AN INTRODUCTION
TO
TROPICAL PATHOLOGY
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AN INTRODUCTION
TO
TROPICAL PATHOLOGY

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WITH A FOREWORD BY
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To
The Memory of My Father
C. RAMUNNI MENON
A Surgeon
FOREWORD.

To the many books dealing with Tropical Diseases another is now added: it may be reasonably asked why. Grounds for adding to an already considerable literature may be found either in the publication of some new fact, or in the compilation of several facts recording the recent discoveries of others, or in a new presentation of material already before the medical public. All these conditions have, I think, been fulfilled by Dr. Bhaskara Menon and the present work on Tropical Pathology brings knowledge of that subject to date by inclusion of recent work in that rapidly extending branch. At the same time the book puts the knowledge before the student in a novel and succinct form and without repetition of the symptoms and physical signs of the various diseases. The description is confined to the pathology of tropical diseases, a branch that has been of recent years probably the most rapidly changing feature in Medicine: it is convenient that the student of Tropical Medicine should have available a brief account of recent accepted work in this subject, and convenient also that the knowledge be available without the lengthy symptomatology and therapeutics with which such descriptions are usually combined. In such a book as this sets out to be, the repetition of the symptoms of diseases is unnecessary; for there is but little change in such accounts from decade to decade.
The symptoms of a disease are almost constant phenomena. The descriptions of Hippocrates and of the Arabian Rhazès can be accepted after many centuries as good accounts of the diseases as seen to-day. It is true that some diseases seem to alter somewhat in character, more notably epidemics of infectious disease which may vary in virulence and even in appearance. Particular epidemics of relapsing fever or of influenza, for example, may differ so much from the type disease as to be at first not always recognized. But such variations are occasional and the disease returns to its usual type in the next epidemic. If, however, the subjective symptoms and even the objective physical signs of a disease are so constant through the passage of time, how more constant should we expect to be those morbid changes in the body which are the causes of those signs and symptoms? But it is just those morbid findings that have appeared to us to alter of recent years and that render the publication of this little book on Tropical Pathology necessary. The truth is that the pathology has not changed, but our knowledge of it has advanced with more rapidity during the last 30 years than in any other branch of medical science. Constant reading of current literature on tropical disease is necessary if the physician wishes to keep himself well-informed. After an abstinence of two years from such literature the physician would find that his views were out of date on some matters and that recent research had shown he must change his consideration of others. It is partly to put before the physician the most recent accepted tropical pathological knowledge and partly to serve as an
FOREWORD.

instruction book for the student that Dr. Bhaskara Menon has written this little book. I think there is a place for it and I wish it a wide circulation.

MADRAS,
March 15, 1931.

C. A. SPRAWSON.
PREFACE.

The novel idea of writing a textbook of pathology, where each disease process is considered as a whole instead of piecemeal, is that of Professor G. W. MacCallum who has shown us how morbid anatomy should be linked up with infectious processes. It is only by a study of this clinico-pathological parallelism that a true understanding of disease is possible. This book is an attempt to apply the methods of this teacher to those diseases which are of importance in the tropics. Descriptions of the morbid anatomy and histology of the commoner tropical diseases met with in India are, to some extent, the result of personal observation and will vary somewhat from those found in works on tropical medicine.

It is intended mostly for undergraduate students in the tropics, where the requirements in pathology are somewhat different from those of students in Europe. It has been found that the course laid down by the Universities in Great Britain is inadequate to meet the requirements of medical students in India where obviously more stress is laid on tropical diseases. It goes without saying that for a proper understanding of the symptoms, treatment, and even the prophylaxis of disease the underlying pathological processes are of prime importance. It is hoped that this book will serve to introduce the student to the further study of those tropical diseases that he meets with in the wards and in practice in
later life. It is also hoped that it will be of some use to the postgraduate student and to medical practitioners.

Dogmatism is to a certain extent inevitable in a book intended mostly for students; but this has been minimized as far as possible. The importance of creating in the student what might be called the scientific attitude of mind is never so apparent as in tropical medicine where so little is known and so much has yet to be accomplished. Even in problems where etiological relationships are definitely established, as for instance in protozoal diseases, how little is known of the factors that upset the harmony between the parasite and the host without which disease in the strict sense does not arise.

The author is under a debt of gratitude to Major-General C. A. Sprawson, not only for the very great interest he has shown in the production of this small book, but for the kind and extremely helpful criticism, in regard to the language, as well as to the omissions that had occurred in the text. The author is also greatly indebted to Professor Clifford Dobell of the National Institute of Medical Research, Hampstead, for his kind permission to copy his published drawings of the human amœbae and of the intestinal flagellates. To Professor T. S. Tirumurti, the author offers grateful thanks for the loan of microscopical specimens. It is a pleasure to acknowledge the assistance received in the selection of specimens from Dr. P. Ramachendra Rau. The author is also indebted to the artists Mr. Veeraperumal, Mr. Letoille and Mr. Appaladoss for some of the illustrations.
CONTENTS.

Chapter I.-Types of Bacterial Infections.
Cholera Asiatica; Bacillary Dysentery; Plague; Undulant Fever; Leprosy; Oroya Fever...
II.-Types of Spirochetal Infections.
The Relapsing Fevers; Rat-bite Fever; Infectious Jaundice; Yaws; Seven-day Fever of Japan...
III.-Types of Infections with Filterable Viruses.
Yellow Fever; Dengue; Phlebotomus Fever...
IV.-Types of Infections Associated with Rickettsiae.
The Typhus Group; Typhus Fever; Rocky Mountain Fever; The Tsutsugamushi Disease; Trench Fever...
V.-Types of Infections with Fungi.
Mycetoma; Rhinosporidiosis...
VI.-Types of Protozoal Infections.
Amœbiasis; The Amœbae living in Man...
VII.-Types of Protozoal Infections.
Leishmaniasis; Trypanosomiasis...
VIII.-Types of Protozoal Infections.
Giardiasis...
IX.-Types of Protozoal Infections.
Malaria; Blackwater Fever; Sarcosporidiosis...
X.-Types of Protozoal Infections.
Balantidiosis...
XI.-Diseases of Unknown or Indefinite Causation.
The Beriberi Group; Pellagra; Sprue; Infantile Cirrhosis; Inguinal Granuloma...
XII.-Types of Helminthic Infestations; Trematode Infestations.
Schistosomiasis; Clonorchiasis; Intestinal Distomiasis; Paragonimiasis...
XIII.-Types of Helminthic Infestations; Cestode Infestations.
Hymenolepiasis; Intestinal Tæniasis; Hydatid Disease...
CONTENTS.

CHAPTER XIV.—TYPES OF HELMINTHIC INFESTATIONS; NEMATODE INFESTATIONS.
Filariaisis; Dracontiaisis; Loaiaisis; Onchocerciaisis .................. 163—180

XV.—TYPES OF HELMINTHIC INFESTATIONS; NEMATODE INFESTATIONS.
Ancylostomiasis; Ascariasis .................................. 181—187

XVI.—TYPES OF INJURY.
Snake Poisoning ........................................ 188—190

APPENDIX I. IMPORTANT LABORATORY METHODS FOR THE TROPICS ........... 191—205

II.—AUTOPSIES IN THE TROPICS .................................. 206—210
### LIST OF ILLUSTRATIONS.

