrin containing amœbæ. Pus cells are also frequently found in large numbers in bacillary disease, and to a less extent red corpuscles. In the diarrhœal form of amœbic colitis the protozoal parasites are seen among the fæcal material, but comparatively few red or white corpuscles, whilst not infrequently the common small oval flagellate tricomonads are also present.

The appearances and best methods of finding the causative amœbæ have already been described in Chapter III.

Appearances of Washed Stools.—Dr. Goodeve, when Principal and First Physician of the Calcutta Medical College Hospital, introduced the plan of washing dysenteric stools so as to enable any sloughs, mucus, &c., to be readily seen. Each stool containing fæcal matter is freely diluted with water in a vessel, and after allowing a minute or two for mucus and sloughs to sink to the bottom, the supernatant fluid is gently poured off, taking with it most of the fæcal matter. This process is repeated until only the pathogenic material apart from fæcal matter remains, the results of the washings of all the stools being kept for inspection in the morning, together with an unwashed morning stool to enable its characters, and especially the amount of blood present, to be noted. This very valuable method was used by Goodeve's contemporaries, but subsequently fell into neglect; for some time past I have revived it in Calcutta, and am convinced that it affords much diagnostic and prognostic informa-

tion. Although Goodeve never published his plan, fortunately Norman Chevers has recorded the principal conclusions derived from Goodeve's experience, which are as follows. The dysenteric products retained after the washings are placed in a large white dish containing water to display them clearly, everything except fæces and blood being displayed, the chief products consisting of mucus and sloughs of various kinds, inspection of which gives important information regarding the state of the mucous membrane of the bowel from which they have come. Chevers described the indications to be obtained from the method as follows: 'A quantity of gelatinous rose mucus with fæculent matter—a case of not more than twelve hours' duration. The same mucus without fæculent matter—probably this case has gone on unchecked by treatment for from six to thirty-six hours longer than the last. Branny mucus—this is a case from five to eight days old, doing well under treatment. Ropy mucus in great abundance—a very favourable case approaching recovery. Pus-infiltrated sloughs—a case of five or more days' duration, in a tolerably good constitution, which will probably do well under treatment. A brown or black cellular slough, scarcely distinguishable at first sight from an old black cobweb pinched together to the same size and placed in the water beside it—an evidence of gangrene and presage of certain death.'

The most important of the above-described dysenteric products are the pus-infiltrated and black sloughs, as I have only met with these in severe cases of amœbic disease, and look on them as abso-

lutely diagnostic of that condition with very extensive ulceration and separation of portions of dead mucous membrane and masses of the tawny yellow infiltrating material in the submucous coat of the large bowel, which are illustrated in Plates III and IV. I agree with Chevers in regarding the appearance of black shreds of mucous membrane in the stools as of almost certainly fatal significance under the methods of treatment until very recently available, but since I have introduced the use of subcutaneous injections of soluble emetine salts I have seen several recoveries in such cases. In my experience the presence of large quantities of mucus, with little or no blood, is most frequently met with in bacillary dysentery, white fibrinous masses being not uncommon in that variety in cases which are doing well, as Chevers states. As the patient improves the amount of mucus in the washed stools steadily decreases and the progress of the case can be judged from day to day, and valuable indications, such as when it is safe to increase the diet, are thus obtained. The rapidity of the decrease in the quantity of dysenteric products in amœbic cases under emetine treatment is especially striking; in bacillary cases the process is a much slower one as a rule, although generally sure under careful treatment once the severe constitutional symptoms have come to an end and improvement set in before the process has had time to become chronic.

Subjective Abdominal Symptoms.—Fairly severe amœbic dysentery is always accompanied by well-marked subjective abdominal symptoms of pain usually with tenderness of some part of the large

bowel, and often definite thickening of the tube, which can be palpated through the abdominal wall. The degree of these symptoms gives much valuable information regarding the extent and severity of the lesions present. The patient will practically always complain of griping pains, produced by irregular peristalsis and the passage of the intestinal contents over the inflamed or ulcerated mucous membrane. These pains are especially severe shortly before and during the passage of a stool. They must be carefully distinguished from true tenesmus, which is the actual straining and bearing-down pain in the rectum during the escape of the stool, and continuing for some little time afterwards, which is a sign of actual involvement of the rectum in the dysenteric process. As this part of the large bowel more commonly escapes the affection than in the case of bacillary dysentery, true tenesmus is often absent in amœbic colitis. The abdominal pain, apart from tenesmus, is usually referred to the neighbourhood of the navel. Frequently it is situated right across the lower part of the abdominal cavity, including the two iliac fossæ, or it may be more marked in one or other of them. Again, the pain may be localised over one or more of the divisions of the large bowel, and may thus affect the regions traversed by any portion of the colon, in which case it is usually accompanied by tenderness and thickening of the area of gut involved, and is more persistent and acute in character. I have seen either the cæcum, ascending, transverse, or descending colon thus singled out, or more than one portion

may be simultaneously affected, such cases often being particularly severe.

Tenderness on gentle palpation is an even more important sign than mere pain, as it is evidence of an acute inflammatory process of the portion of bowel displaying it. It is most frequently met with over the cæcum and ascending colon, or in the sigmoid colon, and when well marked in both these situations is very suggestive of the presence of amœbic disease. When limited to the sigmoid colon it is less helpful, as tenderness in that position is also not uncommon in bacillary disease, although in my experience not usually so well marked as in the protozoal form. If tenderness is present over a large proportion of the great bowel the case may be expected to prove a serious one. This symptom should be very gently elicited, especially in acute or in old chronic cases, as there may be little but the peritoneal coat remaining intact, which any force may rupture and a fatal peritonitis be precipitated. Thus, an Indian patient was admitted for a large hydatid tumour of the spleen, and after having been examined by a large number of Indian students became very ill and died in a few days. Post-mortem a very chronic latent form of amœbic ulceration was present, and some adhesions of the descending colon in the left lumbar region had been broken down and extravasation of the bowel contents had taken place. The condition of the large gut in such cases described on page 70 will suffice to prove how real this danger is.

Thickening of the Large Bowel.—Of even greater diagnostic and prognostic value in amœbic dysentery

is palpable thickening of the bowel, as in its more marked and characteristic forms it is practically diagnostic of the disease. It affects the same parts as the tenderness just described, being most common in the positions of the cæcum and sigmoid colon, but is most important in the former situation as the sigmoid may be to some extent thickened in bacillary dysentery, especially in chronic cases, but not to the same degree as it is in some cases of acute amœbic disease, in which it feels like a large sausage and is extremely tender to the touch. The cæcum may also be greatly enlarged and closely simulate appendicitis, for which I have several times seen it mistaken by both physicians and surgeons in cases in which the appendix proved not to be involved, although this organ may also be affected by amœbic disease, as already described under pathological anatomy. If extensive areas of the large bowel are greatly thickened the case falls into the very acute fulminant class, and the prognosis is exceedingly grave. In ordinary severe cases the thickening and tenderness is confined to the cæcum and sigmoid, and this combination is highly suggestive of amœbic disease, and should always lead to an immediate careful search for amœbæ to allow of the specific treatment being adopted without delay.

The Blood Changes.—The diagnostic and prognostic value of the blood changes in dysenteries have not yet been adequately recognized. The following data are based on sixty consecutive cases in which I have made blood-counts on admission to hospital for amœbic dysentery, all verified by

finding pathogenic amœbæ in the stools or by post-mortems. The most characteristic change is a leucocytosis, commonly of a high degree. Thus, an actual leucocytosis was found in three-fourths of my cases, whilst in eight more a relative leucocytosis was present—i. e. one in which, on account of anæmia reducing the number of the red corpuscles, although the total leucocytes do not exceed 10,000 per cm., yet the ratio of the white to the red corpuscles is greater than the normal maximum of 1 to 500. This leaves only seven cases, or 11·4 per cent., in which not even a relative leucocytosis was present, and three of these seven had enlarged spleens, probably due to kala-azar, which accounted for their scanty white corpuscles. On the other hand, as shown on page 275, of cases of bacillary dysentery in less than one-fourth was there any increase in the white corpuscles, and in only 11·8 per cent. was there an actual leucocytosis.

The degree of leucocytosis is also of great diagnostic as well as prognostic significance, for in amœbic dysentery the extent of the increase of white corpuscles often met with is very striking. Thus, in ten of my sixty cases over 30,000 per cm. were present, while in seven more between 20,000 and 30,000 were found. Compared with this in twenty-one non-amœbic cases in none did the number exceed 15,000, although higher counts have occasionally been recorded by others in very acute bacillary dysentery, but as a rule only in severe cases with well-marked fever, such as are not likely to be mistaken for amœbic disease. I therefore regard the presence of leucocytosis in dysentery as highly

suggestive of the amœbic type, whilst if it is of exceptionally high degree, such as over 20,000, it is almost diagnostic of that disease as against bacillary dysentery.

Again, a count of 25,000 and upwards is of very serious prognostic significance, for only one out of nine such cases treated with ipecacuanha was cured, while of four 'discharged otherwise' at their own request only one had improved while in hospital. Yet the fact is that out of five such cases treated with emetine injections four recovered, the fatal case showing a count of 61,750 and dying within one day of admission in a hopeless state: a striking testimony to the value of the new method in these terribly acute cases, which I had come to look on as almost inevitably fatal under the ipecacuanha treatment. On the other hand, four out of seven cases without any leucocyte increase also proved fatal, usually with gangrene of the large bowel, so that the total absence of leucocytosis in a serious case is of very bad prognostic import, being a sign of feeble resisting powers.

The high degrees of leucocytosis can be readily detected by a glance at the edge of a stained blood film, and when found it is an indication for immediate vigorous treatment with the specific anti-amœbic remedy. In fact, I look on such high leucocyte counts in amœbic colitis, as well as in hepatitis of the same origin, as of prognostic value equal to finding numerous malignant tertian parasites in every field of the microscope in malaria, for as in the latter case it enables the dangerous nature of the infection to be recognized, even when the

clinical signs are not alarming, in time to adopt special measures to get the specific remedy into the system in full doses by the most rapid method available.

The differential leucocyte counts are of less importance, except that a high proportion of polynuclears is a sign of an acute amœbic infection.

The number of the red corpuscles is about normal in early acute cases, but secondary anæmia appears in chronic ones.

FULMINANT OR GANGRENOUS AMŒBIC DYSENTERY

By far the most important and serious class of amœbic colitis is the very acute affection of the large bowel with great thickening due to extreme inflammatory infiltration of the mucous and muscular coats, and tending to run on rapidly to extensive sloughing of the bowel wall, and accompanied by local peritonitis over the most affected parts, usually without actual perforation, owing to the process having reached the serous coat of the intestine. As already described under the head of pathological anatomy, the whole thickness of the bowel wall may become gangrenous in a number of places and be so softened as to resemble damp blotting-paper. Such a hopeless condition may be reached within a few days of the onset of the disease, or not infrequently of the commencement of an acute exacerbation in a previous comparatively mild or even chronic condition. As only the promptest use of full doses of the specific remedy for amœbic disease given at the onset of the acute symptoms will suffice to save such cases, the recognition of their nature as early

as possible is of the utmost importance. Unfortunately, it is just in these cases that the regular symptoms of dysentery may sometimes be absent, although as a rule they are typical enough, unless paralysis of the large bowel, due to extensive gangrene, has already set in when the patient first comes under observation. Very important assistance in the early recognition of these cases may be obtained from an examination of the blood, for, as shown in the preceding description of the blood changes in amœbic dysentery, a very high leucocyte count of from 25,000 to 50,000 or more white corpuscles is often found in such cases, if hopeless gangrene has not already set in, when the count may occasionally be normal. I therefore take a blood-count on admission in all dysentery patients, and if a very high degree of leucocytosis is found I lose no time in commencing active specific treatment, as described later.

Clinically the most frequent symptoms of a fulminant attack of amœbic colitis are, firstly, very numerous stools, usually of pure blood and mucus, with a preponderance of blood, or not rarely large hæmorrhages, as was pointed out by Strong in Manila. If the ulceration is mainly high up in the large bowel the blood may be black and tarry looking, and in one case this sign, together with severe epigastric pain, subsequently found to be connected with great thickening and tenderness of the transverse colon, led me at first to suspect duodenal ulcer, until I noticed some small pieces of mucus in the blood, in which I found numerous amœbæ with the microscope, and was able to rescue the patient from a very serious condition by the prompt sub-

cutaneous injection of emetine hydrochloride, this being the first case in which I tried the new method, with the happy result that the patient was convalescent in three days. If, however, extensive gangrene has already set in the stools may be infrequent, or even constipation, due to paralysis of the sloughing bowel, may be present. It is in these cases that the ominous black sloughs may be found in the washings of the stools. Secondly, abdominal signs will be pronounced, severe general pain being present, together with well-marked tenderness in the course of the large intestine, some parts of which can generally be felt as greatly thickened and usually very tender portions of the large gut, resembling rounded or elongated sausage-like masses, as already mentioned. The cæcum and ascending colon are especially liable to be affected, and such cases may be mistaken for appendicitis, with the unfortunate result that the time during which they might be saved by anti-amœbic treatment may be irretrievably lost. In the worst cases the palpable involvement of the large bowel may extend from the cæcum to the sigmoid, but fortunately is only rarely so extensive. If the intestine is greatly thickened without being tender in an acute case gangrene is usually present and the general condition of the patient very bad. If the pain and tenderness is localised over certain parts of the large bowel it is due to involvement of the patches of peritoneum over the most affected parts of the gut, but without any general infection of the serous sac. Less commonly actual perforation may have taken place, accompanied by signs of general peritonitis, for which

surgical measures will be of no avail on account of the extensive gangrene of the gut. Yet again, post-cæcal or post-colic perforation may occur, leading to abscess formation behind the peritoneum, in some cases closely simulating appendicular suppuration, but distinguishable by finding amœbæ in the stools. On the other hand, perforation, generally of the descending colon or sigmoid, produces general peritonitis, without localised tumour formation, and is a very fatal complication of gangrenous amœbic disease.

VERY MILD AND FREQUENTLY LATENT AMŒBIC COLITIS

The importance of this variety of the disease lies in the frequency with which it is overlooked and subsequently gives rise to serious complications, usually hepatic in nature, which are in their turn liable to be wrongly diagnosed and treated if the nature of the antecedent bowel trouble is not realized. The number of cases of hepatitis occurring in India, often drifting on into abscess of the liver, in which a history of some previous bowel irregularity is obtained, usually slight occasional diarrhœa without the appearance of blood or mucus, and often alternating with constipation, but really caused by mild amœbic ulceration of the colon, is alone sufficient proof of the above statement. The reason why dysenteric symptoms are so commonly absent in these cases is that the lesions are generally limited to the cæcum and ascending colon, as shown in the pathological anatomy section of this work (see page 73). Careful palpation of the abdomen in such cases may elicit evidence of tenderness of the

first portion of the large bowel and sometimes also slight increased resistance due to thickening of the wall of the gut, while repeated examinations of the stools may reveal the presence of pathogenic amœbæ, although they may be difficult to demonstrate when the infection is so limited in extent.

Apart from complicating hepatitis, any persistent or irregularly recurring diarrhœa in warm climates should be regarded as being possibly amœbic in nature and a microscopical examination of the stools carried out repeatedly to verify or exclude this possibility. When such cases are under observation in hospital a little blood-stained mucus containing numerous amœbæ will often be obtained sooner or later, and enable the condition to be clearly identified. Now that it is practically certain that the amœbic infection can easily be completely eradicated, and all risk of later serious hepatic or other complications effectually prevented, the early detection of such cases by the systematic use of the microscope in all diarrhœas as well as dysenteries in the tropics cannot be too strongly and repeatedly urged.

CHRONIC AMŒBIC COLITIS

Cases in which the bowel symptoms have persisted for a month or more may be considered for purposes of description to be chronic, although any hard-and-fast line must be artificial, but necessary for purposes of clinical classification. There are few diseases which so frequently pass into a chronic and, hitherto, intractable stage as amœbic colitis, the ulceration continuing for months or even for

years, fresh portions of the mucous membrane becoming involved as the earlier attacked parts heal, extreme organic change of the bowel wall eventually resulting, as already fully described and illustrated in the pathological section. The symptoms also vary greatly in accordance with the activity or quiescence of the bowel disease, any degree from an acute gangrenous exacerbation down to mere slight irregularity of the bowels being met with, whilst for weeks or even months the disease may be practically in abeyance, once more to light up suddenly as a fairly severe attack of dysentery.

By this time the patient will have become emaciated, although this is not due to loss of fluid from the body, as the specific gravity of his blood will have fallen much below the normal point proportionately to the loss of hæmoglobin. Anæmia of considerable degree will be present, and will be evident from the pallor of the mucous membranes. The muscles will be greatly atrophied and the strength proportionately reduced. The stools, although less frequent than in the earlier stages, are yet sufficiently numerous and painful to be a cause of constant suffering to the patient, whose condition is altogether a most pitiable one, and if no relief is afforded by treatment he gradually sinks into extreme asthenia, and, worn out by his sufferings, eventually finds a happy release in death.

Duration of the Disease.—The great chronicity of these cases will be seen from the data in the next Table, in which an analysis of thirty cases in my wards is given.

TABLE OF DURATION OF THE DISEASE IN CHRONIC AMŒBIC COLITIS

Duration	1 month.	1 to 3 months.	3 to 6 months.	6 to 12 months.	Over 1 year.	Total.
No. of cases	5	12	7	4	2	30

The period entered is that during which the symptoms had never long been absent, but in addition many of the patients had suffered from previous attacks, which in the majority were probably amœbic. The great difficulty in obtaining a complete and permanent cure in this class of case is only too well known, the tendency being for relapse after relapse to occur until the patient succumbs to the exhausting process or to hepatic complications after a long period of misery.

Fever is commonly completely absent, a subnormal temperature being the rule, and usually persists up to the time of death. In a minority of cases slight intermittent fever may occur, often as a result of hepatic or other complication, for which a constant watch must always be kept, as their onset is commonly very insidious and easily overlooked. An analysis of the degree of fever in chronic amœbic bowel disease has already been given (see page 90).

The Number of Stools is very variable, but as a rule they are fewer than in the earlier more acute stages of the disease; during exacerbations they may occasionally exceed twenty daily, most frequently varying between six and twenty, but in very mild types the number may be less than the lower figure.

Abdominal Pain and Tenderness are less marked than in the acuter forms, but are similar in distri-

bution, affecting chiefly the cæcum and sigmoid flexure. Tenesmus is usually well marked owing to the more frequent involvement of the rectum in the chronic disease.

Thickening of the Large Bowel is less frequent and prominent than in very acute cases; it is usually limited to the sigmoid, and less commonly affects the cæcum than is the case in the earlier stages of amœbic colitis. As the same change in the sigmoid is often met with in chronic bacillary disease it is here of comparatively little diagnostic importance.

THE COMPLICATIONS OF AMŒBIC COLITIS

Most of these have been referred to incidentally in the foregoing description of the different types of the disease, but they are so important that it will be well briefly to discuss them seriatim, for a fatal issue is much more frequently due to one or other of these than to any general constitutional toxæmia or exhaustion, as in the bacillary type. It is especially in the acute fulminant variety that they are the common causes of death, although the more chronic affections are not wanting in their own forms of lethal complications.

Local Peritonitis without Perforation.—Stress has repeatedly been laid on the tendency for amœbic infection to spread through the whole thickness of the bowel wall until it involves the peritoneal coat. As a result of this patches of local peritonitis, without actual perforation of the gut but with the deposition of lymph on the surface, occur, giving rise to local pain and tenderness in one or more

areas over the course of the large bowel, sometimes accompanied by rigidity of the abdominal muscles over the affected part, although this may not be so great as to prevent the thickened and very tender intestine being felt by careful palpation. As this condition is most commonly found involving the cæcum and ascending colon it is very important to bear it in mind in the tropics, lest the fatal mistake of diagnosing acute appendicitis be made, and an operation undertaken, which can do no good, while the delay will almost certainly sacrifice the remaining chance of saving the patient by prompt specific anti-amœbic treatment. In some of these grave cases complete gangrene of the whole thickness of the large gut may have occurred in one or even in several places, in which case no treatment can be of any avail, and death takes place within a day or two of the supervention of this terrible complication. Unfortunately it is not very rare for Indian patients to be first brought for treatment in this hopeless state. On the other hand, the recent discovery of the remarkably rapid specific curative effects of emetine has already enabled some desperate cases, with local peritonitis well developed and the passage of large black sloughs in the stools, to be saved, so that their early recognition is of the greatest practical importance.

Perforative Peritonitis.—This is happily a less common sequel of amœbic colitis than the localised inflammation of the serous coat of portions of the large bowel, as its prognosis is even more grave. It occurs in two totally different classes of case, firstly in acute gangrenous dysentery, and secondly

in very chronic cases of the disease, or as a late sequel after apparent recovery from a severe attack. In the first case, as the whole thickness of the bowel wall has been destroyed by the intensity of the process, not infrequently in several places simultaneously, nothing of a surgical nature will be of any avail. In the second class the rupture of the bowel wall is most commonly due to breaking down of some adhesions formed during the healing of extensive sloughing of the mucous membrane of the colon. Thus, in a patient in the Calcutta European General Hospital a complete cast of the interior of the cæcum, including portions of the ileo-cæcal valve, was passed, but the patient eventually recovered from a desperate condition under the influence of very full doses of ipecacuanha, and was invalided to England, where, strictly against the instructions he had received, he played a violent game and soon after developed fatal peritonitis, doubtless due to breaking down of adhesions round his greatly thinned cæcum. Another case of fatal rupture of adhesions round old amœbic ulceration of the descending colon has already been mentioned (see page 81). In this class of cases the diagnosis may be very difficult and the precise condition is often not recognized in time to allow of successful surgical intervention, which in any case would be of an exceedingly difficult nature owing to the seriously damaged state of the bowel wall, unless, indeed, it should prove feasible to utilize a portion of the omentum for sealing the opening. The perforation is most likely to be found in the sigmoid or descending colon.

Post-colic Abscess.—In writing of the pathological anatomy this condition has already been mentioned as most frequently occurring in the cæcal or right iliac or lumbar regions, where I have repeatedly met with it, although I have not seen it occur in relation to the descending colon. In the acuter cases it is accompanied by considerable swelling and great tenderness and a high degree of leucocytosis, which in one case reached 49,000 per c. cm., and the disease is then rapidly fatal. Occasionally it may be a more chronic process with the formation of an abscess in the right lumbar region, which may be opened and drained, but unless the amœbic nature of the disease is recognized and treated accordingly the prognosis is bad.

Appendicitis.—Amœbic ulceration may sometimes involve the appendix, but if perforation or gangrene has not already occurred it will yield to the specific remedy.

Severe Intestinal Hæmorrhage.—Strong and other Philippine workers have called attention to the not very rare occurrence of severe hæmorrhages from the bowel in acute amœbic dysentery, due to a large vessel in the submucous coat being opened by the spreading inflammatory process. I have already mentioned one such case which I at first mistook for duodenal ulcer, but on finding amœbæ in some small mucous flakes mixed with the tarry blood, was able successfully to treat the patient with emetine injections. This condition should, therefore, be always borne in mind in warm countries and amœbæ sought for in the stools in cases of intestinal hæmorrhage.

DIAGNOSIS OF AMŒBIC DYSENTERY

There is but little to be said under this heading that will not be a repetition of points already dealt with in the clinical description of the disease. It has been repeatedly remarked that the diagnosis can only be safely based on finding the pathogenic variety of amœbæ in the evacuations, and that the character of the stools will not as a rule allow of a positive opinion being formed as to the type of dysentery present. Still less will anything short of a microscopical examination for the protozoal parasite suffice in the mild type in which only occasional diarrhœa is present, although these are likely to lead to dangerous complications if not detected in good time.

Recently an important practical help in the differential diagnosis has been furnished by my discovery of the very rapid curative action of hypodermic administration of soluble salts of emetine, for this treatment is only specific for amœbic dysentery, whilst the improvement brought about by it is so great, that if the stools have not much improved in numbers and character within two or three days of its administration in proper doses, it is practically certain that the disease is not amœbic in character. As no harm is done by the use of this drug in bacillary dysentery and other forms of bowel disease, its administration is of the utmost diagnostic value (see pages 121–132). With two such reliable guides as the presence of amœbæ in the stools and the almost immediate good effect of the specific treatment for the disease, it is useless further to labour

over minor and inconstant clinical differences between the amœbic and other forms of dysentery.

The Mortality and Prognosis of Amœbic Dysentery.—Owing to the difficulties in clearly differentiating amœbic from other forms of dysentery by purely clinical methods, there appear to be few reliable estimates of its mortality on record. Andrew Davidson in *Allbutt's System of Medicine* states that the case mortality cannot be under 20 per cent., and sometimes is much higher, and that the intractable nature of the disease must be borne in mind. Moreover, the late liver complications are alone a considerable cause of mortality. In an analysis of 1,000 consecutive medical post-mortems in Calcutta I found 5·7 per cent. clearly due to amœbic dysentery, while 0·7 per cent. more were classed as doubtful forms of dysenteric disease. Liver abscess accounted for 2·2 per cent. more, apart from the much more numerous cases in the surgical post-mortems. Omitting the latter, amœbic disease was thus responsible for one-twelfth of the total medical post-mortems, or almost one-fifth of those due to tropical diseases. The mortality depends very much on the period at which the cases come under observation and the thoroughness with which the specific treatment of the disease is carried out. Still, it is generally acknowledged that even with full and persistent doses of ipecacuanha the difficulty in completely curing the disease is very great and too many of the patients drift into a chronic condition of amœbic colitis, which renders their lives miserable for years, although such cases are less frequent in proportion to the efficiency with which

the ipecacuanha treatment has been carried out. Among the Indian patients, who are so often admitted to hospital in an advanced stage of the disease, the mortality is still very high in spite of full doses of the Brazilian root. Thus, among thirty consecutive cases treated by me at the Calcutta Medical College Hospital with from 20 to 60 grains of ipecacuanha daily I still lost no less than eleven, including four admitted in such an extremely bad condition that they succumbed within less than three days. Moreover, six more were discharged 'otherwise' uncured, further treatment being refused, two of these being taken away by their relatives in a dying condition, whilst only one was better. This leaves only thirteen cases, or 43·3 per cent., discharged 'cured', but how many of these subsequently relapsed it is impossible to say. Including the two patients removed in a moribund condition, the death-rate in this series was therefore no less than thirteen out of thirty cases, or 43·3 per cent. Even allowing that these were of an exceptionally severe and advanced type, they still show the deadly nature of the disease if it is not promptly dealt with, and demonstrate the comparative failure of ipecacuanha in the later stages of amœbic disease.

Fortunately this sombre picture is now greatly relieved by the remarkable success of my new treatment by the hypodermic and intravenous injection of emetine hydrochloride described under that heading, for I am now able to record thirty cases of amœbic dysentery treated in the same ward with only three deaths from dysentery (although two patients died of other diseases some days after complete cure

of their dysentery, and are therefore omitted from the calculation). The mortality was then 10 per cent., or one-fourth of that in an equal number treated by ipecacuanha, all the fatal cases having succumbed within three days of admission in an extremely critical condition, although I now think that one of them might possibly have been saved by the intravenous administration of the drug immediately on admission. Further, the average duration of the symptoms under emetine treatment was only 2·35 days. All the evidence yet available points to complete and permanent cures, apart, of course, from reinfections, being rapidly obtainable even in very chronic cases of several years' duration, with consequent most gratifying lessening of the sufferings hitherto inseparable from old amœbic infections of the colon, while the frequent and very dangerous hepatic complications are likely to be almost, if not entirely, prevented, and, should further experience confirm the results already obtained, perhaps the greatest scourge of warm climates will in future have as favourable a prognosis as it has formerly had an unfavourable one.

CHAPTER VI

THE TREATMENT OF AMŒBIC DYSENTERY

It has already been shown in the discussion on the history of the use of ipecacuanha in dysentery that this drug has been regarded as the most important remedy in its treatment by just those physicians who worked in countries where the amœbic form is now known to be the prevalent type of the disease. Shortly after I first discovered the presence of amœbic dysentery in India in 1901 I came to the conclusion that ipecacuanha is a specific remedy for this disease, but of comparatively little use in the bacillary form. Several years later this view was confirmed by my discovery that early cases of amœbic hepatitis are rapidly curable by the same drug, and that tropical abscess of the liver can thus be easily prevented. More recently still I observed that in some of the most severe and advanced cases of amœbic colitis it was frequently impossible to administer sufficient ipecacuanha by the mouth in time to save the patient. This led me to try if the soluble salts of emetine, the chief alkaloid of ipecacuanha, could safely be given hypodermically, for Vedder has recently shown that in very high dilutions emetine kills cultures of non-pathogenic amœbæ, whilst I found it to be equally effective against pathogenic amœbæ in dysenteric stools. The remarkably good results I have obtained by this method, which will

presently be detailed, have conclusively shown that ipecacuanha through its active alkaloid is, indeed, a most powerful specific against amœbic dysentery and its hepatic complications, which is unsurpassed, if it is equalled, by any other drug treatment yet known. The treatment of amœbic dysentery may therefore be summed up by saying that adequate doses of ipecacuanha, or better, of its active alkaloid, should be administered as soon as possible.

Methods of Administration and Doses of Ipecacuanha.—With the exception of some very acute cases already showing symptoms of local involvement of the peritoneal coat of the large gut, it is always well to commence with a mild purge, both to clear out the fæcal contents of the bowel, which may irritate the damaged mucous membrane, and to lessen the tendency to sickness after the ipecacuanha. For this purpose an ounce of castor oil, followed by an emulsion of the same in drachm doses three to four times a day, is the simplest and best remedy, salines being of little value in amœbic dysentery, if not actually harmful.

Ipecacuanha should then be given in full doses, which in themselves act as a powerful laxative, so that in urgent cases no time should be lost in waiting for the action of the castor oil before commencing the specific drug treatment. I agree with Maclean that large doses of ipecacuanha often cause less vomiting than small ones, while if a full dose is given there is a much better chance of an effective portion passing on into the intestines before the stomach empties itself. I, therefore, do not use less than 20 to 30 grains as a dose in adults, and

in acute cases give the larger quantity twice a day, or a single dose of 60 grains may be administered, as advised by Docker, the following precautions being taken against vomiting. No food or fluid should be given for three hours before and at least that time after the dose, while the patient should lie quite still with only a low pillow, if any, and is on no account to raise his head. As a further aid a preliminary dose of either 20 minims of tincture of opium or 20 grains of chloral hydrate may be given twenty minutes before the ipecacuanha, while a still better plan is the Madras one of adding 10 grains of tannic acid to each dose of the specific powder in a mixture containing mucilage, and administered with as little fluid as possible. Another very useful method is the Philippine one of making up the ipecacuanha in 5-grain pills and coating them with melted salol, so that they may not dissolve until they reach the intestine, or a coating of keratin may be used for the same purpose. In either case the protective covering should not be so thick as to endanger the pills passing unchanged through the whole length of the intestinal canal, so that in acute cases it is better to give the drug in the tannic acid mixture in order to avoid the possibility of a failure of absorption, which might occasion a fatal loss of time in obtaining the specific action of the drug. It is only exceptionally that the tannic acid does not avert vomiting, its power in this respect being apparently due to its action in inhibiting the profuse secretion of mucus by the lining membrane of the stomach caused by ipecacuanha alone, the mucus being eventually rejected by the organ, for it will

be shown presently that emetine when injected subcutaneously, or even intravenously, does not cause sickness, indicating that the emetic action must be a purely local one on the gastric mucous membrane.

If the case is not an urgent one the best time to give the drug is at bed-time, as then the patient will often sleep through the dose, whilst his feeding will be less interfered with than if it is administered during the day. In severe cases full doses must be given both morning and evening, although this is a severe tax on the patient's strength, but one which has fortunately now become unnecessary with the introduction of the hypodermic emetine treatment presently to be described.

Disadvantages of the Ipecacuanha Treatment.—The great difficulty with the ipecacuanha treatment is that in spite of all precautions the nausea and sickness may be so distressing in some subjects that the patient refuses to continue the drug. An even more serious drawback is that in the most severe cases, with great thickening of the bowel wall and perhaps the passage of black gangrenous sloughs, sufficient ipecacuanha cannot be got into the system in time to save the patient's life. Again, in chronic cases the nauseating drug has to be continued for a long time to obtain a complete cure, and disappointing relapses are frequent, while only too often the patient becomes tired of the treatment and leaves it off before he is well.

Results of the Ipecacuanha Treatment.—Out of thirty consecutive cases in my wards, verified by finding pathogenic amœbæ in the stools, and treated

with full doses of ipecacuanha, the results of which have been already given under the head of prognosis (see page 115), only 13, or 43·3 per cent., were discharged cured, while an equal number died in hospital or were taken away in a dying state, the remainder being discharged uncured. Four of the eleven fatal cases were admitted in an extremely grave condition, and died within less than three days and before the specific drug had a chance of acting. It must be mentioned that the patients admitted to my wards are almost all natives, and mostly advanced severe or very chronic cases, so that considerably more favourable results may be expected in earlier ones, but the figures are mainly of value for the purpose of comparison with those of the emetine treatment under the same conditions given below.

In the recovering patients the average number of days in hospital was 16·4, while the average duration of the dysenteric symptoms after the ipecacuanha was begun was 11·4, during which on the average 406 grains of the drug were taken. These figures may be contrasted with those of the emetine series on page 123.

The Emetine Treatment.—On realizing the frequent failure of even large doses of ipecacuanha in the very serious amœbic dysentery cases I had to deal with, I sought for an improved method of treatment, and for the reasons already mentioned I decided to try if soluble salts of emetine could be safely injected hypodermically. I had not long to wait for a suitable case, as a patient, originally admitted to my ward for suspected cholera, proved

to be suffering from very severe hæmorrhagic amœbic dysentery with a greatly thickened and tender transverse colon, and could not retain a single grain of ipecacuanha even when given with opium in the form of Dover's powder by the mouth. As she had passed six large black hæmorrhagic stools in which amœbæ were found, the condition was a desperate one, and I had no hesitation in injecting hypodermically one-sixth of a grain of emetine hydrochloride, being equal to 15 grains of ipecacuanha ; finding to my surprise that it produced neither sickness nor depression, I gave one-third of a grain four hours later, and repeated this dose on the following morning. In two days she was convalescent, all traces of blood and mucus having disappeared from the stools, and she went out quite well a week later, but I was not able to follow her up as she sailed for Japan soon after.

My next case was at the other extreme, namely, a very chronic one of two and a half years' duration with some remissions, but continuous for the last six months, the patient having become reduced from 130 lb. in weight to 76 lb., while colotomy had been proposed as a last resource by several very experienced medical men. Some twenty to thirty very foul stools of blood and mucus were being passed daily, whilst he was totally unable to take any ipecacuanha by the mouth. I injected one-third of a grain of emetine hydrochloride twice a day, and after ten days the last of the dysenteric stools was seen, and he put on nine pounds in weight during the next three weeks, being already on solid diet. I heard from him five months later, when he

was quite well and his weight had risen to 126 lb., a total gain of 60 per cent., which shows to what a desperate condition he had sunk before the emetine was used.

The following case is also a good example of the rapidity of the cure of very acute amœbic dysentery by emetine hypodermically.

Very Acute Amœbic Dysentery with greatly thickened Cæcum and high Leucocytosis treated with Emetine.—Native male, aged 30, admitted to my ward for cholera with a history of having passed fifteen stools in the last twelve hours, the last containing blood. Specific gravity of blood, 1059;

	First Day.	Second Day.	Third Day.	Fourth Day.
Number of stools—				
Day	9	3	2	1
Night	1	2	1	1
Emetine hydrobromide	1 gr.	1⅓ gr.	1 gr.	Ip. 40 gr.
Mucus	Much	Nil	Nil	Nil
Blood	Much	Nil	Nil	Nil
Amœbæ	Numerous	Nil	—	—
Leucocytes	30,050	22,500	12,250	9,250
Ratio to red	1 to 206	1 to 308	1 to 409	1 to 651
Polynuclears	90·8	84·4	72·4	52·8

blood pressure, 112. On examining the stools no cholera organisms were found either microscopically or on culture, but very numerous small amœbæ were present. The abdomen was distended and the cæcum could be felt as a greatly thickened mass, extending into the hypogastrium and very tender to the touch, while the sigmoid showed less marked but similar changes. He gave a history of three previous attacks of dysentery, the last being

one month ago. Hypodermic injections of emetine hydrobromide were at once begun, and the progress of the case, together with the leucocyte counts, can be seen by a glance at the accompanying table.

The blood and mucus and the amœbæ had disappeared from the stools in twenty-four hours, and by the fourth day the whole of the thickening and tenderness of the cæcum and sigmoid, as well as the leucocytosis, had vanished, and the patient was convalescent. Further progress was uneventful, and he was discharged cured eleven days after his admission.

Fatal Gangrenous Dysentery in which the Amœbic Infection was destroyed in sixty hours by Emetine Injections.—Native male, aged 45, a confirmed opium-eater taking about 30 grains

	First Day.	Second Day.	Third Day.
Number of stools—			
Day	4	11	2
Night	15	4	—
Emetine hydrobromide	1½ gr.	2 gr.	Nil
Mucus	Much	Less	Trace
Blood	Much	Less	Nil
Amœbæ	Numerous	Numerous	Nil
Leucocytes	22,250	16,000	14,250
Ratio to red	1 to 268	—	—
Polynuclears	88·4	81·6	82·0

a day, admitted for dysentery of twelve days' duration, having had another attack a month before. Passing about twenty very foul stools a day with blood and mucus containing numerous amœbæ. Abdomen somewhat distended and marked thickening and acute tenderness of the large bowel from

the cæcum to the splenic flexure, but most marked in the right iliac fossa, and a high degree of leucocytosis. Progress :—

Three ½-grain doses of emetine were given the first day, and the patient appeared to be rather better in the evening. The next morning he was passing more frequent stools again, so two 1-grain doses were given hypodermically, each equal to 90 grains of ipecacuanha, without any apparent depression and no nausea or vomiting. The washings of the stools of the first twenty-four hours showed a cupful of large raw-meat-like sloughs, and those of the second twenty-four hours were similar, but smaller and less blood-stained. The second night, after the two 1-grain doses of emetine, he had only four small stools containing a very little thin mucus faintly streaked with blood, while the morning stool was watery brown fæcal, with only a minute trace of white mucus and quite free from amœbæ. In spite, however, of large doses of opium, he had been unable to get any sleep, and suffered much from the great restlessness of opium-eaters, being worn-out, cold, and clammy. The tenderness and thickening of the large bowel had disappeared except in the right iliac fossa, where they were as marked as before, so I recognized that local peritonitis, with either a post-cæcal abscess or gangrene, must be present, for which nothing more could be done, and he died on the evening of the same day. A post-mortem examination was obtained, which revealed most extensive amœbic ulceration affecting the whole length of the large intestine, although the rectum was but slightly involved.

The caput coli was gangrenous, with little but the peritoneal coat remaining, while inflammatory recent lymph on the surface bound it loosely to the ileum. A prolonged microscopical examination of scrapings of the ulcers in various parts of the bowel failed to reveal a single living amœba, and sections through the walls of some of the more recent ulcers stained with hæmatoxylin showed not a single parasite, although they are ordinarily quite easily demonstrated by either of these methods. Thus, in spite of the terrible acuteness and extent of the lesions, every single amœba appears to have been killed by the $3\frac{1}{2}$ grains of emetine injected subcutaneously during the two and a half days he was in hospital, and thus the failure to save this opium-eating patient furnished the most conclusive evidence of the specific nature of the new method of treatment, and fully explained the remarkably rapid recovery in the preceding case.

Further experience has only served to confirm the above results, but the most conclusive evidence in its favour will be found in the following analysis of thirty-two consecutive cases of amœbic dysentery in my ward treated with emetine, which can be compared with the ipecacuanha series above recorded.