<table>
<thead>
<tr>
<th>Fig.</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Smear from a stool showing cholera vibrios</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Appearance of small intestine in cholera (coloured)</td>
<td>Facing 3</td>
</tr>
<tr>
<td>3</td>
<td>Acute bacillary dysentery</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>Showing the diphtheritic reaction and the hemorrhages into the submucosa</td>
<td>Facing 8</td>
</tr>
<tr>
<td>5</td>
<td>Bacillary dysentery, intestine</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td><em>Xenopsylla cheopis</em></td>
<td>11</td>
</tr>
<tr>
<td>7</td>
<td>Smear from fluid from lymphatic gland showing <em>B. pestis</em></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td><em>B. lepra</em> in masses inside the cells and in clumps surrounded by 'globi'</td>
<td>Facing 18</td>
</tr>
<tr>
<td>9</td>
<td>Section of an early cutaneous leproma</td>
<td>19</td>
</tr>
<tr>
<td>10</td>
<td>Leprosy showing the flattening of the papillae and the infiltration of the corium (coloured)</td>
<td>Facing 22</td>
</tr>
<tr>
<td>11</td>
<td><em>Treponema recurrentis</em></td>
<td>27</td>
</tr>
<tr>
<td>12</td>
<td><em>Spirillum minus</em></td>
<td>30</td>
</tr>
<tr>
<td>13</td>
<td><em>Leptospira icterohemorrhagiae</em></td>
<td>32</td>
</tr>
<tr>
<td>14</td>
<td><em>Treponema pallida</em></td>
<td>35</td>
</tr>
<tr>
<td>15</td>
<td><em>Phlebotomus papatasii</em></td>
<td>46</td>
</tr>
<tr>
<td>16</td>
<td><em>Rickettsia prowazeki</em> inside an epithelial cell</td>
<td>48</td>
</tr>
<tr>
<td>17</td>
<td><em>Mycetoma</em> (coloured)</td>
<td>Facing 56</td>
</tr>
<tr>
<td>18</td>
<td><em>Maduromyces: Actinomyces</em></td>
<td>57</td>
</tr>
<tr>
<td>19</td>
<td><em>Mycetoma</em>, showing the edge of the fungus</td>
<td>58</td>
</tr>
<tr>
<td>20</td>
<td>An abscess showing the dense wall</td>
<td>59</td>
</tr>
<tr>
<td>21</td>
<td>Polypus of <em>Rhinosporidium seeberi</em> from nose</td>
<td>61</td>
</tr>
<tr>
<td>22</td>
<td>Polypus showing ripe cyst containing cells</td>
<td>62</td>
</tr>
<tr>
<td>23</td>
<td><em>Entamoeba histolytica</em> (× 2,000) showing character of pseudopodia (coloured)</td>
<td>Facing 63</td>
</tr>
<tr>
<td>24</td>
<td>Section of the intestine showing amoebae in submucosa (coloured)</td>
<td>Facing 66</td>
</tr>
<tr>
<td>25</td>
<td>Subacute amoebic dysentery</td>
<td>67</td>
</tr>
<tr>
<td>26</td>
<td>Amebic 'abscess' of the liver</td>
<td>69</td>
</tr>
<tr>
<td>27</td>
<td><em>E. histolytica</em> in the wall of the abscess</td>
<td>70</td>
</tr>
<tr>
<td>28</td>
<td>Liver abscess</td>
<td>71</td>
</tr>
<tr>
<td>29</td>
<td>Amebic abscess of the liver</td>
<td>72</td>
</tr>
<tr>
<td>30</td>
<td><em>Entamoeba coli</em></td>
<td>74</td>
</tr>
<tr>
<td>31</td>
<td>The amoebae of man</td>
<td>75</td>
</tr>
<tr>
<td>32</td>
<td>Enlarged spleen in kala-azar</td>
<td>80</td>
</tr>
<tr>
<td>33</td>
<td>Liver in kala-azar</td>
<td>81</td>
</tr>
<tr>
<td>34</td>
<td><em>Leishmania donovani</em> inside an endothelial cell from the spleen (coloured)</td>
<td>Facing 83</td>
</tr>
</tbody>
</table>
## LIST OF ILLUSTRATIONS.

<table>
<thead>
<tr>
<th>Fig.</th>
<th>Illustration</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>35.</td>
<td>Oriental sore</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>36.</td>
<td>Schema of the relationships of the trypanosome</td>
<td></td>
<td>88</td>
</tr>
<tr>
<td>37.</td>
<td><em>Trypanosoma gambiense</em> (coloured)</td>
<td></td>
<td>Facing 89</td>
</tr>
<tr>
<td>38.</td>
<td>(1) <em>Giardia intestinalis</em>. (2) <em>Trichomonas hominis</em>. (3) <em>Chilomastix mesnili</em></td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>39.</td>
<td>The malarial parasites (coloured)</td>
<td></td>
<td>Facing 100</td>
</tr>
<tr>
<td>40.</td>
<td>Spleen in acute malaria</td>
<td></td>
<td>106</td>
</tr>
<tr>
<td>41.</td>
<td>Malarial cirrhosis with contraction</td>
<td></td>
<td>108</td>
</tr>
<tr>
<td>42.</td>
<td>Malarial liver</td>
<td></td>
<td>109</td>
</tr>
<tr>
<td>43.</td>
<td>Section of brain in malaria</td>
<td></td>
<td>110</td>
</tr>
<tr>
<td>44.</td>
<td>Sarcosporidium encysted in muscle of man</td>
<td></td>
<td>116</td>
</tr>
<tr>
<td>45.</td>
<td><em>Balantidium coli</em></td>
<td></td>
<td>117</td>
</tr>
<tr>
<td>46.</td>
<td>Large intestine showing <em>Bl. coli</em></td>
<td></td>
<td>118</td>
</tr>
<tr>
<td>47.</td>
<td>Infantile cirrhosis</td>
<td></td>
<td>135</td>
</tr>
<tr>
<td>48.</td>
<td>Tendency of fibrous tissue</td>
<td></td>
<td>136</td>
</tr>
<tr>
<td>49.</td>
<td>Inguinal granuloma</td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>50.</td>
<td><em>Schistosomum haematobium</em></td>
<td></td>
<td>140</td>
</tr>
<tr>
<td>51.</td>
<td><em>japonicum</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52.</td>
<td>Pancreas showing clonorchis sinensis</td>
<td></td>
<td>149</td>
</tr>
<tr>
<td>53.</td>
<td><em>Fasciolopsis buski</em></td>
<td></td>
<td>151</td>
</tr>
<tr>
<td>54.</td>
<td><em>Paragonimus ringeri</em></td>
<td></td>
<td>152</td>
</tr>
<tr>
<td>55.</td>
<td>Head of <em>Tænia solium</em>; <em>Hymenolepis nana</em>; <em>Tænia saginata</em>; proglottis of <em>T. solium</em>; <em>Hymenolepis nana</em>; proglottis of <em>T. saginata</em>; ovum of <em>T. solium</em>; ovum of <em>Hymenolepis nana</em> and ovum of <em>T. saginata</em></td>
<td></td>
<td>155</td>
</tr>
<tr>
<td>56.</td>
<td>Diagrammatic structure of a proglottis of a tapeworm</td>
<td></td>
<td>157</td>
</tr>
<tr>
<td>57.</td>
<td><em>Tænia echinococcus</em></td>
<td></td>
<td>159</td>
</tr>
<tr>
<td>58.</td>
<td>Section of a degenerate hydatid cyst in the liver</td>
<td></td>
<td>160</td>
</tr>
<tr>
<td>59.</td>
<td>Scolices in hydatid fluid</td>
<td></td>
<td>161</td>
</tr>
<tr>
<td>60.</td>
<td>Schema of a hydatid cyst; development of daughter cysts; development of scolices</td>
<td></td>
<td>162</td>
</tr>
<tr>
<td>61.</td>
<td><em>Microfilaria bancrofti</em>; <em>Microfilaria loa</em></td>
<td></td>
<td>164</td>
</tr>
<tr>
<td>62.</td>
<td>Mosquito, development of larval filaria</td>
<td></td>
<td>167</td>
</tr>
<tr>
<td>63.</td>
<td>The parent worms</td>
<td></td>
<td>169</td>
</tr>
<tr>
<td>64.</td>
<td>Elephantoid tissue</td>
<td></td>
<td>172</td>
</tr>
<tr>
<td>65.</td>
<td>Skin</td>
<td></td>
<td>173</td>
</tr>
<tr>
<td>66.</td>
<td>Section of guinea-worm</td>
<td></td>
<td>176</td>
</tr>
<tr>
<td>67.</td>
<td>Cyst of fibrous tissue formed round a guinea-worm</td>
<td></td>
<td>177</td>
</tr>
<tr>
<td>68.</td>
<td>Head of <em>Necator americanus</em>; <em>Ancylostoma duodenale</em>; <em>Ancylostoma braziliense</em></td>
<td></td>
<td>182</td>
</tr>
<tr>
<td>69.</td>
<td>Ancylostomes fixed to the mucosa of the jejunum</td>
<td></td>
<td>183</td>
</tr>
<tr>
<td>70.</td>
<td>Ova of <em>A. lumbricoides</em></td>
<td></td>
<td>186</td>
</tr>
<tr>
<td>71.</td>
<td>Helminths</td>
<td></td>
<td>204</td>
</tr>
</tbody>
</table>
CHAPTER I.