Two cases in which the patients died of other diseases some days after being completely cured of amœbic dysentery are omitted, as it would obviously be unfair to count them as failures of the treatment. Among the thirty remaining cases three died, all within three days of admission, in a very grave condition, too late to give a fair chance of recovery,

making a mortality of 10 per cent., against 43·3 per cent. in the ipecacuanha series. All the remaining cases were completely cured, none having been discharged otherwise uncured at their own request, as so often happens with the ipecacuanha treatment. Still more striking is the fact that the average duration of the dysenteric symptoms after the commencement of the emetine injections was only 2·35 days against 11·4 days in patients recovering under ipecacuanha, while the average amount of emetine used per case was only two grains. That this series included a number of very severe cases will be evident from the fact that four of the recovering patients showed the very high degree of leucocytosis, namely, 25,000 and over, which was almost always a fatal sign in the ipecacuanha series.

Methods of Administration and Doses of Emetine Salts.—The hydrochloride and the hydrobromide of emetine are equally effective in the treatment of amœbic disease, but the former is the more convenient on account of its great solubility, as the hydrobromide requires about 2 c.c. of water to dissolve a full dose, whilst it tends to crystallize out again. I have used the hydrochloride by the mouth, hypodermically and intravenously, with success. When given by the mouth it requires the same precautions as when powdered ipecacuanha is administered, although, as it is very much less bulky and more rapidly absorbed, it possesses considerable advantages over the latter, and less frequently causes sickness if given on an empty stomach, but is not so rapid in its action as when given by one of the other methods; emetine should thus only be

used orally when there is any difficulty in injecting it hypodermically, and never in serious cases if it can be helped. Kerotin-coated tabloids of emetine hydrochloride suitable for oral administration are now made by the leading manufacturing chemists.

The subcutaneous method is the most generally useful one, and it is seldom necessary to give it in any other way, except in very urgent cases, when it should at first be injected intravenously to obtain the full effect in the shortest possible time.

As with the hypodermic method I occasionally lost a patient within less than three days of admission in a grave state, usually with greatly thickened and tender large bowel and signs of local peritonitis, I recently in such a case injected the emetine hydrochloride directly into the median basilic vein in doses of from one-half to one grain dissolved in 5 c.c. of sterile normal saline, the injection being given slowly and the pulse watched. Neither sickness nor depression followed, except after the first dose in a patient who was already suffering from bilious vomiting. In this case the effect was very favourable, as the tumour-like tender mass in the right iliac fossa disappeared within a few days, in spite of a number of black sloughs being passed, indicating a gangrenous condition of the mucous membrane. Unfortunately, twelve days after admission he nearly succumbed to hæmorrhage from the bowel, and after getting over this hypostatic pneumonia developed, to which he succumbed on the nineteenth day in hospital. A post-mortem was obtained, and only healthy healing ulcers were found in the large gut, without any thickening of the

bowel wall. This case, however, clearly shows that the salt may safely be injected intravenously in full doses, and in very severe attacks this would appear to be the best method of administration, although further experience is required on the point.

Dosage of Emetine Salts.—To get the best results I find it is advisable to inject a total of one grain in the twenty-four hours for three or four days, preferably in half-grain doses morning and evening. In severe cases I frequently give a grain at a time (this being equivalent to 90 grains of ipecacuanha), and repeat it two, or even three, times a day, although this is not often necessary. Intravenously from a half to one grain may also be given at a time with perfect safety in adults. It is also surprising what large amounts may be given in children, for I have several times injected one-third of a grain (equal to 30 grains of ipecacuanha) in children of about eight years of age with amœbic dysentery with excellent results, while one-sixth of a grain may be given in still younger patients.

The local effects of the injection are usually nil, the salt being rapidly absorbed. Very occasionally a considerable amount of pain has been noticed for a few hours, possibly due to injection near some small nerve. Either the upper arm or the flank are convenient places for the injection.

If given by the mouth in tabloid form it is advisable to use doses of not less than one-half to one grain to get a full effect quickly.

Do Emetine Injections radically cure Amœbic Dysentery ?—We have seen how difficult it often is to obtain a permanent cure of chronic amœbic

dysentery by the use of ipecacuanha, so the very important question arises as to whether the rapid disappearance of all dysenteric symptoms under the influence of emetine injections results in a complete cure of the disease by destroying all the amœbæ in the tissues, or if some survive its effects and may bring about a subsequent relapse, as so often occurs in the case of other specific remedies, such as quinine in malaria and salvarsan in syphilis. Although it is too early to give a final answer to this question, yet the evidence as far as it goes up to the time of writing points to the conclusion that we have in the emetine treatment a permanent as well as a rapid curative procedure. We have already seen that the amœbæ may all have disappeared from the tissues within two or three days of the use of the drug, whilst the two following cases also prove that after only a few days' treatment with emetine salts very extensive amœbic lesions of the large bowel may rapidly heal and leave no trace of remaining infection.

Case 1.—A Mohammedan male, who had been rapidly cured of a very severe attack of amœbic dysentery by emetine injections, after ipecacuanha had failed to control it, was readmitted for dysentery three weeks after he left hospital. I examined the loose stools, but found neither blood, mucus, nor amœbæ present, while his leucocyte count was low, so I felt sure his present illness was not amœbic in nature. He had persistent hiccup, and died in three days, and at a post-mortem examination I found pneumonia at the left base. The large intestine from the cæcum to the transverse colon was

much dilated, firmly adherent to surrounding structures, and so thinned that it was torn in several places in removing the gut. On laying it open a remarkable condition was found, for there was no trace of any recent dysenteric lesions, but very extensive smooth-floored, healed ulcers of former amœbic disease. Both scrapings and sections showed no amœbæ, but the muscular coat of the bowel had been so extensively destroyed by the former dysentery as to lead to a paralytic dilatation of the large gut. In addition there was a small encysted abscess in the liver about two inches in diameter, with a nearly smooth wall and neither amœbæ nor bacteria present.

It is therefore clear that the six half-grain injections of emetine, which he had received on his first admission five weeks before his death, had completely destroyed the amœbæ in the extensive infection of the large intestine and also in the liver abscess—in short, a complete sterilization of the tissues had taken place.

Case M.—A Hindu male, admitted to my ward for chronic relapsing dysentery, was given three one-grain doses of emetine hydrochloride hypodermically, one on each of three successive days, at the end of which time his stools were normal, and he left hospital well at the end of a week. He was readmitted for dysentery under me four weeks later in a moribund condition, and died on the following morning. I examined the first stool passed after his readmission and found mucus, but no amœbæ. A post-mortem was fortunately obtained, and revealed in the upper part of the large intestine

a number of transverse scars of recently healed amœbic ulcers, but no active lesions. The lower half of the gut showed the characteristic lesions of an acute bacillary dysentery, Shiga's organism being obtained on culture, while no amœbæ could be found with the microscope.

Thanks to the opportunities for making autopsies, these two cases proved not to be relapses of amœbic dysentery, but to furnish the strongest proof that emetine injections can bring about rapid and complete healing of both very acute and very chronic amœbic lesions.

Local Treatment of the Bowel in Amœbic Dysentery.—Numerous forms of medicated enemata have been advised from time to time in the treatment of amœbic dysentery. In the acute stage I do not think it is safe to inject large quantities of fluid into the great bowel, as I have so frequently seen nothing but the peritoneal coat preventing perforative peritonitis in fatal cases. Ewart long ago recorded a lethal result from an enema in such a case, and he never repeated the treatment in any subsequent dysentery patient under his care.

In chronic cases this danger is a much more remote one and rectal injections may be given with due care. Quinine bisulphate solutions of a strength of 1 in 500 to 1 in 1,000 have been most frequently used, but even when given daily through an appendicostomy opening for months at a time they have often failed to have much effect on the disease. Nor is this surprising when we remember that the pathogenic amœbæ are situated deeply in the submucous coat of the bowel, where they are quite

beyond the reach of local medication. Others have found that normal saline solution is quite as effective as solutions containing powerful drugs, while it doubtless helps to keep the ulcers clean and so favours their healing. The only form of bowel wash I have seen good results from in amœbic dysentery was permanganate solution, but as the potassium salt causes too much pain to allow of a greater strength than 3 to 6 grains to the pint being used, I prefer the calcium permanganate, beginning with 6 grains to the pint, and, if it does not cause pain, increasing it to 10 or even 15 grains in the same amount of water, or better, normal salt solution. Before I began the emetine treatment I frequently met with chronic cases in which ipecacuanha had reduced the number of stools from fifteen to twenty down to three or four daily, but still containing a little mucus and blood. In these cases the addition of the calcium permanganate bowel wash frequently completed the cure within a few days, apparently as the result of the action of the injections in healing the remaining ulcers. However, since I began the emetine treatment I have rarely had occasion to give any form of bowel wash in amœbic dysentery.

Appendicostomy and Colotomy have been advocated by some American and English writers in the treatment of obstinate chronic forms of amœbic dysentery, but since the recent revival of full doses of ipecacuanha these operations have fallen increasingly into disfavour. Musgrave, with a very extensive acquaintance with amœbic disease in the Philippine Islands, has recently condemned such

measures as useless and unnecessary ; for it has now been conclusively proved that the whole length of the large intestine can be completely washed out by the injection of three or four pints per rectum, preferably through a soft catheter passed in for about eight inches, as any further length of tubing only curls up in the lower bowel without entering the sigmoid. I have long been on the look-out for suitable cases of dysentery in which to try appendicostomy, but have found that chronic amœbic cases generally do so well on continued full doses of ipecacuanha and calcium permanganate bowel wash, and are so rapidly cured by emetine injections, that I have not yet met with an instance in which I felt justified in recommending surgical procedures. Moreover, cases have been recently recorded in which after the complete failure of prolonged irrigation through an appendicostomy wound, persistence with ipecacuanha has cured the patients, while with the emetine treatment I feel sure that operative interference will rarely if ever be necessary or admissible.

Diet.—In acute amœbic dysentery a fluid diet is essential, milk, citrated to prevent the formation of large irritating coagula, being the main stand-by, while soups are useful as a stimulant. Great caution is required in going back to solid diet, especially if the ipecacuanha treatment is being relied on, lest a relapse should be brought about. In native patients, who will seldom remain in hospital if their diet is long restricted to fluids, I often have to give a little soft rice as soon as the stools have become reduced in numbers and somewhat improved

in character, although still not quite free from mucus or blood. In chronic cases the strength has to be maintained through a long and exhausting illness, and as the small bowel is not involved in the disease a more liberal diet is possible than would otherwise be the case, as long as it does not leave solid residue which may irritate the large gut. Such food as arrowroot and custards may, therefore, be added to the milk and the effect carefully watched. In cases treated with emetine the difficulties are much less, and some solid food can usually be given about the third or fourth day after admission.

CHAPTER VII

THE REMOTE COMPLICATIONS OF AMŒBIC DYSENTERY

A PRIMARY amœbic infection of the large intestine may sooner or later result in the protozoal parasite finding its way through the portal system, most commonly to the liver, but in rare instances also to the spleen or even more distant parts, such as the brain and other tissues, in any of which it may set up inflammatory processes ending in suppuration. Nor are such extensions of the infection by any means limited to the more acute cases of amœbic colitis. On the contrary, they tend to occur as remote complications months, or even years, after the primary dysenteric attack, which may have been a very slight one, so that the connexion with it is quite liable to be overlooked. Further, amœbic hepatitis not rarely occurs in subjects who give no history of ever having suffered from actual dysentery, although sometimes careful inquiry will elicit that there has been a tendency to slight attacks of diarrhœa alternating with constipation, which are really mild amœbic infections. Still more puzzling are the cases in which even such a history of intestinal irregularity cannot be obtained, yet amœbic hepatitis, too often drifting on to suppuration in the liver before its true nature is suspected, may occur. The solution of the difficulty lies in

the fact, which I have been able to demonstrate from an extensive post-mortem experience in Calcutta, that in such cases if the liver abscess proves fatal a few small latent amœbic ulcers, or scars proving their previous existence, will almost invariably be found in the large bowel, usually limited to the cæcum and ascending colon, although the lesions may have been too slight to have produced definite bowel derangement (see Diagram 3, illustrating bowel lesions, at end of the work). My Calcutta experience shows that in 98 per cent. of fatal amœbic abscesses of the liver either a history of previous dysentery or actual bowel lesions post-mortem were present, the disease being always of the amœbic type, and never bacillary in nature, which affords the most conclusive evidence of the causal relationship between the two conditions, the infection of the liver taking place through the portal system.

The practical importance of these facts cannot be overrated, as their demonstration has enabled me to prove conclusively that the same specific remedy which rapidly cures amœbic colitis is equally effective in its hepatic complication, provided that the latter is detected before the stage of suppuration has been reached, as may almost invariably be done by finding a leucocytosis present in the blood. Once extensive abscess formation has taken place in the liver or spleen surgical intervention becomes almost always necessary, so that the early recognition of what I have termed 'the pre-suppurative stage of amœbic hepatitis' is most essential, and this condition must first be described and its treatment

indicated, before the extensive subject of amœbic abscess of the liver is dealt with.

THE PRE-SUPPURATIVE STAGE OF AMŒBIC HEPATITIS

Attacks of hepatitis secondary to active or latent amœbic ulceration of the colon vary very widely in their clinical symptoms, from an easily recognized acute inflammatory condition of the liver down to the most insidious process, revealing itself solely by chronic low fever and a leucocytosis, with no signs pointing to the liver as the seat of the disease, except sometimes slight painless enlargement of that organ. The cases must, therefore, be divided up into several classes for purposes of description, beginning with the obvious acute cases closely related to an attack of dysentery, and ending with the difficult insidious ones resulting from a latent amœbic infection of the bowel, illustrative examples being recorded of each variety.

Acute Hepatitis complicating or shortly following an acute attack of Amœbic Dysentery.—In this class there is no difficulty in recognizing the condition, for in the most acute form, during or very soon after an attack of dysentery, severe pain appears in the hepatic region, whilst the temperature rises several degrees and often becomes remittent in type. Rapid painful enlargement of the liver soon becomes apparent, so that its lower edge may extend several fingers' breadths below the right costal margin and in the epigastrium, whilst the dullness may also extend in an upward direction. With the onset of the acute hepatic symptoms the number of the dysenteric stools usually becomes

much reduced, or active bowel symptoms may entirely subside for a time. Should the dysenteric symptoms continue after the onset of acute hepatitis, the latter is likely to be very severe and rapidly to end in multiple small amœbic abscesses in the organ and lead to a fatal termination. More frequently the hepatitis only ensues after the dysenteric symptoms have subsided, and then the former condition is less rapid in its course and more amenable to proper treatment. The hepatic pain may sometimes be very severe, so that the patient can only lie in one position and is quite unable to turn over to one side on account of the distress occasioned by the movement. Yet all the pain may be completely alleviated by a very few doses of the specific remedy for amœbic disease, clearly showing that the hepatitis is due to the protozoal parasite.

The acuteness of the hepatic symptoms is often such as to suggest that actual suppuration has already occurred, and it is in this class of cases that aspiration of the liver is so frequently performed with a negative result, although not many days later a second exploration may reveal pus in the same place, showing that at the earlier operation the disease was still in the pre-suppurative stage, and consequently would have proved amenable to full doses of ipecacuanha or emetine. The following is a very conclusive example of such an occurrence.

Acute Hepatitis not treated with Ipecacuanha and developing into Liver Abscess while in Hospital.—A European male was admitted for fever of three weeks' duration, of uncertain nature. A few days later signs of acute hepatitis developed, and leuco-

cytosis being also found, an exploratory laparotomy was performed, as the left lobe of the liver was much enlarged and very tender. The liver was palpated and repeatedly aspirated with a negative result. Ammonium chloride and saline purges were accordingly continued, and the temperature was lower for a time. Four weeks after his admission the fever again became higher, and on the thirty-eighth day in hospital a second operation was per-

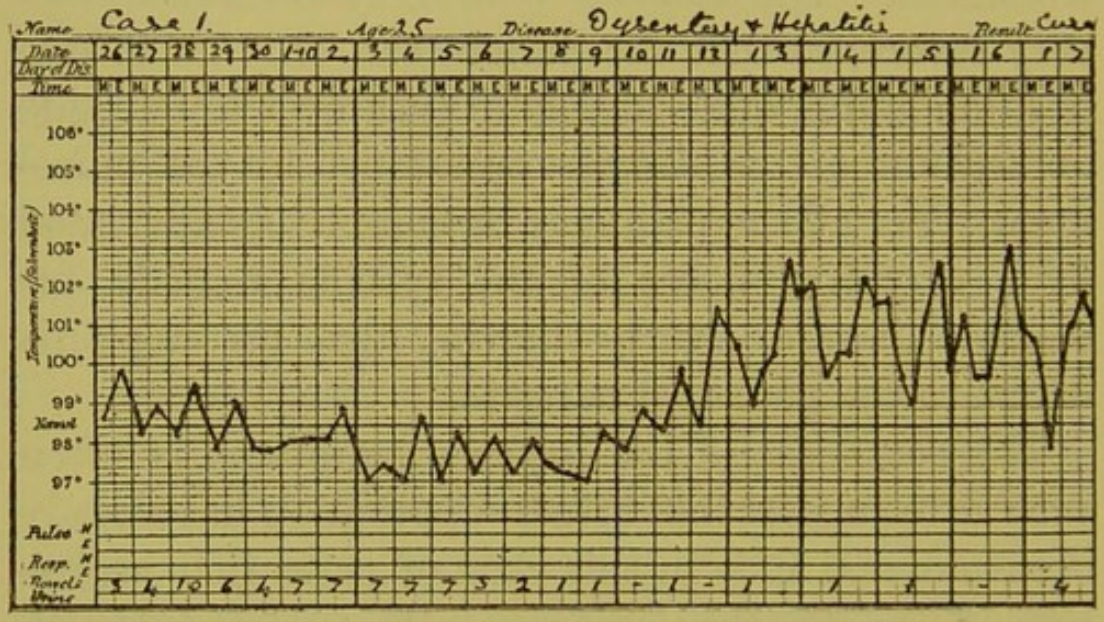


CHART I. Dysentery and Hepatitis.

formed, and an abscess opened in the very part of the left lobe of the liver which had been proved to be free from suppuration at the first operation twenty-nine days before. The case terminated fatally. The patient had never had any ipecacuanha, the routine treatment with ammonium chloride and large doses of quinine having been used in accordance with the general teaching of recent times. Yet this case showed far less urgent signs of hepatitis when first admitted than the great majority of those which cleared up so readily under the

ipecacuanha treatment. I venture to think that such misfortunes will become increasingly rare with the increasing use of the method here advocated.

As a contrast to the above case the following is a good example of an acute attack of amœbic hepatitis ensuing on dysentery, in which, although suppuration was diagnosed by a very experienced medical man, all the symptoms rapidly subsided under the influence of full doses of ipecacuanha.

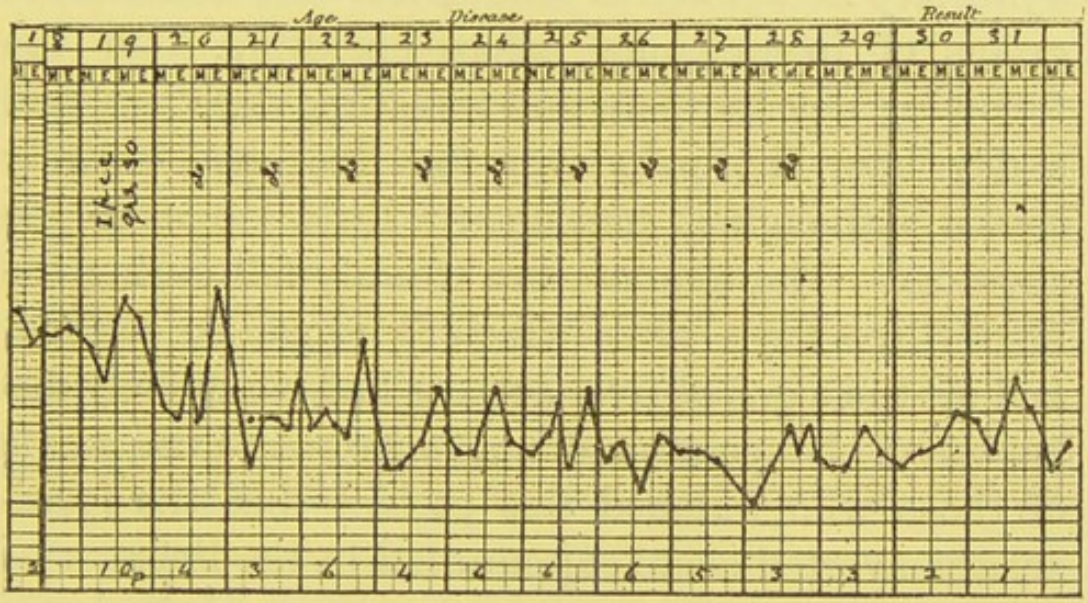


CHART I (continued).

Very Acute Hepatitis with suspected Liver Abscess following immediately on Dysentery.—A European male, aged 25, was admitted for dysentery of six weeks' duration. About six stools of blood and mucus daily, without pain or straining, which subsided in ten days under treatment with castor oil mixture and creolin enemas. Seven days later he began to suffer from pain in the hepatic region and right shoulder, while his temperature, which had been normal for twelve days, rose to a remittent type of fever ranging between 99° and 103° F. The

pains continued to be severe, the breath sounds at the right base became diminished and profuse sweats occurred, and on the eighth day of the hepatitis the right side of the diaphragm was found by X-rays to be quite motionless, and there appeared to be a slight shadow in the right lobe of the liver. Abscess within this organ was, therefore, confidently diagnosed by the very experienced medical man in charge, but as the patient had recently suffered from dysentery he agreed to take a few full doses of 30 grains of ipecacuanha before operating. On the following day the pain and sweating were less, and a day later the pain over the liver had entirely ceased, although it continued a little longer in the shoulder. The temperature steadily fell during the next three days, after which it remained normal, and all the signs of liver abscess had completely disappeared. No possible doubt remained in the minds of those who watched this patient that the ipecacuanha averted acute suppuration in the liver.

The next case is one of an insidious febrile hepatitis following dysentery, which was detected by finding leucocytosis.

Insidious Attack of Hepatitis following closely on Dysentery, detected by means of a Blood Examination, and rapidly cured by Ipecacuanha.—Case 1.—A male, aged 38, who had been in hospital two and a half months previously for a slight attack of hepatitis, which yielded to ammonium chloride treatment in three days. He had suffered from dysentery on and off for seven months before this first attack of hepatitis, and on readmission was passing mucus and blood, but showed no signs of

hepatitis. The dysentery improved under bismuth, but the irregular intermittent fever continued in spite of quinine, and one month after he came into hospital I found slight increase of the leucocytes not amounting to an actual leucocytosis. Six days later, his liver having become tender, a second examination showed 15,250 white corpuscles per cubic millimetre, a leucocytosis having now developed. Although all active symptoms of dysentery had long ceased, I suspected a latent form of the disease as the cause of the hepatitis, and advised the ipecacuanha treatment, which was followed by a permanent cessation of the fever within two days, as seen from Chart 1, although the case was just one of those which ordinarily drift on into liver abscess.

Such cases as the above could be multiplied almost indefinitely, including patients sent from long distances to Calcutta by very experienced medical men for operation for liver abscess (mostly before I described the condition and its cure by ipecacuanha) in which all the symptoms rapidly subsided under the specific treatment, but this class of straightforward case is too well known at the present time to need further illustration.

Cases of Amœbic Hepatitis without previous history of Dysentery, recognized by Blood Examinations, and rapidly cured by Ipecacuanha.—In cases of this class there are obvious clinical symptoms of hepatitis, but in the absence of any history of dysentery their amœbic nature is very likely to be overlooked and treatment other than large doses of ipecacuanha adopted, when they are liable to drift on into hepatic abscess formation necessitating

serious surgical interference. If, however, a blood examination is made, a leucocytosis, either actual or relative, with or without some increase of the percentage of the polynuclears, will always be found, and this furnishes an indication for the exhibition of ipecacuanha in large doses without delay. The following are examples of this condition.

Acute Hepatitis, with involvement of the base of the right lung, clearing up under Ipecacuanha.—A European male, aged 43, admitted with a history of fever for one month, with severe pain over the liver during the last few days. The liver extends from the sixth rib to one inch below the costal margin. Temperature from 100° to 102° F. X-rays showed the diaphragm on the right side to be high and nearly fixed, while the base of the left lung was darker than normal and the outline of the diaphragm blurred. No shadow in the liver. There were also a few crepitations to be heard at the base of the right lung. An abscess was suspected at the upper part of the liver, with extension of the inflammation to the base of the right lung, but he was put on ipecacuanha in the hope that suppuration might not actually have taken place. On the following day the pain over the liver was much less, but the temperature only very slowly declined to some extent during the first six days. At the end of this time X-rays showed the right diaphragm to be moving almost as well as the left, while the opacity at the base of the right lung had almost gone, leaving the vault of the diaphragm clearly defined. On the eighth day the temperature remained quite normal, but the following and third days after this a high

intermittent rise occurred, which proved to be benign tertian malaria; this yielded at once to quinine, and he made a complete recovery.

Chronic Hepatitis without Dysentery rapidly cured with Ipecacuanha after the failure of other drugs.—A European male, aged 29, admitted for chronic hepatitis of six months' duration, but much worse for the last seventeen days, with slight fever, sweats, and pain over the liver and in the right shoulder. He was treated in hospital with sodium sulphate and ammonium chloride, arsenic and dilute hydrochloric acid for thirty-one days, with very little result, his temperature being higher at the end of this period than on his admission. He was now put on ipecacuanha in 30-grain doses every evening, and his fever finally ceased in five days.

Acute Hepatitis without Dysentery cured by Ipecacuanha.—CASE 8.—A male, aged 38, admitted for acute hepatitis without any history of dysentery, and no present bowel trouble. His temperature showed the rapid oscillations produced by the frequent profuse perspirations so common in acute liver inflammation, a marked leucocytosis was present, and he had occasional rigors. Nevertheless, the pyrexia and all the acute symptoms yielded in four days to 20-grain doses of ipecacuanha morning and evening.

In these cases the presence of leucocytosis with little or no increase in the percentage of the polynuclears, as in amœbic abscess of the liver, and the rapidly curative effect of the specific anti-amœbic drug furnish good evidence as to the true nature of the hepatitis.

Latent Amœbic Infection with Fever, but no definite Hepatic Symptoms, yielding to Ipecacuanha.—Lastly, we come to the most difficult cases of all, in which there is neither a history of dysentery nor any very evident signs of hepatitis, although there may be slight painless enlargement of the liver, but which, nevertheless, show the same type of leucocytosis, and whose real nature is revealed by the chronic fever rapidly yielding to ipecacuanha. I only discovered this important condition during a prolonged investigation of fevers in the Calcutta European General Hospital, during which I made blood examinations and obtained full clinical notes and four-hourly temperature charts of 1,350 consecutive fever admissions, in the course of which I met with several cases of chronic pyrexia showing leucocytosis of the above-mentioned type. Suspecting them to be latent forms of amœbic hepatitis, I advised the exhibition of full doses of ipecacuanha, with the happy effect of rapidly curing the fever, thus confirming the correctness of my supposition. The following are typical examples of this puzzling condition.

Fever, without Dysentery or active Hepatitis, for fifty-three days rapidly cured by Ipecacuanha.—Case 13.—Male, aged 28, admitted for fever of three weeks' duration, which persisted under quinine treatment, although no cause could be found for it. Bowels normal, both sides of the diaphragm moving well, as seen by the X-rays. Liver slightly enlarged, but not tender, although becoming larger. Leucocytosis was found by me both one week and three weeks after admission, so the liver was explored for

abscess with a negative result. Three days later, or fifty-three days after the fever commenced, the ipecacuanha treatment was commenced, and on the fourth day the temperature was normal, but slight low fever up to 100° F. recurred for several days more, after which convalescence set in.

This was a most remarkable case, as the nature and cause of the fever was quite a puzzle until the presence of leucocytosis led to a suspicion that latent amœbic dysentery and hepatitis might be at the bottom of it, while the rapid success of the ipecacuanha treatment in such a persistent fever appears to me to lend some support to the correctness of this view of the case.

Fever with Leucocytosis, but neither Dysentery or active Hepatitis, rapidly cured by Ipecacuanha.—Case 14.—Male, aged 24, admitted for irregular intermittent fever, not yielding to quinine, and with no obvious cause. As over 20,750 leucocytes were found the ipecacuanha treatment was again adopted with the happiest results, the fever finally ceasing two days later, and convalescence being quickly established, as in the preceding case.

In this last series of cases the discovery of leucocytosis is of great help in the diagnosis, as this blood change is not found in malaria, kala-azar, and other chronic fevers with which the disease is most likely to be confused, with the possible exception of Malta fever, which is not met with as an indigenous disease in Calcutta. The importance of its recognition can hardly be over-estimated, for it is just these cases which drift insensibly into liver abscess, sometimes after the patient has left the

tropics, although such a disaster can be easily prevented by correct diagnosis and treatment in the often prolonged pre-suppurative stage.

CASES OF AMŒBIC HEPATITIS TREATED WITH EMETINE INJECTIONS

During the last few months I have found that hypodermic injections of soluble salts of emetine are more rapid and efficient in the treatment of amœbic hepatitis than crude ipecacuanha powder, a further important advance which may be illustrated by the following cases.

Acute Hepatitis in a patient who could not take Ipecacuanha by the mouth cured by Emetine Hydrochloride, Hypodermically.—A European lady who had been suffering from fever and pain over the liver for ten days had had an attack of dysentery some two months before. Widal tests for typhoid and paratyphoid were negative. Ipecacuanha was now given by the mouth for three days, with the result that the hepatic pain became less and the temperature declined to a lower level.

On account of the great nausea and vomiting she now refused to continue the ipecacuanha, and during the next three days the temperature rose steadily to reach 103° F. in the evenings, and the hepatic pain recurred. At this period I was asked to see her in consultation, and injected one-third of a grain of emetine hydrochloride in the afternoon. The temperature fell steadily during the next twenty-four hours to 100° F., and the pain had also disappeared. I now gave a second injection of half a grain, equal to 45 grains of ipecacuanha. No vomiting, and

practically no nausea, was caused by these doses, and her medical attendant reported to me that she was much better.

Four days later I was again asked to see her, as the temperature had once more risen to 103° F., and it was feared that liver abscesses would result if the disease was not quickly cured. I repeated the former doses on that and the following day, and the temperature declined steadily, to reach the normal in three days, when two more similar doses were given to guard against any recurrence, and no more fever or other trouble has occurred.

Very Acute Hepatitis with threatened Liver Abscess cured by Emetine and Ipecacuanha.—Case VII.—A native male, aged 17, admitted with very acute hepatitis with marked enlargement and extreme tenderness of the lower border of the liver. An evening rise of temperature to 101° F. had persisted for ten days, in spite of 30 grains of ipecacuanha daily during the last four evenings. Two half-grain injections of emetine were now given, and within eight hours of the first dose the tenderness had remarkably decreased, and on the following day the temperature became normal and remained so for four days. It then rose again in the evenings, and X-rays showed a shadow suggestive of liver abscess. A needle was passed into the lower part of the right pleura and a little purulent lymph was drawn off. Ipecacuanha was persisted with and the condition cleared up entirely without any further operative procedures being necessary. The beneficial effect of a single grain of emetine in the early acute stage of this case was very striking.

Acute Hepatitis cured by Emetine Injections after a negative aspiration for Liver Abscess.—Case VIII.—A European male, aged 29, was admitted for acute hepatitis with intermittent fever, and 20-grain doses of ipecacuanha were given every evening. As the fever and hepatic pain persisted for five days the liver was explored for pus under an anæsthetic, but with a negative result. Emetine hydrobromide was now injected daily in half-grain doses, and the temperature at once fell to normal and the pain subsided. Ipecacuanha was reverted to after four days, but the improvement was less marked than under the emetine, so the daily half-grain dose of the latter was recommenced, and at once rapid improvement set in, going on to complete convalescence after a few doses, and accompanied by a fall in the previously high leucocyte count.

The Duration of the readily curable Pre-suppurative Stage of Amœbic Hepatitis.—The extent to which the occurrence of tropical abscesses of the liver can be reduced by the use of large doses of ipecacuanha will evidently depend on the duration of the pre-suppurative stage, in which alone it can be expected to be successful. I have analysed a number of cases of liver abscess to determine this point with the following results. Among twenty liver abscess cases in the European hospital, in 50 per cent. fever or hepatitis had been present for over one month before the abscess was found, in 34 per cent. more these symptoms had been evident for between two weeks and a month, while in the remaining four cases the time was from

nine to thirteen days. Again, out of fifty-three native patients, in 51 per cent. a history of over two months' illness was obtained, in 38 per cent. one of from one to two months, in 9 per cent. from two weeks to a month, and in only one case less than two weeks. Of course, many of the native patients had developed abscesses some time before they came to hospital, but allowing for this, there still remains a good margin of time, in the vast majority, during which the preventative ipecacuanha treatment might have been carried out, with great saving of life and prolonged suffering.

The Reduction in the death-rate from Amœbic Abscess of the Liver by the cure of the Pre-suppurative Stage by Ipecacuanha.—If the foregoing views are correct, then a marked reduction of the number of cases of amœbic abscess of the liver should have resulted where my methods have been adequately carried out. Evidence has now accumulated to prove that this is actually the case. At the Calcutta European General Hospital during four consecutive years of which I have records, no case of hepatitis went on to abscess formation after the admission of the patient, while the number coming with suppuration in the organ already established has fallen considerably. Moreover, Lieut.-Colonel Pilgrim, for many years superintendent of the hospital, has recorded that during the four years subsequent to the introduction of my methods, out of an average of over 200 cases of dysentery, nearly all treated with ipecacuanha, not a single one developed hepatitis, and out of a yearly average of eighty-two hepatitis cases treated in the same way

none developed a liver abscess, while the admissions into his wards with suppuration already established in the liver had fallen to about one-third of the previous number.

Again, in the British Army in India the prevalence and mortality of liver abscess has fallen steadily since 1907—when my paper on pre-suppurative amœbic hepatitis was published—to under one-half of the former number, although the rate had been stationary during the previous thirteen years, as shown in the next table. It has been pointed out that the admissions for alcoholism, an important predisposing cause of tropical liver abscess, have equally fallen greatly during the last five years, but this fall had been well marked for several years before the decline in the liver abscess cases began, so will not account for the latter.

TABLE SHOWING THE REDUCTION IN THE DEATHS FROM LIVER ABSCESS IN THE BRITISH ARMY IN INDIA SINCE THE REVIVAL OF THE IPECACUANHA TREATMENT OF HEPATITIS.

	Admissions per 1,000.	Deaths per 1,000.	No. of cases.	No. of deaths.
1894–1903 (average)	2·39	1·39	157·5	92·5
1904	2·6	1·36	184	96
1905	2·1	1·17	152	83
1906	2·6	1·52	183	107
1907	2·4	1·01	165	70
1908	1·7	0·80	115	55
1909	1·4	0·48	100	34
1910	1·0	0·48	75	35
1911	—	—	71	33

With the much more rapid cures of amœbic disease now obtainable by means of hypodermic

and intravenous injection of soluble emetine salts, the above results should be capable of still further improvement, especially among Europeans and in the soldiers of the British Army in warm countries, who come early under skilled medical treatment. Further, with the radical cure of amœbic dysentery by the new treatment both immediate and remote hepatic and other complications should become very rare, while amœbic abscess of the liver should practically disappear, although up to 1907 it was the second largest cause of death in the British Army in India. In short, it is now not too much to say that the vast majority of early cases of amœbic hepatitis should be rapidly cured and the formation of tropical liver abscess should become a very exceptional occurrence, and one which ought to cause serious questionings in the mind of the medical man under whose care it has been allowed to develop.

The Treatment of Pre-suppurative Amœbic Hepatitis.—In view of the details already recorded there is but little remaining to be added under this head, especially as the methods of administration and doses of ipecacuanha and emetine have already been fully dealt with under the treatment of amœbic dysentery, from which they do not differ. The active alkaloid will doubtless replace the crude powdered root, and it is of especial value in amœbic hepatitis on account of its rapid action in relieving the pain and in preventing the grave danger of abscess formation, if that has not already taken place. In fact the results of the emetine treatment are so remarkable as to raise the question whether

a small abscess may occasionally encyst under this treatment, as the instance given on page 149 seems to prove. The value of the drug after suppuration has taken place is considered later (see page 227).

The ipecacuanha and emetine treatments are so satisfactory in early amœbic hepatitis that no other measures are necessary beyond keeping the bowels open with some very mild purge such as castor oil, rest in bed, and a light fluid diet for a few days.

AMŒBIC SUPPURATIVE HEPATITIS OR TROPICAL LIVER ABSCESS

Suppuration occurs in the liver in several forms. Firstly, we have pyæmic affections due to septic organisms. These may either be part of a general pyæmic infection, with abscesses in the lungs, spleen, &c., as well as in the liver; or a portal pyæmia (pylephlebitis), due to septic infection arising in some part of the gastro-intestinal tract and producing multiple acute abscesses throughout the liver originating in the distribution of the portal veins. This form of portal pyæmia may arise from sloughing dysentery in the tropics, but is less common than might have been expected. I have not met with an example among over one thousand post-mortems in Calcutta during the last few years. At an earlier period several cases recorded as pyæmic abscesses of the liver following dysentery were found post-mortem, but as occasionally small amœbic abscesses may be multiple, without any pyogenic bacteria being present, it is impossible, in the absence of bacteriological examinations, to say how many of these cases were septic portal pyæmia.

Secondly, there occur multiple abscesses of the liver in the biliary canals. Among twenty cases of this rare disease which I collected some years ago, eighteen were secondary to gall-stones, the infection probably spreading up the common bile duct from the duodenum; one was due to an hydatid cyst and the remaining one to a primary cancer of the bile duct. I have recorded one case of this nature occurring in Calcutta, which I diagnosed during life and in which I removed a large mass of gall-stones from the hepatic ducts, but the suppuration tracked along the inferior vena cava to open into the lungs with fatal results (*Brit. Med. Journ.*, 1903, vol. ii, p. 706). One other case of this nature is noted in the thirty-five years' record of Calcutta post-mortems, but it is a rare disease which it is difficult to recognize during life.

These forms of multiple abscesses throughout the portal veins or bile ducts of the liver are usually of a very acute nature and seldom recognizable during life apart from the primary diseases on which they are dependent. For this reason they differ clinically very widely from the so-called tropical liver abscess, which follows an attack of more or less acute hepatitis, and nearly always produces one or more large localised collections of pus, with or without smaller multiple abscesses quite unconnected with each other, being generally quite free from the ordinary pyogenic bacteria, both in their early and late stages. This very distinct variety of liver abscess is now known to be constantly associated with the presence of active protozoal amœbæ, and hence is best described simply as amœbic suppurative hepatitis.

As it occurs almost exclusively in tropical or sub-tropical climates, or in persons who have resided in such places, it is also commonly spoken of as tropical liver abscess, in distinction from the portal and biliary multiple abscesses, which are nearly, if not quite, as common in the temperate zones. In this article only amœbic suppuration is dealt with.

GEOGRAPHICAL DISTRIBUTION OF AMŒBIC LIVER ABSCESS

This disease is met with most frequently in low-lying, moist tropical climates. Thus, it is common in the large Presidency coast towns of India, at Colombo in Ceylon, Singapore, the East Indies, Philippine Islands, Hong Kong, and the more southern parts of China. It also occurs inland in these countries, being met with in all parts of India, including the comparatively dry Punjab and Central India. It is least common among British troops in the Peshawar division in the extreme north-west of India and in Burma than in any other area, but only in proportion to the infrequency of dysentery in these parts. In Africa it is not uncommon in Egypt and Algiers as well as upon both coasts, while cases have also been reported from the interior. It is relatively rare in the West Indies, but occurs to some extent in the hotter parts of both North and South America. Owing to the chronic nature of the amœbic form of dysentery on which it is dependent, persons invalided from the tropics not very rarely develop the disease after returning to temperate countries, but these cases show a smaller proportion of the very acute multiple

liver abscesses than do those arising in the tropics themselves.

PREDISPOSING CAUSES OF TROPICAL LIVER ABSCESS

Age, Sex, and Race Incidence.—The following table shows the age and sex of 300 liver abscess cases among natives of India and 92 Europeans treated in the Calcutta hospitals.

Age.	Natives.						Europeans.			
	Hindus.	Mohammedans.	Males.	Females.	Total.	Percentage.	Males.	Females.	Total.	Percentage.
0–10 . . .	0	2	2	0	0	0·7	0	0	0	0·0
11–20 . . .	15	1	16	0	16	5·3	4	0	4	4·4
21–30 . . .	86	19	102	3	105	35·0	24	1	25	27·2
31–40 . . .	94	17	107	4	111	37·0	34	1	35	38·0
41–50 . . .	46	7	58	1	53	17·6	19	1	20	21·7
Over 50 . .	11	2	13	0	13	4·3	7	1	8	8·7
Total . . .	252	48	353	8	298	—	88	4	92	—
	%	%	%	%			%		%	
Percentage .	84	16	97·3	2·7	—	—	95·6	—	4·4	—

These figures show that the age incidence is very similar in Europeans and natives, especially when allowance is made for the fact that a much smaller proportion of native patients belong to the later decades of life. The well-known very low incidence of liver abscess in the first decade is clearly brought out by the table, only 0·6 per cent. of the native patients, and none of the Europeans, having been under 10 years of age. Further, only 5·3 per cent. of the former and 4·4 per cent. of the latter were between 11 and 20, two-thirds of the natives being entered as 20, this being only their approximate age, for they are not very accurate in this respect. Over

two-thirds of the cases among natives and almost as many among the Europeans occurred during the third and fourth decades. In each race the fourth decade showed more cases than the third, so that the disease becomes increasingly frequent up to the age of 40, especially when we remember that many more native hospital patients are admitted in the third than in the fourth decade of life. Between 41 and 50 the disease is also quite common in proportion to the numbers of such patients, but over 50 becomes less frequent.

The **Sex** of incidence of liver abscess is of still greater interest and importance, for the great rarity of the disease in females is certainly the most striking fact in the distribution of the disease, and one regarding which I know of no adequate explanation. Thus, only 2·7 per cent. of the native patients and 4·4 per cent. of the Europeans were females, although one-fifth of the surgical admissions among natives are females. During the last nine years at the European General Hospital the whole of the sixty-two admissions for liver abscess of which I have notes were males. The European female patients at the Medical College Hospital with liver abscess were nearly all of mixed European and Indian blood. It is noteworthy that pre-suppurative amœbic hepatitis is equally rare among females of both races, only one out of about fifty cases in my European series having been of the female sex. The Medical College post-mortem records show an equally great rarity of tropical liver abscess among native females.

The lesser consumption of alcohol by females is probably an important factor in their relative escape

from liver abscess, but it will by no means fully explain the difference. It is more likely connected with a lesser incidence of amœbic dysentery in women, the reasons for which will only be fully known when we have more exact knowledge of the etiology of that disease.

The **Race** incidence of amœbic abscess of the liver has next to be considered. It is commonly stated in text-books that the disease is rare in natives of India as compared with Europeans, figures in support of this contention being quoted from army and jail returns. Thus, during the fourteen years from 1894–1908, the admission rate per thousand for liver abscess averaged 2·35 among British troops, but only 0·1 in the Native Army. It is also very rare in Indian jails compared with the number of cases of dysentery, namely, 0·1. This is partly explained by recent investigations which show jail dysentery to be largely of the bacillary type, amœbic cases being very rare. Moreover, dysentery in the Indian army and jails always comes under early and efficient treatment, while liver abscess is especially liable to follow chronic neglected dysentery. Again, the excellent sanitary condition of the army barracks and jails in India may be expected greatly to lessen the incidence of amœbic dysentery among their occupants as compared with the general population. Nor are the conditions under which European and Native troops serve strictly comparable, for the two races are unequally distributed over Indian stations, British troops alone being sent to the hills in large numbers in the hot and rainy seasons, while sudden change of climate notoriously predisposes to both

dysentery and hepatitis. Alcohol is also much more largely consumed by British than by Native troops. For these various reasons the figures of a number of years' admissions for liver abscess to the large Calcutta hospitals may be expected to furnish more reliable data for comparing the incidence of tropical abscess of the liver in different races, and the following data are of interest in this connexion.

My tables of Medical College cases contain most of the admissions from 1899 to 1908, and the post-mortems for the last thirty-five years. They show 300 natives and only thirty-one Europeans, so one-eleventh of the patients belonged to the latter race, while one-third of the beds are for European patients; so that in proportion to the beds available there were three times as many cases among the natives. On the other hand, if the incidence is calculated on the relative proportion of natives and Europeans in the population from which the admissions are derived, then the disease is more common among Europeans. It is not possible to arrive at any exact estimation of the incidence of the disease in the two races from these data, but it is at least clear that liver abscess is very common among natives of India, much more so than has commonly been admitted hitherto. Lieut.-Colonel Hatch in 1898 drew attention to the frequency of the disease among the native population in Bombay.

The incidence among Hindus and Mohammedans is also shown in the table. No less than 84 per cent. were in Hindus and but 16 per cent. in Mohammedans, although both the admission rates for all diseases and the census figures give but two and

a half times as many Hindus as Mohammedans. It is, therefore, clear that there is relatively twice as high an incidence among Hindus, probably largely as a result of their greater indulgence in alcohol, although this habit is unfortunately by no means uncommon among the lower classes of Mohammedans in Calcutta.

Duration of Residence in the Tropics of European Patients.—Among forty-five cases of liver abscess in Europeans, of which I have records regarding the time they had been in India, one-third had been born and bred there and two-thirds were immigrants. The duration of the residence in the tropics of the latter class was as follows:

Time in India.	Under 1 year.	1 to 3 years.	3 to 10 years.	Over 10 years.	Total.
Cases	8	6	8	8	30
Percentages . .	26·7	20·0	26·7	26·7	100

Thus just over one-fourth were attacked in the first year, and another one-fifth in from one to three years of coming to India, so that long residence does not appear to increase the predisposition to the disease as much as might have been expected.

Alcohol, especially in excess, has long been known to be an important predisposing cause of liver abscess, although the extreme rarity of the disease in temperate climates makes it clear that it is not in itself an exciting cause of suppurative hepatitis. The histories of the cases in the Medical College Hospital are not always very full, but J. W. D. Megaw, I.M.S., found that in 170 out of 229 a note was recorded regarding the use of alcohol by patients admitted for liver abscess. In 119 of these, or about

70 per cent., the stimulant had been habitually used in some form, while in 51, or about 30 per cent., the habit was denied. At the European Hospital the records are much more complete, a note of the habits regarding alcohol having almost always been recorded. Among fifty-five cases all took alcohol in some form, such being the nearly universal custom among Europeans in India. In 62 per cent. the quantity taken was not noted. Of the remaining 38 per cent. a moderate amount was recorded in twenty-two, namely, up to two or three whisky pegs a day. In the remaining 16 per cent. excess was noted; a very high proportion, especially when we remember the tendency of alcoholics to deny their failing, clearly indicating a marked effect of alcoholism in predisposing to liver abscess in the tropics. It has already been pointed out that the low incidence of liver abscess in the native army, in Indian jails, among Mohammedans, and in the female sex are all in accordance with the view that alcohol predisposes to the disease in a marked degree, so that there can be no doubt that its habitual use is an important factor in the etiology of tropical liver abscess. Nevertheless, it is by no means essential to its causation, for suppurative hepatitis may occur in those who never take alcohol as well as in persons who are extremely moderate in its use.

Malaria has often been accused of favouring the formation of liver abscess, especially by earlier writers in the days when nearly all forms of fever in hot climates were attributed to miasmatic influences. The fact that the fever, so constantly present in the pre-suppurative stages of liver abscess

in the tropics, was very generally looked on and treated as malarial, is the probable origin of such a belief. In the many blood examinations I have made in the early febrile stage of this affection I do not remember to have ever found malarial parasites, while the almost constant leucocytosis present is alone sufficient to exclude malaria as the cause of the fever in most cases. In fact I know of no reliable evidence that malaria in any way predisposes to the formation of liver abscess.

Chills are commonly looked on as predisposing or exciting causes of liver abscess in the tropics, but the fallacy of regarding the rigor, occurring as a symptom of the presence of acute hepatitis, as a chill causing the disease must be carefully guarded against. Nevertheless, the occurrence of severe hepatic symptoms following exposure to cold on a railway journey, or on going from the hot plains to a hill station, is sufficiently frequent in persons who have suffered from dysentery or previous hepatitic congestion of the liver to constitute chills an important predisposing cause of liver abscess, when the exciting cause, active or latent, amœbic dysentery, is also present. Such cases may indeed be of a very acute nature ending in multiple abscesses, so great care is necessary after amœbic dysentery or hepatitis to avoid any sudden changes of temperature.

ETIOLOGY

Tropical abscess of the liver presents many points of difference from collections of pus due to ordinary septic bacteria. They sometimes form very slowly

and insidiously, occasionally with little or no fever or other constitutional disturbance. Rarely they may become spontaneously encysted and dry up, their remains being found unexpectedly at a post-mortem examination years after. A large tropical abscess may not infrequently be present in the liver without any fever whatever. Pus collected on first opening differs markedly from that of ordinary septic abscesses, whilst on culture it is quite free from cocci and bacteria in the great majority of instances. In all but very acute cases the abscess is quite localised and presents a dense fibrous wall separating it from healthy surrounding liver substance, whilst it is usually single; thus differing strikingly from the multiple septic suppurations in this organ of a pyæmic, pylephlebitic, or cholangitic nature. All these facts point to the tropical liver abscess being different in its etiology from suppurations of bacterial origin.

The discovery of a protozoal amœba in the pus of tropical liver abscess furnished a simple explanation of these differences. Yet there has been much dispute with regard to the exact rôle played by this organism in the causation of suppuration in the liver. This was largely due to its having been found very inconstantly in the small number of cases reported in the earlier papers of Kartulis in Egypt and Councilman and Lafleur in America. It has been held, especially by French writers, that pyogenic organisms may be present in the earlier stages of the abscess formation but die out later. I am not aware of any acceptable explanation having been given why such an event should occur so commonly

in an abscess of the liver, when it is so exceedingly rare, if indeed it occurs, in septic abscesses in other parts of the body. As I have probably had unique opportunities during the last ten years of investigating this subject, with the abundant material afforded by the large Calcutta hospitals, my experience may here be recorded.

The Constancy of the Presence of Amœba in the Walls of active Tropical Abscess of the Liver.—Earlier observers had pointed out that the amœba is more readily found in the wall of a liver abscess than in its contents. This I confirmed in Calcutta. In order to get a large number of cases I obtained (through the kindness of a succession of surgical colleagues at the Calcutta Medical College and European hospitals) at the time liver abscesses were opened some of the thick pus in one sterile test-tube, and in another a small scraping of the wall of the abscess taken with a sterile Volkmann's spoon. In other cases similar scrapings were taken at subsequent dressings. I was thus able to demonstrate living amœbæ in thirty-five consecutive cases examined either at the time of operation or within nine days afterwards. In two cases, not examined until twelve and fourteen days respectively after opening, when only a little thin yellow pus was present, I did not find them. I have since confirmed these observations many times, so that it may be confidently asserted that in the wall of an active tropical liver abscess, that is, at the seat of the disease process, amœbæ may invariably be found by such examinations made at the time of operation or within a few days after. Post-mortem I once

found amœbæ absent from an encysted liver abscess, but present in an active one in the same organ, so that the organism may occasionally die out when the active process subsides. An operation undertaken in such a late stage might very occasionally reveal an abscess free from amœbæ.

The next important question is that of the exact conditions prevailing in the earliest stages of the abscess formation. This can only be studied in the fortunately rare acute multiple amœbic abscesses met with in tropical climates. I have been able to examine several such cases post-mortem, and have found that in nearly all of them cultures from a number of the small purulent collections showed their contents to be sterile as far as micrococci and bacteria are concerned. On the other hand, the microscope readily revealed active amœbæ in the smallest points of suppuration, but no bacteria of any kind. In one exceptional case a boy died unexpectedly while in hospital for fractured femur, for which the tendo Achillis had been cut, the wound becoming septic. Several medium-sized and numerous very small abscesses were found in the liver, which all contained both amœbæ and streptococci, the latter organism being also present in the suppurating wound. The larger liver abscesses were doubtless antecedent to the tenotomy, so there can be no doubt that the streptococcal complication of the older hepatic suppurations was secondary to the wound infection. This curious case, therefore, affords no support to the theory that tropical liver abscess is originally due to septic organisms, and not to the amœbæ, but rather shows how a primarily

sterile unopened amœbic abscess may be secondarily infected by bacteria through the blood-stream.

Once more, if sections are cut through the walls of an acute spreading liver abscess before any surrounding fibrous tissue wall has formed, amœbæ may readily be found extending along the blood-vessels, whilst suppuration will also be seen spreading into the neighbouring tissues in the same manner. All this may occur in the total absence of any pyogenic organisms other than the amœbæ.

Lastly, the evidence given in the section on treatment shows that quinine—which has been proved readily to kill the amœbæ, but not pyogenic organisms—when repeatedly injected into the cavity of a liver abscess without any drainage, will in a large proportion of cases completely cure the condition and bring about a cessation of the formation of pus and of all symptoms of the disease. For these various reasons I hold that the amœba is the active cause of tropical abscess of the liver, and does not require the assistance of any bacterial pyogenic organisms in any stage of the disease.

Primary Sterility as regards Bacteria of the great majority of Amœbic Abscesses of the Liver.—If the pus of an amœbic abscess of the liver is received directly into a sterile vessel or test-tube and examined microscopically and by culture without delay, it will be found in the great majority to be free from bacteria. Thus, during an investigation of eighty-seven consecutive cases, seventy-five, or 86 per cent., were sterile as regards bacteria, both microscopically and on culture. Cantlie has since stated that he observed this feature in China as long ago as

about 1895. The absence of bacteria from this form of liver abscess is clearly not due to the contents being unfavourable to their growth, for in the damp, germ-laden air of Calcutta bacilli and cocci rapidly make their appearance in the pus once the liver abscess has been freely opened. In fact it is almost impossible to prevent this, especially if the discharge be abundant. I have recently examined the pus from a large number of cases both at the time of operation and again within a few days after, and in no single case did the originally sterile pus remain so for as long as three days. This is not surprising when we remember that the sterile blood-serum-like contents of a liver abscess afford an ideal culture medium for the organisms which must inevitably gain access to the wound either at the time of opening or at an early dressing. The bearing of these important facts on the treatment of the disease will be considered later.

Relationship of Antecedent Dysentery to Amœbic Liver Abscess.—The association of dysentery with tropical liver abscess has long been recognized. Yet until recently there has been much difference of opinion as to the exact relationship between the two diseases and the frequency with which they are connected. Thus Andrew Duncan, in opening a discussion on dysentery at the British Medical Association in 1902, expressed the opinion that the large tropical abscess of the liver did not bear any special relationship to antecedent dysentery, although multiple abscesses did. This view was largely based on the rarity of liver abscess following dysentery in Indian jails and among native troops, as well as

in the South African War. With the recognition by me of amœbic dysentery in India further light was thrown on the subject, for the bowel disease in the above-mentioned conditions is now known to be chiefly of the bacillary type.

During the last ten years I have had exceptional opportunities for investigating this question in Calcutta and have collected the following data bearing on it, including an examination of the post-mortem records for the last thirty-five years. Dysenteric lesions may frequently be found post-mortem in cases in which there was neither a history of the disease nor symptoms of it while the patient was under treatment for liver abscess. It is therefore necessary to examine a series of cases in which both clinical and post-mortem records are available in order to ascertain the true incidence of dysentery in relation to tropical liver abscess. The following table gives such data of sixty-three cases:

RELATIONSHIP OF DYSENTERY TO TROPICAL LIVER ABSCESS

		Percentage.	
Clinical and post-mortem evidence of dysentery .	35 cases	55·5	
No history, but post-mortem evidence, of dysentery	13 „	20·6	90·4
History, but no post-mortem evidence, of dysentery	9 „	14·3	
No history or post-mortem evidence of dysentery .	6 „		9·5

Thus, both a history and lesions of dysentery were recorded in over half, no history but post-mortem lesions in 20 per cent., and a history without lesions in 14 per cent., giving a total of 90·4 per cent. in which evidence of dysentery was forthcoming. The cases in the above table include old records dating back to 1872, when the relationship of the two diseases was less well known than later.

The post-mortem records of liver abscess cases during the last ten years at the Calcutta Medical College Hospital, most of which autopsies have been performed by me, give the following figures:

BOWEL CONDITIONS IN RECENT FATAL LIVER ABSCESS CASES

		Percentage.	
Amœbic dysentery present	35 cases	77·0	97·0
Scars of former dysentery present	9 „	30	
No evidence of former dysentery found	1 „		2·2

Evidence of dysentery, always of the amœbic type, is thus seen to be almost constantly found after death from amœbic abscess of the liver, while the few negative results can easily be explained on the ground that a mild latent bowel infection has completely healed before death from hepatic complication, leaving no very evident scarring.

The clinical records of the native patients are not sufficiently complete to afford accurate data regarding the frequency of previous histories of dysentery in liver abscess cases. An analysis of the excellent European hospital notes of the last nine years have yielded the following data:

			Percentage.	
Dysentery.	In hospital	18		
	Within three months of admission	10	36	72
	Over three months before admission	8		
Diarrhœa only			7	14
Nil			7	14

There existed thus a definite history or symptoms of dysentery in 72 per cent., while in 14 per cent. more there was one of diarrhœa, which is the only symptom produced by some mild cases of amœbic disease of the large bowel. This leaves only 14 per cent. with no evidence of intestinal flux, while we

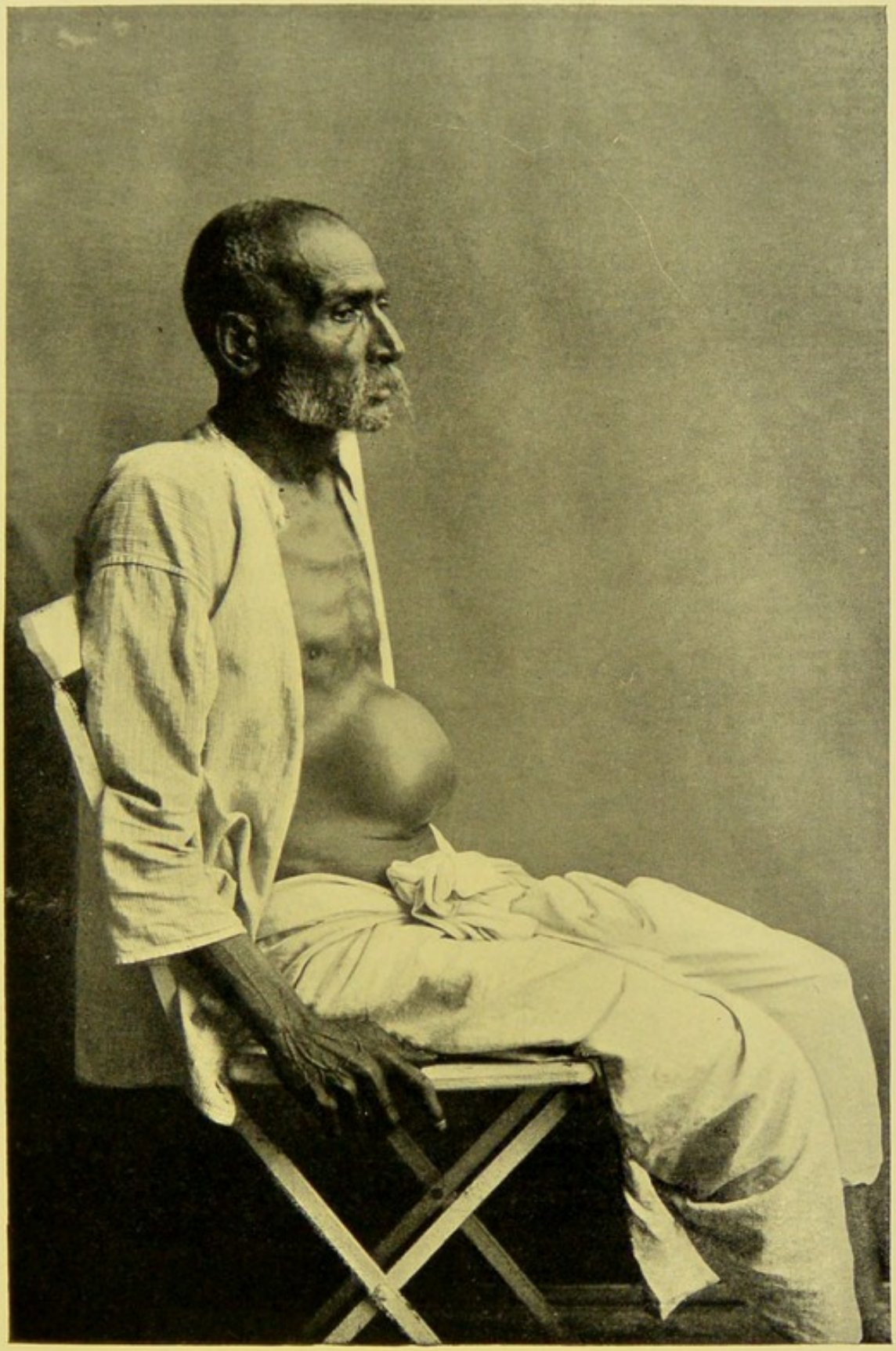
have already seen that this symptom may not rarely be absent when typical amœbic ulcers are found after death from liver abscess. It is also of interest to note that dysenteric symptoms frequently abate when those of acute hepatitis supervene, and the previous bowel trouble may not be mentioned by the patient unless carefully inquired for.

Moreover, the dysentery is nearly always clearly antecedent in date to the hepatitis, for even in those patients who showed bowel trouble while in hospital for liver abscess, the history of dysentery antedated the liver complication in the very great majority. In the native series the dysentery certainly preceded the liver abscess in 80 per cent. of the cases in which full histories were recorded, while when the bowel trouble supervened after signs of hepatitis, it was frequently only a recrudescence of old intestinal disease. The whole of the evidence, then, points to amœbic dysentery, often of a latent character, as constantly preceding the formation of tropical liver abscess.

Mode of Formation of Liver Abscess secondary to Dysentery.—The constant presence of amœbæ in all but the rare encysted stage of tropical liver abscess, taken together with the very close association of amœbic dysentery, either active or latent, with the amœbic hepatitis, can leave but little doubt that this protozoal parasite does pass from the large bowel to the liver in some way or other. Difficulties arise when we come to explain how this common complication is produced, particularly when in the form of a large localised collection of pus. The organisms must either travel across the peritoneal

cavity to the liver, or pass through the portal circulation. Infection by the former route is probably very rare, although I have seen it occur in a case of post-colic abscess due to perforation of the ascending colon by an amœbic ulcer, with adhesions to the liver and direct infiltration of the organ with pus to a slight extent. Infection by the portal route might be expected to produce multiple abscesses in the liver of the pylephlebitic type, such as occasionally arise from septic bacterial infections in sloughing of some part of the gastro-intestinal tract. We require much further information regarding the pathogenic properties of intestinal amœbæ to enable us fully to understand the liver complications they produce, yet a study of the lesions produced in the liver in different stages and degrees of acuteness of the disease throws considerable light on the subject.

Pathological Anatomy of Amœbic Abscess of the Liver.—The microscopical changes in the liver vary very widely according to the acuteness and duration of the disease, which are naturally in inverse ratio to each other. The more common and characteristic large single abscess is surrounded by a dense fibrous wall, which effectually shuts it off from the surrounding healthy liver substance. Once this limiting membrane is formed the swelling increases by expansion and pushing on one side of the liver substance rather than through its further destruction. Thus, I have several times seen a huge single amœbic abscess in the right lobe of the liver, which had expanded downwards to the level of the anterior superior spine of the ilium or even further, and



Large Amœbic Liver Abscess projecting in the Epigastrium.

formed a fluctuating bag containing four or more pints of thick pus. Yet the greater part of the right lobe, as well as the whole of the left, remained quite healthy in appearance. Were this not the case it is difficult to conceive a patient surviving long enough to enable abscesses holding four to six pints of pus developing in the substance of the liver. Moreover, the rapid and complete recovery which has ensued, even in such cases treated without open drainage, in the manner to be described later, proves conclusively that in extreme cases of amœbic abscess most of the liver substance escapes destruction. In this stage we have what we may well call a pyogenic membrane secreting pus, but prevented from further encroachment on the surrounding liver substance by a dense fibrous wall, formed by a chronic inflammatory process of a protective nature. In this advanced condition all trace of the mode of origin of the abscess is necessarily lost.

At the other extreme we have the most acute and rapidly advancing amœbic hepatitis, usually producing multiple abscesses, some of a considerable size, but others still in a very early condition. It is in these cases that the primary stages of the process can best be investigated. Taking first the larger ragged-walled, actively advancing abscesses, sections show the process to be extending along the veins into the surrounding tissue. Clots containing amœbæ are seen in the lumen of the veins, some of the organisms showing granular degenerative changes. The circulation is thus obstructed, a further zone of liver substance breaks down, and so the process extends. In these cases there will

commonly also be found some minute multiple abscesses down to the size of a pin's head, and sometimes they are very numerous. Sections of the smallest of these clearly show the process to commence in one of the distributaries of the portal vein, within the lumen of which amœbæ entangled in breaking down blood-clot may be seen, together with an excess of leucocytes. It is clear that in these instances the protozoal organisms have been brought to the liver through the portal vein, while Councilman and Lafleur have found them in the origins of the portal system in the submucous coat of the large bowel in amœbic dysentery. As already mentioned these primary stages of multiple amœbic liver abscesses are usually quite free from all bacteria, and the same is true of very large acute sloughing cavities, so the amœba is certainly able by itself to break down the liver substance, and the formation of numerous amœbic abscesses of the liver secondary to amœbic dysentery by infection through the portal vein is easily understood.

The production of a single, or a very few, circumscribed large abscesses with dense fibrous walls remains to be accounted for. In 1903 I suggested the following explanation of this seeming anomaly. It has been shown in the section on pre-suppurative amœbic hepatitis that acute inflammation of the liver, with high fever, profuse sweating, extreme tenderness and marked leucocytosis following amœbic dysentery may continue for a considerable time without any actual abscess formation, as shown by the rapid subsidence of all the symptoms under appropriate treatment. In this condition there can

be little doubt that the hepatitis is set up by amœbæ carried to the liver in considerable numbers through the portal circulation, producing acute congestion and probably clotting in some of the smaller branches of the portal veins, where they may become entangled and undergo degenerative changes without being able to escape through the vessel walls to break down the liver substance into an abscess. As long as the organisms are widely distributed in small numbers through the organ no suppuration may take place, but if at any one or more parts of the liver they should chance to be sufficiently numerous to produce clotting in a number of contiguous vessels, to such an extent as to cut off the circulation through a small part of the liver, then a necrotic focus will be formed, which will produce softening of the vessel walls, and enable the amœbæ to escape and break down the liver substance. Once this process has been started the organism will invade the vessels of the surrounding tissue, as seen in the wall of an advancing liver abscess, producing further clotting and breaking down of another layer. The abscess thus commenced will extend by disintegration of concentric layers, until it becomes limited by a fibrous capsule, formed by the reaction of the liver substance, when the cavity will continue to enlarge by the secretion of pus from the containing wall and expand the organ until eventually a huge single localised tropical abscess results. All the very various degrees of amœbic abscess of the liver, from the most acute multiple ones, arising within a week or ten days, to the chronic single ones of months' duration, may thus

be readily explained as being solely caused by this protozoal parasite.

VARIETIES, PROGRESS, AND COMPLICATIONS OF TROPICAL LIVER ABSCESS

Before the days of early surgical interference tropical liver abscess commonly ran a long and varied course, frequently involving surrounding cavities or viscera, in accordance with the part of the organ in which they arose. Among native patients, more especially, such terminations are still not infrequently seen on account of their habit of coming to hospital only after having suffered for months and tried all kinds of quack remedies. The complications which may thus arise are numerous, and often present considerable difficulties in arriving at a correct diagnosis. For example, in one obscure abdominal case post-mortem examination revealed an abscess of the left lobe of the liver opening into the stomach, together with strangulation of the small intestine by extensive fibrous peritoneal adhesions, secondary to amœbic dysentery of a chronic nature. A study of the various conditions observed post-mortem in 164 fatal liver abscesses during the last thirty-five years at the Calcutta Medical College Hospital, will best enable the relative frequency and importance of the different terminations of the disease to be described. The subject is further complicated by the frequency with which two or more large abscesses may be present at the same time, as well as multiple small ones.

The Relative Frequency of Single and Multiple

Amœbic Liver Abscess.—In the first place it is important to know what proportion of cases are single and multiple respectively, for the latter will be less rapidly fatal and more amenable to treatment. As the records go back over so many years, during which the treatment of the disease has undergone considerable modification, I have divided them up into two periods. The first includes all the post-mortems up to 1886; the second those from the latter date to 1908. The cases showing multiple abscesses have been subdivided into two groups. One group includes those in which two or more large or moderate-sized, well-circumscribed abscesses were found, which are clearly similar in nature to the typical single large abscess. The other group show one or more large or fair-sized cavities, together with a number, sometimes very many, small acute suppurative points, evidently of more recent and acute formation, and quite different in character from the fibrous-walled localised collections of the former class. These last multiple acute abscesses are commonly accompanied by well-marked dysentery, and they run an acute course not amenable to surgical measures, although I believe they are readily preventable in the pre-suppurative stage by the treatment already described. When, however, patients only come under observation in this late stage no treatment is likely to be of any avail. In others small multiple abscesses are found after death in addition to a single large cavity of much earlier date, which has been opened some time before the fatal event. Here the multiple abscesses must have formed after the operation in one of two ways. Firstly, from continued

infection of the liver from a persistent amœbic dysentery, perhaps of a latent type, which has not been treated with ipecacuanha. This is not an uncommon event, but one which is easily preventable by the use of the same drug which is effective in pre-suppurative amœbic hepatitis. Secondly, fresh suppuration may be due to the infection of the original large abscess cavity, after it has been opened, by septic bacteria. That the latter is not very rare is clear from the fact that in several of the post-mortems of the last two decades pyæmic abscesses were found both in the liver and in other organs such as the lungs, spleen, and brain, in addition to typical opened tropical abscess with thick fibrous wall. This septic complication is exceedingly difficult to prevent in a damp, hot climate as already explained. It is noteworthy that the figures in the table below show a larger proportion of the combination of a single large abscess with a number of small ones during recent years than before 1886. This is probably partly due to the recovery of a greater proportion of single liver abscesses with improvements in surgical treatment, and also in part to the greater neglect of the ipecacuanha treatment of acute hepatitis, which was empirically advocated by Maclean and Norman Chevers many years ago, and recently revived and placed on a more scientific basis by the writer.

The following table shows the number and proportions of the different forms of liver abscess just described.

These figures show that just over half the total fatalities were single abscesses. The recovery rate

during the last two decades is just 40 per cent. (see figures under mortality), which will almost invariably be composed of single abscess cases. To get the proportion of single abscesses among the total admissions we must add the 40 per cent. of recoveries

THE FREQUENCY OF SINGLE AND MULTIPLE LIVER ABSCESS POST-MORTEM

	1873–86.		1886–1908.		Total.	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Single abscess	33	55·9	52	49·5	85	51·8
Two or more large abscesses . .	16	27·1	23	21·9	39	23·8
Large plus several small . . .	10	17·0	30	28·6	40	24·4

to half the deaths among the 60 per cent. of fatalities, and we thus find that 70 per cent. of the total admissions are single abscesses. There is evidently much room for improvement in the death-rate if any safer and less exhausting method of treatment than the open operation can be devised.

The Frequency and Distribution of Two or more Large Abscesses.—Among the cases showing more than one localised collection of pus in the liver the number and distribution was as follows.

Two abscesses	17	44·7 per cent.
Three ,, ...	10	26·3 ,,
Four ,, ...	7	18·4 ,,
Over four	4	10·6 ,,
All in the right lobe of the liver . . .	15	
Abscesses in both lobes	13	
All in the left lobe	0	

Thus in nearly half the cases only two abscesses

were present, in one-fourth three were found, and in the remaining 29 per cent. four or more. I have records of several cases in which more than one liver abscess has been opened and drained during the admission, but in only one of them did recovery take place. Sir Havelock Charles mentions a recovery from three liver abscesses, but such cases must be exceedingly rare. It is obvious that very few patients with such a serious illness as two or more large collections of pus in the liver will be in a condition to stand the shock and exhaustion of each being opened and drained. Even when close together they do not tend to drain into each other on account of the dense fibrous wall which usually separates them, while nearly half of the above multiple cases showed abscesses in both lobes of the liver. Yet these very unpromising cases under ordinary surgical treatment form a considerable proportion of the total admissions for liver abscess. Possibly some of them may be saved in future by my plan of repeated aspiration and injection of quinine, by which means more than one collection of pus could be readily dealt with, if recognized and located by exploration, guided when possible by previous X-ray examination.

Distribution and Course of Single Liver Abscess.—1. **Abscess of the Left Lobe.**—Only 14 out of 85 single abscesses were in the left lobe, that is, 16·4 per cent. One involved both lobes. On account of their small size, left-lobe collections of pus become clinically evident while the abscess is still small and readily amenable to surgical treatment. Uncomplicated cases are therefore rarely fatal. Thus, among

the 14 cases examined post-mortem no less than 13 showed some serious complication due to involvement of surrounding viscera, as will be seen from the following data.

COMPLICATIONS OF LEFT-LOBE ABSCESSES

Supra-hepatic abscess	1
Abscess in the base of the right lung	1
„ „ left lung	3
Abscess opening into the pericardium	2
Suppurative pericarditis without perforation	1
Sub-hepatic abscess	1
Abscess opening into the stomach	2
„ „ „ and pericardium	1
„ opening into the omental bursa	1
Uncomplicated	1
Total	14

Most of these complicated cases occurred among the earlier records, but they are still met with in patients admitted late in the disease. In two cases opening into the pericardium, as well as in the case of pericarditis without perforation, no less than 20 oz. of pus were found in the sac. The involvement of the base of the left lung is important to bear in mind, as it is much rarer than that of the similar complication at the right base secondary to right-lobe abscesses, so may easily be overlooked. On the other hand, when a left-lobe abscess bulges on the under-surface of the liver adhesions are quickly formed as a result of localised peritonitis, and it tends to open into the stomach. The tendency of left-lobe abscesses rapidly to spread to surrounding structures indicates the necessity for early surgical measures in their treatment.

Large Abscesses of the Right Lobe.—On account

of the much greater bulk and deeper situation of the right lobe of the liver large amœbic abscesses occur much more frequently and attain a greater size before implicating surrounding parts. They show the same marked tendency to incite the formation of adhesions when they reach the surface of the organ, and may thus open through the diaphragm into the bases of the lungs or into the gastro-intestinal canal, or even discharge externally, without any of their contents escaping into the pleural or peritoneal cavities. The commonest position of right-lobe abscesses is in the upper posterior part coming to the surface just beneath the diaphragm and rapidly forming adhesions to it. Those situated more anteriorly produce enlargement of the organ downwards and come into contact with the anterior abdominal wall just below the costal margin. Less frequently they appear on the under-surface of the lobe, when they may open into the colon or duodenum, or occasionally form a retro-peritoneal abscess extending down into the lumbar region. The frequency of these various terminations, together with some rarer ones met with in the thirty-five years' Calcutta records, may be seen from the following data.

By far the most frequent complication is the spread of the disease through the diaphragm to involve the base of the right lung. It is especially noteworthy how rarely empyema results in such cases owing to failure of the formation of adhesions between the base of the lung and the perforated diaphragm. Yet, when the pleural cavity is opened in draining a liver abscess cavity through the diaphragm before such adhesions have taken place,

fatal suppurative pleurisy only too frequently results. In analysing the cases the striking fact was ascertained that among fifty right-lobe abscesses in the post-mortem records up to 1886 in none did empyema follow operation, which during those days was most commonly performed at a late stage of the disease when adhesions had formed. Yet subsequently to that date this serious complication of the trans-pleural operation occurred in no less than sixteen

COMPLICATIONS AND TERMINATIONS OF RIGHT-LOBE LIVER ABSCESS

Peri-hepatic suppuration in addition	4
Secondary abscess in the base of the right lung	26
Empyema preceding operation	3
,, after operation through the right pleura	16
,, doubtful if after operation or not	3
Opening into right flexure of the colon	3
,, ,, cæcum	1
,, ,, duodenum	1
,, ,, pericardium	1
,, ,, inferior vena cava	1
Acute general peritonitis without operation	3
,, ,, ,, following operation	10
,, ,, ,, of omental bursa	3
Post-peritoneal secondary abscess	1
Hæmorrhage after operation	5
Total	81

out of ninety-nine right-lobe abscesses, and possibly in three more. Similarly, in the earlier series, peritonitis only once followed the opening of a liver abscess by the abdominal route, while in the later cases this fatal complication occurred nine times. In one case a large thin-walled abscess had been aspirated only. Acute peritonitis followed, which was found post-mortem to have been caused by a rupture of the wall at its thinnest part about one

inch from the puncture; doubtless by hydrostatic pressure at the time of the puncture. Earlier operations must have saved some cases from developing serious complications, but it is clear that incisions across the pleural and peritoneal sacs before adhesions have formed add grave risks to the operation.

The next most frequent complication is opening of the abscess into the colon or duodenum, and in one case into the cæcum after tracking down along the colon. None of the right-lobe abscesses opened into the stomach. One abscess in the left upper part of the right lobe opened into the pericardium, while another near the posterior inferior surface perforated the inferior vena cava.

Hæmorrhage after Operation caused death in five cases, all during the more recent years of early operations. In four the bleeding took place into the abdominal cavity following puncture of the liver, while in one an abscess, which had been opened through the thoracic wall, was filled with large blood-clots.

Peri-hepatic Abscesses.—We have already seen that amœbic abscesses of the liver tend to involve surrounding structures. They may thus form the so-called supra- and sub-hepatic abscesses about which much has been written. The question arises whether an amœbic abscess may originate in one of these positions, without the liver itself having been first involved. The post-mortem appearances may at first sight suggest such an occurrence, the collection of pus being bounded on one side by what looks like a thickened capsule of the liver. If, however,

microscopical sections through this wall are examined it will be found that the liver substance has been involved and the limiting membrane is but the deeper fibrous wall of a primary abscess of the liver, the superficial part of which has merged into the peri-hepatic collection of pus. I have carefully examined several such cases, as well as the post-mortem records of many more, and have never been able to satisfy myself that any amœbic peri-hepatic abscess arose primarily outside the liver itself. What happens is that when a superficial amœbic liver abscess opens into some surrounding area, the original cavity soon contracts down to leave but a slight excavation of the surface of the liver, and the primary seat of the suppuration is thus obscured. For example, a large amœbic abscess affecting the greater part of the lower lobe of the right lung may, at the time of death, be only connected with its origin in the upper surface of the liver by a small perforation of the diaphragm, leading to a depression in the surface of that organ admitting but the tip of the finger: the contents of the hepatic cavity having all been discharged into the lung abscess. The precise nature of such cases may be impossible of recognition at the time of the operation for opening a supra-hepatic or secondary lung abscess.

Old Encysted Liver Abscess.—It is well known that tropical abscess in the liver may occasionally be encysted and dry up, spontaneous cure thus resulting. That this is not an extraordinarily rare event is shown by the fact that no less than seven such instances are recorded in the Calcutta post-mortems on patients dying of other conditions, while in two

more an encysted abscess was found in addition to an active amœbic one in the liver. In one instance I found an encysted abscess with smooth walls and containing no amœbæ, together with two recent ones containing the protozoal parasites in an active form. The frequency of these cases is of particular interest and importance as an encouragement to imitate and assist nature's method of cure, as by aspiration of the pus and injection of some substance which will destroy the causative amœbæ.

SYMPTOMS AND PHYSICAL SIGNS

The foregoing account of the very varying course and complications of amœbic liver abscess will have prepared us to expect equally marked differences in the clinical symptoms of this serious disease. These are indeed so great that clear ideas on the subject can best be conveyed by subdividing the subject according to the degree of acuteness of the cases, it being clearly understood that they shade off one into another, so as to form a regular gradation, from the fulminant multiple abscesses, to the most insidious chronic ones, with few or no local symptoms leading the observer to suspect the liver as the origin of an obscure illness. Between these two extremes lie the subacute cases which constitute the most frequent and typical condition.