TYPES OF BACTERIAL INFECTIONS.

Cholera Asiatica.

A SEVERE type of catarrhal enteritis with a high mortality sometimes occurring in epidemic form and caused by a highly infectious vibrio, the comma bacillus.

Some individuals are naturally immune while others get severe symptoms, very often within 24 hours after infection. The infection occurs through drinking-water or food contaminated with the dejecta of cholera patients. The 'carrier' stage exists and is possibly responsible for the commencement of epidemics.

The vibrio of cholera is a small organism about 1 to 2μ in length and is generally comma-shaped, or slightly curved, and shows rapid motility from the presence of a single polar flagellum. Sometimes two vibrios may be attached together with alternating curves—the S-forms—and sometimes two are arranged to form a semicircle. It is Gram-negative and grows best in alkaline media which inhibit the growth of the ordinary faecal organisms. Growth occurs thus in alkaline bouillon or peptone water as a pellucid film on the surface. On gelatine, growth occurs with liquefaction of the medium, so that in stab cultures funnel-shaped areas of liquefaction result. The comma bacillus forms indol in alkaline peptone water and this fact is made use of in what is called the 'cholera red reaction,' for the demonstration of which a drop of sulphuric acid is added to a 24-hour culture of the vibrio, resulting in a violet red coloration of the medium. The typical vibrios are non-haemolytic; but atypical organisms exist which differ in this property. Many species of the genus vibrio exist, exhibiting close biological relationship with M, TP
V. cholera and some definitely pathogenic. These latter are the 'para cholera' vibrios found in cases of diarrhoea. Some of these, such as El Tor Vibrio, are mere serological strains with slight differences in haemolytic property and are undoubtedly pathogenic, but produce milder infections. Similar organisms have also been found in water, and these

should be regarded as potentially pathogenic though most of the organisms are merely saprophytic in water. The disease has been reproduced in rabbits by intravenous injection of cholera vibrios.

The pathological lesions met with vary with the severity of the attack and the stage of the disease. Of the vibrios that are ingested, many are killed by the acid of the gastric juice, but some escape into the alkaline intestinal juices. The normal intestinal bacteria appear to be antagonistic. Possibly some pre-existing catarrh or alteration of the bacterial flora favours infection.

The intestines in the acute stage show signs of a severe catarrhal enteritis. The blood vessels on the serous coat stand out as bright red lines while the serosa is dull and sticky.
Fig. 2. Appearance of small intestine in cholera.
The peritoneal cavity is generally dry and injected, the omen-
tum also taking part in the vascular reaction. The mucous
membrane of the intestine shows intense congestion while in
some cases actual petechiae may be present. Depending on
the stage of the disease, the intestines may be full or empty.
Thus, in the early stages, they contain large quantities
of a thin, serous, watery fluid with flakes of shed mucous
membrane, the typical rice-water of cholera. In acute cases,
the contents might be pinkish red from admixture with
blood. Microscopically, there is a desquamative catarrh
affecting the superficial cells of the mucous membrane
which are cast off and form the characteristic flakes in the
thin serous exudate, which is regarded as a hypersecretion.
This fluid may show almost a pure culture of the vibrios
which may also be found in numbers on the surface and
inside the glands, but never very deep, the reaction being
essentially superficial. In some cases the lymphoid follicles
may show surrounding areolae of congestion. During the
stage of reaction, the intestine may rarely present a picture
of a severe membranous inflammation, which is, however,
due to infection with secondary organisms. The mesenteric
lymph glands may be enlarged and congested.

The spleen and the liver show congestion, but enlarge-
ment is not a feature. The gall bladder contains thick
inspissated bile, the absence of the normal biliary flow
being probably due to catarrh affecting the ducts. In
some cases, definite cholecystitis is present as in typhoid
fever and the gall bladder may serve as a reservoir of
organisms. Microscopically, there is catarrh and desquama-
tion of the epithelium while the vibrios may be found in the
submucosa.

The serous cavities in the chest are usually dry, the heart
and the great vessels contain but little blood, which is dark,
thick and tarry from the profuse excretion of its fluid constitu-
ents. The lungs are generally dry, but may sometimes
show irregular broncho-pneumonia with vibrios inside the
alveoli.
The kidneys show marked congestion and cloudy swelling in the early stage, but in patients who die in the stage of reaction there is severe degeneration of the tubules ending in necrosis of the renal epithelium, the condition being one that goes under the name of 'nephrosis,' a term applied to these purely degenerative changes without any inflammatory reaction. Such extensive necrotic changes form the pathological basis of the condition of post-choleraic uræmia, which is now regarded as toxic and not the result of a depletion of the blood.

Among general features of interest are the very early onset of rigor mortis, the bluish-grey colour of the skin of the hands which is wrinkled and shrivelled like that of a washerwoman's, the dryness of the subcutaneous tissues, and the hard rigidity of the calf muscles which are dark, red and dry and may even show rupture. The urine generally contains albumin and sometimes casts.

The blood becomes highly concentrated and shows a high specific gravity and a relative increase in the number of erythrocytes per c.cm. The alkalinity of the blood is diminished and the pressure falls.

Isolation and demonstration of the vibrios can be carried out during life as well as post-mortem, by picking off the white flakes in the motion and after washing in saline, inoculating into plates of Dieudonné's alkaline blood agar, which is a selective medium that suppresses types of B. coli. At the same time inoculation should be made into peptone water, from which they can be directly examined microscopically.

**Bacillary Dysentery.**

This is an acute form of ulcerative ileo-colitis caused by the invasion of the intestinal tract by a group of bacteria classed together as dysentery bacilli.