Fulminant Multiple Abscesses of the Liver.— These are fortunately somewhat uncommon, only 12 per cent. of the Calcutta European Hospital cases during the last nine years having been of this type. In one of these the total duration of the hepatitis before death was six and seven days respectively,

in another eleven days, and in the remaining two sixteen and eighteen days. In one such case the patient developed acute hepatitis following a chill at a dance. When I first saw him soon afterwards he had no leucocytosis and I advised ipecacuanha. I had not then devised the method of giving it in keratin capsules: he vomited and his doctor left it off. I saw him again a week after, when the liver had increased considerably in size and was extremely tender, whilst leucocytosis was now present. He was operated on the same day and the liver found to be riddled with abscesses breaking down one into another and with no localising fibrous wall; he died the same day. The acute suppurative stage was here certainly under one week's duration. The only chance of saving such cases is the early and persistent use of the ipecacuanha treatment, or, better still, emetine injections, from the first onset of the acute hepatic symptoms. In almost every case of this fulminant type there is a clear history of dysentery, generally within a short time previously and frequently persisting during the development of the hepatitis, so that the origin and nature of the disease are easily recognizable at an early period. The symptoms are those to be described under the subacute type in an aggravated degree. There is fever of high remittent type with rapid rises and falls of the temperature curve, frequently with rigors accompanying the exacerbations and nearly always very copious sweats with the declines. More rarely continued fever may be present. The liver rapidly enlarges and becomes acutely painful and tender, so that the weight of the bed-clothes cannot be tolerated.

A slight degree of jaundice is more frequent in this form than in less acute cases.

Subacute and usually Single Abscess of the Liver.—In this class the great bulk of cases fall, so that it best illustrates the usual symptoms and course of the disease. The following description is mainly based on an analysis of full notes of sixty consecutive cases treated at the European Hospital during nine years, the great majority of which I had an opportunity of watching, and on a much larger number in the Medical College Hospital.

Fever.—The premonitory fever in the pre-suppurative stage has already been fully illustrated by a number of cases in Chapter VI. The type of fever in cases with actual abscess formation was variable. In over half it was of the remittent variety, usually falling to below 100° in the morning and rising to 103° or 104° in the evening, but in one-fifth of the cases it was of a higher remittent type, not falling below 100° for several days together. In only one-seventh was a high continued fever recorded, that is, a temperature keeping above 101° and not varying more than 2° F. in the twenty-four hours, these cases being commonly fatal, or at least very severe. In one-fifth the temperature was intermittent in character, while in two out of fifty-seven it was normal for the few days the patient was in hospital before the abscess was opened. Among native patients, coming to hospital with a large bulging liver abscess, it is by no means rare for the temperature to remain quite normal as long as the abscess is intact, although unfortunately the almost inevitable bacterial infection which

follows the open operation is commonly accompanied by a rise of temperature. Thus, the degree of fever is highest in actively enlarging, deeply-seated abscesses, whilst in the more chronic type, especially when the tension is reduced by the abscess bulging through the capsule and making its way towards the surface, the fever is less, and may even entirely subside, only a history of its having been present at an earlier stage being obtained.

Copious Sweats are a frequent symptom, especially in the more acute cases, and may produce two or more depressions in the temperature curve within twenty-four hours. They may be so copious as to soak through the bed-clothes.

Jaundice is not a marked symptom of amœbic hepatitis, although a slight degree may be present in acute cases. In the more slowly developing abscesses it is usually absent altogether. In one patient in whom intense jaundice was present, sterile amœba-containing pus was aspirated from the liver, after which the jaundice decreased somewhat. He died a few days later, when a very large single acute abscess was found occupying the greater part of the right lobe and containing large sloughs. It had completely dissected out the neck of the gall bladder and pressed on the bile ducts, which, however, readily allowed the passage of a probe. Such pressure had been suspected by me during life.

The **General Condition** of the patient is very variable. Usually there is great weakness and exhaustion with rapid wasting and loss of weight. The appetite is usually, but not always, lost. The facial expression is anxious and pinched.

The **Local Symptoms** will vary from mere discomfort and heaviness in the right hypochondrium in the more insidious cases, to severe pain and tenderness in the acute ones. A very common symptom is inability to lie on one or other side. Usually the patient cannot turn over on to his left side on account of a dragging pain due to the weight of the enlarged organ causing some displacement on movement. If the abscess is situated in the upper part of the liver just beneath the diaphragm, the pain may also be referred to the tip of the right shoulder or even pass down the inner side of the right arm. This symptom was seldom noted in abscess of the left lobe. It is most frequent, and indeed rarely absent, in those right-lobe abscesses which make their way through the diaphragm to involve the base of the right lung. When the abscess involves the anterior portion of the liver the organ is enlarged below the costal margin, and the pain is felt chiefly in the right hypochondrium and epigastrium. In left-lobe abscess it may extend into the left hypochondrium, where I have known a liver tumour to be mistaken for an enlargement of the spleen. The liver may be so tender that the abdominal wall becomes rigidly contracted over it so that the edge cannot be felt, and the degree of enlargement can only be ascertained by light percussion. Friction may occasionally be heard due to localised peritonitis which results in the formation of adhesions over the advancing abscess. At a later stage, when a bulging swelling has formed in the epigastrium, there may be little or no pain and tenderness, especially in native patients.

All the foregoing symptoms, including even a slight degree of tumour formation in the epigastrium, are common to both the pre-suppurative stage and to the actual abscess formation in the liver. In fact there is no symptom, other than some of the physical signs still to be mentioned, by which it is possible positively to say that pus has already formed in the organ. Hence before marked tumour formation, indicative of a localised abscess, has made its appearance, the only way of deciding this question was to do an exploratory puncture under an anæsthetic. Unfortunately such punctures are far from being the harmless procedures which might be gathered from some text-books, several fatal hæmorrhages following them having already been mentioned. This subject will be further dealt with under the head of treatment.

The Duration of Symptoms before Local Physical Signs of Liver Abscess are present.—Before all cases of acute hepatitis were treated with ipecacuanha at the European Hospital, it was a common event for a patient to be admitted some time before signs of liver abscess developed, although such cases do not now occur there. The duration of illness before abscess of the liver was recognizable has been worked out from the histories and notes of the cases, and the data are given in the following table.

The short course of multiple abscesses has already been pointed out. Next to these come small abscesses in the left lobe of the liver, which rapidly produce local swelling in the epigastrium within one to four weeks of the first symptoms. The larger right-lobe abscesses, coming to the surface in

the right epigastrium, are very much more variable in their size and in the duration of the symptoms in accordance with the depth at which they arise. In the still more deeply-situated abscesses in the upper part of the right lobe beneath the thoracic wall, the duration of the symptoms before operation was over a month in a slight majority of cases, whilst in only two was the time recorded as less than two weeks. One of these short cases was diagnosed early by a blood

DURATION OF SYMPTOMS BEFORE LIVER ABSCESS IS CLINICALLY EVIDENT

	Multiple.	Left lobe.	Right lobe pointing through—				
			Abdominal wall.	Ribs.	Lung.	Total.	Per cent.
Under 1 week . . .	2	—	—	—	1	3	5·2
1 to 2 weeks . . .	1	2	1	2	2	8	13·4
2 weeks to 1 month . .	2	2	4	8	3	19	32·9
1 to 2 months . . .	—	—	2	5	—	7	11·9
Over 2 months . . .	—	1	3	8	6	18	30·5
Time doubtful . . .	—	2	1	1	—	4	6·7
Total	5	7	11	24	12	59	
Percentage	8·4	11·9	18·6	40·7	20·8		

examination and X-rays. The last group includes right-lobe abscesses opening through the lungs. Half of these had a history not exceeding a month, including one of less than a week, but some of these doubtless belonged to the insidious variety which developed without any definite localising symptoms pointing to the liver in the earlier stages. The remaining half had histories of over two months' duration, two of the patients having been ill two

and four months respectively, so that this form is commonly the most chronic of all. Taking all the varieties together, only one-fifth had a history not exceeding two weeks, one-third from two weeks to a month, and nearly one-half a duration of over one month. It is impossible to say in each case the length of time which elapsed before actual suppuration took place, and, consequently, how long an abscess had been present before it made its presence felt. Still, it is clear that the more deep-seated the position of the pus, the longer is the latter period and the larger is the abscess likely to be, and vice versa.

THE DIAGNOSTIC PHYSICAL SIGNS OF LOCALISED LIVER ABSCESS

The local physical signs of tropical liver abscess vary widely according to the position of the collection of pus, so that each of the classes shown in the above table must be separately described.

Abscess of the Left Lobe of the Liver.—Among the European Hospital cases 11·9 per cent. belonged to this class, while at the Medical College Hospital, where the great majority of the patients were natives, the proportion of left-lobe abscesses was 18·3 per cent. They frequently form prominent swellings in the epigastrium, usually accompanied by local pain and tenderness. In a late stage they become adherent to the anterior abdominal wall and present evident fluctuation, when there may be very little pain. Such cases may be very easily mistaken for an abscess in the abdominal wall itself, and I have known a liver abscess pointing in this position to be opened as such in the out-patient

department, its origin in the liver being only recognized on the escape of a large amount of the characteristic thick reddish pus of an amœbic abscess. Left-lobe abscesses bulging on the under-surface of the liver present greater difficulties in diagnosis. They produce signs of localised peritonitis in the upper abdomen, and tend to open into the stomach if not detected and evacuated in good time. In one patient, who had been unsuccessfully explored in several places for liver abscess, a quantity of typical pus was vomited on the following day, and he eventually made a good recovery by nature's method of cure. A disproportionately great increase in the liver dullness in the epigastric region accompanying acute hepatitis would indicate the probability of suppuration having taken place in the left lobe. Still more difficult of localisation is an abscess in the upper edge of the left lobe, which may only reveal itself by the suppuration extending to the pericardium or base of the left lung.

Right-Lobe Abscess in relation with the Anterior Abdominal Wall.—This class is a fairly large one, as an abscess in the anterior and lower part of the right lobe enlarges the organ downwards into the right hypochondrium. They only differ from the common form of left-lobe abscess in the swelling being placed more to the right and much more frequently attaining a large size. They form local tender swellings, producing marked extension of the liver dullness downwards below the costal margin, while the lower ribs may be pushed somewhat outwards and upwards by the tumour. Friction sounds may sometimes be heard over them, but disappear

as adhesions are formed to the parietes, when superficial œdema may appear. In some very advanced cases a fluctuating swelling, continuous with the liver dullness, may extend far down into the right lumbar region and even reach the iliac area. If evacuation occurs into the colon or duodenum liver pus may be passed in the stools coincidentally with a marked reduction in the extent of the liver dullness, and recovery may eventually take place.

Abscess of the Right Lobe in relation with the Thoracic Wall.—This is the commonest situation of a large single liver abscess, no less than 40·7 per cent. of the European series and 45·5 per cent. of the operation cases among natives belonging to this variety. Owing to the less yielding nature of the thoracic, as compared with the abdominal wall, these abscesses are longer in producing clear indications of their presence, and cause greater difficulties of diagnosis in their earlier stages. The first physical sign will be a marked increase of the liver dullness, mainly in an upward direction, but also extending below the costal margin to some extent. Then bulging of the right lower ribs with an increase in the circumference of the chest of that side will appear. On auscultating the base of the right lung there will be diminution of breath sounds, due to cessation of the movement of the right half of the diaphragm, which is readily demonstrable with the aid of the X-rays. The lower costal spaces may be wider than normal, and in advanced cases they will be full and even present actual fluctuation. Localised œdema of the superficial parietes is often a

valuable diagnostic sign of suppuration having taken place, and one which some surgeons consider to be certain evidence of pus. I have, however, several times seen it quite distinct in cases of acute hepatitis which rapidly yielded to the ipecacuanha treatment, so that, at any rate, its presence is not a certain sign that surgical interference is necessary. When the abscess is nearing the surface the skin may in addition present a glossy appearance, indicating the position in which it will point. This variety often reaches a large size, and may contain from one to three or more pints of pus. Exploratory puncture is more frequently required to confirm a suspicion of liver abscess beneath the ribs than in the case of the former varieties.

Liver Abscess opening through the Lungs.—This variety comprised 20·8 per cent. of the European series, but only 7·8 per cent. of the native cases. The latter figure is doubtless an under-estimate, as this class is commonly admitted to the medical wards, and some of the notes may not have reached my hands. These abscesses may be very acute, and rapidly perforate the diaphragm to form a secondary abscess in the base of the right lung. More frequently they belong to the chronic insidious class, with obscure fever, being eventually quite unexpectedly evacuated through a main bronchus, producing copious thick, reddish, purulent expectoration with little or no odour; differing widely in the last respect from most primary pulmonary abscesses. In the acuter cases there will be similar physical signs to those described in the last class, with the addition of those dependent on involvement of the

lung, namely, dullness and marked or total loss of breath sounds at the right base, often extending up to the angle of the scapula. Vocal resonance may be increased at first, due to inflammatory consolidation of the lung, but diminished as it breaks down into pus. X-rays are of great diagnostic value here by revealing a dense shadow in the affected part of the lung, in addition to the fixation of the diaphragm so commonly present in hepatitis alone. I have, however, once seen a shadow appear at the base of the right lung during subacute hepatitis, which quite cleared up under ipecacuanha, so that presumably actual suppuration had not taken place. Great difficulty may arise in determining whether a shadow and dullness at the base of the right lung, continuous with that of the liver, are due to primary pulmonary disease, or are secondary to hepatitis. The blood changes to be described later are here of great assistance.

Insidious Chronic Abscess of the Liver.—Lastly, we have a class of very slowly forming liver abscesses, which present great difficulties in their recognition. The illness begins with a feeling of being out of sorts, and on taking the temperature a slight evening rise will be found, sometimes not exceeding 100° F. The bowels may previously have shown some irregularity, such as occasional slight diarrhœa, commonly alternating with constipation, but often there is no history of any recent definite dysenteric attack. The patient is usually treated for malaria or low fever with full doses of quinine for a long period without deriving any benefit, or he is sent for an equally ineffective change. On

further examination slight enlargement of the liver dullness may be detected, or the edge of the organ may be felt below the ribs, but there is no pain or tenderness, only a dull, heavy or dragging sensation in the right hypochondrium. The patient will have lost much weight, his appetite will be poor and all his former energy abated. At length one day he develops a cough, and his physician is astonished at his suddenly expectorating a large quantity of pus, similar in appearance to that of a tropical liver abscess, and the obscure illness at once becomes intelligible. In one such case a distinguished medical man, after retiring from the Indian service on account of a long illness, coughed up a liver abscess in England, and recovered his health once more. In another, a Government official had for four months been suffering from an obscure low fever, which would not yield to quinine. The day before he was to sail for England on leave he began to cough up pus. A blood examination indicated that it was coming from the liver; he went into hospital, where an hepatic abscess was opened and he eventually recovered after a long illness. In other cases enlargement of the liver becomes more pronounced and leads to an exploratory puncture which locates the abscess. It is in cases of chronic hepatitis such as these that we possess in the blood changes described in Chapter VII a method of diagnosis from other chronic tropical fevers, leading to a line of treatment which will assuredly prevent abscess formation if the condition is detected in time. Hence the importance of bearing this difficult class of case in mind, and not negativing the possi-

bility of serious liver disease because there are no definite signs implicating this organ. Should such a chronic hepatitis fail to yield to a course of ipecacuanha of two or more weeks' duration, or emetine injections for one week, the advisability of an exploratory puncture of the liver must be considered, and X-rays may be of use by revealing the shadow of a deep-seated, well localised collection of pus in the organ.

The Blood changes in Liver Abscess and their Diagnostic Value.—A few years ago I looked on the presence of leucocytosis as an important diagnostic sign of the presence of abscess formation in cases of acute hepatitis, in accordance with the general opinion on the subject. I have, however, recently shown that even high degrees of this change may be present in the pre-suppurative stage of amœbic hepatitis. Illustrative cases will be found on pages 143–50, as many as 28,500 white corpuscles having been recorded in a case which completely subsided without abscess formation. The following data show the degree of leucocytosis in a series of liver abscess cases in European patients, which will be seen to be closely similar to those of hepatitis without purulent collections. The two cases with the highest counts were both instances of rapidly fatal multiple abscesses with 35,000 and 38,000 leucocytes respectively. With the exception of these extreme cases the degree of leucocytosis present does not appear to be of much prognostic value.

Of greater importance than the total count is the proportion of the polynuclears present. In Chapter V

I have pointed out that the characteristic feature of the leucocytosis of amœbic hepatitis is the less marked increase of the polynuclears than is usual in ordinary septic bacterial inflammations. This is equally true of both the pre-suppurative and the suppurative stages of the disease. In the majority of the cases the polynuclears form from 70 to 80 per cent. of the whole, but in chronic liver abscesses

LEUCOCYTOSIS IN LIVER ABSCESS

	Recovering cases.	Fatal cases.	Total.
11,000 to 15,000	2	4	6
15,000 to 20,000	4	6	10
20,000 to 30,000	1	2	3
Over 30,000	0	2	2
Total	7	14	21

they may even be below 70. On the other hand, in a few very acute ones, especially when multiple abscess formation or secondary bacterial infection is present, they may rise to over 80, but I have only once seen as many as 90 per cent.

In all the cases of tropical liver abscess examined by me in the European hospital some degree of leucocytosis was present. In the more chronic and late admissions among native patients I have several times found the total number of leucocytes to be less than 10,000, no actual leucocytosis being present even with a very large abscess. In these cases, however, there has always been, in my experience, a marked degree of anæmia, so that the leucocytes were almost invariably relatively increased to a

considerable extent as compared with the number of the red corpuscles. For example, the first case of the kind I met with showed red corpuscles 2,860,000, white 8,625, ratio of white to red 1–332. The red corpuscles were therefore reduced by nearly one-half, so that the proportion of white to red was double the normal. A similar proportion in a blood containing a normal number of red corpuscles would have been 16,000 white, so that a relative leucocytosis was actually present. I did not recognize this at the time, and thought that the count excluded the presence of suppurative hepatitis. On the death of the patient not long after three pints of pus were found in the right lobe of the liver. I have several times since found a similar relative leucocytosis in liver abscess cases and recognized its significance.

The Diagnostic Value of X-Rays.—A very useful aid in the diagnosis of deep-seated inflammatory conditions of the liver has been placed in our hands by the discovery of the X-rays. In the first place, examination with the screen allows of the detection of any diminution in the movements of the right side of the diaphragm, which is an important early sign of acute hepatitis, especially when the upper surface of the liver is affected. This sign is very commonly present in the early pre-suppurative hepatitis, and is in no way an indication of actual pus formation. The right diaphragm may be nearly or quite motionless, while resumption of its action is one of the characteristic signs of the subsidence of the liver inflammation. When the liver is enlarged, or an abscess is present in its upper part, the right diaphragm may be raised above its normal level as

well as being fixed. Valuable information is also obtainable regarding the spread of the inflammatory trouble to the base of the right lung, which will be indicated by a loss of transparency immediately above the diaphragm. If the shadow is extensive in this position it will generally mean a secondary abscess in the lung, but a case has already been mentioned in which a slight shadow was seen there without any abscess developing.

Of much greater importance is the detection of a definite localised increase in the density of the liver shadow, for when well marked it may be an important sign of the presence, as well as an indication of the position, of a liver abscess. In the thin left lobe comparatively small collections of pus may throw a well-defined shadow. In the thick right lobe, however, an abscess holding a pint or so of pus may fail to be revealed by the X-rays, as occurred in several of the comparatively early European series. The shadow is better marked in a well-localised chronic abscess with thick fibrous walls. Moreover, in at least one case a dense patch was seen in the liver shadow in which abscess was subsequently proved by a post-mortem not to exist, but this is much more exceptional than to find an abscess when no darker shadow was detected. In native patients, with advanced disease, the shadow cast by a liver abscess is more frequently quite distinct, and often of aid in precisely locating the collection of pus, although in this stage the diagnosis is usually clinically evident. On the whole the X-rays do not afford quite as much assistance as might have been expected, and some experience is required in drawing

reliable conclusions from the appearances seen. In particular the absence of any increased density of the liver shadow in no way negatives the presence of a collection of pus in the liver.

Terminations and Causes of Death in Liver Abscess.—The following table shows the causes of death in a series of fatal liver abscesses in European subjects, together with the period after operation at which it occurred:

	First week.	1 to 2 weeks.	2 to 4 weeks.	Over 4 weeks.	Total.
Shock and exhaustion . .	4	1	2	—	7
Hæmorrhage	2	—	—	—	2
Dysentery	1	—	—	—	1
Fever, ? septic infection .	1	2	2	2	7
Complications	—	2	—	1	3
Total	8	5	4	3	20

Of the two cases of fatal hæmorrhage one occurred on the day of the operation and one on the fourth day. Shock and exhaustion were the most frequent causes of death during the first week. The later fatalities were chiefly due to fever continuing after the abscess had been opened and drained. In several there was little or no rise of temperature for a few days after the operation, but it then recurred and continued until death. Most of these were almost certainly due to septic bacterial infection of the cavity, for it was repeatedly noted that an originally sweet discharge had developed a foul putrefactive odour. Another occasional cause of fever is the recurrence of acute hepatitis secondary to unhealed amœbic ulcers in the large bowel, but

this is preventable by the administration of ipecacuanha as soon after the operation as the patient can stand it. Fever persisting in spite of the wound being in a healthy condition has several times been stopped by this treatment during the last few years. Bacterial infection should also be preventable by the methods of sterile evacuation to be described later, which will also materially diminish the shock and exhaustion incidental to the open operation.

The Stay in Hospital after Operation of European patients who recovered from liver abscess is shown in the following table. Cases of cure by discharge of the pus through the lungs are also given.

	Under 1 month.	1 to 2 months.	2 to 3 months.	3 to 4 months.	Over 4 months.	Total.
After operation .	3	4	9	6	2	24
Opening through the lung	1	2	1	—	1	5

Of the three cases cured within one month the only one treated by the ordinary open operation was a very small left-lobe abscess containing but 1 oz. of pus. The second was a deeply-seated right-lobe abscess rapidly cured by my plan of aspiration and injection of quinine—the first case so treated. He was convalescent in a week, but was kept under observation for two weeks more, and seen again in perfect health over a year later. The remaining case was the first patient treated by sterile siphon drainage by means of my flexible sheathed canula described later. He was discharged cured with the wound soundly healed in twenty-four days from the operation. Of the four cases cured in from one to two months three were small left-lobe abscesses, the fourth a small right-

lobe one treated by resection of a rib, who left hospital on the fifty-eighth day after operation, so that all the right-lobe cases treated by the open operation took over eight weeks to heal, while almost one-half of them were over three months before discharge from hospital. Such lengthy illnesses are a very severe strain on the system, and subsequent long leave is almost invariably necessary before return to work. It is to be hoped that by improved methods these tedious and exhausting convalescences may be greatly shortened and ameliorated.

The Mortality.—This will vary with the class of patient and the stage of the disease in which he comes under treatment. Thus the death-rate is comparatively low among Europeans coming early under observation in a fairly good general condition. In the Calcutta European Hospital the mortality among sixty-four recent cases of which I have notes was 53 per cent., leaving 47 per cent. of recoveries. Among British troops in India for the fifteen years from 1894 to 1908 the fatalities averaged 56 per cent. and showed little yearly variation. At the Calcutta Medical College Hospital Captain J. W. D. Megaw analysed all the available clinical records for ten years up to the end of 1905, amounting to 292 cases, and estimated the mortality at about 60 per cent. Among 231 cases at the same institution of which I have notes, many at a later date than Megaw's, the mortality was 60·1 per cent., thus agreeing with his figure. In 1907 I found the mortality among all the cases, notes of which were in the hands of the registrar, was as high as 73 per

cent. among fifty-two cases, the open operation being in general use. A few patients taken away by their friends when in a hopeless condition are included in the deaths, while those leaving uncured, but improving, have been classed as recovered. This high mortality among the liver abscess patients of the very experienced surgeons of this institution is largely due to many of them coming to hospital in such an advanced stage of the disease as to have extremely little chance of surviving the shock and exhaustion of the copious discharges following incision of the abscesses, so that little improvement can be expected in the results from the methods hitherto in general use.

During the last few years better results have been obtained, especially in the formerly very fatal deep-seated right-lobe liver abscesses, by the adoption of my plan of repeated aspiration and injection of quinine without drainage, some apparently almost hopeless cases having thus been cured. Further experience will be necessary before the exact value of this plan can be estimated, but it is now certain materially to reduce the mortality of the disease, if given a trial in all suitable cases before the open operation is resorted to.

The Mortality of Different Varieties of Liver Abscess.—The figures given above show the mortality in a large number of liver abscess cases of all degrees of acuteness, positions, and stages treated by very experienced surgeons in a tropical country. The death-rate, however, differs greatly according to the position of the abscess and the direction in which it is opened. The following table, worked out

from a series of Medical College Hospital cases, illustrates this point:

MORTALITY IN DIFFERENT FORMS OF LIVER ABSCESS

Opened through abdominal wall.									Opened through chest wall.			Through lungs.		
Left Lobe.			Right Lobe.			Total.								
Cases.	Deaths.	Mortality.	Cases.	Deaths.	Mortality.	Cases.	Deaths.	Mortality.	Cases.	Deaths.	Mortality.	Cases.	Deaths.	Mortality.
33	4	% 12	51	30	% 59	84	34	% 40·5	79	58	% 73·4	13	6	% 46

The total mortality being nearly 60 per cent., it is clear that the small early left-lobe abscesses have only one-fifth of the average mortality, while taking all the abscesses opened through the abdominal wall the death-rate is but two-thirds of the total rate, and only a little over one-half of that of the large deeply-seated abscesses opened through the thoracic wall. Abscesses of the right lobe drained by the abdominal route have a much higher mortality than left-lobe ones, because they commonly reach a far larger size before being opened. The higher mortality of the transthoracic operation is partly due to the greater frequency of secondary purulent pleurisy, in these days of early operation before firm adhesions have had time to form. Those opening naturally through the lungs have a lower mortality than any other form except left-lobe ones, this being far lower in cases not operated on than in those in which the abscess is opened, partly due to the former including the less severe cases.

It is clear from these data that in estimating the results of any particular operation or line of treatment, the proportion of the different classes of cases in the series must be taken into account. Thus, in the less acute and less frequently multiple abscesses seen in patients in Europe, the results will necessarily be better than in a series treated in the tropics. Again, the comparatively low mortalities reported by some individual operators may in part depend on a certain amount of selection of cases, either conscious or accidental. For example, at the Calcutta Medical College Hospital a number of the most hopeless cases are sometimes operated on by the resident surgeon on their admission as urgent cases, and will thus be excluded from the list of the visiting surgeon: greatly to the advantage of the statistics of the latter operator. In these advanced cases, often with evident fluctuation, the mortality will not depend on the particular hand which thrusts the knife into them, but on the well-nigh hopeless condition of the patient on admission. For this reason the figures of all the cases admitted to a large hospital given above afford the most accurate information regarding the true mortality of the disease in a tropical country.

PROGNOSIS

From the account already given of the great variations in the number, acuteness, size, and complications of amœbic abscess of the liver it is clear that the prognosis in any given case will depend on a number of factors, some of which it may not be possible accurately to gauge before operative pro-

cedures are undertaken. The most important of these are the following.

The Number of Abscesses present will clearly be the most essential element in the prognosis. Once the liver has become riddled with rapidly extending collections of pus the time to save the patient's life will be past. Fortunately, these cases are rare, and are sometimes accompanied by a hopelessly advanced amœbic dysentery. Even if only a small number of localised abscesses are present, the chances of successful treatment will be very much less than if there is only a single cavity, however large it may be, on account of the great difficulty of finding and evacuating each collection. Multiple abscesses of the liver, therefore, are most essentially cases in which prevention is much easier than cure, and as the value of the ipecacuanha and emetine injections in the pre-suppurative stage becomes generally recognized and acted on, this class of hopeless case will become more and more rare. Fortunately, even without this preventive method, 70 per cent. of all cases are single abscesses. The further remarks will apply to single abscesses alone.

The effect of the **Position** of a single abscess has been indicated in a preceding paragraph, and is closely related to the size the collection reaches before it can be recognized and adequately dealt with.

The **Size** of the abscesses is also an important factor, especially if they are submitted to the open operation, as has for many years past been the generally recognized method of treatment. In the first place, a large abscess will presumably destroy a greater amount of liver substance than a smaller

one. This, however, applies rather to very acute and often multiple collections containing large sloughs, than to single more chronic abscesses. The latter almost invariably have thick fibrous walls completely localising them, and microscopical sections show that immediately beyond this membrane the liver cells are commonly quite healthy. Moreover, a large single abscess quickly reaches the surface of the organ, and then increases in size by distending the thickened capsule and pushing on one side the liver substance without further destroying it. If long neglected, as is so often the case in native patients, the system becomes much enfeebled by the disease, leaving the patient unfit to stand the shock and strain of the exhausting discharge following the open operation. Recent experience of repeated aspiration and quinine injection to destroy the causative amœbæ without drainage has, however, shown that very feeble and emaciated patients, with an enormous single abscess containing three to six pints of pus, may rapidly improve and completely recover. It is clear, therefore, that the largest single amœbic liver abscesses do not commonly destroy sufficient of the secreting substance of the liver to make recovery impossible.

Bacterial Infection secondary to the Open Operation is a far more important factor than mere size in rendering the prognosis unfavourable. The practical impossibility of maintaining the sterility of the discharge has already been shown. The seriousness of such infections, even by organisms of low pathogenicity, has been acknowledged by such experienced surgeons as Sir Havelock Charles and Major G. C.

Spencer, Professor of Military Medicine at the Royal Army Medical College. The last writer has well summed up the question in the following words: 'The chief cause of this high mortality, apart from the presence of more than one abscess, or extreme debility of the patient before operation, is undoubtedly infection of the abscess cavity by pyogenic organisms through the open wound. This is extremely difficult to prevent, no matter how much care is taken: the large amount of viscid discharge necessitates frequent changes of dressings, air and pus are sucked in and out of the cavity by respiratory movements, and it is very difficult to keep the skin around the wound aseptic, especially in a hot, moist climate. The great majority of amœbic abscesses are sterile when first opened, and every surgeon with Indian experience is familiar with the usual course of fatal cases—the patient does well for the first few days after operation, then infection occurs, the temperature goes up again, and death from septic poisoning slowly but surely follows.'

If the abscess is a small one the patient may ultimately recover in spite of bacterial infection. The process of healing is, however, much delayed by this complication, as is clearly shown by the case related later of the sterile sinus of an abscess healed up to the surface in three days, and completely in seven with but a few drops of serous discharge.

The Presence of Active Dysentery is another important factor in the prognosis. In the first place it renders it more likely that multiple abscesses are present in the liver, or that further ones will continue to develop; and secondly, the dysentery may

increase and prove fatal after the liver complication has been successfully dealt with, as I have seen occur. The routine use of ipecacuanha or emetine in the after-treatment of liver abscess will do much to lessen these dangers.

TREATMENT

In dealing with the treatment of liver abscess it will be necessary first to describe the methods which have been in general use for many years past, and subsequently to deal with the modifications introduced by the writer, which have now been favourably reported on by several surgeons; revolutionary as they may appear to those to whom an abscess, whatever its course, can indicate nothing but the knife.

The Open Operation.—The usually accepted treatment is to localise, freely open and drain the abscess as soon as possible. Formerly some surgeons treated liver abscess by repeated aspirations without opening them. Thus in 1892 E. Lawrie, I.M.S., recorded 18 cases treated by repeated aspiration, of whom 15 were cured and the remaining 3 died of dysentery. In 5 more aspiration was followed later by opening and all recovered. Of the cases cured by aspiration 8 only required one such operation, 3 two aspirations, 3 three and 1 six aspirations. One case after being aspirated 27 times was eventually opened and the patient recovered. No harm appears to have been done in any case by the operation, and even when opening was necessary afterwards, the patients were often in a better position to stand

drainage. With the perfecting of the aseptic methods, which greatly reduced infection of the wounds by the more virulent types of bacteria, the plan of aspirating alone has been almost entirely abandoned by surgeons on account of its frequent failure rapidly to cure cases. It appears to be open to question whether the pendulum has not now swung too far the other way, aspiration being too much neglected.

Exploratory Puncture to Localise a Liver Abscess.—It is important to evacuate a liver abscess as early as possible before it has set up serious complications by involving neighbouring structures and cavities. When the presence of pus in the liver is either clearly evident, or has been rendered exceedingly probable by the failure of a course of ipecacuanha or emetine to abate an acute hepatitis, exploratory puncture should be undertaken without delay to locate the collection, everything being prepared for any further proceedings which may be required. A general anæsthetic is usually necessary for this purpose, but in debilitated subjects with advanced disease Sir Havelock Charles prefers local anæsthesia, as he considers chloroform to be badly borne in liver inflammation. A fine cannula should be used to lessen as far as possible the danger of hæmorrhage. In the absence of any definite indications of the site of the abscess the same surgeon first explores through the lowest thoracic space in the anterior axillary line, and then a space higher, the search being carried out in a systematic manner. The trocar should be inserted to a full depth, which according to Mr. Cantlie should not exceed three

and a quarter inches. Aspiration is then applied, and if the result is negative the cannula is slowly withdrawn, the suction being repeated at each step, but not during the actual withdrawal. If no pus is obtained a firm bandage, extending below the costal margin, is applied to support the liver, and a dose or two of calcium chloride given to increase the coagulability of the blood. With these precautions Sir Havelock Charles states that he has not been troubled with hæmorrhage into the abdomen, although other Indian surgeons have not been so fortunate in this respect.

Hæmorrhage after Exploratory Puncture of the Liver.—Four such fatalities recorded in the Calcutta post-mortem notes have already been referred to, and I know of others both at the Medical College and European hospitals, although few surgeons have the courage to report them. A notable exception is a valuable paper published in 1898 by Lieut.-Colonel Hatch, I.M.S., in which he narrates no less than six cases occurring in Bombay of this disaster. It is especially noteworthy that most of these cases occur in patients in whom no abscess is found by the exploratory operation, as has been proved by the absence of suppuration in the liver post-mortem. It appears, then, that there is the greatest danger of fatal hæmorrhage occurring as a result of such operations performed in the acute hepatic congestion of the pre-suppurative stage of the disease. These may be entirely prevented by never doing an exploratory puncture of the liver in any case in which liver abscess is merely suspected, without first treating the patient with a course of

ipecacuanha or emetine, as the rapid subsidence of the disease, if no abscess has formed, will obviate the necessity for carrying out the operation.

Some surgeons are so greatly impressed with the danger of puncturing the liver in these cases, that they advocate opening the abdominal cavity in every doubtful case, and locating the position of the abscess by palpating the organ before aspirating or incising it. A. Powell advised this procedure in 1898, and Wilson and Lane came to a similar conclusion in 1905. In early acute cases with absence of adhesions this plan is worthy of consideration, especially as it has the great advantage of enabling more than one localised collection to be detected and dealt with. In the more chronic fibrous-walled abscesses there is very little likelihood of serious hæmorrhage, whilst adhesions will limit the practicability of the suggestion.

Incision through the Abdominal Wall.—If pus is found with the aspirator the next step is to open the abscess at once. The incision will necessarily vary with the position of the collection. The simplest cases are those in which it is situated in the epigastrium or right hypochondrium, and can readily be reached by cutting through the anterior abdominal wall, either in the middle line, the linea semilunaris, or through the right rectus muscle. If firm adhesions shutting off the peritoneal cavity are present nothing can be simpler than to open and drain a liver abscess in this position. In early cases adhesions may be absent or insufficient, and the peritoneal sac has to be opened to reach the liver. The capsule of the organ must then be

carefully sutured to the abdominal wall before the abscess is opened, so as to prevent any pus entering the cavity. If difficulty arises owing to the softness of the organ, and the least doubt arises whether the peritoneal sac is completely and permanently shut off, it will be far safer to plug the wound with gauze and wait for two or three days, to allow of the formation of firm adhesions, before incising the abscess. The tension may be relieved, if thought necessary, by aspirating some of the pus through a fine cannula. When adhesions are present, but not very firm, the edges of the opening into the abscess should be sutured to the abdominal wall in the upper part of the incision, to give a stronger hold and prevent the retraction of the liver with the emptying of the cavity in it.

Incision through the Thoracic Wall.—Here, again, the operation is simple if the abscess has approached so close to the surface as to have obliterated the pleural sac over it by adhesions. It is nearly always advisable to resect two or three inches of a rib to allow of very free drainage, and then to incise the abscess cavity and insert a large rubber drainage tube. If the pleura is opened at the operation the two layers should be carefully sutured at the upper edge of the wound completely to shut off the serous sac from the site of the incision through the diaphragm. This muscle may also be united to the thoracic wall, if thought necessary, to prevent it falling away as the contents of the abscess escape, which would tend to separate the wounds through the chest wall and the diaphragm from each other and make the drainage less simple and free. It

would appear to be wise to resect as low a rib as possible to allow for any fall in the height of the diaphragm with the reduction in the size of the liver due to emptying the abscess. In very advanced cases necrosis of one or more ribs may be found and necessitate removal of the affected portions. After some of the pus has escaped a large drainage tube is inserted to the bottom of the wound, and a cross-piece, or other device, adopted to prevent it slipping in. When the abscess is deeply seated the aspirating needle should be left in as a guide in opening the abscess.

Manson's Method.—Another method of draining a liver abscess is that devised by Sir Patrick Manson. He uses a trocar three-eighths of an inch in diameter, through which he passes a rubber drainage tube stretched by a long stiletto, the extremities of which are placed in buttons tied into the ends of the tubing. On withdrawing the cannula and the stiletto the rubber tube contracts, fitting tightly into the puncture wound in the liver and serving to bridge over any passage through a serous sac, preventing pus from entering them and also lessening hæmorrhage. The end of the tube left in the abscess has several large holes previously cut in its sides for drainage, while the protruding end with the other button is cut off to let the pus escape by it. An ordinary small aspirating cannula is used to locate the abscess when necessary before inserting the large special one. This method does not appear to have been given the trial it deserves by surgeons in India. By combining it with siphon drainage (a long rubber tube joined on by a glass-piece being carried

into a vessel on the floor containing an antiseptic) sterility of the contents should be obtainable in a manner which is not usually possible with the open operation. Mr. Cantlie by this means has had 82 per cent. of recoveries in 100 cases: a remarkably good result even when allowance is made for most of his cases having been of the single and less acute varieties most commonly seen in patients invalided to England. Sterile daily washing out with quinine solutions might with advantage be combined with this method, to kill the amœbæ in the abscess wall. In the absence of special instruments the advantages of siphon drainage may be obtained by fixing one end of a long piece of large rubber tubing into the abscess cavity and carrying it through the dressings into a bottle of antiseptic under the bed.

The Author's Flexible Sheathed Trocar for Sterile Siphon Drainage and Quinine Irrigation.—In order to carry out sterile drainage in those liver abscesses in which the method of aspiration and quinine injection to be described presently fails to effect a cure, I have devised a trocar with a flexible sheath, which can safely be left in the abscess as a drainage tube. It is to be connected with a long rubber tube carried into a vessel containing an antiseptic lotion under the bed of the patient. This instrument has been made for me by Messrs. Down Bros., to whom I am much indebted for their care in making it. It consists of an aspiration trocar and cannula, the sheath of which is made of flexible silver-nickel tubing, so that it can safely be left in as a drainage tube which will accommodate itself

to the altered relationship of the traversed parts due to emptying the abscess cavity. The break in the cannula within the handle should be joined up by a piece of pressure rubber tubing, through which the trocar passes. This enables it to be clamped on withdrawing the trocar, so that no air is admitted in the process of connecting up the cannula with the aspirator or injection syringe. A plug is provided to fit the proximal end of the cannula for connexion with the tubing leading to the aspiration bottle. A silver Y-tube is also supplied to facilitate the daily aspiration and quinine injection. This tube can also be reversed so as to allow a current of lotion being run down one limb, past the inner opening of the other limb connected with the drainage cannula, into a vessel under the bed, which would exert a continuous suction action on the contents of the abscess cavity and thus keep it more completely empty. For irrigation purposes the single limb is connected by pressure tubing with the end of the cannula, and one of the branches by similar tubing with the aspirator. The other limb allows of sterile quinine solutions being injected by means of a glass syringe after aspiration without having to disconnect the tubes, this injection limb being clamped or closed with the fingers during aspiration. In passing the trocar through the cannula before use the end of the cannula should be supported by the fingers to prevent the sheath being unduly stretched. The inside of the tube is smooth, so that it can be readily sterilized after use. Experience has shown that the break in the tube in the handle is not absolutely necessary, and

Messrs. Down Bros. have also made for me a simplified pattern in which the proximal end of the cannula only projects for an inch beyond the flange which limits the depth to which it is inserted. A further slight improvement is the provision of a slit in the flange on either side, through which a piece of tape is passed and tied round the body or the ends fixed with strapping to keep the cannula from slipping out.