The disease is world-wide in its distribution and occurs sometimes in epidemic forms in armies; but sporadic cases occur frequently in tropical and subtropical countries.
The infection occurs by faecal contamination of food or drinking-water. Flies are an important source of indirect transmission, while human carriers are possibly more important in the starting of epidemics.

The dysentery bacilli are short rod-shaped organisms about 1 to 2½ in length, and are of two main types, the Shiga bacilli, so named after its discoverer, being the more virulent. The Shiga bacillus does not ferment mannite and is thus distinguished from the other type which is a mannite fermenter and goes under the name of the Flexner group. Various strains of this latter group are recognized by their specific agglutinating reaction. Two other types have been recently recognized, the Sonne type allied to the Flexner being a mannite fermenter, while the other, the Schmitz type, is allied to the Shiga and does not ferment mannite. The organisms are highly toxic and intravenous injections into animals are followed by severe diarrhoea and dysenteric symptoms, believed to be due to the excretion of the toxin into the large intestine and not to the local action of the bacilli. The Shiga types are more toxic. The pathological effects are mostly due to an endotoxin formed by the bacilli, since filtered cultures containing exotoxin produce only nerve lesions and paralysis in animals.

In acute infections in man the organisms cause an attack of dysentery, characterized by the passage of blood and mucus in the motion, with colicky pain and sometimes a febrile reaction. In Flexner infections the clinical features may sometimes be those of a simple diarrhoea rather than true dysentery. In chronic cases, apart from chronic dysentery, a chronic diarrhoea may be met with and the true nature of the condition overlooked. The Sonne type is responsible for severe epidemics in children.

The carrier stage may result after infection, some cases showing no clinical features of the disease. Thus carriers may be mere contact carriers or convalescent carriers.
Acute Bacillary Dysentery.
Pathological lesions in bacillary dysentery.

The earliest lesions met with consist of small specks of necrosis covered by greyish-white sloughs on the mucous membrane over the lymphoid follicles or on the crests of the folds of mucous membrane. These small greyish-white sloughs are surrounded by zones of intense congestion of the mucous membrane, and a diffuse congestion would thus appear to be the earliest lesion before the necrotic reaction commences. In other cases, the earliest noticeable lesions are capillary hæmorrhages, which soon become covered over by necrotic sloughs. The lesion then spreads along the folds of the mucosa in a transverse direction to form irregular serpigenous ulcers, which have a moth-eaten or worm-eaten appearance. The slough gradually becomes bile stained and a dirty green or greenish-grey in colour, while the surrounding mucous membrane shows intense hyperæmia and even points of capillary hæmorrhage.

The lesions are generally met with in the large intestine; but the terminal coils of the ileum may also be affected. The sigmoid and the rectum are, however, the parts that are most commonly affected while the flexures of the colon are also frequently involved.

The reaction is toxic from the endotoxin formed by the dysentery organisms and, depending on the virulence of the toxin formed by the different organisms, mild cases may be met with showing only patchy areas of necrotic false membrane and severe types where the whole of the mucous membrane is covered by sheets of irregular dirty greenish necrotic slough. In hyperacute infections a gangrenous process may be met with, involving large areas of the mucous membrane. The reaction is generally on the surface and the ulcers do not extend deep down, and so perforation is comparatively rare and general peritonitis is uncommon. Toxic absorption, however, may cause a variable peritoneal reaction, and the mesenteric lymph nodes are generally swollen and hyperæmic.
In cases where the toxic action is not marked the reaction may subside and the sloughs are cast off exposing raw bleeding ulcers with undermined edges communicating with neighbouring ulcers. The ulceration is superficial and no compensatory thickening of the bowel wall is usual, though in the acute stages owing to inflammatory œdema and spasm the whole of the gut may be rigid and contracted.

Healing occurs by the formation of granulation tissue followed by fine scarring, so that greyish irregular radiating scars may be met with in healed cases. The mucous membrane is generally thinned out and may have a moss-covered appearance somewhat resembling wet flannel. In chronic cases, obstructive changes in the glands may occur giving rise to the formation of mucous retention cysts of variable size projecting into the lumen of the intestine. In some cases, the mucous membrane may undergo chronic proliferative changes resulting in polypoid growths into the intestine, a condition called colitis polyposa. In other cases, mixed infections may occur giving rise to varying degrees of thickening and fibrosis.

The histology of the lesions differs from that of amoebic dysentery in that the reaction is inflammatory rather than a lysis of tissue. In the earlier stages, the surface of the mucosa is covered with a sheet of false membrane consisting of fibrin, leucocytes and necrotic cells. The inflammatory reaction passes down and involves the whole of the mucous membrane down to the muscularis mucosae and the lymphoid follicles. There is a necrosis of the columnar cells and the cells lining the crypts, and an inflammatory exudate, consisting of fibrin, polymorphs in various stages of necrosis, large endothelial and mononuclear cells, some of which are actively phagocytic and containing ingested red blood cells, may be met with surrounding the glands. Hæmorrhages into the mucous membrane form another important feature. The submucosa is very much thickened and œdematous, the blood vessels are engorged, capillary hæmorrhages are usually present. Inflammatory cells and mononuclear phagocytic
Fig. 4. *Slide 5351*. Acute bacillary dysentery. Showing the diphtheritic reaction and the hæmorrhages into the submucosa.
cells derived from the capillary endothelium may be met with in the submucosa in large numbers. The muscle coat may not be infiltrated and the serosa is generally unaffected. In chronic cases, the submucosa becomes converted into a delicate granulation tissue, and regeneration of the mucous membrane may occur to a slight extent. The bacilli may be met with by proper staining at the base of the ulcers.

Besides intestinal lesions as a result of toxic action, a synovitis of the knee joint is sometimes present. In other cases, a polyarthritis may occur, but the fluid is usually sterile. Eye complications such as conjunctivitis and iridocyclitis are rare features. A parotitis may sometimes be found. Intussusception may occur in children. Hæmorrhage and perforation may be met with in the acute stages. In the chronic stages of healing, stenosis of the gut and adhesions may give rise to clinical symptoms of constipation. The syndrome called sprue is by some authorities believed to be commoner after bacillary dysentery. A peripheral neuritis following dysentery has been described; but is of uncommon occurrence.
The intestinal contents in bacillary dysentery show characteristic features. Microscopically, there are large numbers of polymorphonuclear cells with rounded clear outline and vesicular nuclei, shed from the mucous membrane. Large mononuclear cells sometimes containing ingested red blood cells might be mistaken for ameobae. Organisms are few in number and red blood corpuscles are numerous and lying free. The motion is usually alkaline in reaction.

The blood usually contains agglutinins and bacteriolysins, and this may be of value for diagnosis. Leucocytosis is not a feature.

The bacilli may be isolated from the intestinal contents in the earlier stages by inoculating a MacConkey’s agar plate with a loop-full of the freshly passed mucus. The colonies are bluish, refractile, transparent and small. They may be picked off and subcultured on agar and final identification should be made by agglutination tests, using homologous sera for differentiation of the strains.

Identification of the bacilli, post-mortem, is possible if a scraping is made from the bases of recent ulcers after cutting through the slough with a hot knife. Isolation is extremely difficult in chronic cases, since the other organisms in the bowel overgrow the dysentery group. They may, however, be recovered from the fluid inside the small mucous retention cysts that are sometimes present. A scraping taken deep from the base under the overhanging edge of a chronic ulcer may be successful.

**Plague.**

An acute infection characterized according to type either by a severe lymphangitis and lymphadenitis, or by haemorrhagic broncho-pneumonia, or by a rapid severe septicæmia, the infective organism being in all types *Bacillus pestis.*

The course of the disease is extremely rapid and it is attended with a heavy mortality. Man gets the infection from the rat, the transmitting agent being the rat-flea, *Xenopsylla cheopis.* In the pneumonic form of the disease
the spread occurs by 'droplet infection' and possibly by the organisms floating about in the air. While the rat is here the most important reservoir of infection, in parts of Russia a marmot is the rodent that harbours the bacillus, while in America a ground-squirrel and in Africa a ground-squirrel, mice and gerbils are implicated. The disease is world-wide in its distribution though more prevalent for sometime in the tropics. An epizootic breaks out in rats before human epidemics arise in places where the rat is the reservoir of infection.

Fig. 6.
Xenopsylla cheopis (× 15).

The infective organism, Bacillus pestis, is a short thick coco-bacillus about 1.5 to 2μ in length by about 0.5 to 0.7μ in thickness. It is Gram-negative and exhibits bipolar staining. It grows easily on ordinary media and is stained by aniline dyes. Extreme variation in size and shape occur in culture. In broth, with a thin layer of oil on the surface, it forms thin thread-like stalactiform down-growths from the surface. It is easily transmissible to animals and this, together with its fermentation of sugars and the character of its colonies, serve to distinguish it from the Pasteurella
group which resembles it morphologically. A very closely allied organism is *B. pseudotuberculosis rodentium* which is serologically indistinguishable and which causes lesions like those of tuberculosis in animals. In the rat, *B. pestis* causes enlargement of the submaxillary nodes with hæmorrhage, necrotic nodes in the liver, pseudotubercles in the spleen, and hæmorrhages into the serous membranes. In the rat-flea, *Xenopsylla cheopis*, the bacilli multiply rapidly in the proventriculus, where they cause a curious condition of blockage resulting in a regurgitation of an almost pure

![Image](attachment:image.png)

**Fig. 7.** Smear from fluid from lymphatic gland showing *B. pestis* (*×* 1,000). Note the bipolar staining.

culture during subsequent feeding, so that the puncture becomes infected. The bacilli are also excreted in the faeces, so that infection often occurs by infected faeces which are deposited by the flea during feeding.

The pathological lesions are the result of a hæmorrhagic septicæmia with localizing features. In bubonic plague they consist of a primary lymphangitis affecting the lymphatics at the site of inoculation, followed by acute lymphadenitis of the affected group of glands forming the so-called primary
PLAGUE.

bubo. However, the primary lymphangitis is often unnoticeable and mild. The femoral group is most often involved since the legs are most commonly infected; but the inguinal, axillary or other gland-groups may show primary involvement. From these primary foci the bacilli spread and cause secondary involvement of the neighbouring lymph nodes in the line of lymphatic spread. The bacilli enter the blood even in bubonic types, the bacteriæmia increasing with the progress of infection. The affected glands are matted together and surrounded by an inflammatory cœdema sometimes showing areas of hæmorrhage. The glands are swollen, soft and pink on section and generally show areas of hæmorrhage and necrosis in the late stages. This hæmorrhagic cœdema, which is regarded as a toxic effect, distinguishes this from other types of acute hyperplastic lymphadenitis. The bacilli are usually found in scrapings from the glands. The spleen is markedly enlarged and is in a state of acute hyperplasia. Underneath the tense capsule are numerous tense points of hæmorrhage. The cut surface is convex and greyish pink in colour and shows areas of hæmorrhage and necrosis. The necrotic foci are in relation to bacillary emboli. The bacilli are found in numbers in spleen smears. The liver is enlarged and markedly congested and shows cloudy swelling. Submucous hæmorrhages are met with in the intestine and similar hæmorrhages are a frequent feature in all serous cavities. Thus, subpleural ecchymosis, pin-point hæmorrhages underneath the endocardium and pericardium are common. The heart may show cloudy swelling of the myocardium. The lungs often show congestion and cœdema. Sometimes, bronchitis, broncho-pneumonia or hæmorrhagic infarcts are met with. Increasing importance is now attached to the secondary pneumonias which occur in bubonic plague. Externally, the skin may show small areas of ecchymosis, which may be extreme in some epidemics justifying the name the ‘black death’ of the middle ages. Papular cutaneous rashes, boils and abscesses may be met with. The blood shows a marked polymorphonuclear leucocytosis.
It is now believed that primary pneumonic plague owes its commencement to infection from a secondary pneumonia in bubonic plague, 'droplet' infection being the mode of spread. Subsequent cases occur by aerial spread, the bacilli floating about during coughing. The effects of overcrowding and defective ventilation thus become apparent in the spread of this type. The bacilli pass down the bronchial tract resulting in an alveolitis and lobar or lobular pneumonia. The mucosa of the larynx, pharynx and trachea are intensely congested and the bronchial glands are involved. The broncho-pneumonia is of the hæmorrhagic type. Sometimes pseudolobar consolidation may be met with affecting, however, both the lungs. Subpleural hæmorrhages and pulmonary infarcts are common. The whole lung may show a hæmorrhagic œdema. The bacilli are found in numbers in the inflammatory exudate. They may be demonstrated by lung puncture during life. There is generally an associated septicæmia possibly due to spread from the lung. The visceral changes met with in bubonic plague such as enlargement and congestion of the spleen, the liver and the kidneys with severe parenchymatous degeneration, may sometimes be met with. Leucocytosis is not marked owing to the severity of the infection.

Though septicæmia is a feature of all types of plague, in septicæmic plague, the bacilli are found in enormous numbers in the blood and consequently, the course is much more rapid and petechial hæmorrhages and slight glandular enlargement may be the only features since reactive changes do not occur. Owing to the severity of the infection, there is no leucocytosis in the blood, but a leucopenia. The bacilli may be passed out in the urine and in the ëæces in severe septicæmia.

Undulant Fever.

An acute infectious disease characterized by a sub-acute septicæmia with a prolonged course and irregular waves of pyrexia, the infective organism being Brucella melitensis.
The disease is endemic in Malta and on the coast of the Mediterranean. Other endemic centres exist in India, China and Africa, while isolated cases occur in all subtropical and even in temperate regions.

The goat is the carrier of infection, the organism being transmitted to man through goat’s milk. Goats harbour the organisms without giving rise to any symptoms and thus serve as ‘passive carriers.’ Other modes of infection, such as by direct spread and by inoculation, are possible, but of rare occurrence. Besides goats, mares, cows and asses may serve as carriers, the infection being spread to these animals by goats. Products of goat’s milk, such as ice-cream, cheese, etc., are fruitful sources of infection. Contamination of the soil may occur since the bacilli are excreted in the faeces and the urine of goats.

*Brucella melitensis* is a small non-motile cocco-bacillus which occurs singly or in pairs or in short chains. In culture there is a tendency to assume coccoid forms, but the organism is in reality a short bacillus about 1.5 to 0.5\(\mu\) in length and about 0.4\(\mu\) in thickness. It is Gram-negative and has a slight tendency to bipolar staining. A serological strain, *Br. paramelitensis*, is a mere variant playing a similar pathogenic rôle. A bacillus causing epidemic abortion in cattle, *Br. abortus*, is also a serological variant, but the question of its pathogenicity to man has not been settled. The organism grows on all ordinary media such as nutrient agar or glucose agar. A characteristic biochemical reaction is the formation of hydrogen sulphide from protein containing sulphur. Inoculated into monkeys it produces lesions identical with those met with in man. Other laboratory animals, such as rabbits and guinea-pigs, are also susceptible. The pathogenic action is due almost entirely to the endotoxin.