The whole principle of the instrument is to enable a liver abscess cavity to be drained aseptically, and daily washed out with sterile quinine solution to kill the causative amœbæ. The strictest antiseptic precautions are therefore essential, including boiling the quinine solution and the syringe used for its injection. When the abscess is deeply seated it must first be located by aspiration with an ordinary fine cannula, but without removing much of the pus. The flexible sheathed trocar is then inserted into the cavity, alongside the smaller one if thought advisable, and the latter withdrawn. On withdrawing the large trocar from its sheath the tube is connected with the aspirator and the cavity emptied as far as possible. From 2 to 4 oz. of a sterile bihydrochloride of quinine solution (10 grains to the oz.), is now injected into the cavity, and retained for five to ten minutes. The end of the cannula is then connected to a long large-calibre drainage tube, the distal end of which is carried into a bottle containing one in forty carbolic acid or other antiseptic. By placing the bottle beneath the patient's bed siphon action will be set up and keep the cavity drained. A small dressing

is now applied over the puncture wound, through which the tubing projects, the cannula being prevented from slipping out by strapping or tape.

The After-treatment is very simple as there are no copious discharges into the dressings, which need not be touched for some days. Each morning the rubber tubing is detached, the aspirator connected up to remove any thick pus which may not have drained, and the cavity irrigated with sterile quinine solution.

Case treated with the Flexible Sheathed Trocar. —The following notes of the first case treated with this instrument will sufficiently illustrate its advantages. A man, aged 24, was admitted to the Calcutta European Hospital under Dr. J. G. Murray, I.M.S., to whom I am greatly indebted for trying my method. He had suffered from dysentery recently and presented well-marked signs of a liver abscess beneath the right lower thoracic wall. Dr. Murray aspirated 10 oz. of pus through the ninth costal space in the mid-axillary line, only partially emptying the cavity. The flexible sheathed trocar was inserted by the side of the other, and siphon drainage established as above described. I found the pus to be sterile. On the first day after the operation a few ounces of pus had drained into the bottle, and a little thick material was withdrawn with the aspirator. An attempt was made to run in quinine solution through a funnel, but little entered. On the second day the discharge was less and only a few drachms of pus could be aspirated. Quinine solution was injected through a sterile glass syringe. On the third day only a little shreddy

pus had drained and only a few drops could be removed by aspiration. The cavity had already contracted so much that it would admit but half an ounce of quinine solution. Progress continued in much the same way, and within a week no pus could be got by the aspirator, and drainage was stopped at night, the tube being clamped. The cannula was kept in for a week more as a matter of precaution, although so long a period was probably unnecessary. Three days after its removal the four-inch sinus left by it had filled completely up to the surface with only a very few drops of serous discharge on the dressing, and in a week from the tube being taken out the wound was soundly healed and the patient left hospital. He was seen from time to time for upwards of a year, at the end of which his liver appeared to be quite normal under the X-rays. It is noteworthy that his stay in hospital after the operation was less than half the shortest time of that of any liver abscess case in which the open operation through the thoracic wall had been performed in the hospital during the previous nine years.

The above instance is sufficient to prove that the instrument fulfils the objects for which it was devised, and will allow of sterile drainage and quinine irrigation of liver abscesses, and thereby greatly simplifies and shortens the duration of after-treatment in these cases. During the last few years the still simpler method of aspiration and quinine or emetine injection, without drainage, has proved so effective in a number of cases as to limit the rôle of sterile drainage, but in cases in which repeated

aspirations fail to complete the cure the above plan is worthy of trial.

The Treatment of Liver Abscess opening through a Lung.—These cases often present considerable difficulty in deciding whether operative procedures are advisable or not. The majority make a good recovery without the necessity for surgical interference, while operative measures are often of considerable difficulty owing to the primary abscess in the liver rapidly contracting to a small size, and being then very troublesome to locate. In my European series out of five cases operated on three recovered and two died, while of seven cases not operated on five recovered and two died. One of the last was a man who refused any operation, even before the lung was involved, and the other died of exhaustion a few days after the abscess burst through the lung. In my native series out of eight cases operated on six died, while five not submitted to surgical measures all recovered. The latter include the less serious and the former the worst cases, so the two classes are not strictly comparable. Nevertheless, it is clear that operative procedures in this complication are of a very serious nature and to be avoided whenever possible. Recent experience has shown that the very great majority of cases of liver abscess opening through the lungs are rapidly cured without operation if full doses of ipecacuanha are given by the mouth, or better, emetine hydrochloride injected subcutaneously. Major Whitmore, I.M.S., has kindly sent me notes of a case of abscess of the liver opening through the lungs, at Rangoon, which he treated by aspiration and injection of quinine

solution by means of a funnel attached by rubber tubing to the cannula, so as to avoid forcing in the fluid at a high pressure, with the result that the expectorated pus rapidly became reduced and recovery ensued.

Liver abscesses opening into the bowel are also fairly often spontaneously recovered from, so that nature's methods of evacuating amœbic abscesses of the liver are frequently entirely successful in curing the patient, while they are far less often accompanied by the extension of serious inflammation to the pleura or peritoneum, or septic infection of the abscess cavity, than are the surgeon's attempts in the same direction.

If the expectorated discharge is becoming less, there is little or no fever and the patient is not losing weight, it is better to watch events. Under the reverse circumstances, in which the patient is clearly losing ground, it is evident that his powers are unequal to the strain being put upon them, and the abscess in the base of the lung and upper part of the liver must be drained through the chest wall without delay. Adhesions of the pleura are pretty certain to be present, so after locating the pus with the aspirating needle this can be used as a guide while cutting down on it. When it appears clear from the first that the patient's strength will not suffice to allow him to cough up a liver abscess it should be opened as soon as possible after pus appears in the sputum, and before its cavity has contracted and become difficult to find. In one old, exhausted European, in which this was done without delay, the communication with the lung and expectoration

of pus ceased at once on the abscess being freely drained. He made a good recovery, although his illness was prolonged by a continuation of fever, when the wound was in a healthy condition, but the temperature yielded to ipecacuanha, being clearly due to a recurrence of hepatitis independently of the original abscess.

Other Complications.—Now that tropical abscess of the liver is usually recognized and surgically treated at a comparatively early stage, other complications are not very commonly met with. Rupture into any part of the gastro-intestinal tract, with vomiting or the passage of pus by the bowel, is not unfrequently recovered from spontaneously, and does not require any operative measures. When, however, a liver abscess opens into the pleura or pericardium these sacs should be drained without delay. The same remark applies to the peritoneum, although here the nature of the disease is less likely to be recognized in time for success to be probable.

After-treatment of the Open Operation.—Very extensive dressings are required to absorb the copious discharges of the first few days unless siphon drainage is used. If they are soaked through it is imperative to change them completely as soon as possible. Merely covering them over with further absorbent material is equivalent to shutting the stable door after the horse has been stolen, for the soaked dressings will already have been infected from the air, and the putrefactive process will rapidly spread through the deeper layers, which are saturated with serum-like culture fluid, to reach the

wound. In such cases an originally sterile and sweet discharge may rapidly become extremely foul and swarm with cocci and bacteria. The practical impossibility of keeping the discharge of a liver abscess treated by the open operation completely sterile has already been dwelt on, but with great care the bacterial infection may be limited to a comparatively slight and mild infection, which may only result in a prolongation of the period of healing, unless the abscess is a large one, when fatal exhaustion may ensue. Antiseptic lotions are often used to wash out the cavities at the daily dressings. If the pus is originally sterile, and remains so, there is no necessity for their use, whilst if the wound is infected it is very doubtful if irrigation will materially lessen the contamination. Those I have seen used do not appear to kill the causative amœbæ, as I have often readily found them in the pus taken at the dressings, even when there was marked bacterial infection. Of much greater value is the plan of washing out with sterilized quinine solutions, which in a strength of 1 per cent. will readily kill the protozoal parasites and rapidly diminish the discharge, if no serious bacterial infection has taken place. This plan has been used in the Madras General Hospital and in Calcutta with good results. If the abscess is not a very large one and can be kept sterile, the discharge will dry up to a great extent in a very few days under quinine irrigation.

If the discharge becomes foul smelling from bacterial infection, I have found that daily irrigation with a 1 in 1,000 solution of permanganate of potash until the fluid is no longer decolorized,

is of great value and rapidly reduces the amount and improves the character of the pus.

Ipecacuanha in the After-treatment of Liver Abscess.—One of the greatest trials of the surgeon in the tropics is to have a patient doing well after operation for liver abscess whose convalescence is interrupted by a recurrence of the fever, in spite of the wound being in a healthy state. Another abscess is probably forming in the liver, which will almost certainly prove fatal to the patient in his weak condition. Many a case has thus been lost in the past, but fortunately we are now in a position to prevent the recurrence of amœbic abscesses, and should also, in these days of aseptic surgery, be largely free from the bugbear of secondary septic ones. The method of cutting short an acute hepatitis in the pre-suppurative stage applies equally well to the prevention of further abscess formation after one has been surgically treated. The fact that the disease is always secondary to amœbic dysentery, very often in a latent condition, clearly indicates that the cure of this exciting cause should not be neglected, as it generally has been in past years. As soon as the patient is in a position to stand it, a course of ipecacuanha or emetine injection should be given in the after-treatment of every amœbic liver abscess. If given in one of the ways described under the pre-suppurative stage of the disease it will cause very little trouble to the patient. For some time past this has been the routine treatment in the Calcutta hospitals, and I attribute not a little of the recent improvement in the results to this simple measure. One European patient had been operated

on four times for liver abscess in as many months, a large fresh one being opened at the last. He was still getting high fever and severe pain and steadily losing ground, and although a powerful man he had nearly given up hope of recovery. He was now put on ipecacuanha and the wounds washed out with quinine solution. The next day he was free from pain and soon after the fever subsided, the discharge was much less, and he made a good recovery, although it took some weeks for the extensive incisions to heal. In another case reported to me by Captain Foster Reany, I.M.S., a sepoy developed fever when an opened liver abscess had nearly healed. The sinus was dilated, but no collection of pus was found, and the temperature continued to rise higher. He just then read my advocacy of ipecacuanha in amœbic hepatitis, so at once put the patient on the drug. The fever declined rapidly and the patient made a good recovery. A recurrence of the disease had been prevented by this timely treatment. Such cases speak for themselves.

TREATMENT BY ASPIRATION AND INJECTION OF QUININE WITHOUT DRAINAGE

There is no difference of opinion about the necessity of opening and draining as soon as possible any collection of pus containing the ordinary pyogenic bacteria. This treatment was, however, found to be sometimes disastrous when applied to cold abscesses, now known to be caused by the tubercle bacillus; for septic organisms were liable sooner or

later to gain access to the large cavity, and the last state of the patient was worse than the first. The discovery of a protozoal parasite in the pus of some abscesses of the liver, and the knowledge that pyogenic bacteria and cocci were frequently absent altogether from them, does not appear to have led to any change of principle in the treatment of these purulent collections. This is probably largely due to the earlier workers only occasionally having found the amœba, so that for long it was not generally looked on as the causative agent of the disease. When, by the methods already described, I was able to show that the amœba is constantly present in the walls of active tropical liver abscesses, and that 70 to 80 per cent. of them are otherwise sterile, I naturally set to work to find some non-poisonous agent which had the power of destroying the protozoa in the thick pus of a liver abscess. In September 1902 I recorded that a 1 in 500 solution of quinine (either a soluble salt or quinine sulphate dissolved in very weak acid) would readily destroy amœbæ in the wall of such an abscess in vitro. I therefore suggested the treatment of sterile liver abscesses by withdrawing as much pus as possible with an aspirator, and injecting through the cannula a sterile solution of 30 grains of quinine in 2 to 4 oz. of water, the cannula being then removed and no drainage attempted. Owing to unexpected difficulties in getting surgeons to adopt this simple method, it was not until four years later that I was able to report the results of its trial. I was frequently told that it was an 'unsurgical procedure'. Looking at it purely from the patient's point of

view, I could never understand how that was a valid objection to its being tried, when it was obviously quite harmless, while there was good reason to believe it might save him from a much more serious surgical procedure. In 1906 Roger P. Wilson, I.M.S., carried out my suggestion in two patients with deep-seated right-lobe liver abscess with the most striking success, and since then it has been favourably reported on by several surgeons who have used it. In January 1909 Professor G. C. Spencer, of the Royal Army Medical College, recorded three successful cases, two of which were cured by a single injection of 15 to 20 grains of quinine hydrobromide. The third was a greatly emaciated subject from whom 50 oz. of pus were removed at the first aspiration, 40 grains of quinine being injected, which was followed by some collapse and deafness of short duration. A fortnight later 53 oz. of pus were evacuated and 20 grains of quinine injected, and after another week 40 oz. of pus were removed and the injection of 20 grains of quinine repeated. From that time he steadily recovered and put on several stones in weight. As a result of his experience Major Spencer advises that this method should first be tried in every case, as even when unsuccessful it gives temporary relief and may place the patient in a better position to stand the open operation. During 1909 a number of liver abscesses were cured by this method by Major O'Kinealy and Major C. R. Stevens, I.M.S., at the Calcutta Medical College Hospital. The following table shows a consecutive series of cases which I have been able to watch in the Calcutta hospitals.

CASES OF LIVER ABSCESS TREATED BY ASPIRATION AND QUININE INJECTION IN CALCUTTA

		Cured.	Died of other Diseases.	Died of Liver Abscess.
Aspiration and quinine injection only	Cured	16	—	—
	Liver abscess cured, died later of dysentery	—	1	—
	Liver abscess cured, died later of pneumonia	—	1	—
	Died of liver abscess	—	—	3
Total		16	2	3
Ditto and opened later	Cured	3	—	—
	Died	—	—	3
Grand total		19	2	6
Abscess evacuated through the thoracic wall 24				
Ditto ditto abdominal wall 3				

Out of the eighteen cases treated by aspiration and quinine injections sixteen were completely cured, two were cured of the liver abscess but subsequently died of other diseases, and three died of the liver abscess. As all but three of these cases were evacuated through the chest wall, which class when treated by the open operation has a mortality among native patients (who formed a large proportion of the whole) of over 70 per cent., these are very encouraging results, which are enhanced when we consider the nature of the three cases it failed to save. One was admitted in a very bad condition, for whom only very temporary relief was possible. From another no less than 112 oz. of pus were aspirated at the first operation, when he was in an extremely critical state. He rallied, however, and a week later 20 oz. were removed, while after

another seven days only 10 oz. could be got. He picked up considerably and was able to walk about, but evidently attempted too much as he died unexpectedly of heart failure when there seemed every chance of his recovery. The third was a very acute case with destruction of most of the right lobe of the liver, the cavity containing very large sloughs which prevented complete evacuation. Here the open operation would have enabled more complete emptying of the abscess, but the patient was in a hopeless condition with extreme jaundice due to the neck of the gall bladder being completely dissected out by the suppuration, so recovery was scarcely possible. In none of these cases, therefore, is there any probability that the open operation would have saved the patient. Of the two cases dying of other diseases after cure of the liver abscess one succumbed to dysentery nearly three months after his abscess had dried up. The other died of lobar pneumonia of the left apex quite unconnected with the liver trouble after the abscess had ceased to form pus. He had been admitted in an extremely debilitated condition with a huge liver abscess, the treatment of which by the open operation was recognized to be practically hopeless. No less than 86 oz. of pus were removed by aspiration and 15 grains of quinine bihydrochloride injected into the cavity. He improved slowly, and nine days later a second aspiration only withdrew 18 oz. of pus, while seven days later still only 10 oz. were obtained, quinine being injected each time. At a fourth aspiration eight days after only 5 oz. of thin bile free from pus were removed, so no quinine was

introduced. He had picked up considerably by this time, but shortly afterwards was attacked by pneumonia and quickly died. At the autopsy the cavity in the liver, which had held over 4 pints of pus just four weeks earlier, had contracted down so as to contain but $2\frac{1}{2}$ oz. of clear bile with no pus. Its walls were formed of a very thick layer of fibrous tissue, its inner surface being quite smooth and free from amœbæ, whilst the contents were sterile on culture, as they had been at each operation. He had been given a course of ipecacuanha while in hospital, and in the cæcum some recent scars, together with a few slit-like depressions of almost healed ulcers, were found. Left pneumococcal apical pneumonia was present, but for which accidental complication there can be no doubt he would have recovered, for the liver substance beyond the encysted abscess was quite healthy. This case affords striking evidence of the value of the new method of treatment, even in very large chronic abscesses in debilitated subjects, in whom the open operation would almost inevitably be fatal. Out of twenty-one cases treated throughout by aspiration and quinine injections only three died of liver abscess, or 14 per cent., although all but two belonged to the deep-seated right-lobe class, the mortality of which by the open operation is over 70 per cent. If the cases in which the abscess was opened subsequently to the use of aspirations and quinine injections be added the mortality rises to 22 per cent., but some of these were early cases only aspirated once, and might very possibly have done better by a repetition of the process.

As the mortality in different forms of liver abscess differs very greatly the cases have also been classified in the next table, and the mortality of each class, calculated from a large number of cases treated in the Medical College Hospital by the open operation, has been added for comparison. By this means alone can the true effect of any alteration in the treatment of a given series of cases be correctly estimated. Two cases in which the liver abscess was cured, but the patients died of independent left

TABLE I. LIVER ABSCESS TREATED BY ASPIRATION AND QUININE INJECTION WITHOUT DRAINAGE

Site of puncture.	Cases.	Cured.	Died.	Mortality by open operation.	Estimated mortality of these cases by open operation.
Through chest wall	16	13	3	73%	11·68
Below right ribs	1	1	—	59%	0·59
Epigastrium	2	2	—	12%	0·24
Totals	19	16	3	—	12·51

apical lobar pneumonia in one and of dysentery two months afterwards in the other, have been omitted, although they might equitably have been included among the liver abscess cures.

The last column gives the estimated death-rate in the particular cases in accordance with the previous rates by the open operation in each class of case. The reduction in deaths in this series by the new method is thus shown to be a fourfold one.

The most remarkable case was a patient of Major O'Kinealy's; no less than 6 pints (120 oz.)

of sterile pus were aspirated from a single huge abscess in his liver on the day of admission. Before the operation the liver dullness extended from the second right rib to a little below the navel, and the history of his illness was of over one year's duration. He was in an extremely weak and emaciated condition, and was kept up by strychnine injections. Five days later 36 oz. of pus were aspirated and 40 grains of the bihydrochloride of quinine injected. He improved steadily from that time; the liver dullness subsided until it only extended from the fourth rib to just above the costal margin, and the diaphragm was seen by the X-rays to be moving well. He put on $18\frac{1}{2}$ lb. in five weeks and left the hospital quite recovered. Such a case clearly proves that the most advanced liver abscesses are amenable to this simple plan of treatment, so I venture to think the patient should always be given the benefit of its trial before the open operation is resorted to.

In carrying out this plan of treatment the following points require attention. The skin at the seat of puncture must be most thoroughly sterilized to prevent any bacteria being carried into the cavity. If the presence and position of the abscess are accurately known a full-sized aspiration trocar should be used to allow as much as possible of the thick pus being withdrawn through it. For the same reason it is also an advantage to use a T-tube of large calibre fitting into the exhausted bottle. Messrs. Down Bros. have made a suitable one for the purpose. The cavity is emptied as far as possible, some of the first pus being run directly into a sterile test-tube for bacteriological examina-

tion. An additional ounce or two of very thick pus can often be withdrawn by forcible aspiration by a large syringe with closely-fitting piston attached by a short piece of thick rubber tubing to the cannula, as used by Major C. R. Stevens, I.M.S., in Calcutta.

The blunt stiletto should then be inserted to clear the tube, and a previously boiled solution of the very soluble bihydrochloride of quinine, of a strength of 10 grains in 1 oz. of water, or preferably 1 grain of emetine hydrochloride in 1 or 2 oz. of sterile water, is now injected into the abscess cavity through the cannula by means of a sterile syringe, and the cannula is then withdrawn and collodion applied externally. If only a few ounces of pus are obtained it will be sufficient to inject 2 oz. of the quinine solution, but if a pint or more is present then 4 oz. containing 40 grains of quinine should be used, so as to saturate the whole wall. In some cases the temperature falls finally, all the symptoms disappear, and weight is rapidly gained after a single injection, as happened in eight cases. More frequently the effect is only temporary if the quinine solution is used, and it is then advisable to repeat the little operation after about a week, when less pus is commonly obtained. A third injection is not rarely required, and in large abscesses even more, four or five, as in two cases. I have noticed that if an originally present leucocytosis completely disappears, little or no pus is usually obtained at a second aspiration, and an uninterrupted convalescence ensues. The continued presence of even a slight leucocytosis is generally an indication for repeating the aspiration. In the common fibrous-

walled single abscess no cinchonism results, even from the injection of as much as 60 grains of quinine, but in more acute ones the drug may be absorbed to some extent into the circulation.

The pus removed at each aspiration has been examined both microscopically and by culture, with the result that primarily sterile abscesses almost invariably remain so throughout. The pus should be examined as soon as possible after removal, for if kept for twenty-four hours it commonly shows bacteria on culture, due to rapid multiplication of organisms which have entered from the air during the collection of the pus. For this reason when no bacteria are found microscopically the occurrence of a very few isolated colonies on culture indicates only an accidental contamination and not an infection of the abscess. Several such cases have done perfectly without any drainage being necessary. One case in which bacterial infection was found at the third and fourth aspirations recovered without drainage. If numerous bacteria are found both microscopically and on culture the abscess is clearly infected, and drainage will, as a rule, be necessary, as quinine only kills the amœbæ and not bacilli and cocci. Such cases are fortunately quite exceptional, and usually show thin greenish-yellow pus, sometimes with foul-smelling gas formation, instead of the typical thick reddish pus of a purely amœbic abscess. Occasionally a thin watery fluid may first escape from a purely amœbic case, followed later by thicker material, and such cases usually do well. In very acute large abscesses, with much liver destruction, the quinine injections may sometimes

fail. Unfortunately these cases also do badly with the open operation, so that even here the aspiration method has the advantage of being less exhausting, and may possibly afford time for the patient to recover sufficient strength to stand drainage of the cavity, if this can be done in a sterile manner.

Another great advantage of this method is that it is more likely than the open operation to be successful if more than one localised abscess is present, for any continuation of the symptoms after one abscess has been dealt with will lead to further exploration, which may very possibly come upon a second collection of pus. Further experience is necessary before the exact limitations of this treatment can be laid down, but it is clearly worthy of an extended trial in all cases in which there is no definite contra-indication to its adoption.

Recently I have injected 1 grain of emetine hydrochoride in about 1 oz. of water into liver abscesses, in place of quinine, with very satisfactory results as shown by the following cases.

Epigastric Liver Abscess Cured by Aspiration and Emetine Injections after Failure of the Quinine Treatment.—A native lad, aged 15, admitted for a liver abscess bulging in the epigastric region. Six oz. of liver pus were removed by aspiration, and 1 oz. of saline containing 10 grains of the soluble bihydrochloride of quinine injected into the cavity and the puncture sealed with collodion. Intermittent fever continued and the abscess cavity refilled within four days. A second aspiration was now done, 8 oz. of liver pus being removed, and 1 grain of emetine hydrobromide, dissolved in

2 oz. of sterile salt solution, was injected into the cavity. The emetine salt was also injected subcutaneously in half-grain doses every morning for four days, and again on the sixth day. In addition, 10 grains of ipecacuanha were given by the mouth every evening. After two days the temperature fell to normal and never again rose above 99° F. The abscess cavity steadily contracted and the tissues became firm, and the patient was discharged cured just under one month after the emetine injection, having been detained under observation to make sure that the abscess did not refill. This case is one which would, in all probability, have done well by the open operation, as the abscess was a comparatively small one, but the rapid subsidence of the fever and cessation of pus-formation under the influence of emetine was very striking.

Right-Lobe Liver Abscess Cured by Aspiration and Injection of Emetine.—A native male, aged 30, admitted for liver abscess following dysentery six months before. On aspirating through a lower right intercostal space, 8 oz. of typical liver abscess pus were withdrawn, and 1 grain of emetine hydrobromide dissolved in 2 oz. of sterile salt solution injected into the cavity and the puncture wound sealed with collodion. Half-grain doses of emetine were injected subcutaneously on each of the four following mornings and 25 grains of ipecacuanha given in the evenings, my supply of emetine being then very limited. The temperature rapidly fell to normal, but on three occasions during the next thirteen days it reached 100° F. in the evening.

At the end of this time the liver was normal in size and there were no signs of further collection of pus, but to make quite sure a second exploration under an anæsthetic was now performed, with a negative result, and subsequent convalescence was only interrupted by a mild attack of benign tertian malaria.

In addition to the above cases, a third, very similar to the last, has done equally well. On the other hand, in two others the pus obtained at the time of aspiration and injection of emetine was found on culture to contain large numbers of staphylococci, and consequently the abscesses had to be opened and drained, with ultimate recovery. I have previously pointed out, in connexion with my method of treating amœbic liver abscesses by aspiration and injection of soluble quinine salts into the cavities, that such a plan should only be persisted in if the pus is free from marked secondary bacterial infection, as occurs in my experience in 85 per cent. of cases.

Amœbic Liver Abscesses Cured by Aspiration and Subcutaneous Injections of Emetine.—In two other cases, one of which is still under observation, liver abscess pus was evacuated by aspiration and emetine injected subcutaneously, but not into the abscess cavity. In one the emetine injections were given for acute hepatitis, which greatly improved, but, as leucocytosis persisted, the liver was explored and several ounces of pus withdrawn, after which steady convalescence ensued and the leucocytosis disappeared. In the other the emetine injections were commenced two days after the aspiration of

liver pus, with an equally happy result. A single aspiration so exceptionally cures such cases that these two successive recoveries are in all probability due to the action of the subcutaneous injections of emetine in destroying the amœbæ in the walls of the liver abscesses, so that it may eventually prove unnecessary to inject the drug into the cavities; although in view of the harmlessness of the procedure, and the certainty that it will kill the parasites in the superficial parts of the lining membrane, it is advisable to do so in the present state of our knowledge.

Amœbic Abscess of the Spleen Cured by Aspiration and Emetine Injections.—A native male, aged 32, admitted with enlargement of the spleen to 2 inches below the left costal margin and a tender prominence of the lower ribs, with redness of the skin over it. On exploration 8 oz. of thick reddish pus and blood, closely resembling that of amœbic liver abscesses, were withdrawn. Three days later there was evidence of refilling of the cavity, so a second aspiration of 4 oz. was performed, and this time 1 grain of emetine hydrobromide in 2 oz. of water was injected. I examined the pus microscopically, and found amœbæ to be present, while it was sterile on culture for bacteria. On each of the next two days half a grain of emetine was injected subcutaneously, but the temperature once more rose, and six days after the second aspiration there was again slight bulging. A third aspiration was now done, but only a little pus and much blood was obtained, and a grain of emetine hydrobromide was again injected into the

cavity, and two more half-grain doses given subcutaneously. The temperature finally fell to normal two days later, and the abscess did not again refill, but complete recovery ensued.

This case is of great interest, both on account of the rarity of amœbic abscess of the spleen and because of its successful treatment by the new method; for when opened these abscesses are liable to heal very slowly and to leave obstinate sinuses. It was for this reason that a repetition of the emetine injection into the cavity was carried out, with the fortunate results recorded.

Taken as a whole, the cases above detailed of amœbic abscesses of the liver and spleen treated by emetine injections are full of promise. If further experience should confirm them a new era will have commenced in the treatment of this very serious and fatal disease, for the causative parasite can be destroyed by injections of emetine salts into the abscess cavities, after very thorough evacuation of their contents by aspiration. Subcutaneous injections, too, of the same drug will kill the organisms in the deeper layers of the abscess wall by way of the blood-stream (as well as in any latent amœbic ulcers in the large bowel which may have produced the liver trouble), and thus the necessity of resorting to the much more serious and open operation, with prolonged drainage and almost inevitable secondary bacterial infection of the wound in damp, hot climates, may be largely dispensed with, greatly to the comfort and benefit of the patients.

CHAPTER VIII

ETIOLOGY AND BACTERIOLOGY OF BACILLARY DYSENTERY

The history of the differentiation of bacillary dysentery having been recorded in the opening chapter, the main facts regarding the causative organisms will now be given and their bearing on the etiology of the disease discussed.

Methods of isolating Dysentery Bacilli.—The most conclusive proof that a given case of dysentery is bacillary in nature will clearly be the successful isolation of the organisms from the patient's stools. Owing to the innumerable other bacteria likely to be present this is commonly a somewhat difficult task requiring special technique, while more than one examination is often necessary before a reliable result is obtained. The process has been simplified during the last few years by the discovery of culture media inhibiting largely the growth of organisms other than those belonging to the coli group, which includes the dysentery bacilli, while litmus is also added which is turned red by colonies of the B. coli communis, but not by dysentery organisms, which are stained pale blue and can thus be picked out and further tested. These principles are made use of in the following procedures.

In making cultures from dysentery stools it is

important that these should be as fresh as possible, as within a short time in warm climates the number of dysentery bacilli will become materially diminished in numbers by putrefactive changes. Vedder and Duval advise that the stool should be passed on to sterile gauze in a previously boiled bed-pan and either examined on the spot or taken to the laboratory at once. A small piece of mucus is then taken, preferably according to some workers one containing blood, although there is some difference of opinion on this point. If fæcal matter is adherent to the mucus it should be washed in several changes of sterile salt solution in test-tubes to free it from such contamination. A small fragment of the selected piece is next smeared over the surface of a large-sized plate of the desired culture media, for which purpose a glass rod bent at right angles may be used, so as to uniformly inseminate the whole surface, two or three plates being thus treated in succession with the same piece of mucus so as to ensure sufficient isolation of the colonies for ready subculture.

Culture Media.—The most convenient is the Drigalski-Conradi litmus-lactose-crystal-violet medium, which in warm countries should be made up with agar, as gelatine will melt at most seasons of the year in the tropics. The crystal-violet serves to inhibit the growth of organisms other than the coli group, while the litmus allows of the red acid-producing coli colonies being distinguished from the pale-blue dysentery ones. To 2–3 per cent. of lactose agar of a slightly alkaline reaction sufficient litmus is added to produce a bluish-violet tint and

also 1 in 10,000 crystal violet; after sterilization it is poured out in large Petri's dishes, and when the film has firmly set, inoculated as above described, and incubated at blood-heat in the reversed position to avoid aqueous condensation on the medium.

After twenty-four hours the plates are examined, and all red colonies passed by as coli organisms. By this time the dysentery bacilli will be seen as very small pale-blue transparent colonies, some of which are now planted out on agar or other media. Many of the dysentery bacilli, however, will not develop into visible colonies until between twenty-four and forty-eight hours, so at the end of two days further blue growths will have appeared and should also be planted out. For this reason Duval and Bassett advise that after twenty-four hours all the blue colonies should be ringed with a wax pencil, and at the end of forty-eight hours' incubation the blue colonies which have developed since the previous day should be isolated and further tested in glucose broth, all which produce gas being rejected and the others submitted to the sugar and agglutination tests for the identification of the variety of the dysentery bacilli as described below.

At autopsies, after the removal of all fæcal matter by thorough washings with sterile saline, scrapings of the mucous membrane are used for inoculating the plates and subcultures made as just described.

Darling has recently reported a case in which the dysentery bacilli were grown directly from vein blood in a very acute case, but ordinarily such a procedure gives negative results in dysentery.

Additional help can be obtained by aid of a

serum which agglutinates both the Shiga and Flexner types of dysentery bacilli in high dilutions, obtained by repeatedly inoculating rabbits with suitable non-lethal doses of the dead organisms. By adding a colony or culture to a drop of a strong serum on a blood slide, if it is a true dysentery bacillus, it will show almost immediate clumping, and only those colonies which give a positive reaction are subcultured and further tested.

Morphology and Cultural Characters of the Dysentery Bacilli.—We have already seen in the historical section that we have to deal with several varieties of dysentery bacilli as revealed by their powers of fermenting certain sugars, a useful although highly artificial method of distinction. Their general appearance on ordinary culture media is, however, very similar in all, so one description will suffice.

Morphology.—The dysentery bacilli are rods from 1 to 3 μ in length and very similar in appearance to the B. typhosus, only slightly thicker. In cultures much longer forms are also seen, especially after three or four days' growth, when involution forms will have appeared. The Shiga type are not actively motile, only oscillatory movements without progression being seen in fresh specimens, in which respect they differ materially from the typhoid bacillus. The Flexner group show slight motility, while both groups are free from cilia and do not form spores. They stain readily with the ordinary aniline dyes, and may show bipolar staining, especially with fuchsine, but they decolorize by Gram's method.

Cultural Characters.—The dysentery bacilli grow best at blood-heat, and more slowly at the room temperature, but below 40° F. they do not develop.

In **Broth** at the end of twenty-four hours they produce a uniform turbidity with a slight flocculent precipitate, which becomes more marked day by day, a slight degree of acidity being also produced, but no pellicle is formed on the surface.

On **Gelatine** in a stab culture no liquefaction takes place, whilst a light-yellow line of growth with a thin translucent surface layer forms. On a slope a narrow, thin transparent streak appears with a slightly wavy border very similar to a typhoid culture.

On **Agar** the appearances are very similar to surface gelatine cultures.

On **Blood Serum** a yellowish-white growth is formed.

On **Potato** after one or two days a very thin, not very easily seen, moist shining pellicle forms, which later becomes a thick yellowish-white layer containing many involution forms.

The **Indol** reaction in peptone broth is negative for the Shiga type, but positive for the Flexner group and Strong's bacillus.

In **Litmus Milk** no coagulation occurs, although a purple tinge appears due to acid formation after one day and later again disappears, the blue alkaline reaction returning.

The **Sugar Fermentation Tests** vary with the types of the dysentery bacilli which serve to differentiate them from one another. Thus, the Shiga bacillus only ferments glucose with the production

of an acid formation, but no gas. The Flexner group differ from the Shiga organism in having the power of acting on mannite to form acid, and also similarly on saccharose, maltose, and dextrose. As subvarieties of the Flexner bacillus we have the Y bacillus of Hiss, which acts on mannite, but not on either saccharose, maltose, or dextrose.

Strong's bacillus, found by him in Manila, but not yet obtained by any other worker, acts on saccharose in addition to mannite, but not on maltose or dextrose.

The above are the best recognized varieties of dysentery bacilli, although numerous other strains have been described by various workers, the reactions of some of which are shown together with the foregoing ones in the following table.

TABLE OF THE SUGAR REACTIONS OF DYSENTERY BACILLI

	Motility.	Indol reaction.	Litmus milk. Days.			Glucose.	Mannite.	Saccharose.	Maltose.	Dextrose.	Lactose.
			1	3	15						
Shiga	−	−	Ac.	Neut.	Alk.	+	−	−	−	−	−
Y (Hiss) . . .		+				+	+	−	−	−	−
Strong	−	+				+	+	+	−	−	−
Flexner-Harris .	+	+	Ac.	Neut.	Alk.	+	+	+	+	+	−
Shiga (1904) . .		+	Ac.	Alk.	Alk.	+	+	+	+	+	−
Hiss and Russell						+	+	+	+	−	−
Morgan . . .	+ +	+ +	Ac.	Neut.	Alk.	+	−	−	−	−	−

Vitality.—The resisting powers of the dysentery bacillus are of importance from the etiological point of view by affording indications as to the probable modes of infection. The following are the more important data regarding them.

Temperature Conditions.—The dysentery bacillus is killed in a few minutes by boiling and in one hour at 58° C. On the other hand, it resists low temperatures and lives much longer in water at the freezing point than at room temperatures, whilst it dies out more quickly still at blood-heat. Thus cold tends to preserve its vitality.

It does not resist **Drying** for more than about 12 days. **Sunlight** has a powerful destructive effect on it, for Shiga found that thirty minutes' exposure sufficed to kill it. In dysenteric stools Shiga's bacillus dies out in 2 days, the other organisms present being, according to Pfuhl, highly antagonistic to it. The same experimenter found that in damp garden earth its vitality was maintained up to 101 days, in milk for 17 days, unless other acid-forming bacilli were present, in which case it died out in 8 days.

The duration of its life in **Water** is of great practical importance, and has been carefully investigated by Vincent, who obtained the following results. In **Sterile Water** at 38° C. dysentery bacilli survived 4 to 5 days; at 15° to 20° C. from 6 to 10 days, and at 1° to 4° C. for from 9 to 18 days. In **Unsterile Water** containing a moderate number of other organisms, the dysentery bacillus lives nearly as long as in sterile water, but if there are numerous organisms in it the life of the pathogenic bacillus is short in inverse ratio to the extent of the contamination, owing to the antagonistic action of saprophytic germs. Vincent found that the following organisms had an inhibitory power against the dysentery bacilli: staphylococcus pyogenes, M. pro-

digiosus, pyocyaneus, the typhoid and coli bacilli, the cholera vibrio, proteus vulgarus, and certain anærobic organisms. The rapid disappearance of the dysentery bacillus from stools after their passage is thus readily explained.

The above facts have an important bearing on the etiology of the disease, for they show that the dysentery bacilli will tend to die out rapidly from a grossly contaminated water, especially if it is at a comparatively high temperature as in the tropics. On the other hand, it will live longer in a purer and cooler supply. Exposure of a shallow stream to strong sunlight will also be inimical to the infective organisms of dysentery. Vincent attributes the comparative rarity of bacillary dysentery in the tropics to these destructive influences, but although the amœbic disease is commonly the prevailing form in warm climates, the bacillary variety is more frequent than in colder climates.

Agglutination.—As first shown by Shiga the blood of patients suffering from bacillary dysentery clumps the organism of the disease, and this reaction can be used for diagnostic purposes as in the case of typhoid fever, although it is not nearly as useful as in the latter disease. Further, by repeatedly injecting non-lethal doses of dysentery bacilli into such an animal as a rabbit a serum can be obtained which agglutinates the injected organism in a high dilution. The strongest serums are got by intravenous injections, when it may react in a dilution of 1 in 1,500 or even higher. By this means it has been found that a serum obtained by the injection of Shiga's bacillus only agglutinates that variety of

organism, while one prepared by means of Flexner's bacillus clumps both that and the Y bacillus, but not Shiga's or Strong's, while a Strong's serum only reacts with the same strain; but the last is of little practical importance on account of its extreme rarity. In testing the blood of a dysentery patient its serum should be put up separately with both Shiga's and Flexner's bacilli.

The methods in use are precisely similar to those of the typhoid reaction, either the microscopical test with a time limit of one hour, or the microscopical one in sedimentation tubes kept for a day, being available, with either a twenty-four hour broth or agar culture, an emulsion of the latter being allowed to settle, or better, to be centrifuged for a short time to remove any masses of bacilli which might be taken for clumps. Dead bacilli may also be used, as in typhoid, in the sedimentation test. It is convenient to put up the serum in dilutions of 1 in 20, 1 in 40, and 1 in 100. To be of diagnostic value in the case of the Shiga bacillus a complete reaction should be obtained in a dilution of 1 in 20 to 1 in 30 and upwards, but with the Flexner organism higher reactions are necessary, for according to Dopter only one in a dilution of not less than 1 in 90 is reliable with this strain.