In man, the pathological lesions met with are the result of a bacteriæmia with localizing features. Thus, inflammatory changes occur in joints and nerves resulting in arthritis and peripheral neuritis while in rare instances a tendency to
serous inflammation results in pleurisy and peritonitis. Another feature of this bacteriæmia is the tendency to produce cold abscesses and inflammatory swellings on the ribs.

The most characteristic lesion is an early generalized lymphadenitis most marked in the mesenteric nodes since the organism is absorbed from the intestine. An enlargement of the spleen is always met with, this being more marked in the chronic cases. The spleen is generally congested and in the stage of hyperplastic swelling met with in some acute infections. It shows prominent Malpighian bodies with lymphoid hyperplasia. Infarcts may sometimes be met with. The organisms are usually present in numbers in the spleen. The liver may also be enlarged and congested and histologically shows cloudy swelling and focal necrosis. A mild hepatitis accounts for the jaundice that is sometimes present. The gall bladder may be a reservoir of the organisms, which may be passed out in the fæces. The kidneys may be enlarged and congested and may show cloudy swelling. A true subacute nephritis is sometimes met with, resulting in a large pale kidney. The heart may show a toxic myocarditis in fatal cases, while fatty degeneration may be met with in chronic cases. Endocarditis has been met with. The intestines generally show patchy congestion. Orchitis and epididymitis are common features while ovaritis is rare. Meningitis and encephalitis are rare complications.

Externally, petechiæ and ecchymosis may be met with in severe cases. The organisms are excreted in the urine, which may show a variable albuminuria. Cases may be met with showing no obvious features at autopsy except for the enlargement of the spleen and congestion of the viscera.

The blood shows a secondary anæmia which is generally severe, and a lymphocytosis is usual. Agglutinins are met with in the blood, but are variable, and this fact should be taken into account in diagnosis by serum reactions. The organisms may be cultured from the blood even in early stages.
This is a specific infective granuloma caused by *Bacillus lepræ* and characterized by cutaneous nodular lesions called lepromata and an interstitial neuritis resulting in trophic lesions.

The disease occurs in scattered foci in all the continents; but is extensively prevalent in the tropics, particularly in India, China and Japan and in the Hawaiian Islands. In endemic areas, it has a curious distribution affecting certain regions, while other areas are left alone. It is a disease commoner in youth and adolescence and affects more males than females. There is no direct inheritance of leprosy, the children of leprous parents being infected early in life by contact. With regard to the transmission of leprosy we know nothing definite, except that prolonged contact with lepers is an important factor. The primary lesion would appear to be in the skin, or the mucous membrane of the nose or of the gastro-intestinal tract, and the possible modes of infection are by ingestion, inhalation and sexual transmission, while the question of an insect transmitter has not been decided. The rarity of leprous lesions in the lungs seems to rule out that as a primary focus. Hutchinson's theory of fish-eating as a cause of leprosy cannot hold in India where a large number of lepers do not eat fish. As with tubercle, the question of absorption of the lepræ bacilli through the alimentary canal has also to be considered, though no lesions have been met with in the intestine.

The organism of leprosy, Hansen's bacillus or *Bacillus lepræ*, is a small thin rod-shaped organism about 2 to 4μ in length by 0.4μ in thickness and is shorter and thicker than the tubercle bacillus. As with the tubercle bacillus it is an acid-fast organism, that is an organism that resists the decolorizing action of acids when stained with dyes such as carbol fuchsin. It is Gram-positive and is easily identified by differential staining by the Ziehl-Neelson's method, though the stain should be used cold, and a weaker acid of about 10 per cent should be used for decolorization. In the
possession of this acid-fast staining it resembles both *Bacillus tuberculosis* and *Bacillus smegmæ*. It differs from the tubercle bacillus, however, in that it is found in enormous numbers inside cells, appearing like sheaves or bundles, or in clusters outside the cells and not individually, and in the difficulties met with in cultivation and in animal inoculations. Cultivation is generally unsuccessful, but claims have been made that the bacilli can be cultivated in symbiotic growth with other organisms, and streptothrix-like filamentous forms have been described in cultures, but are of doubtful significance, since animal inoculations were not conclusive. Experimental transmission to animals is extremely difficult, though in rats a similar disease exists, exhibiting histological features of the leproma besides showing acid-fast organisms. Experimental transmission to man is also equally difficult and accidental inoculations have had no results. One case of experimental transmission has been described in which the lesions developed after a long incubation period at the site of inoculation. The experiment loses much of its value since it was carried out in an endemic zone.

The lesions met with in leprosy are of two kinds, the specific cutaneous granuloma called the leproma, and the leprous neuritis. The question of the primary lesion has not been settled, though early location of the bacilli in the lymph glands is probable. So far the evidence is in favour of the skin being the site of the primary infection.

The lepromata are diffuse nodular elevations, which are met with most commonly on the skin of the face, forehead, nose or ears and less commonly on other parts of the body such as the arms and legs. The earlier patches show a hyperaemia with a thickening of the skin which becomes a definite area of solid infiltration giving rise to exaggeration of the usual contours of the face, resulting in the 'leonine facies' of leprosy. On the other hand, the lesions may be definitely nodular and circumscribed. Some nodules may undergo absorption, while in other cases ulceration may occur. Febrile reactions occur during these stages, and
Fig. 8. *B. lepra* in masses inside the cells and in clumps surrounded by 'globi'.
even before the granulomatous deposit. On section, the leproma is a dense solid growth, white in colour, sometimes yellow or brown, which cuts with resistance and leaves a convex cut surface which is glistening and vascular and quite unlike tubercle. The skin over the nodule is thinned and glossy and may show a pitted appearance not unlike the

![Image](https://example.com/image)

**Fig. 9.**

(× 50). **Section of an early cutaneous leproma showing the infiltration around the hair follicles as well as a more diffuse growth.**

rind of an orange, the hair generally having fallen out. Histologically the well developed leproma is made up of a type of granulation tissue consisting mostly of large mononuclear cells most of which have a foamy protoplasm, the so-called 'lepra' cells. They contain numbers of bacilli which are acid-fast with Ziehl-Neelson's method. Besides these mononuclear cells, the endothelial cells of the vessels and
lymphatics are also swollen and may show numbers of bacilli. Sometimes clumps of bacilli appear outside the cells surrounded by a mucinous substance called 'glea' the whole forming what are called 'globi,' where the containing cell has disintegrated. Some believe that these are really masses formed by the multiplication of the bacilli which subsequently undergo mucoid degeneration. Endarteritis obliterans is not a feature. Giant cells containing three or more nuclei are sometimes met with, somewhat resembling the giant cells met with in gummata. Sometimes typical giant cells of Langhan's type may be met with. Caseation necrosis is not a feature, though necrotic changes may be met with following superficial ulceration. The very early lepromata occur as small granulomatous masses under the skin or involving the hair follicles and the sweat glands, so that atrophy and falling of the hair and diminution of the sweat are early features met with in the affected area. The process can be seen to implicate the small terminal branches of the cutaneous nerves and the sympathetic fibrils resulting in disturbances of keratinization, hyperkeratosis and parakeratosis. Engorgement of the superficial capillaries may be met with in acute lesions. The skin shows a flattening of the papillae even in early stages and a hyalinization has been described in the superficial connective tissue while the granuloma is underneath. When extensive ulceration has occurred, the bacilli are being discharged in numbers, but the same is not true of old lepromata where absorption is taking place. Trophic ulcers met with in the late stages, however, are not infective.

In the mucous membranes, particularly of the nose, palate, pharynx and larynx, lesions occur quite commonly, particularly in the later stages, and consist of the specific granulomatous deposits which, however, assume ulcerative types. Thus nodules occur on the septum of the nose, break down and destroy the septum and cause deformity. Bacilli are found in numbers in smears from the nasal mucous membrane. The tongue may be affected. Lesions occur
on the conjunctiva and cornea and lead to the loss of the eye. The lymph nodes of the various parts may show early involvement and it is believed that they may act as reservoirs for the bacilli.

Besides these nodular lesions which are characteristic of the type called nodular leprosy, another type exists where nerve lesions predominate, nerve leprosy, while cases occur where both types of lesions coexist, mixed leprosy.

The peculiar feature of nerve leprosy is the tendency to involve peripheral nerves while the central nervous system is unaffected. Leprous neuritis is essentially a nodular perineuritis in which the individual nerves become involved. The ulnar nerve or the posterior tibial are often involved and thickened in fusiform nodes. Histologically, the lesion consists of a granulomatous infiltration of the epineurium and the perineurium so that the nerve bundles are widely separated by a tissue in which bacilli can be demonstrated. The endoneurium, the delicate connective tissue between individual fibres, is also involved, and the axis-cylinders are compressed and fibrosed. Early macular depigmented lesions occur in the skin even before noticeable thickening occurs in the nerve trunks. So the question arises whether the skin lesions are primary and the bacilli travel up the sheath of the nerves and set up a nodular perineuritis, or whether the skin lesions are merely the result of trophic disturbance. Ascending infection can sometimes be demonstrated where the disease first starts as a cutaneous lesion and the gradual spread of infiltration along the nerves can be traced when the process affects the limbs. The skin lesions may sometimes show marked depigmentation or hyper-pigmentation or hyperaemia and are in the later stages anaesthetic. The hair is generally absent and the skin smooth, shining and atrophied. Bacilli are found in these early macular lesions.

Trophic lesions occur in the muscles owing to involvement of the motor nerves. Wasting may be a marked feature in the interossei of the hands, and this is often followed
by contracture resulting in the 'main en griffe,' the griffin's claw of leprosy. Involvement of the muscles of the leg may result in ankle-drop, and rarely facial paralysis has been met with.

Trophic lesions involving the soft tissues may result in perforating ulcers of the foot, pressure ulcers may result and secondary septic processes are frequent.

Trophic lesions may occur in bone leading to absorption of bone—osteoporosis—particularly in the terminal phalanges. A leprous osteomyelitis is another feature leading to necrosis of bone. Similar lesions may implicate joints leading to synovitis and dis-organization and dropping off, of toes and fingers.

Apart from these lesions which occur in nerve leprosy, changes occur in the viscera in the nodular form of the disease. These consist of granulomatous nodules, the miliary lepromata, scarcely visible to the naked eye, but fairly frequent microscopically. These miliary lepromata are masses of endothelial cells containing the bacilli, and are found in the liver and spleen and often in the testes, where even the epithelial cells of the tubules are affected, so that atrophy often results. A true glomerular nephritis may be present. The regional lymphatic glands show chronic hyperplasia and contain bacilli. Lardaceous disease may occur as a complication while secondary infections, such as tuberculosis, syphilis or pneumonia, may be met with. The blood shows no obvious microscopic features, while the question of an early bacillæmia is not yet decided, though undoubtedly it exists in those cases where visceralization is met with. The blood shows a positive Wassermann reaction in a large number of cases. Of great interest are the leprous reactions met with, where a fresh eruption of cutaneous nodules occur due to the sudden bacillæmia, probably by reason of the bacilli coming into direct contact with the tissue fluids and entering the circulation. It is believed that the situation of the bacilli inside lepra cells and surrounded by 'glœa' outside the cells prevents marked tissue reactions.
Fig. 10. Section of leproma showing the flattening of the papillae and the infiltration of the corium.
While the bacilli occur in the nasal secretion, this is only in cases with obvious nasal lesions, and for demonstration in the nodular type, an incision should be made into the cutaneous nodule and a scraping obtained from the tissue juices, care being taken not to include blood. From the early macular lesions and anaesthetic patches they may be obtained by blistering the skin and examining the blister fluid. In the late ulcerative stages where the lesions are mostly trophic the bacilli are difficult to demonstrate, and this accounts for the fact that the disease is much more infectious in the early stages.

**Oroya Fever.**

This is an acute infection caused by an organism, *Bartonella bacilliformis*, manifesting itself in two stages, a febrile stage with anaemia followed by a stage of granulomatous warty growth on the skin called Verruga Peruviana.

The two stages of the disease have till recently been regarded as different. The febrile stage of the disease is called Carrion's disease, after a medical student who injected himself with blood from a case of Verruga Peruviana and got severe fever and anaemia with a fatal termination. Noguchi has conclusively proved that the virus can be recovered from both the stages. The disease occurs in Peru, Chile and other parts of South America. Sometimes it assumes epidemic prevalence and the outbreak that gave it this name occurred among workmen in a railway construction near Oroya.

The causative organism, *Bartonella bacilliformis*, is met with in the blood inside the red blood cells. It occurs in small coccoid forms 0.5μ in size often in chains or sometimes in longer bacillary forms 1.5μ to 2μ in length inside the red blood cells. The organisms have also been found in the endothelial cells of the lymphatic glands. Different grades of motility are described.

The first stage of the disease is that of a remittent or intermittent pyrexia with marked anaemia and enlargement of the spleen and liver. The second stage is characterized by
the occurrence of crops of cutaneous nodules of variable size. Some are small and miliary, others warty, and still others pedunculated, while sometimes large tumour-like masses of the size of a lime may be met with showing superficial ulceration. Lesions occur also in mucous membranes.

The pathological lesions met with in the first stage of the disease which is the more severe and oftentimes fatal, are those of an acute infection with marked anaemia. Externally, besides the marked pallor and anaemia, petechial haemorrhages and ecchymosis may be met with. There is early enlargement and inflammatory changes in the lymphatic glands. The deeper nodes are often involved, particularly the retroperitoneal and the mesenteric nodes. The organisms may be met with in the lymphatic glands. Petechial haemorrhages are common affecting the serous membranes such as the pericardium, the pleura and the peritoneum. Similar punctate haemorrhages or even more diffuse haemorrhages are met with in the mucous membranes. All the internal organs show marked cloudy swelling. Besides this, the liver may show fatty changes and areas of necrosis. Microscopically, there is a central necrosis of the lobules and a deposit of pigment also occurs. The spleen is enlarged as in an acute infection, flabby, and shows areas of infarction. Microscopically pigment granules may be present. The endothelial cells and leucocytes may contain organisms. Ulceration may be met with in the large intestines and the organisms may be demonstrated in the perivascular cells.