The **Period of the Disease** at which the reaction appears is after eight to twelve days in cases of a severe or average type, but in mild ones it is often absent for a much longer period, yet may eventually show itself. In both severe and chronic cases the reaction may continue up to two or three months after convalescence, and thus allow the type of the

disease to be verified after an attack is over. A positive reaction is therefore of considerable diagnostic value, but a negative one will not exclude bacillary dysentery during the first week or two of an acute attack or for much longer in a chronic one. This materially detracts from the clinical value of the test, as proper treatment based on a correct diagnosis is essential from the outset. Moreover, many workers have found the test of little practical value, while I have not infrequently obtained a positive reaction in cases which proved to be amœbic in nature, possibly due to earlier bacillary infection.

The Differentiation of Dysentery Bacilli by the Agglutination Test.—This test may be carried out by adding serums of known agglutinating powers to broth cultures of bacilli recently isolated from dysentery cases. From one to five drops of a Shiga antidysenteric serum are added to a twenty-four hour broth culture of the organism to be tested, and to another similar tube a similar amount of Flexner serum. After twenty-four hours' incubation if agglutination has taken place in one of the tubes it will show a precipitate of clumped bacilli with clear supernatant fluid, while the other culture will present a uniform cloudiness. In this case the bacillus being tested will belong to the type whose serum has agglutinated it. The test works equally well if the serum is added to the broth culture at the time it is inoculated with the organism under examination, whilst a day's time is thereby saved. This test may also be performed by the more rapid microscopical method already mentioned.

Bordet's Fixation Test.—In addition to agglu-

tinins anti-dysenteric sera contain specific sensitizing bacteriolytic substances, which can be demonstrated by means of Bordet's fixation test, which depends on the principle that in the process of combination of the sensitizing substance to the dysentery bacilli a certain amount of complement is absorbed and rendered inactive. If, then, to a small measured quantity of the serum of the blood which is to be tested for the presence of the bacteriolytic substances a suitable quantity of complement (contained in fresh guinea-pig's serum) and of dysentery bacilli are added, and the tube incubated at blood-heat for an hour or two, the complement will be used up and disappear if the bacteriolytic substance is present; while if the latter is absent the complement will remain active, as can be demonstrated by the production of hæmolysis on the addition of washed sensitized red corpuscles, as in the Wassermann test. In carrying out this procedure for dysentery specific substances a control should be made by using typhoid instead of dysentery bacilli in a second set of tubes. These should give a negative result, as shown by hæmolysis taking place in the final procedure, thus proving that the complement used is an active one, and has been actually used up in the dysentery set of tubes, in which no hæmolysis has taken place. These procedures are unfortunately difficult and lengthy, but are of great theoretical as well as practical interest.

The Diagnostic Value of the Fixation Test.—As the bacteriolytic substances appear in the blood of dysentery patients between the fifth and seventh days, that is, a little earlier than the agglutination

reaction, the test for them is of diagnostic value, for it is negative in amœbic dysentery. Again, Dopter finds that the bacteriolytic sensitizing substances produced by every one of the different varieties of dysentery bacilli are identical, so that a serum obtained by injecting one variety into an animal will give the fixation test with each of the other dysentery organisms, but not with other members of the coli group, such as the typhoid or coli communis bacilli. The test may therefore be applied to any organism isolated from a dysentery case to ascertain if it be a true dysentery bacillus or not.

Dopter's observations are also of importance in proving that all the dysentery bacilli are extremely closely allied, being in fact brought closer together by this common production of specific anti-dysenteric substances than they are divided by the agglutination reactions and sugar tests. In fact, Dopter maintains that there is only one specific dysentery bacillus, which may vary slightly in its fermentative powers, and that this shows that a curative bacteriolytic serum made from one variety will have an equal action against all the other forms of bacillary dysentery—a point on which there is still some difference of opinion, which will be referred to when we come to deal with the serum treatment of the disease (see page 290).

Dysentery Toxins.—Shiga first showed that the injection of his bacillus into rabbits produced death with the lesions in the large intestine resembling those of dysentery. Later it was found by other workers that dead bacilli produced precisely similar effects in very much the same doses as living ones,

thus indicating that the symptoms and bowel effects are produced by the action of a toxin in the organisms, which may be demonstrated in several ways. The simplest procedure is to make an aqueous emulsion of the bacilli, which is rendered more toxic by incubation at blood-heat for twenty-four hours to allow autolysis to take place. The remaining bacilli may be killed by heating to 60° C. for one hour or by chloroform, or they may be separated by means of a fine porcelain filter. Todd found that a powerful toxin was obtained by growing the organism in alkaline broth at 37° C. for twenty days and then filtering as before. As little as 0·01 c.c. of the filtrate administered intravenously killed a rabbit. The toxin is mainly, if not entirely, intracellular, that found in the twenty-day broth culture being derived from the dissolution of dead organisms.

The Shiga bacillus alone produces much toxin, while the Flexner group and Strong's bacillus are but slightly harmful to such animals as have been tested. Horses and rabbits are very susceptible to the Shiga toxin, while guinea-pigs are least affected by it. It does not, however, follow that an organism is not toxic for man because it is harmless to laboratory animals, for Strong produced a typical attack of dysentery in the person of a condemned prisoner who swallowed a culture of his dysentery bacillus.

Antitoxins.—As early as 1898 Shiga obtained an antitoxic serum by repeatedly injecting goats and horses first with dead and later with living dysentery bacilli, and got good results by its use in cases of the disease. Krause, Todd, Rosenthal,

Vaillard and Dopter, the Lister Institute, Ruffer, and others have all prepared active serums against the disease, which possess strong agglutinating and bacteriocidal properties. In animals they have been found to have both a curative and a protective effect, although the latter is of short duration as with other antitoxic serums. Vaillard and Dopter maintain that an anti-dysenteric serum made by the injection of one variety of organism is equally effective against all forms, and cases have been recorded in which a Shiga serum was quite active against a Flexner type of dysentery. On the other hand, Ruffer at El Tor in Egypt found that he got considerably better results with a serum prepared from the strains of dysentery bacilli obtained from local cases (see page 291). Great care is necessary in the handling of horses used for preparing these serums, as they are extremely susceptible to dysentery toxins. The best results are obtained by the intravenous injections of bacilli and toxins respectively on alternate weeks, the doses being only very gradually increased, beginning with one-fourth of a c.c. of a twenty-four hour broth culture, as severe febrile reactions constantly result.

Experimental Dysentery.—In addition to Strong's convict, several workers have developed dysentery after an incubation period of several days, as a result of accidentally swallowing the Shiga organism, so there is no doubt as to the pathogenicity of these bacilli.

In addition to rabbits, dogs and pigs can be readily infected by injecting a twenty-four hour broth or agar culture of the organisms either sub-

cutaneously or intravenously, the latter method being the most certain. Subcutaneous injections produce marked inflammatory œdema locally within a few hours and the temperature rises to about 104° F. On the following day the animal becomes acutely ill and mucous diarrhœa appears, which may later become blood-stained; paralysis, generally paraplegic in type, ensues and death takes place after three or four days unless the dose was a small one, when it is longer delayed. Post-mortem, extensive inflammation and necrosis of the mucous membrane of the large intestine is found, precisely as in bacillary dysentery in the human subject, leaving no doubt as to the relationship of the bacilli to the disease.

CHAPTER IX

THE PATHOLOGICAL ANATOMY OF BACILLARY DYSENTERY

Early Stages.—In the bacillary class of dysenteries the primary lesion is essentially one of the mucous coat of the large bowel, just as that of the amœbic variety is one of the submucous layer. This difference is best seen in the early stages of the disease, which are seldom seen in the post-mortem room except in the very acute forms which are rare. These were, however, well illustrated in the case of a patient suffering from another serious disease, who succumbed rapidly to a Shiga bacillary dysentery. The cæcum and ascending colon showed the characteristic thickening due to a fibrinous granular-looking deposit in the mucous membrane, while in places the epithelial layers had separated to leave superficial ulcers with a red slightly depressed base situated on a generally thickened mucosa. Scattered through the remainder of the large bowel were a number of minute yellowish-white dots not much larger than a pin's head, which constitute the earliest lesions on the very surface of the mucous membrane, being inflammatory deposits in its epithelial layers. This is the only specimen I have seen in such an early stage of the bacillary disease, and it clearly showed

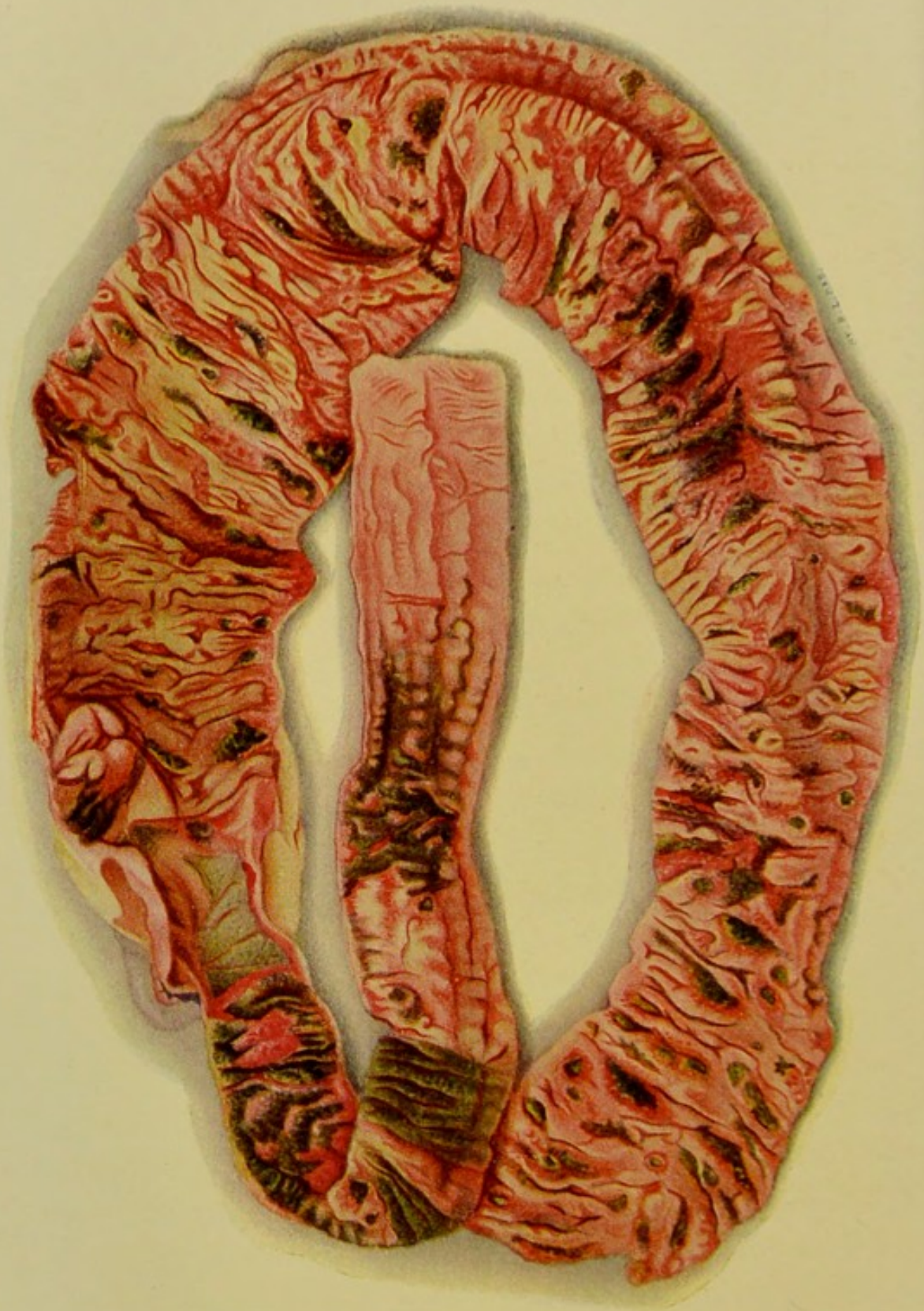


PLATE VIII.—THE ADVANCED STAGES OF ACUTE BACILLARY DYSENTERY.

[*To face p.* 259.

the limitation of the primary lesions to the superficial layers of the mucous membrane of the large bowel. In the portion of the ascending colon where the lesions were most advanced they formed a large patch affecting the whole circumference of the gut for several inches of its length, presenting general thickening and inflammatory œdema and granular degeneration of the mucous membrance; thus affording a great contrast to the discrete small round or oval thickenings of the submucous coat already described as so characteristic of early amœbic disease. (See page 66 and Plate II, opposite page 65.)

Ulcerative Stage.—Plate VII illustrates very well the more advanced changes of acute bacillary dysentery. In the first place it will be noted that the whole extent of the large bowel is involved, no extensive area of healthy mucous membrane remaining, as is the case in the acute amœbic dysentery represented in Plate III, opposite page 68. Next it will be seen that the lowest foot or two of the ileum presents inflammatory changes of the mucous membrane similar to those in the large bowel, the disease not being limited by the ileo-cæcal valve, as is nearly always the case in amœbic dysentery. The actual lesions only differ in degree from those of the early stages above described. Thus, throughout the large bowel, as well as in the lowest part of the ileum, there is marked general thickening of the mucous membrane, with patches of a greenish granular appearance, due to fibrinous deposit in necrosis of the surface epithelial layers, as shown in the ascending colon in Plate IV, opposite page 72. In addition there is very extensive serpiginous ulceration presenting

slightly depressed red inflamed floors, between which portions of yellowish-white relatively raised intact mucous membrane remain, being parts which have passed through the early inflammatory stage without having sloughed away, as in the areas where depressed serpiginous ulcers have appeared. The very marked congestion depicted in Plate VIII is only seen when a post-mortem is obtained very shortly after death, so it represents as well as possible the conditions actually present during a severe attack of acute bacillary dysentery.

The disease does not always involve the whole length of the large bowel even in cases proving fatal in the acute stage, but when a smaller length of the intestine is attacked that part will be uniformly affected, and no extensive and abruptly defined healthy areas will remain within it, as is so commonly the case in advanced amœbic dysentery. The absence of the discrete rounded raised yellow ulcers of early amœbic dysentery is conspicuous in Plate VIII, in which the ulcers are extremely irregular in outline, running one into another and relatively depressed beneath the level of the remaining islets of unnecrosed mucous membrane. The pictures of the two diseases are, therefore, quite different from each other, and although doubtless in rare instances one may complicate the other, this is altogether too exceptional to cause much difficulty in interpreting the lesions found post-mortem.

Fibrinous or Diphtheritic Dysentery.—These terms were frequently applied to the lesions of dysentery by older European writers on epidemic bacillary

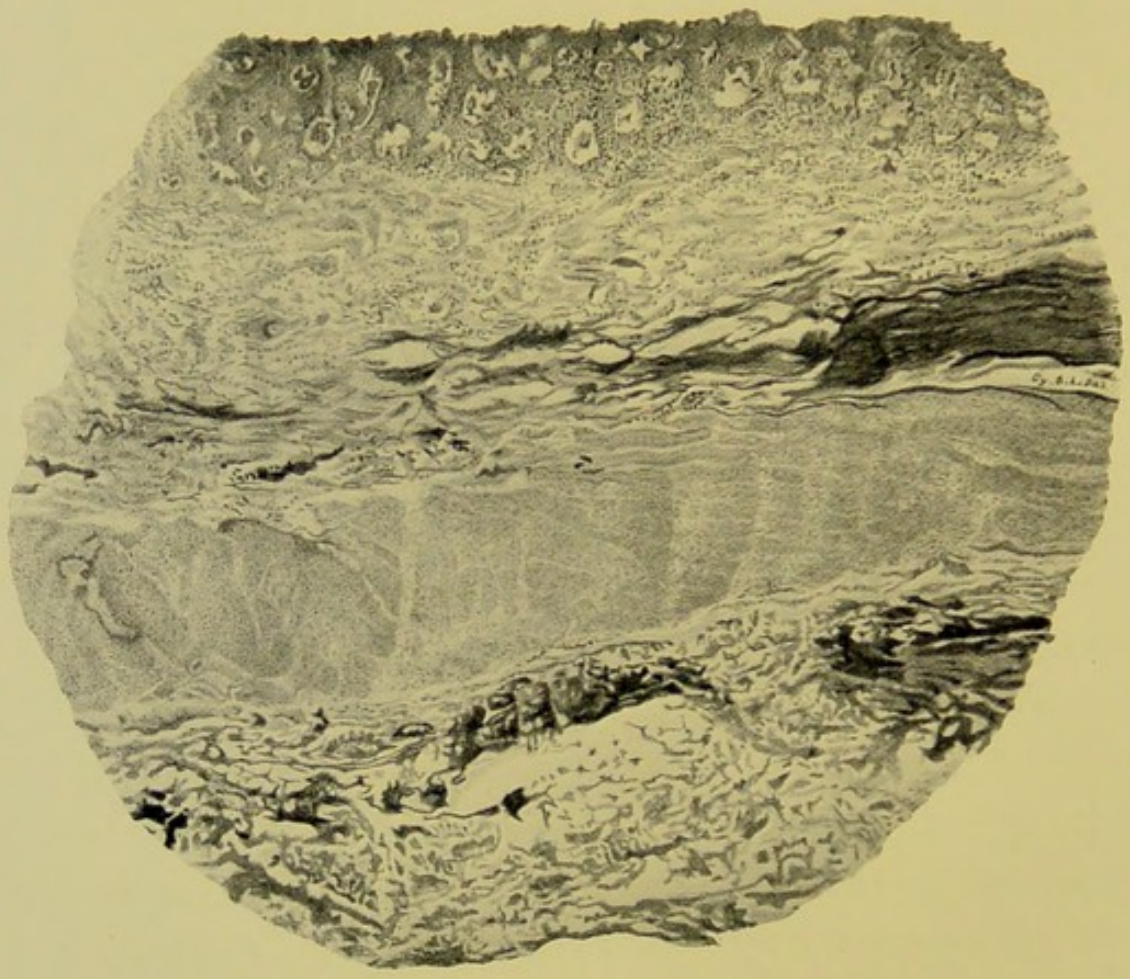
dysentery, and also less frequently by those whose experience was gained in tropical countries where the amœbic form predominates, much confusion having thus arisen in their use. Both the grey or greenish granular necrosis of the mucous surface of bacillary dysentery and the tawny yellow exposed infiltration of the submucosa of amœbic disease have been described as fibrinous or diphtheritic by different writers, although quite distinct in nature, as will appear from the account of their microscopic appearances on pages 75 and 78. It is particularly in acute epidemic forms of bacillary dysentery in temperate climates that an actual diphtheroid membrane resulting from fibrinous deposit and necrosis of the mucous membrane itself is most frequently seen, so it is well to confine the term to that condition, and not to apply it to the very different purulent gelatinous amœbic infiltration of the submucous layer, which cannot correctly be called diphtheritic if any analogy to the throat affection is to be maintained.

I possess one illustration of an exceedingly acute bacillary dysentery, from which the patient died so rapidly that the body was brought for a medico-legal examination as a suspicious death. The cæcum and ascending colon alone were affected, the mucous membrane being so extremely inflamed as to measure nearly half an inch in thickness, and it was covered with a dense white membrane, which could be peeled off in large thick flakes, showing that it was a surface deposit, and so totally different from the submucous infiltration of amœbic disease. Such cases are very rare in my experience, and only differ

from ordinary acute bacillary dysentery in that the patient dies of toxæmia before actual ulceration has time to take place. These cases are obviously very far removed from the chronic membranous colitis occurring in temperate as well as in tropical climates.

Chronic Bacillary Dysentery.—When we come to consider the distribution of the lesions it will be shown that the feature in which chronic bacillary dysentery most differs from the acute stage is that in the latter all, or nearly all, of the large gut is involved, while in the former only the lower half or so is ulcerated. The character of the lesions differs mainly in that the early fibrinous granular changes in the mucosa have usually disappeared in the chronic stage, and only leave very extensive irregular depressed ulcers, usually running into each other, with some general thickening of the mucous membrane, the whole presenting a worm-eaten appearance.

In some cases very numerous separate small depressions are seen, containing transparent mucus closely resembling raw white-of-egg, and similar in nature to that so often met with as small flakes in the stools of bacillary dysentery. These ulcers are quite different in character from the small amœbic ulcers, while the whole of the affected portion of the bowel wall is thickened and uniformly studded with them without any intervening healthy portions, such as are found in amœbic dysentery. In fact, the extent of the mucous membrane which is destroyed by the process is the most noteworthy feature of this stage.



Mucous Membrane in Acute Bacillary Dysentery (× 15).

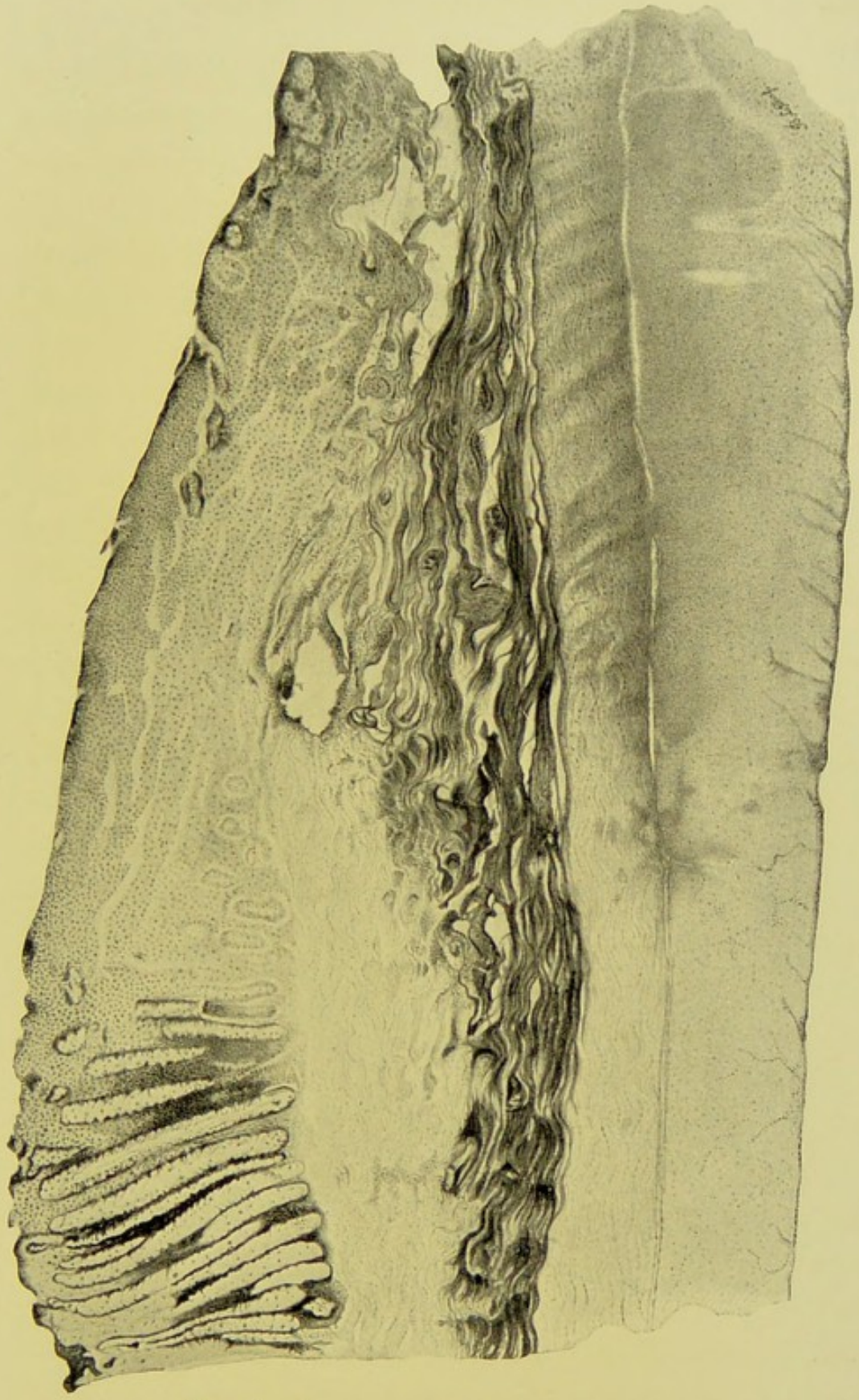
THE MICROSCOPICAL CHANGES IN BACILLARY DYSENTERY

In the acute stages of bacillary dysentery presenting the granular thickening of the inner surface of the bowel wall, without any actual ulceration, the principal changes will be found to have taken place in the mucous coat. This stage of the disease is well illustrated by the drawing in Plate IX, from a typical case of acute bacillary dysentery due to Shiga's organism. Here the process is essentially an acute fibrinous (diphtheritic of old writers) inflammation of the mucous membrane, producing the darkly-stained irregular deposit with a frayed edge seen on the inner surface of the section depicted in Plate VIII. The rest of the mucous layer is infiltrated with the same inflammatory product to such an extent that the tube glands have almost entirely disappeared by a necrotic process, only a few degenerate groups of epithelial cells remaining. This is in marked contrast to the condition in early amœbic disease shown in Plates V and VI, in which the tube glands are clearly seen almost up to the edge of the central ulcerated part. Again, in acute bacillary disease the submucous coat is much less involved than in the amœbic form, and shows but a scanty small-celled infiltration, together with some inflammatory œdema, the latter producing the greater part of the limited amount of thickening. The muscular coat is healthy, while the serous membrane may show some œdematous effusion. In this stage there is no acutal ulceration, the whole process being an acute inflammation mainly affecting the mucous mem-

brane and producing an excessive secretion of mucus, with a variable amount of bloody effusion in proportion to the severity of the process, but often only very limited in amount.

The chronic stage of bacillary dysentery with depressed ulcers is illustrated by Plate X. On the left side of the drawing the tubular glands of the recovered portion of the mucous membrane are seen with slight remaining cellular infiltration and some degeneration of the epithelial cells, which increases as we pass towards the ulcerated portion, the gland tissue first staining very feebly and finally disappearing altogether, shading off into chronic small-celled infiltration of granulation tissue in the floor of the ulcer, which diminishes in thickness as the centre of the depressed bare patch is reached. The submucous coat shows a little chronic inflammatory fibrous tissue formation, while the muscular coat is practically healthy, the appearances thus differing materially from those of the raised greatly thickened submucous coat of amœbic colitis. Here, again, we see that the stress of the bacillary infection falls almost solely on the mucous membrane itself, the other coats of the bowel being but little affected.

The Distribution of the Lesions in the Bowel in Bacillary Dysentery.—In bacillary dysentery the inflammatory thickening of the mucous membrane, and later the depressed serpiginous ulcers, involve large areas of the bowel wall in a uniform manner, leaving little or no completely healthy mucosa between the ulcers, such as is practically always present in amœbic disease. In Diagram 3 at the end of the work it has therefore only been possible to represent



The chronic stage of Bacillary Dysentery.

the affected parts of the bowel by a general shading, except in a few chronic cases in which only scars or small ulcers remained in the upper portions of the large intestine. The cases have been subdivided into acute and chronic in accordance with the clinical histories, those in which the disease had lasted for a month or more being taken as chronic, although necessarily one class shade off into the other. The acute cases of less than one month's duration vary from the choleraic form lasting only two or three days down to those of three or four weeks. That such a division is of practical importance will be seen from the following considerable differences between the two classes.

Acute Bacillary Dysentery involves the whole, or nearly the whole, of the large bowel. If the lesions extend as high as the cæcum, then the lowest part of the ileum for from one to three feet is also inflamed, as shown in Plate VIII and illustrated by Cases 1 to 4 and 9 to 11 of the first line of Diagram 3. The acuter the case the more marked is the general inflammatory thickening and granular appearance of the mucous membrane and the less the extent of acutal ulceration, death having been produced before the sloughs have had time to separate to form the depressed ulcers of the later stages. Thus, Nos. 1 and 2 were admitted to the cholera ward with choleraic symptoms and died within eighteen hours, uniform acute inflammatory changes of the mucous membrane throughout the whole of the large intestine, together with granular thickening of the lowest part of the ileum, being found after death. At the other extreme of this

series we have No. 8, in which the duration of the disease was just one month, the cæcum showing only small depressed ulcers, while the rest of the large bowel presented the typical general thickening of the mucous membrane with very numerous irregular depressed ulcers, the disease being on the verge of becoming chronic. Nos. 9 to 11 respectively illustrate acute bacillary dysentery complicating cirrhosis of the liver, kala-azar, and pulmonary phthisis without tubercular involvement of the intestines. They were thus acute attacks of bacillary dysentery proving rapidly fatal in patients already worn out by other serious diseases. I have repeatedly obtained cultures of dysentery bacilli in such cases, showing that there was nothing peculiar about them such as would warrant their being called 'terminal dysentery', if by that term it is meant in any way to imply a special variety of the disease (see further page 279). The same remark applies to Nos. 25 to 27 of line 1 of the diagram, which are examples of fatal chronic bacillary dysentery at the end of the same diseases.

Chronic Bacillary Dysentery is illustrated by Cases 12 to 27 of the first line of the diagram. With a few exceptions the lesions are limited to the lower half or two-thirds of the large intestine, while only in No. 14 was the whole of the large bowel uniformly involved, the case being diagnosed clinically as 'chronic dysentery', although its duration was not recorded, so it may have been an acute final exacerbation. In Cases 12, 13, and 19 the first part of the large bowel showed only small ulcers or scars, while the lower portion presented the

characteristic general thickening with extensive serpiginous ulcers. In none of the chronic cases was the lowest part of the ileum involved, as was so commonly the case in the acute series. In no less than 12 out of the 16 cases only the lower part of the large gut presented dysenteric lesions: an important point which it has been already shown is in great contrast with what obtains in chronic amœbic disease (see page 71). The ulceration is usually very extensive in the affected portions of the bowel, and only small tags of relatively raised intact mucosa may remain between the extensive intercurrent depressed ulcers surrounding them. If some healing has taken place the bowel may be contracted as well as thickened.

The most essential difference between the distribution of the lesions of typical acute and chronic bacillary dysentery respectively is, then, that in the former the whole, or nearly the whole, length of the large bowel and often also the lowest part of the ileum are uniformly involved in an acute inflammatory process which rapidly proves fatal; while in the latter the process is limited to the less vital lower portions of the large gut, and the patient survives long enough to allow of more extensive destruction of the mucous membrane of the affected areas.

CHAPTER X

CLINICAL DESCRIPTION OF BACILLARY DYSENTERY

Bacillary dysentery is remarkable for the great variations in its virulence, extending from very acute cases, closely simulating cholera, down to a mild disease with the passage of a little mucus, and readily amenable to simple purgative treatment. On the other hand, the classical symptoms of the disease are much less seldom absent than is the case with amœbic colitis, which so frequently produces simple diarrhœal stools without blood or mucus, as already described (see page 105). Moreover, when bacillary dysentery passes into a chronic stage it becomes much less amenable to treatment than in the earlier ones, so this condition requires special consideration. The typical average case will therefore first be described, and afterwards both the very acute and the chronic forms will be separately dealt with.

The General Characteristics of Bacillary Dysentery.—It has already been pointed out in considering the epidemiology of dysenteries that the bacillary form tends to assume epidemic characters and to attack a number of persons within a short time, either in a household or in some such institution as an asylum or jail, in which respect it differs from the usually sporadic amœbic disease. In Japan the bacillary

disease is often epidemic and attended with a high mortality of about 30 per cent. In such cases the disease begins suddenly and runs an acute course with a considerable degree of pyrexia, often of a remittent character, and accompanied by marked constitutional symptoms, which may even approximate to those of typhoid fever, while in extreme cases they may at first be mistaken for cholera in tropical countries, several such cases having been admitted to my cholera ward in Calcutta. Such severe febrile and toxæmic symptoms accompanying the frequent passage of blood and mucus are of considerable value in differentiating the disease from amœbic colitis, in which high persistent fever and severe constitutional disturbance are uncommon in the absence of serious inflammatory complications, such as extensive involvement of the peritoneal coat of the large bowel or acute hepatitis. Great depression of the vital powers ensues, involving a tardy convalescence in recovering cases, during which the greatest care is necessary to prevent a recrudescence of the symptoms. If the patient comes early under proper treatment the disease tends to get well after a longer or shorter time, and with due care should be completely cured in the great majority of cases. If, however, the condition is neglected at the first it may soon pass into a chronic and intractable form, which only too often terminates fatally after a protracted course, especially in feeble, badly fed, poor native subjects. Consequently the slightest signs of dysenteric disease should never be lightly regarded or neglected, as there is no affection in which the old adage ‘a stitch

in time saves nine' is truer than in bacillary infection of the large bowel.

Onset.—In bacillary dysentery the symptoms usually begin suddenly, although there is often a feeling of uneasiness and abdominal discomfort for a short time before a griping sensation is felt, quickly followed by the passage of mucus with or without blood, and as a rule accompanied by straining and tenesmus, which is a more constant symptom

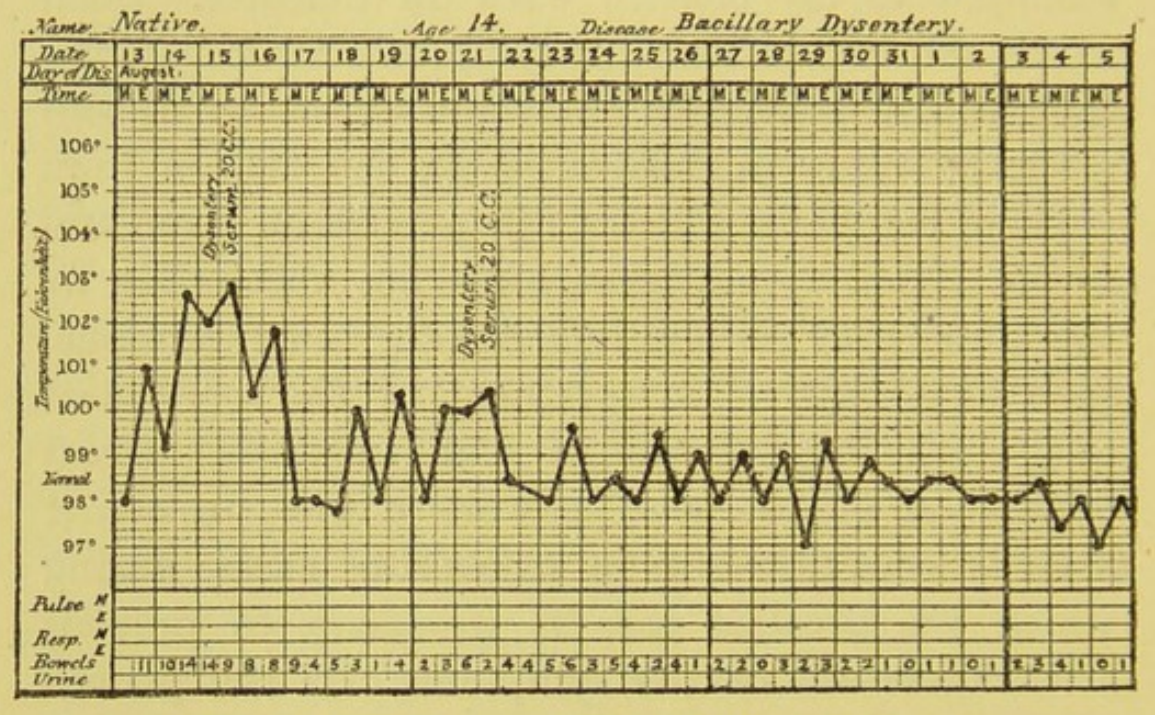


CHART 2. Temperature Chart of a Case of Severe Bacillary Dysentery.

in bacillary than in amœbic colitis on account of the marked tendency of the former to attack the rectum early in the disease. Exceptionally bacillary dysentery may commence with diarrhœa for a day or two before the appearance of mucus and blood in the stools.

Fever.—With the onset of all but the very mildest forms the temperature rises to 101° or 102° F., in the acuter cases to a still higher point, and this is

accompanied by great lassitude and depression or even drowsiness. In mild cases the febrile curve may be intermittent throughout, but it often assumes a remittent type for the first few days and gradually declines to the normal in the morning, while still rising to from 100° to 102° in the afternoon. Although the temperature curve seldom remains high for long, yet its observation is of great importance, for even a rise to just over 99° F. indicates that the disease is still active, while such a slight return of the fever after the curve has been normal for a time is almost always accompanied by an exacerbation of the symptoms, and is a sure sign of the necessity for the utmost vigilance, especially as regards diet. As convalescence becomes established the temperature often becomes subnormal, and I regard it as a favourable sign if it does not rise above 97° to 98° for several days at a time in a patient who is otherwise progressing favourably. This is shown in the latter part of the chart above, which illustrates several of the above-mentioned points, the curve being remittent at first, then intermittent, and finally subnormal as convalescence ensued. The case was a severe one, although recovery was complete, as I saw the patient in good health some weeks after his discharge from hospital.

Abdominal Pain and Tenesmus.—The griping pains within the abdomen are very characteristic of dysentery, and are doubtless due to the passage of the intestinal contents over the inflamed mucous membrane, as they commonly immediately precede a call to stool. They must be carefully distinguished from true tenesmus, which is the bearing-down pain

experienced in the rectum during and for a time after the actual evacuation of the bowels, and is a sign of the involvement of the rectal mucous membrane in the disease process, as is usually the case early in bacillary dysentery. It may be so troublesome as to cause nearly constant calls to stool, making the patient reluctant to leave the commode or bed-pan, although only a few drops of mucus are passed at a time. In addition to the griping pain a more constant dull sensation is experienced, which is most frequently referred to the neighbourhood of the navel or across the lower part of the abdomen. This pain is much less frequently localised over some part of the large gut than in the amœbic disease, for the reasons already pointed out (see page 267). When tenderness on gentle pressure is present in bacillary dysentery it is most usually found over the sigmoid colon in early acute cases.

Thickening of the Bowel.—This is much less common in bacillary than in amœbic colitis, and when present is nearly always limited to the sigmoid, which is often rather contracted to form a firm elongated mass without much actual thickening of the wall of the gut. Moreover, this condition is much more common in chronic cases, so is quite different in nature from the greatly thickened tender cæcum or colon of acute amœbic dysentery (see page 66).

Number of Stools.—This will vary enormously with the nature of the case, being naturally more numerous in the acute types, especially if the rectum is severely attacked, when from twenty to forty

motions may be passed in the twenty-four hours, although in Calcutta this great frequency is not very common, less so than is the case in amœbic disease. In ordinary early bacillary dysentery from six to fifteen stools is about the usual number, being somewhat less frequent in the chronic cases.

Character of the Stools.—This also varies within very wide limits, so that in a large proportion of the cases it is impossible to form any safe conclusion as to the type of dysentery from the appearance of the stools; for although as a general rule the presence of much blood is a more marked feature of amœbic as opposed to bacillary dysentery, in the early acute stages of the latter variety very blood-stained mucus is often passed precisely similar in its naked-eye characters to the typical stools of amœbic disease. In milder early as well as in chronic cases there is often little or no blood visible in many of the stools in bacillary disease, but abundant thick, opaque and sometimes stringy mucus forms the bulk of the material passed other than fæcal matter; but even this may be simulated by amœbic disease, so, as was emphasized in dealing with that form, microscopical and bacteriological examinations are essential in order to be certain of the correct diagnosis, and therefore of the best treatment. Unfortunately, facilities and time for the latter are only too often absent in the tropics, and a provisional diagnosis has to be made and corrected, if necessary, in the light of the results of the treatment adopted.

Microscopic Examination of the Stools.—Here again the simple microscopic characters of the mucous discharges from the bowel will not in them-

selves always allow of a correct differentiation between the different forms of dysentery being made, although certain points are often of great assistance in arriving at a correct conclusion. If the pathogenic amœba is met with there can be no doubt as to the presence of that type of the disease, and the specific anti-amœbic treatment may be confidently adopted, the cases in which the two forms are simultaneously present being too rare materially to affect the issue. The warning already given as to the necessity of making several examinations before excluding amœbic infection being borne in mind, the absence of that parasite greatly increases the probability of the disease being bacillary dysentery, although such causes of the passage of blood and mucus as cancer and tubercle should not be forgotten.

In either type of dysentery pus corpuscles may form the bulk of the mucous discharge, although in my experience this is more common in the amœbic variety. On the other hand, in bacillary disease fibrin and columnar epithelial cells are often present in abundance, the latter being sometimes seen in rows adherent to each other as if just cast off from the internal surface of the bowel. It will be remembered that the characteristic lesion of bacillary dysentery is an acute inflammation of the mucous membrane with resulting necrosis of the superficial layers, so these microscopical features are exactly what might be expected and are of considerable diagnostic value, their detection having often afforded me the first reliable clue to the nature of the infection, especially as these appearances are rarely met with in amœbic disease.

When possible endeavours should be made to clinch the diagnosis by cultivating the dysentery bacillus from the stools by the methods already described (see pp. 244–6).

Blood Changes.—It has previously been shown that in amœbic disease either actual or relative leucocytosis is almost invariably present in the absence of liver complication (see page 100). On the other hand, in bacillary dysentery as seen in Calcutta it is quite exceptional to find any increase of the leucocytes. Thus, out of seventeen cases in which there was either post-mortem or cultural proof of the disease being of bacillary origin, in only two was there an actual leucocytosis and in another two a relative one, so that in less than one-fourth was there any increase and in only 11·8 per cent. an actual leucocytosis was found. Probably in severe epidemic dysentery a more frequent excess of white corpuscles might be met with, but in some extremely acute cases of bacillary dysentery I have found a complete absence of leucocytosis, which is practically never the case in very acute amœbic disease unless the patient is in a nearly moribund condition with gangrene of the bowel wall. Again, in chronic bacillary dysentery I have not met with actual leucocytosis and very rarely with even a relative increase; this being also in marked contrast to the very frequent increase of the white cells in chronic amœbic disease. Further, the few cases in which I found an actual leucocytosis in bacillary dysentery were acute cases which ultimately did well, and in these the total count did not exceed 15,000, although others have recorded higher counts. This is also

a point of considerable diagnostic importance, as it has already been shown that counts of from 20,000 to 40,000 or more are comparatively common in amœbic disease.

The differential leucocyte counts do not show much variation from the normal proportion, the two cases with actual leucocytosis not yielding particularly high polynuclear percentages, although this is generally raised in the acuter forms of amœbic disease.

The red corpuscle counts are of less importance, except that in the very acute choleraic forms they may be much increased owing to the concentration of the blood, which is also revealed by the high specific gravity, and affords an important indication for intravenous salines. In chronic bacillary disease fairly marked anæmia is shown by a fall in the number of red corpuscles and in the specific gravity of the blood, which is often below 1,045, while the hæmoglobin is proportionately diminished.

THE VERY ACUTE CHOLERAIC FORM OF BACILLARY DYSENTERY

This is a somewhat rare but important type of the disease, which is worthy of special note on account of its liability to be temporarily mistaken for cholera or ptomaine poisoning, and of the necessity for intravenous saline injections in some cases. The most characteristic feature is the very acute onset, accompanied by great loss of fluid from the system which, with the toxæmia due to absorption of the bacillary toxins from the large bowel, rapidly leads to serious collapse closely resembling the algid

stage of cholera. Indeed, I have treated several such cases as cholera on their first admission, and only realized their true nature when large mucus evacuations were passed, with or without blood, which were found to be free from cholera vibrios. The specific gravity of the blood may be raised from a normal of 1,056 up to about 1,064, indicating the loss of several pints of fluid from the system, and necessitating the intravenous injection of 3 or 4 pints of saline solution, preferably the hypertonic solution containing 120 grains of sodium chloride, together with 6 grains of potassium chloride and 4 of calcium chloride to the pint, as advised by me in the treatment of cholera.

The most remarkable case of this nature I have met with was found to be due to the Shiga bacillus. The patient was admitted as a case of cholera in a pulseless condition and showed a rectal temperature of 106·2° and a specific gravity of 1,064, so was given 4 pints of the hypertonic saline solution intravenously at room temperature of 86° F., and other measures were taken to reduce the hyperpyrexia. After the infusion the pulse returned at the wrist, but was still very feeble, so I injected per rectum a quart of a solution of 10 grains of calcium permanganate to the pint with a view to destroying as much as possible of the bacillary toxins in the large bowel—as I had found experimentally that the salt had that power—and repeated this injection in the evening. On the following day he had a good pulse and made a rapid recovery, although these cases often prove fatal in spite of the utmost care. Leucocytosis was absent in this case, which is an im-

portant point in differentiation from cholera, as well as from acute amœbic dysentery.

CHRONIC BACILLARY DYSENTERY

In its more chronic forms bacillary dysentery has much less characteristic features than in its early acute manifestations, so that it is usually impossible to differentiate it from amœbic disease by purely clinical appearances. This is due to fever being frequently entirely absent, or when present being of a low intermittent type such as may occur in other forms, while the naked-eye characters of the stools cannot be relied on to differentiate the two great classes of dysentery in this condition. Although the acute stage insensibly merges into the chronic disease, so that no hard and fast line can be drawn between them, yet for purposes of analysing my cases I have taken a duration of a month or more to indicate chronicity. As a general rule bacillary dysentery terminates in either death or recovery within a few months, and comparatively rarely lingers on with longer or shorter remissions for from one to several years, as is not uncommonly the case with inadequately treated amœbic disease. Nor are the remissions so complete and lengthy in the bacillary type, the disease tending to run on unchecked until the patient eventually develops some immunity to the infection and slowly recovers, or more often, worn out by his sufferings and the steady loss of albuminous fluids in the bowel discharges, succumbs to exhaustion. Extreme emaciation with a retracted abdomen is a striking feature of the clinical picture, but in the terminal stages it

may be partly masked by dropsy due to cardiac weakness, while atrophy of the general muscular tissue is also great, together with anæmia as already described. The stools are often extremely foul, this being an unfavourable sign. Severe hæmorrhage from the bowel is less common than in the amœbic form, but I have seen fatal loss of blood from a deep ulcer in the upper part of the rectum in chronic bacillary dysentery. Temporary improvement without complete cessation of the dysenteric discharges is not infrequent, but is too often followed by a recrudescence of the disease, often accompanied by a slight rise of temperature.

'TERMINAL DYSENTERY'

This very unsatisfactory term has been applied by certain Anglo-Indian writers to attacks of dysentery occurring as a late complication of some other chronic disease, the fatal termination of which it materially hastens, being particularly common in kala-azar. It is by no means a special type of dysentery, for I studied a number of such cases both clinically and in the post-mortem room, and have repeatedly met with either the amœbic or the bacillary types in different cases. Nor should it be regarded as a hopeless condition, for the amœbic cases are readily curable by ipecacuanha or emetine; whilst the disease may produce a considerable increase of the leucocytes, and in this way prove beneficial to the kala-azar, more than one desperate case of which I have seen steadily improve and ultimately recover after such an attack. I have, therefore, sometimes thought it may be inadvisable to cure

too quickly an amœbic infection in kala-azar, as long as it is kept under sufficient control to prevent it seriously weakening the patient. The so-called 'terminal dysentery', then, is no special type of the disease, but these cases require the same careful differentiation of the particular form present to enable correct treatment to be undertaken as in uncomplicated bowel trouble, and it would be well if this unfortunate term disappeared from medical nomenclature.

COMPLICATIONS OF BACILLARY DYSENTERY

Owing to the tendency of the disease process to be limited to the mucous and to a less extent the submucous coats of the bowel, and very rarely to extend deeply through the muscular layers to reach the peritoneum, abdominal complications are much less commonly met with in bacillary than in amœbic dysentery, as has been shown in the section on pathological anatomy. There may be slight tenderness on pressure, generally over the sigmoid flexure, but actual local peritonitis is most uncommon, although some sero-purulent fluid was found in the lower abdomen in one very acute case ending fatally on the second day. Perforation of the large bowel is also rare in bacillary disease, although only too common in the amœbic form, and the same remark applies to serious hæmorrhage from the bowel.

Hepatitis.—We have already seen that hepatitis, often going on to suppuration, is a very common remote complication of amœbic colitis, and it might at first sight be expected that acute and chronic bacillary ulceration of the large bowel might not

infrequently result in infection of the liver through the portal system, if only by secondary pyæmic organisms, as the dysentery bacillus itself rarely enters the circulation, but is ordinarily limited to the intestinal wall. Portal pyæmia with multiple small abscesses of the liver may, indeed, occur as a complication of bacillary dysentery, but it is most remarkable how rarely this happens, when we consider the destruction of extensive areas of the mucous membrane of the large intestine which is so generally found after death from chronic bacillary dysentery. Thus in 125 post-mortems in both primary and secondary dysentery cases in Calcutta during the last twelve years, 36 per cent. of which were bacillary in nature, I have not met with a single instance of portal pyæmia or other serious disease of the liver resulting from bacillary intestinal ulceration. Multiple small abscesses were not infrequently seen in the liver, but they have always been amœbic in nature, and usually contained the protozoal parasite alone, without any bacteria whatever, whilst they only occurred in amœbic dysentery cases. The explanation of the rarity of portal infection in the bacillary disease must be the limitation of the disease to the inner coat of the bowel.

These facts are of great practical importance, as it follows that the occurrence of hepatitis during or after dysentery is an almost sure sign that the bowel trouble is amœbic in nature, and not bacillary. In the very rare cases of true portal pyæmic abscesses secondary to bacillary dysentery the clinical signs of the liver infection are liable to be overlooked during life on account of the serious illness of the

patient, but as the condition is beyond the range of successful treatment it is of more academic than practical interest.

Arthritis.—A more important complication is swelling of one or more of the large joints of a very obstinate character, which is met with in certain outbreaks, and was a not infrequent sequel of bacillary dysentery during the South African war. It appears to be due to absorption of toxins from the bowel, and tends to get well eventually without going on to suppuration, although it may take some months to resolve. I have not yet met with it in India, but Brodribb has recorded a case occurring there (*Ind. Med. Gaz.*, 1907, p. 172).

The Diagnosis of Bacillary Dysentery.—In this form there is rarely any difficulty in recognizing the presence of a dysenteric process, with the exception of the early stages of the choleraic type; but it is a much more difficult matter to differentiate the bacillary from the amœbic disease, especially in warm climates where the latter is so prevalent. As, however, the treatment of the two diseases is very different, and the specific remedy for one is of no use in the other, the clinical distinction between the two is of the utmost practical importance. From the foregoing description it will be seen that in the early stages of acute bacillary dysentery the more marked febrile and constitutional disturbance will often afford a clue to the nature of the case. In the milder and also in the chronic forms, however, the clinical signs usually fail to separate the two affections, and microscopical and bacteriological methods are essential to success. The discovery of a patho-

genic type of amœba will establish the diagnosis of that variety and go far towards excluding the bacillary form. Apart from this there is no simple and reliable microscopical character of the stools which will enable bacillary dysentery to be recognized, although the presence of large numbers of columnar epithelial cells in the mucus is an indication of the probable presence of this type, but the naked-eye characters of the evacuations are usually quite unreliable.

Bacteriological methods are therefore necessary, but unfortunately opportunities and leisure for making use of the rather complicated technique are seldom available in the tropics where they are most wanted. The serum agglutination test is also of little practical value, for, in the first place, the reaction only appears one or two weeks after the commencement of the disease, so that it is absent just when it is most wanted, while even when it is present in the later stages it has been found to be a very unreliable guide.

The Diagnostic Value of the Emetine Treatment.—Treatment has, therefore, usually to be undertaken without waiting for a certain diagnosis of the type of disease to be dealt with, but the important fact has been already recorded that the failure of hypodermic injections of emetine to bring about very marked amelioration of dysenteric symptoms within two or three days is sufficient to exclude the presence of amœbic disease, and thus make it so extremely probable that bacillary infection is present as to indicate active treatment against the latter disease being adopted. The preliminary purgative treat-

ment, which is indicated in all forms of dysentery, can be combined with the emetine, and but little time is lost in thus excluding the common amœbic infection.

The possibility of the presence of tubercle or cancer as a cause of the discharge of blood and mucus from the bowel must not be lost sight of. A preliminary microscopic examination of the stools on admission, which should never be omitted, will have already enabled the presence of amœba and of the balantidium coli to have been detected if present.

Mortality.—In the epidemic form bacillary dysentery is always a serious disease, the mortality in Japan having been about 30 per cent. before the discovery of the serum treatment, while it is also comparatively high in asylums and to a less extent in jails, especially in the more unhealthy provinces. The case mortality of bacillary dysentery in India is not known, as in the official statistics it has not yet been possible to separate this disease from the amœbic variety. In Calcutta, in my ward, before I began the emetine treatment for amœbic dysentery the mortality of that form was higher than in bacillary cases, but my cases of the latter verified by bacteriological examinations are too few to furnish a reliable figure. On the other hand, at the Campbell Hospital, where many chronic cases of dysentery have been admitted in the past year, during which I have been studying the disease there, in the majority of fatal cases post-mortems revealed bacillary disease. At the Medical College Hospital, where I have recently found only one-third of the

dysentery admissions to be for bacillary disease, the post-mortem records show that 43·6 per cent. of the cases dying primarily of dysentery were found to be bacillary in nature, which indicates a high case mortality, probably somewhere about 30 per cent. In both these hospitals a considerable proportion of the patients only come for admission after they have been suffering from the disease for some time, often several months, so it is not surprising that the death-rate among these neglected patients should be so high, that for all forms of dysentery together during the five years 1907–11 having been 41 per cent. At El Tor among the Mecca pilgrims the mortality of bacillary dysentery was 64·4 per cent. in 1909, but was reduced during 1910 by the serum treatment to only 10·8 per cent.

On the other hand, when dysentery cases come early under skilled treatment the mortality is much lower, as shown by the figures in Table II of the official figures for the army and jails in India, which include all forms of dysentery together.

TABLE OF THE PREVALENCE AND CASE MORTALITY OF DYSENTERY IN INDIA, 1906–10

	Admissions per mille.	Case mortality.
British Army . .	12·0	2·93 per cent.
Indian Army . .	33·6	0·51 ,,
Indian Jails . .	70·3	5·29 ,,

Prognosis.—In individual cases the most important elements in the prognosis are, firstly, the severity of the initial symptoms; and secondly, the duration of the disease before the patient comes under treatment. In epidemic outbreaks, whether in an institution or in a household, the disease is likely

to be especially severe, while in the very acute choleraic cases the mortality is also high. With these exceptions, in the great majority of bacillary dysentery cases coming under early observation the ultimate prognosis is good, although convalescence may be tardy. It is far otherwise with neglected patients who have suffered from dysentery for from one to several months, often without any treatment, so that extensive ulceration of much of the large bowel is already present on their admission to hospital. Treatment now often fails to avert a fatal termination, or at the best they leave incompletely cured and very liable to fatal relapses. Emaciation and anæmia are bad signs, and in these advanced cases bacillary dysentery is only exceptionally a curable disease, even under the more favourable conditions in Indian jails, where relapses frequently recur until the patients are released by death or the termination of their sentences. In short, chronic bacillary dysentery is a much more difficult disease to deal satisfactorily with even than the amœbic form was until recently, which is saying a great deal.

CHAPTER XI

THE TREATMENT OF BACILLARY DYSENTERY

Unfortunately we have no drug with a specific curative action on bacillary dysentery such as ipecacuanha has on the amœbic disease, so, apart from serums and vaccines, the treatment is largely empirical. However, with proper attention the disease can be controlled and time afforded for the natural production of immunity except in the most virulent infections, or when patients are first seen with advanced chronic dysenteric ulceration.

In **Acute** cases coming early under observation the first thing to be done is to clear out the bowels with a purge. As there is often for a time some uncertainty as to the precise type of the disease present, an ounce of castor oil, followed by one-drachm doses in an emulsion every four to six hours, is the best preliminary treatment, together with fluid diet mainly composed of citrated milk. If the stools show no pathogenic amœbæ and the symptoms point to the presence of bacillary disease, the saline treatment should now be commenced, as it usually affords most relief in the early stages. For this purpose sodium sulphate is the best salt, as it is less griping than magnesium sulphate, although some prefer to combine the two. To get the best results from them they should be given in saturated solutions, the first dose being half an ounce, followed

by one to two drachms every two to four hours in accordance with the age and condition of the patient, the fuller amounts being reserved for strong adults. In very mild cases of dysentery treated as soon as the first symptoms appear, it is surprising how quickly all traces of mucus disappear from the watery yellow stools, while at the same time relief is afforded to the abdominal pain and tenesmus; but it seems to me to be still an open question as to how many of the cases yielding to the first few doses of salines are really examples of specific bacillary dysentery (see page 287). However that may be, undoubted mild bacillary infections may sometimes subside within four to seven days, although if the attack is at all severe in its onset a considerably longer time is necessary for its complete cure, and other treatment than salines has often to be resorted to.

The favourable action of saline purges is probably due to their relieving the congestion of the mucous membrane, whilst they may also flood it with opsonins and other specific anti-bodies during the escape of the watery fluid through the bowel wall.

Opium is often necessary if the stools continue to be frequent and distressing, especially if abdominal pain is present in the intervals between the evacuations. It is best given in the form of an enema at bed-time to ensure some rest during the night, and repeated if necessary in the morning; it is only exceptionally necessary to administer it by the mouth, when it is usefully combined with 1 to 3 grains of calomel or given in the form of Dover's powder to counteract its constipating effect,

or morphia may be injected subcutaneously instead, as advised by Morehead.

Ipecacuanha is useless in bacillary dysentery except in so far as it exerts laxative properties, but any advantage in this direction is more than counteracted by its nauseating and depressing effects. Emetine in my hands has proved to be equally useless in this form of dysentery, and may sometimes increase the number of the stools.

In some cases of dysentery perchloride of mercury is efficacious when other remedies have failed, but I know of no rule for guidance in its use, which is empirical. Calomel is much less given in dysentery at the present day than formerly, but is often of use either in one large dose or in doses of one grain combined with an equal quantity of opium and ipecacuanha two or three times a day, a careful watch being kept to avoid salivation. As was long ago pointed out by Twining, calomel is dangerous in cachectic patients, especially if the spleen is much enlarged.

In the acute stage of bacillary dysentery rectal injections are not of as much use as in chronic forms of the disease. The most valuable in my experience are the permanganates, especially when there are marked toxæmic symptoms, as is the case in the very acute choleraic form. I have proved experimentally that these substances have an immediate action on the toxins produced by Shiga's bacillus, oxidizing them into harmless substances, so that several times a lethal dose of dead dysentery bacilli, mixed with just enough permanganate solution to retain a little of the red colour, may be injected into

a susceptible animal without any ill effect. In treatment the calcium salt is preferable to the potassium one, as the former is somewhat less irritating to the bowel, forming calcium hydrate instead of caustic potash when decomposed. The former can usually be given in a strength of six to ten grains to a pint, beginning with the lesser amount, two pints being run in slowly through a slightly elevated funnel and a soft rubber tube passed about eight inches into the bowel. As the dysentery bacilli are to a great extent limited to the large intestine, it may thus be possible to destroy much of the toxin there and prevent its absorption into the system. In chronic bacillary disease this treatment is less efficacious than in acute cases.

Among substances which have been recommended as soothing to the bowel in dysentery are ispaghula, the dried seeds of Plantago ovata, which absorb water and swell up to form a mucilage given in doses of 50 to 150 grains; and kuchi in the form of a liquid extract or a tincture of the strength of 1 in 10, but they are not very active drugs.

The Serum Treatment of Bacillary Dysentery is the only truly specific one we have, and is of great value, especially in the acute stages. It is made by repeated injections of Shiga bacillus toxins in gradually increasing doses into horses over a long period. Shiga was the first to make and use such a serum, and with it he reduced the mortality of the severe epidemic form of the disease in Japan to about half its former rate. The main difficulty with regard to this treatment is that there are a number of varieties of dysentery bacilli in different countries

and even in different outbreaks in the same country, and although there is evidence that a Shiga anti-dysenteric serum may be active against an attack of dysentery due to Flexner's organism, still one made by the use of a particular strain of organism has in some instances been found more active than a stock Shiga one. Thus Ruffer and his colleagues, working at the El Tor quarantine station in Egypt, found it necessary to make a polyvalent serum with the aid of dysentery bacilli isolated from their own cases in order to get the best effects, and with it they obtained remarkably good results in the severe and neglected cases among the Mecca pilgrims, in whom the death-rate in bacillary cases was reduced from 64·4 to 10·8 per cent., whilst in pure infections with their El Tor bacillus it was only 5·7 per cent. The serum proved useless in amœbic cases, as might have been expected, the mortality among that form having been no less than 91 per cent. In Calcutta I have repeatedly seen great improvement follow the subcutaneous injection of 20 c.c. doses of the Lister Institute serum, repeated if necessary after two or three days. At El Tor from 40 to 60 or even 80 c.c. were given at a time. It is said to be most effective when administered intravenously.

In Chronic Bacillary Dysentery the treatment is much more difficult and unsatisfactory than in the earlier stages, as by this time much of the mucous membrane of the large bowel will have been destroyed and extensive serpiginous ulcers will be present, often involving a large extent of the gut, especially in its lower half. In this stage I have seen little good from the saline treatment, which is

often so useful in the early stages. Not only so, but when the patient has become greatly weakened and emaciated by chronic bacillary dysentery saline purges are often actively harmful, and may rapidly exhaust the little remaining strength to a fatal degree, and I have repeatedly had to regret using them in such cases. Moreover, it is now too late to expect improvement from reducing the congestion of the inflamed mucous membrane, as that stage is long past. Nor is much benefit to be derived from drugs administered by the mouth, for if they ever reach the lower bowel in an active form they will quickly be expelled by the irritable large intestine, only the lower half of which is usually involved in these cases (see Diagram 3, at the end). Hence the disease can now be much more readily reached by medicated enemata, combined with prolonged careful dieting to lessen as far as possible the irritation produced by the passage of fæcal matter over the ulcerated bowel wall. Thus it is in chronic bacillary dysentery that astringent enemata are most valuable, the most efficacious of them being *silver nitrate*, as long ago used by Wood in Philadelphia, while Stephen Mackenzie in 1882 reported several very chronic cases which were rapidly cured by 3-pint injections of a strength of $\frac{1}{2}$ to $1\frac{1}{2}$ grains to the ounce. Hewes of Boston has recently advocated as much as 5 grains to the ounce to cut short the early acute stages, a pint or more being injected and retained if possible for half an hour. If a silver nitrate solution is retained too long it may be neutralized by the injection of one containing common salt. Cooke advises touching all the ulcers

which can be reached through a proctoscope with 60 to 120 grains of silver nitrate to the ounce repeated daily until tenesmus is relieved. Copper sulphate in a strength of 1 grain to the ounce (20 grains in a pint) is also often of great value, while it has the advantage of being less painful than silver nitrate. Either the semi-prone or knee elbow position, or marked elevation of the hips, is advisable when giving large medicated enemata.

The Vaccine Treatment of Chronic Bacillary Dysentery.—Shiga first injected dead dysentery bacilli as a prophylactic against the disease in epidemics in Japan, with the result of lessening the mortality. Other observers have used similar procedures in the treatment of the disease, notably W. H. C. Forster in India, whose vaccine consists of an emulsion of dead Shiga bacilli in normal salt solution with 0·5 per cent. carbolic acid, prepared from twenty-four hour agar cultures killed by heating to 60°–63° for twenty minutes. Good results have been obtained with it by Gillett in two Bengal jails, and several cures of very chronic cases have been reported by other writers. On the other hand, Godson's results in an Eastern Bengal jail were very disappointing, no less than 30 per cent. of the cases receiving the full course of four doses at fortnightly intervals having relapsed within a short period after its conclusion, possibly owing to many of the cases having been amœbic in nature. In the Campbell Hospital, Calcutta, the treatment was also not successful, but here a considerable proportion of the cases are amœbic, in which it is not likely to be of any use, whilst it is unnecessary in view of the

specific action of emetine in that disease. I have also treated a few advanced cases of proved bacillary disease with Forster's vaccine with disappointing results, but its great value in certain recorded cases seems to be established, although much further work is required to ascertain the precise indications and limitations of its use. The initial dose for an adult should not exceed one lethal dose for a rabbit, which may conveniently be diluted so as to be contained in 2 minims of the vaccine, and repeated at fortnightly intervals in doses of 4, 6, and 8 minims as directed by Forster. I have occasionally obtained good results with a vaccine made from a dysentery bacillus isolated from a patient's stool, but this is a troublesome and expensive method.

The Diet in Dysentery.—In the acute stages of dysentery a milk diet is indicated, 3 grains of citrate of soda being added to each pint of milk to prevent the formation of irritating large curds. Soups, barley water, and other fluids may also be given, but no solid food until the active process has subsided, when arrowroot, custards, &c., may be added, but great caution is necessary in gradually increasing the diet for fear of incurring a relapse.

In chronic dysentery the dieting is a still more difficult matter, as the duration of the disease necessitates nourishing food, while since only the lower half of the large bowel is usually affected the digestive processes may be fairly efficient and more food can be given than in the acute stage, the effect on the number and character of the stools being carefully watched. In native patients it is usually necessary to allow a few ounces of soft rice or bread

as soon as some improvement has taken place, without which they will seldom remain in hospital long enough to have a chance of being cured. Some mild form of iron is also indicated for the anæmia which is present in these cases, together with other tonic treatment. The abdomen should be kept warm, a flannel binder being of great use for this purpose, as a chill may easily produce an exacerbation of the disease.

CHAPTER XII

OTHER FORMS OF DYSENTERY

DYSENTERY DUE TO THE BALANTIDIUM COLI

This is a rare disease which has been met with in Germany, Russia, the United States, the Philippine and Andaman Islands. The Balantidium coli is met with in larger or smaller numbers in the stools, and in the fresh state is a large oval granular protoplasmic mass from 70 to 100 micromillimetres in length and 50 to 70 in breadth, showing an oval nucleus anteriorly, together with contractile vacuoles and coarse granules of partly digested food. At the anterior end is a slight depression, the peristome, and all around the rest of the surface are cilia, which are longest near the peristome and slope backwards from their attachment to the finely striated cuticle. In stained sections of the affected tissues the parasites are rounded and the nucleus dark, but the cilia do not take the stains. Multiplication is chiefly by transverse division, the other described methods of reproduction being still disputed. The parasites may also encyst, especially if kept outside the body under unfavourable conditions, when they quickly lose their motility and many of them degenerate and disappear. They have been successfully cultivated in the Philippines on Musgrave's medium, and are readily killed by antiseptics and by a 1 in 5,000 solution of hydrochloride of quinine.

These organisms are found both between the tube glands of the mucous membrane and in the submucous layer, where they may enter the blood-vessels and be carried to the liver and set up abscess formation there. The typical lesions are produced in the large intestine, especially in its lower part, being commonly limited to the sigmoid and rectum. Congestion and catarrh with œdematous swelling first appear, going on to produce deep round or oval ulcers covered with mucus, somewhat resembling those of the amœbic disease, but containing numerous Balantidium coli if examined within a few hours of death, while sloughing and even perforation may result. There is no leucocytosis, but the eosinophiles may be increased.

In the Philippines Weston found this parasite only three times in 4,000 routine examinations of the stools of prisoners in the Manila prison, and a few cases of the disease have been reported by other American workers. Anderson met with it five times in 920 dysenteric stools in the Andaman Islands. Infection is believed to be through water, whilst healthy pigs often harbour the parasite and monkeys have been found to be naturally infected, but several experimenters have failed to infect these or other animals artificially.

The symptoms are said to resemble those of amœbic dysentery, and in the early stages diarrhœa only may be present, whilst later typical dysenteric stools are passed. The diagnosis can only be established by finding the parasite in the discharges.

Treatment.—Weston obtained recovery in two cases by treatment with calomel and salines followed

by full doses of ipecacuanha, while Jennings was successful with arsenic, thymol, and quinine enemata. On the other hand, Bowman states that the prognosis is bad even in early cases, and becomes hopeless when dysenteric symptoms ensue. In view of the good effect of ipecacuanha in some cases, hypodermic injections of emetine salts are worthy of trial.

THE BILHARZIA HÆMATOBIA AS A CAUSE OF DYSENTERIC SYMPTOMS

This parasite chiefly affects the bladder and urinary system, but in addition may involve the ileum and especially the large bowel, first producing papillomatous tumours of the mucous membrane, which may slough off and leave superficial ulcers. The wall of the gut is infiltrated throughout all its layers by the parasite, producing great localised thickening of the bowel wall. When ulceration takes place symptoms of diarrhœa or dysentery ensue, the discharges containing the ova of the worm which, together with the nearly invariable simultaneous involvement of the bladder, enables the nature of the disease to be recognized.

Unfortunately there is no effective treatment of the condition known.

THE RÔLE OF THE TRICOMONAS INTESTINALIS

This is a small, rounded or slightly oval flagellate organism from 10 to 15 micromillimetres in diameter with a long flagellum and undulating

membrane arising from a centrosome at the posterior end, and several smaller flagella which give it very active movement. They are frequently found in enormous numbers in both diarrhœal and dysenteric stools, being often associated with pathogenic amœbæ, but are occasionally found alone, more especially in cases of diarrhœa. Castellani has frequently met with them in Ceylon, whilst I have found them in about 20 per cent. of dysentery cases in Calcutta. Anderson met with them in no less than 723 out of 920 dysentery cases, and in 134 out of 210 admissions for other diseases.

It is still an open question whether this organism has any pathogenic action, but they are usually considered to be harmless. I have frequently seen them disappear in cases of amœbic dysentery treated with ipecacuanha or emetine. In cases of diarrhœa showing large numbers of the tricomonas without amœbæ, both the symptoms and parasites have disappeared after the use of enemata of 6 to 10 grains of calcium permanganate to a pint.

THE RELATION OF INTESTINAL WORMS TO DYSENTERIC SYMPTOMS

Ankylostoma and other intestinal worms may produce gastro-intestinal disturbance with the passage of a little blood and occasionally mucus, and thus be liable to be mistaken for dysentery. Indeed, some writers look on these parasites as a definite and not uncommon cause of dysenteric symptoms, especially in jails. Such cases are easily detected if routine microscopical examinations of the stools are

made in all dysenteric patients, for the ova of any worms present in sufficient numbers to cause such derangements will be readily found and lead to the adoption of suitable treatment for their removal. It should, however, be remembered that these parasites are present, usually in small numbers, in about three-fourths of native patients in the tropics, in the vast majority of whom the infection is not sufficient to produce any important symptoms; so the mere presence of ova in a stool is not sufficient reason for adopting drastic measures for immediately expelling the few worms present, possibly greatly to the detriment of a patient suffering from a serious attack of true amœbic or bacillary dysentery, but the latter diseases should first be cured, and then the advisability of dealing with the worms may be considered on its own merits.

IS THERE A NON-SPECIFIC CATARRHAL COLITIS PRODUCING MILD DYSENTERIC SYMPTOMS?

It remains to consider the probability of the occurrence of other common forms of dysentery as yet undifferentiated, whereby an important question is raised to which it is not possible at present to give a categorical answer. The word non-specific is used to indicate a disease not due to the known groups of dysentery bacilli or pathogenic amœbæ, and not to exclude any unrecognized organism, such, for example, as may produce catarrh of other mucous membranes.

In the first place, it would be strange if the mucous membrane of the large bowel were entirely

immune to mild catarrhal changes resulting from chills or indiscretions in diet, or at least if these were not predisposing causes. Secondly, very mild dysenteric attacks with the passage of a little mucus, perhaps tinged with blood, and disappearing at once after the bowels have been cleared out by a mild saline purge, are so common in warm climates that it is difficult to believe that they can be all due to such virulent infections as those caused by the known dysentery bacilli and amœbæ. Thirdly, when a large series of dysentery cases are investigated by modern methods there will always be found a considerable percentage (amounting to no less than 75 per cent. in a recent inquiry at an Indian jail) in which neither of the known classes of causative organisms can be found even by those familiar with the somewhat difficult technique required in such work. Again, it is impossible to reconcile the fact that Colonel W.J.Buchanan, I.M.S., has recorded over 1,000 consecutive cases of jail dysentery in Bengal treated with salines with only one death, with the view that the cases were mainly either bacillary or amœbic in nature, for wherever those diseases have been scientifically diagnosed and differentiated the mortality has been far higher; while Forster, working in a Bengal jail, records that those cases from which he isolated dysentery bacilli did not prove amenable to any drug treatment. Once more, it has been repeatedly pointed out that in jails the prisoners often purposely eat substances likely to produce bowel derangement in order to get into hospital and escape hard labour, and such cases would naturally be readily amenable to a saline purge.

Thus there are strong reasons for thinking that many of the milder cases presenting dysenteric symptoms which have immediately cleared up under purgative treatment may not be specific bacillary or amœbic dysentery. When we consider how recent is our knowledge of a number of organisms producing catarrh of the respiratory passages, it would not be surprising if somewhat similar bacteria capable of causing a mild catarrhal condition of the large bowel, probably assisted by chills and dietetic errors, have so far escaped detection among the extensive intestinal flora. If such exist they would be likely to produce milder and more easily curable forms of dysentery than those already differentiated, only requiring purgatives, rest, and dieting, and consequently the possibility of their occurrence does not materially affect the use of the measures already advised for the specific dysenteries. They should, however, be borne in mind by those engaged in investigating this great class of disease, regarding which we doubtless have still very much to learn, a fact of which no one can be more sensible than the writer of this very imperfect little work.

CHAPTER XIII

HILL DIARRHŒA AND DIARRHŒA ALBA OR SPRUE

The true etiology of these diseases is still unknown, but clinically they are so closely allied that cases beginning as hill diarrhœa not uncommonly run on into the much more serious typical diarrhœa alba or sprue. Indeed, Alexander Grant's classical paper on hill diarrhœa and dysentery includes cases of undoubted sprue with the typical tongue changes. On the other hand, the great majority of attacks of hill diarrhœa are readily amenable to treatment and change of climate, and only neglected cases develop into sprue, so it will be well first to describe hill diarrhœa and subsequently to deal at greater length with the more formidable disease.

HILL DIARRHŒA

A. Crombie well described this condition, the early stages of which he had abundant opportunities of studying in Simla and the more chronic cases in patients returning to Calcutta with the disease from various hill stations.

Symptoms.—The most essential feature of this form of diarrhœa is that it is limited to the early hours of the day, beginning between 3 and 5 a.m. and rarely continuing after 11 a.m., but recurring at the same time each day. From one to six motions may be passed daily, but usually from two

to four, whilst a noteworthy feature is that not only are they unattended by pain or depression of the pulse, but they actually afford relief to the abdominal discomfort and distended feeling which precede the evacuations. The stools are liquid, frothy, and of a light-grey colour, being described by Crombie as resembling whitewash, whilst their odour is fæculent, but not offensive. During the remainder of the day the patients go about their occupations without any discomfort or anxiety, and are thus liable to regard the complaint as too trivial to trouble about, as their general health is for some time but little affected. Associated with the diarrhœa is flatulent dyspepsia affecting both the stomach and intestinal canal, which may commence immediately on the patient arriving in a hill station, and therefore must rather be due to physiological processes than to any infective agency. The almost entire absence of bile from the motions points to deficient action of the liver.

The diarrhœa may continue in this way for many months, and in some cases recurs during each season in the hills for a number of years without the general health being materially affected, but more commonly some degree of emaciation results, which is often first noticed by the sufferer's friends. On returning to the plains, or even to a slightly lower elevation, the symptoms may, if the affection has not been long established, at once subside, again indicating a disturbance of physiological functions, which must be allowed some weight in the production of disease even in the germ-laden tropics. As Crombie pointed out, every gradation may be seen

in people arriving at a hill station, from mild flatulent dyspepsia to typical persistent hill diarrhœa.

Seasonal Prevalence.—Although a few patients develop diarrhœa immediately on arriving at a high elevation, the disease only becomes widely prevalent at certain seasons, namely, as soon as the valleys below become filled with vapour, while it reaches its maximum prevalence at the height of the rainy season, to decline again at the end of the rains late in September or early in October. This distribution is of importance in connexion with the possibility of the disease being a water-borne infection, for it is most prevalent just when the water supply is purest after the hills have become thoroughly washed free of any accumulations of dust and dirt. Grant also observed that those who only drank water which had been boiled or filtered did not escape the disease, while Crombie points out that children under twelve years of age are rarely attacked, which would not be the case with a water infection. It was suggested by Dyson and supported by Duncan that mica in the water supply might irritate the bowel and thus produce the disease. Some years ago at the height of the rainy season, when hill diarrhœa was at its maximum, I obtained some of the Darjeeling water, that being the hill station where the mica theory had been suggested, but even with the aid of a large and powerful electric centrifuge I was unable to recover any of the accused particles, so this theory may be safely excluded.

On the other hand, the rainy season is a time of rapid changes of temperature combined with a moist atmosphere, which has a much greater action on the

human body than a dry one. The patients, moreover, have mostly come up from the hot plains, often in a condition of debility due to long exposure to heat, and are also suddenly exposed to a great decrease of atmospheric pressure, which often produces sickness and other physiological perturbations. It is not, therefore, surprising that chills due to rapid variations of the moist temperature should produce derangements of the delicately adjusted mechanisms of secretion and absorption of some part of the gastro-intestinal canal and the large glands associated with it, and that the ill-digested food should cause flatulent distension of the bowel, leading in its turn to the expulsion during the early morning hours of the irritating remains of the heavy evening meal, so that sometimes in Simla nearly one-third of the population have been affected.

According to Grant, when children suffer from the disease it is mild and may last a long time without apparent ill-effect, and the same observer remarks that the temperate are attacked as frequently, but not so severely, as the less temperate.

Prognosis.—This is good as long as emaciation has not advanced, and removal from the hills is possible after treatment has failed to control the disease. It is only neglected cases running on into true sprue that become dangerous to the health, as in many of Grant's patients. In such the disease may persist after return to the plains, and will then probably necessitate long leave to England to eradicate its effects.

Treatment.—If seen early this is usually very effective. Grant relied on a dose of blue pill and

Dover's powder at bed-time, and in the morning an ounce of castor oil with a little laudanum. Farinaceous diet and confinement to the house for a few days then suffices to stop the trouble. For recurrence he repeated the treatment, ordered warm clothing and careful diet. Opium should only be given with ipecacuanha, as it otherwise checks the liver secretion. Crombie looked on the disease as essentially a disturbance of the gastro-intestinal secretion due to the high elevation combined with chills. He found that 10 to 12 grains of pepsin two hours after meals relieved all the symptoms in mild cases, while one drachm of liquor hydrargri perchloridi fifteen minutes before meals was a useful intestinal antiseptic and liver stimulant. In severe cases nothing but peptonized milk should be given for a few days; in ordinary cases 4 to 6 oz. of plain milk every hour day and night when awake, and as improvement ensues eggs, boiled fish, and then fowl may be added. Protection of the bowels from chills by means of a flannel binder round the abdomen, especially at night, is an important safeguard against attacks and recurrences of the disease. The success of these simple measures and the pepsine treatment support the physiological view of the causation of the disease.

DIARRHŒA ALBA OR SPRUE

Historical.—As long ago as 1766 Hillary of Barbadoes described cases which had a close resemblance to the disease now generally known by the name of sprue, although not much has been heard of the disease recently in the West Indies.

In the writings of the older Anglo-Indian physicians no very clear description of the disease is on record, although Twining recorded cases which may have been of this nature. It was not, however, until Alexander Grant published his paper in the first number of the *Indian Annals of Medical Science* in 1853 that an accurate description of the disease in India appeared, including its relationship to hill diarrhœa.

In 1870 Edward Goodeve, Principal of the Calcutta Medical College, wrote an article in the first volume of Reynold's *System of Medicine* on chronic diarrhœa, in which he admirably described the affection subsequently termed sprue under the heading, 'Chronic Diarrhœa—White Flux—Cachectic Diarrhœa,' although this paper appears to have been strangely overlooked by some later writers on the subject.

In 1880 Sir Patrick Manson published an accurate account of the disease as seen in China under the name 'sprue', derived from a Dutch name for the affection which had long been known in the East Indies, and was fully described by Van der Burg of Batavia in a small book entitled *Indische Spruw*; a term which is now so widely adopted as to have replaced the original Indian name 'Diarrhœa alba or White Flux', although the latter has the advantage of being descriptive of the most important symptom of the disease.

In 1881 Fayrer gave an account of the disease in his Lettsomian lectures, and in 1886 Norman Chevers dealt with it in his *Commentary on the Diseases of India*, while in the same year Maclean described it

in his lectures on *Diseases of the Tropics* under the term 'scorbutic diarrhœa'.

In 1883 George Thin suggested the term 'psilosis', from ψιλόω, to strip bare, and in 1897 the second edition of his small book on the subject was published under this title, which has not been adopted by subsequent writers, as it presents no advantages over the older and well-established terms.

Definition.—Diarrhœa alba or sprue is a chronic tropical diarrhœa characterized by the passage of large, frothy, pultaceous, light-coloured stools, associated with atrophy of the mucous membrane of the alimentary canal and later of the liver, and raw or ulcerated tongue and mouth, commonly ending fatally after a running and protracted course.

Pathological Anatomy.—Nothing is definitely known with regard to the causation of the disease, but the following are the lesions commonly found post-mortem. The tongue is raw-looking and its epithelial coat thinned, whilst small aphthous ulcers may be found on its tip and edges as well as in other parts of the mouth. The œsophagus may show very similar changes, and the stomach may also present minute shallow ulcers and congestive patches.

The most important changes are, however, met with in the intestinal canal, where the mucous membrane of the small bowel is thinned, and on section shows extensive atrophy of the villi and tube glands, together with small-celled inflammatory infiltration, as was well described by Thin, while patches of chronic venous congestion are also seen.

These processes are variable in degree, but in chronic cases fibrotic changes are also met with in the mucous coat, and in one-fourth of the cases minute superficial ulcers are said to be present. The large intestine shows similar changes in a lesser degree.

The **Liver** in the later stages shows simple atrophy and may be considerably reduced in size, but in proportion to the general wasting of the whole body, so that this organ presents no distinctive changes. The pancreas is also usually normal in appearance, and shows no constant changes which will account for the characters of the stools, nor do the other organs present any important lesions.

The above conditions appear to be essentially due to a chronic inflammation of the whole lining of the alimentary canal going on to atrophy of the mucous membrane, especially that of the small intestine, and secondarily of the liver, which no doubt accounts for the deficient digestive powers and peculiar stools, and indirectly to the great wasting and eventual anæmia of advanced cases of sprue.

Etiology.—Although the above-described changes suggest the possibility of bacterial or protozoal action, no such causal agent has yet been discovered. There are, however, certain facts known regarding the distribution and predisposing causes of the disease which are worthy of notice. The most important of these is prolonged residence in a warm and usually damp climate. Table I gives the data regarding the length of residence in India of forty-one cases seen in Calcutta.

Thus only one had been less than one year in the country, and he was a sailor, who probably had

previously visited India; while only four more had been under five years in the country, so that the remaining seven-eighths of the patients had been upwards of five years in a hot climate. This important fact is somewhat against a bacterial

TABLE I. DURATION OF RESIDENCE IN INDIA OF SPRUE CASES.

	Under 1 year.	1 to 5 years.	5 to 10 years.	Over 10 years.	Always.	Total.
Males . . .	1	3	2	6	15	27
Females . . .	—	1	2	—	11	14
Total . . .	1	4	4	6	26	41

origin of the disease, for Europeans are especially liable to such infections as typhoid during their earlier years in India. It is also noteworthy that twenty-six of the forty-one patients with sprue had been born and bred in India, yet none of them were under twelve years of age.

The **Age** and **Sex** incidence of the disease are shown in Table II.

TABLE II. AGE AND SEX INCIDENCE OF SPRUE AMONG EUROPEANS IN INDIA

	Up to 10.	11–20.	21–30.	31–40.	41–50.	51–60.	Over 60.	Tot.
Males . .	—	3	9	5	8	4	1	30
Females .	—	5	2	9	1	—	—	17
Total . .	0	8	11	14	9	4	1	47

Here we find the age incidence is much in proportion to the probable numbers of total patients in each decade, with the exception of the absence of those up to ten years of age, while all those between 11 and 20 had been born in India. The preponderance of males is explained by the much larger number of Europeans of that sex in Calcutta, so

that, beyond the exemption of children, age and sex do not appear to play any important part in the etiology of sprue.

Residence and Occupation.—Out of my fifty patients there was a history in ten of having been first attacked in the hills by diarrhœa, which subsequently developed into typical sprue, usually after their return to the plains. Thirty-five of the remainder appear to have contracted the disease in the plains as far as the histories go, whilst in five the notes upon this point are incomplete. Another noteworthy fact is that no less than ten out of the thirty males were working on railways, chiefly as guards, who obtain their hurried meals at very irregular hours, so that it is not surprising that they should be subject to gastro-intestinal derangements: irregular meals, therefore, seem to be an important predisposing cause of sprue in India.

Seasonal Incidence.—In such a chronic and insidious disease it is somewhat difficult to get exact data regarding the time of onset, but by only taking cases in which the disease had not lasted upwards of a year and in which the history of the onset was carefully recorded, the data in Table III were obtained.

TABLE III. SEASONAL INCIDENCE OF THE COMMENCEMENT OF SPRUE

January.	February.	March.	1st Quarter.	April.	May.	June.	2nd Quarter.	July.	August.	September.	3rd Quarter.	October.	November.	December.	4th Quarter.	Total.
2	2	2	6	5	—	4	9	3	1	3	7	3	7	3	13	35

The figures show that sprue commenced most

frequently in the last quarter of the year, just after the conclusion of the rainy season, and next most commonly in the trying hot weather months, being rarest in the dry and comparatively cold first quarter, which is the healthiest time of the year in Calcutta. It is noteworthy that the largest number of admissions were in November, that is just after so many of the European population return from the hills, which is in keeping with the frequency with which sprue supervenes on hill diarrhœa, as already pointed out. This distribution, taken together with the long residence in India of the majority of sprue subjects, points to the debilitating effect of a hot climate as an important predisposing cause of the disease.

Dysentery is occasionally followed by an attack of sprue, such a history having been recorded in 5 out of my 50 cases. In two more the onset occurred shortly after childbirth.

Onset and General Course of the Disease.—Sprue has been described by some writers as beginning with soreness and superficial ulceration of the tongue and mouth, which later spreads down the œsophagus to the stomach and intestinal canal. Such a characteristic course of the disease would be highly interesting from the theoretical point of view, but it is not in accordance with the facts as far as the disease in India is concerned. On the contrary, I find from an analysis of detailed notes of fifty cases in the European General Hospital at Calcutta that the intestinal symptoms almost invariably preceded the affection of the mouth, often by months. The first sign of the disease was irregularity of the bowels, usually thought at first to be simple diarrhœa, but

tending to occur in the morning and to become chronic, whilst the stools soon became light-coloured and bulky and accompanied by dyspeptic symptoms. Steady loss of weight with occasional temporary improvement, sallow complexion and, in the later stages, anæmia ensue, and after a longer or shorter course a large proportion of the cases eventually terminate fatally or in chronic invalidism predisposing to the supervention of terminal acute infections.

The **Duration of the Disease** at the time of admission to hospital is shown in Table IV.

TABLE IV. DURATION ON ADMISSION AND RESULT OF TREATMENT

	Cured.	Much better.	Slightly better.	Not better.	Died.	Total.
Under 3 months .	1 (?)	2	3	4	—	10
3 to 6 „ .	—	—	2	3	—	5
6 to 12 „ .	1	1	1	10	5	18
1 to 2 years . . .	—	—	—	6	1	7
2 to 8 „ . . .	—	—	2	3	—	5
Total	2	3	8	26	6	45

It appears from these figures that the largest number of admissions occurred between the sixth and twelfth months of the disease, being chronic cases, which partly accounts for the poor results obtained from treatment, which are embodied in the table for convenience, and will be referred to under the head of prognosis. Of the ten patients admitted in the first three months only one came to hospital within less than one month of the beginning of the illness. Further, in just over one-fourth the disease had lasted for from one to eight years, which is evidence of the chronic nature of the affection.

The **Mouth Symptoms** are of great importance both on account of their diagnostic significance and the trouble they occasion. The tongue becomes smooth and glossy, especially at the tip and edges, whilst small aphthous ulcers appear both on the tongue and on the mucous membrane of the mouth, which are very painful and recur again and again, making it difficult for the patient to partake of solid food, hot and pungent substances being unendurable. The data regarding the condition of the mouth on admission are shown in Table V, classified in accordance with the duration of the general symptoms and the severity of the tongue lesions.

TABLE V. THE MOUTH SYMPTOMS IN DIFFERENT STAGES OF SPRUE

Duration of disease.	Under 3 months.	3 to 6 months.	6 to 12 months.	1 year.	Total.
Lesions absent . .	2	2	2	2	8
„ slight . . .	3	3	4	2	12
„ typical . .	3	4	5	11	23
Total	8	9	11	15	43

Thus, in cases of under three months' duration the mouth symptoms were absent in 2 out of 8 cases, while with the advance of the disease this proportion steadily decreased until in those which had lasted for one or more years this symptom was recorded in only 2 out of 15 patients. Moreover, the mouth lesions were much more frequently severe in the older cases of long standing. I have frequently made careful inquiries into the histories of fairly early cases in which the mouth symptoms were absent, and found they had not been present at an earlier period, while in those in which they were found

they had nearly always appeared after the typical diarrhœa, so that the disease does not commonly begin in the mucous membrane of the mouth in India, although this appears to be more frequently the case in China and the Malay Peninsula.

Gastro-intestinal Symptoms.—Flatulent dyspepsia is of frequent occurrence, and is often accompanied by abdominal distension and discomfort following shortly after a meal, which tend to persist until the bowels are evacuated, when relief is obtained. Even the blandest and lightest diet may produce this condition in advanced cases.

The most characteristic sign is in the nature of the stools. They vary considerably in number in different cases, being often not more than from one to three a day, although liable to be considerably increased from time to time with exacerbations of the condition. In other cases they number from four to eight daily for a week or two, during which much weight and strength are lost. When comparatively few in number they are usually all passed in the morning, after which the patient may be more comfortable for the rest of the day.

The typical evacuation is a semi-formed or pasty, very bulky mass, of a light dirty grey or chalky colour, as if almost free from bile, often with a frothy appearance, as if undergoing gaseous fermentation, and with a peculiar acrid, but not very offensive, odour. At times when numerous they may be more watery, whilst if improvement is taking place the stools tend to become formed and of a darker colour with more bile in them.

The **Liver** may be slightly enlarged in the early

stages especially, but later the organ becomes smaller from atrophy, as illustrated by Table VI.

TABLE VI. THE LIVER CHANGES IN SPRUE

Duration.	Normal.	Enlarged.	Slightly smaller.	Atrophied
Under 1 year	11	3	6	5
Over 1 ,, ...	3	3	1	7
Total	14	6	7	12

Anæmia is an important symptom in the latter stages of sprue and is always well marked in the fatal cases, being usually of the secondary type, but occasionally of a progressive pernicious nature with high hæmoglobin value, in which case the course of the disease is very rapid. Out of 28 cases of under one year's duration anæmia was noted in 15, having been of a high degree in 2 of them, while among 15 cases of over one year's duration it was present in 8 and marked in 2.

The **Weight** of the patient should be carefully watched, as unless it is increasing the patient cannot be said to be progressing favourably, whilst a steady loss is of serious import.

Diagnosis.—There is little difficulty in recognizing typical cases of sprue, but as success in treatment depends on early diagnosis it is well to look on any case of chronic diarrhœa with light-coloured stools, very deficient in bile, as likely to be the early stage of the disease, and consequently to treat them with great care, and warn the patients against the serious consequences which may attend any neglect of dietetic and other precautions. The mouth symptoms, when present, are of especial diagnostic importance, but their prolonged absence in no way negatives

a diagnosis of sprue. The character of the stools usually enables the disease to be detected early, whereby appropriate and timely treatment can be adopted and the disease possibly cut short before it has become a confirmed chronic disorder.

Prognosis.—Although in all but advanced cases there is little immediate danger of a fatal termination, yet the prognosis as regards complete recovery is very unfavourable. This will be evident from a glance at the figures in Table IV on page 314, for out of forty-five cases there dealt with only two were discharged from hospital as 'cured', one of which was readmitted for the same disease seven months later, and was subsequently discharged again without any improvement. The other 'cured' patient was in hospital for 383 days, at the end of which she was discharged at her own request very greatly improved and having gained 12 lb. in weight, but her further history is not obtainable. Thus, there was only one probable cure out of forty-five cases, although many of them stayed in hospital for long periods, usually for several months. Further, only three more patients had much improved, two of these having been early cases, whilst eight were slightly better, but very likely to relapse on returning to their homes. On the other hand, in no less than twenty-six no material improvement had resulted from the prolonged care bestowed upon them in hospital, while the remaining six died whilst under observation; so that over two-thirds of the patients received no benefit from the treatment. Nor can it be said that the patients admitted within the first six months of the disease yielded much better results than the

later cases, for out of fifteen of the former only three were materially improved and five were slightly better, whilst seven showed no improvement at all. It is, therefore, clear that sprue requires to be tackled at the very beginning if permanent cures are to be expected, and neglect of the early stages can rarely be made up for later.

The **Deaths** mostly occurred between six and twelve months after the commencement of the disease, during which period five out of the six fatalities took place among eighteen patients, while of twelve who had suffered from the disease for from one to eight years only one died in hospital, and none of those admitted during the first six months of sprue ended fatally while under observation, so it appears that those who survive the affection for a year are likely to continue in a chronic condition for long periods without much probability of an early fatal termination. There is thus ample time for treatment if only an effectual remedy were available.

Treatment.—The extremely unsatisfactory nature of the treatment of sprue will be gathered from the data just given in considering the prognosis. As usual in such cases, a host of remedies have been advocated in the disease, none of which can be relied on to give good results. In fact the drug treatment is of far less importance than careful regulation of the diet, and in most cases the fewer medicines given by the mouth the better will be the chance of improvement, for more harm than good is often done by the administration of strongly-acting substances, which are only likely to irritate

the bare and atrophied lining membrane of the gastro-intestinal tract.

In the Calcutta series of cases bismuth, salol, santonin, beta-naphthol, perchloride of mercury, cyllin, izal, acetozone, ispaghula, and ipecacuanha have all been used in sprue without apparently having been of much service. Recently I have seen some improvement, especially in the amount of bile in the stools, follow the administration of small doses of ipecacuanha, while Fayrer advocated full doses of this drug in sprue; in view of the good effects of emetine in some cases of chronic diarrhœa recently reported, it would appear to be advisable to try small doses of from one-sixth to one-third of a grain of emetine hydrochloride hypodermically once daily in this disease, but I have not as yet had a suitable opportunity of doing so.

Among the drugs to be avoided in sprue, in addition to irritating antiseptic remedies, arsenic should be mentioned, as it may otherwise be indicated for the anæmic condition, but even hypodermically it has been found to be harmful. Iron salts are also usually too irritating to the stomach and intestines to be tolerated, anæmia being thus very difficult to treat and constituting a serious complication.

There remains one drug which requires further consideration, as it has been much vaunted as a specific remedy in sprue, namely, santonin. It was first used by French physicians in this disease under the incorrect impression that the affection was caused by minute intestinal worms, and subsequently Dr. Begg, both in Hankow and in England,

has repeatedly and warmly advocated its use, and recorded cases said to have been completely cured within two or three weeks, but unfortunately his results have not been confirmed to any material degree by other experienced workers. Dr. Begg insists that only yellow santonin is of any use, being prepared from the white form by being exposed to the sun for several months in England or a few weeks in India, of which he gives 5 grains in a teaspoonful of olive oil twice a day for four to seven days, after which it is omitted and the diet rapidly increased. This treatment has only been used in a few of the Calcutta General Hospital cases which I have analysed, but in none of them was any lasting good produced, although some were comparatively early cases, but it is worthy of further trial, combined with careful dieting, the latter being probably the more important of the two.

Dietetic Treatment.—In the absence of any drug which can be trusted to do any good in sprue, the regulation of the diet becomes the most important line of treatment, by means of which rest may as far as possible be given to the gastro-intestinal mucous membrane, and nature thus assisted in restoring the deficient physiological functions. Very numerous dietaries have been proposed, the most important of which are those described below, perseverance for months at a time being the most essential factor in obtaining satisfactory results with them, once that most suitable for the particular patient has been found by trial.

A Purely Milk Diet is the most generally useful one, the quantity being gradually increased until

4 to 6 pints are consumed in the twenty-four hours, and if it suits the patient the abdominal symptoms will be relieved and weight slowly but steadily gained. It may sometimes be necessary to dilute the milk at first with equal quantities of lime or ærated water and to citrate it, while if still not digested it may be previously peptonized or part of the allowance given in the form of whey, although this is less nourishing than milk itself.

A Meat Diet is more successful in some cases, and should be substituted for milk if the latter is found after a careful trial not to suit the patient. Owing to the deficiency of carbohydrates in meat it is necessary to push the quantity up to as much as 2 lb. a day, including as little fat as possible, as the latter is not easily digestible. Beef and mutton are the best forms, but chicken has often to be largely relied on in the tropics, and is easily digested. In advanced cases extracts of meat and raw meat juice may be necessary. As improvement in the stools takes place and weight is gained the diet may be cautiously increased by the addition of eggs, fish, and some fruit.

Lastly, **Fruit** has been largely used as a dietary in sprue in addition to milk, grapes being much given on the continent, as first advised by Van der Burg, or pears during the season ; while in England strawberries have recently been the favourite form, being naturally popular among those who can afford the large quantities necessary, 5 lb. and upwards being consumed daily. In the tropics thoroughly ripe bananas are the most suitable and constantly available fruit as they are highly nutritious, while

lichees, mangoes, mangosteens, and papaya have also been recommended, the last mentioned having the advantage of possessing ferments with digestive powers.

The difficulty in all dietetic treatments of sprue is to induce the patients to continue them long enough to allow of full recovery of the damaged mucous membranes, and until the stools remain formed and contain sufficient bile, and weight is being steadily gained, great caution is necessary in adding solid carbohydrate food, beginning with toast. If we may judge from published accounts of sprue, recoveries would appear to be more frequent among those sent out of the tropics to England; and after a prolonged attack of sprue it is not advisable for a patient to return to a warm climate if it can be avoided, especially to climates which are damp as well as hot, as relapses are very likely to occur and are less easily dealt with than first attacks.

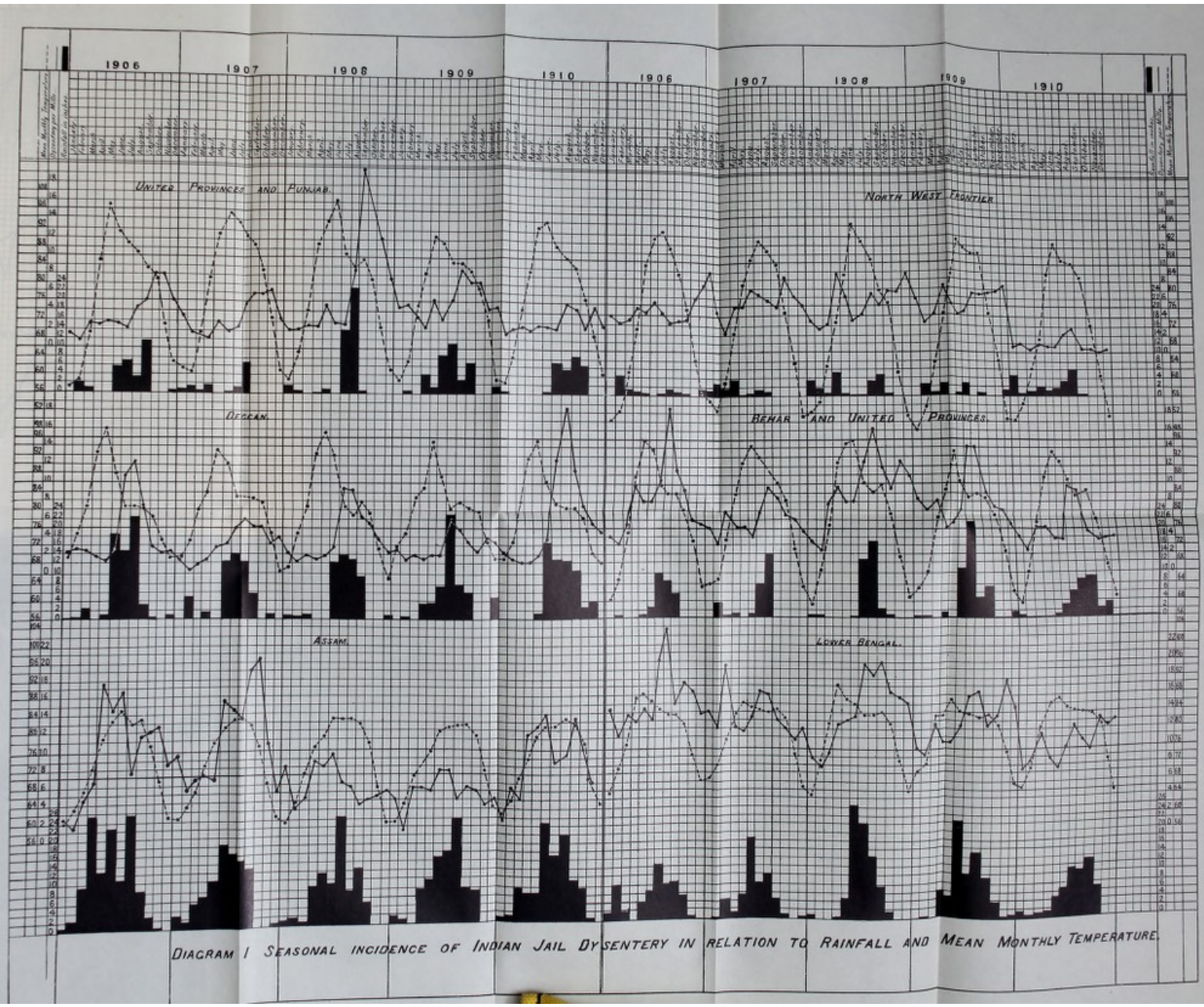
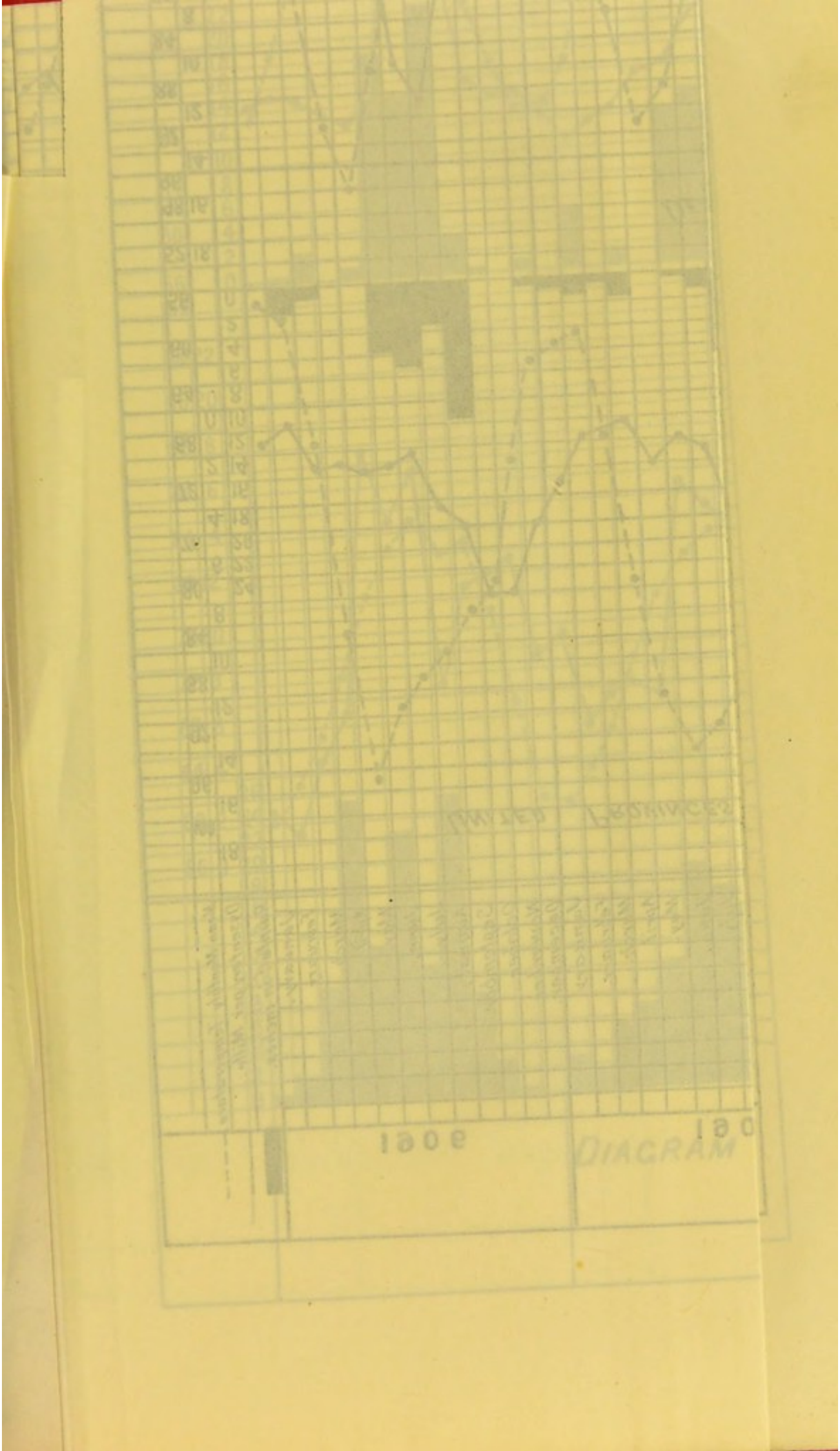


DIAGRAM I SEASONAL INCIDENCE OF INDIAN JAIL DYSENTERY IN RELATION TO RAINFALL AND MEAN MONTHLY TEMPERATURE.



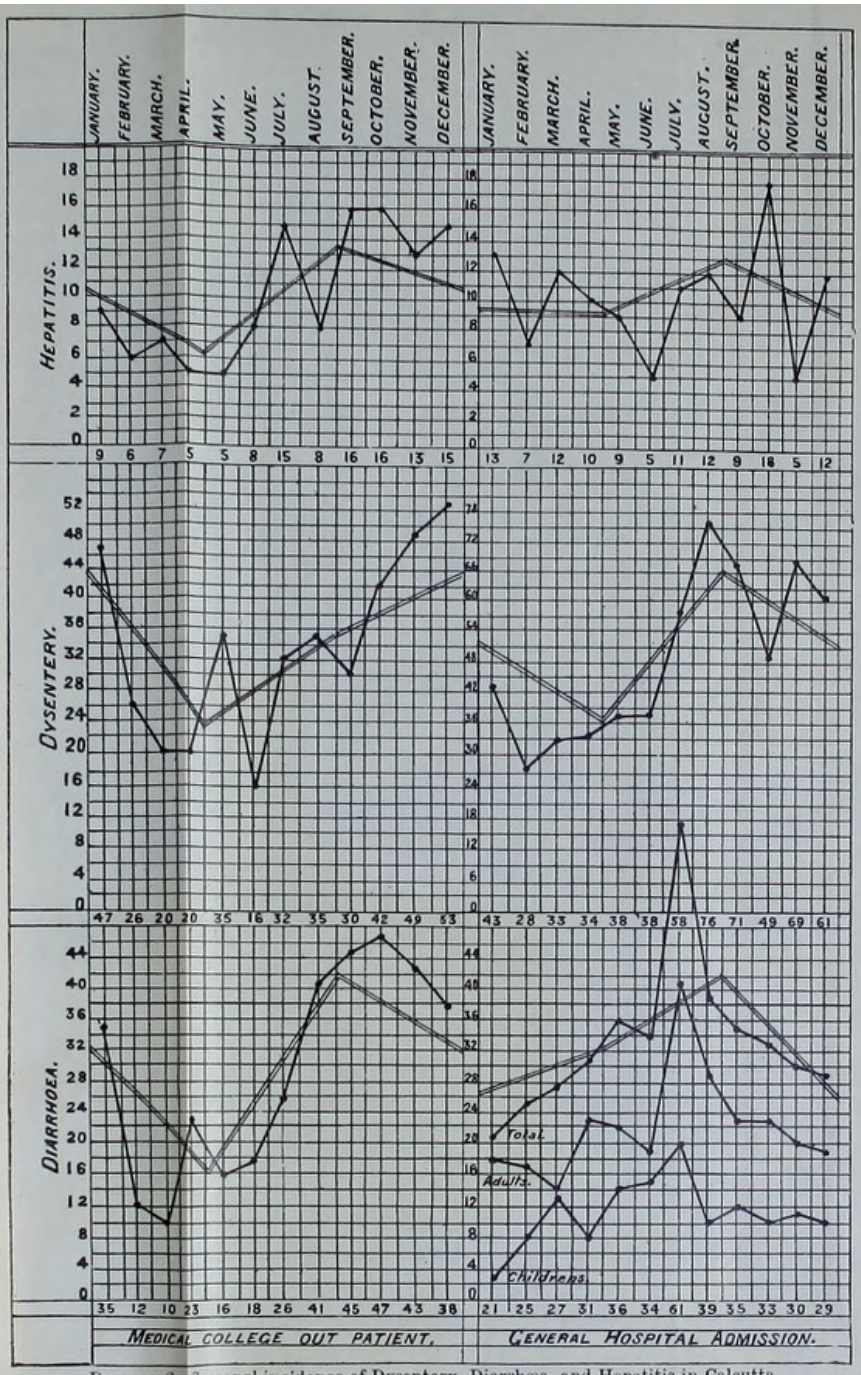
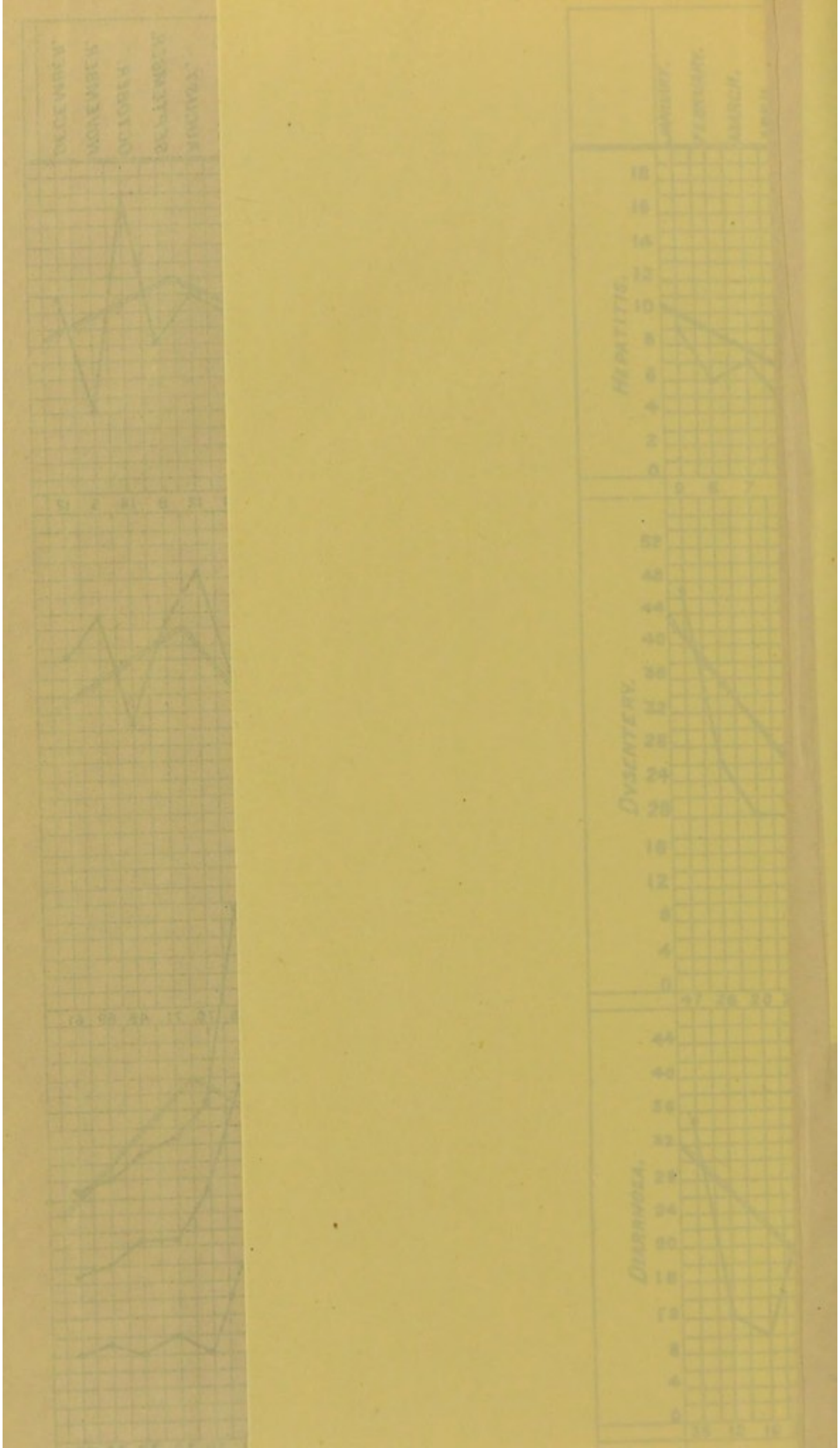


DIAGRAM 2. Seasonal incidence of Dysentery, Diarrhœa, and Hepatitis in Calcutta.



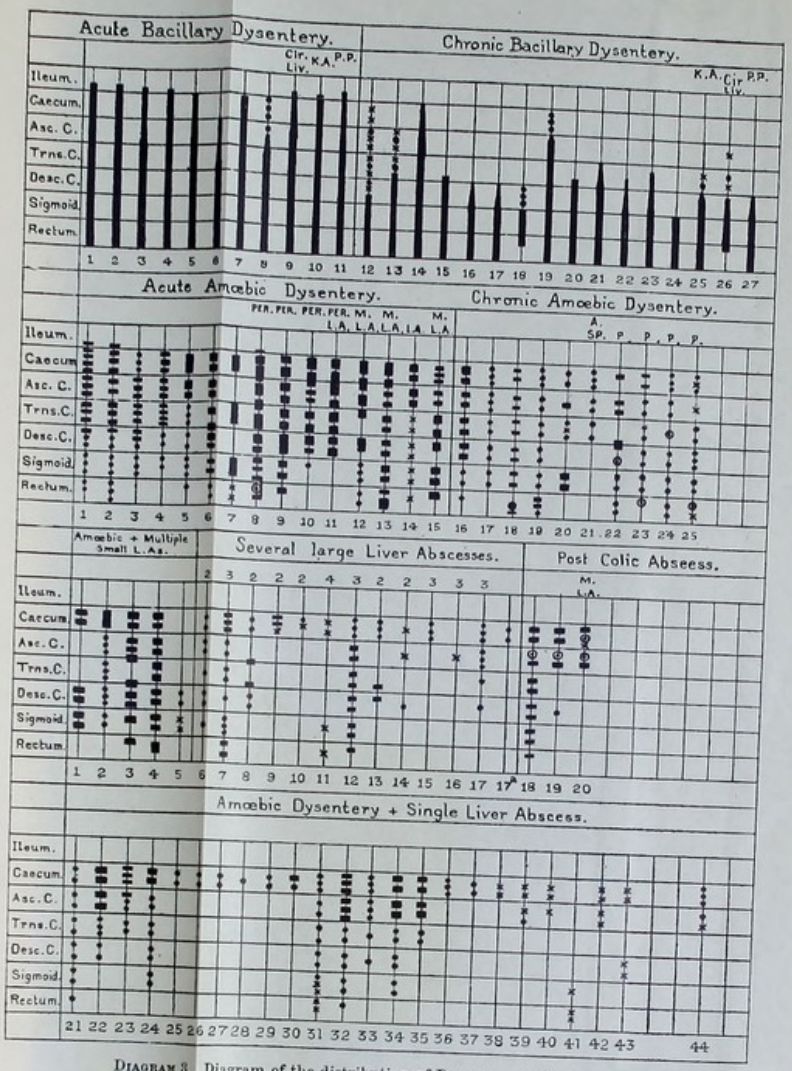
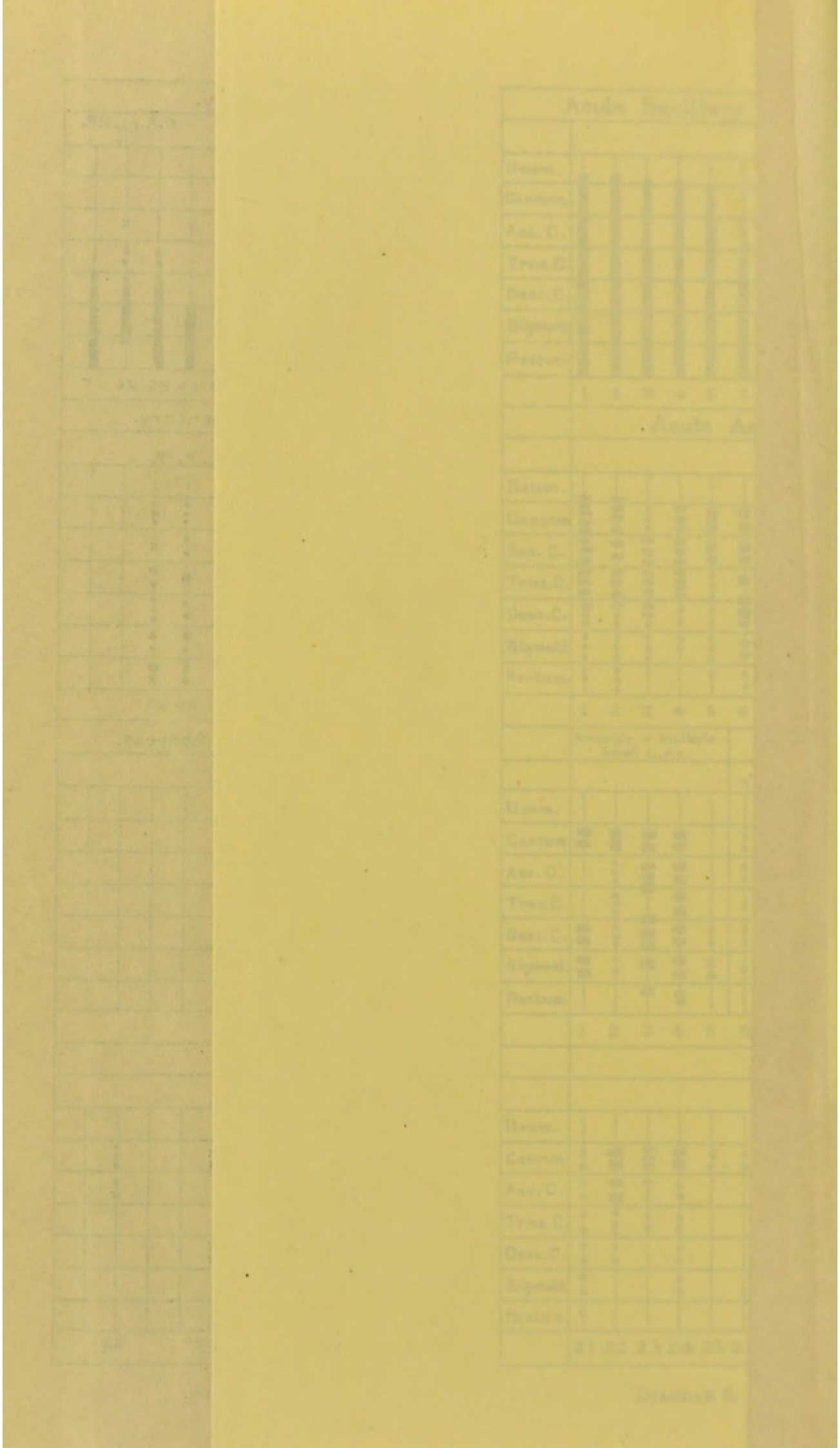


DIAGRAM 3. Diagram of the distribution of Dysentery in the Intestine.



INDEX