During the second stage of the disease the small nodules which occur all over the skin and mucous membranes form the characteristic features. Similar nodules may be met with in all the internal organs. On incision the Peruvian wart shows a congested red granuloma which in the later stages become bluish in colour. Histologically the tissue consists almost entirely of proliferating capillary buds showing marked dilatation of the lumen so as to suggest an angiomatous appearance. In between these proliferating capillaries clusters of cells, mostly lymphoid, may be met with in the
later stages. Thence overgrowth of fibrous tissue occurs and the nodule shrivels up. Vacuolated endothelial cells, the so-called foamy cells, are often met with. A perivascular endothelial reaction is regarded as characteristic.

During the early stage, the blood shows a marked diminution in the number of red blood cells. Megaloblasts and normoblasts are common. Alteration in the shape of red blood cells, poikilocytes and polychromes are met with. The anæmia offers great resemblances to pernicious anæmia.
CHAPTER II.

TYPES OF SPIROCHÆTAL INFECTIONS.

THE RELAPSING FEVERS.

Infections with spirochætes transmitted either by ticks or lice, bouts of febrile paroxysms recurring cyclically form the important features.

The disease has a wide geographical distribution occurring in parts of Central Europe and Russia, in parts of Africa and in many parts of Asia. It is a disease associated with overcrowding and insanitary surroundings such as occur in crowded camps, in armies and in famine-stricken districts, conditions favourable to the incidence of lice and ticks, the transmitting agents. Sporadic cases occur in non-endemic areas from the transport of the infected insect vectors. Infection occurs by the organisms getting into the blood either through contamination of the bite of infected ticks or when infected lice are crushed into the skin, the spirochætes making their way through the abraded skin. The tick-transmitter is Ornithodorus moubata, and infection occurs by contamination of the wound by the fluid secreted by the coxal glands of the tick and possibly directly through the mouth parts, since the salivary glands of the tick are also infected with spirochætes. The infection is transmitted to the eggs which hatch out infective larvæ which can transmit the infection to still another generation. Direct infection occurs through mucous membranes and even through unbroken skin, but this is a rare mode of transmission.

The infective organism, Treponema recurrentis is an actively motile thread-like organism about 17μ in length by about 0.3μ in thickness with tapering extremities. The body is arranged in a number of waves, all in one plane, and
not in cork-screw-like spirals as in other types of spirochætes. There are 4 or 5 bends or waves or even fewer or sometimes as many as 6 or 7. Motility is marked, the movements consisting either of whirling forward or backward movements or bending movements or whip-like lashing movements. Leishman's stain brings out the structure quite clearly, and in the blood elongated, coiled or rounded forms can be met with.

FIG. II.

Treponema recurrentis (x 3,000).

Two or more are often seen joined together end to end forming the so-called ‘long’ forms, some of which are also forms undergoing transverse division. A supporting axial filament is believed to exist while the chromatinic granules of the body are described to break up and to be thrown out from the organism. A coccoid stage of the parasite is believed to occur, by some observers, in the body of the tick, and varying
stages between coccoid granules and spirochaetal forms have been described. But the spirochaætes themselves can be demonstrated in all the organs and tissues of the tick and also in the coxal fluid. This, however, is not the case in the louse, the spirochaætes disappearing from the alimentary canal in a few days after feeding, reappearing again as smaller forms which are infective. A feature that is of great interest is that of spirochaetal periodicity in man, the organisms appearing in numbers with the fever, disappearing, however, during the afebrile intervals. Whether this disappearance is only apparent and due to the scanty numbers present in the peripheral blood, or whether there is an invisible phase is the question. Recently Nicolle has pointed out that the suddenness of the recovery from fever, the simultaneous disappearance of the spirochaætes, the extreme infectivity of the blood to animals at the commencement of the relapse when spirochaætes are few, the occurrence of crisis in relapsing fever and their early disappearance in the louse, all these go to show the existence of an invisible phase of the parasite which, however, is the most infective. The crisis he regards as due to the breaking up of the spirochaætes into invisible forms under the influence of antibodies, followed later on by their regrowth into the infective previsible forms and finally to the spirochaætes again. Others, however, believe that the disappearance is due to destruction of the spirochaætes, which again gradually increase in number, till a stage is reached where the relapse of fever occurs. The existence of a similar subfebrile stage in malaria due to scanty parasites suggests that a similar condition may exist in relapsing fever. Experimentally, the infection can be transmitted to monkeys, ground-squirrels and other rodents, particularly white mice and white rats. Culture is extremely difficult, but has been carried out by Noguchi in ascitic fluid with citrated blood containing a piece of rabbit's kidney. The spirochaætes have been proved to be capable of passing through a Berkefeld filter. Depending on the different regional types of fever, different serological strains have been described.
The pathological lesions in man are those of an acute infection complicated by jaundice.

The liver is usually enlarged, markedly congested and shows microscopically cloudy swelling and focal necrosis. Haemorrhages are few, but there may be slight fatty degeneration. Numerous spirochaetes are found in various stages of degeneration in the Kupffer cells of the liver or lying free in the capillaries. The spleen is markedly enlarged and congested and shows infarcts. It is in a stage of acute hyperplastic swelling. Microscopically, numerous spirochaetes in various stages of phagocytosis are always present. The kidneys show cloudy swelling besides numerous spirochaetes. The bone marrow is hyperaemic, and a similar congestion may be met with in the brain and spinal cord, and the cerebrospinal fluid may contain spirochaetes. Submucous haemorrhages occur in the stomach and intestine.

Externally, jaundice may be marked, and together with the petechial haemorrhages, may suggest yellow fever; but the histological appearances are distinctive.

The blood usually shows a well marked polymorphonuclear leucocytosis and spirochaetes are usually numerous. When they are scanty they may be demonstrated by injection into animals. At autopsy, they are easily found in smears from the internal organs if the examination is carried out early. The urine contains albumin.

Immune bodies appear in the blood about the time of the crisis. An interesting feature recently pointed out is that the relapses are caused by the alternating growth of two strains of organisms which are serologically different.

RAT-BITE FEVER.

An infection transmitted from the rat characterized by relapsing pyrexia, the causal organism being a spirochaete, Spirillum minus.

The disease is common in Japan, and since its first description by Japanese observers, cases have been recognized in India and parts of Europe and America.
TYPES OF SPIROCHÆTAL INFECTIONS.

Rats and mice appear naturally infected with the organism, and the infection occurs by contamination of the bite with infected secretions, possibly lachrymal. Man may rarely get the infection from the bite of other rodents which in turn are infected by devouring diseased rats. Thus, cats, ferrets and bandicoots may transmit the infection.

*Spirillum minus* is a small spirochaete about 2 to 5μ in length with about 4 to 8 coils which, however, are rigid and fixed unlike the flexible spirals of the treponema. It exhibits active motility in a longitudinal direction and lashing movements of its flagella which consist of two or three spiral threads situated at each pole. Long and short varieties are described; but these appear to be identical. The spirilla are met with in the blood only in very scanty numbers, and for demonstration, inoculation into animals is the method of choice. Mice, guinea-pigs and rabbits are all susceptible, and after intraperitoneal injection the organisms appear in the blood in about 8 days. Cultivation is difficult and it is doubtful
whether the organism has been successfully cultured. In man the spirochætes may be demonstrated in the serum at the site of the primary wound.

The primary lesion generally heals, but in some cases ulcerates and produces a hard, nodular, chronic ulcer resembling an extra-genital chancre. In most cases, there is a regional lymphadenitis and lymphangitis which reappear with every bout of fever at the site of the primary lesion. The spirochætes can easily be demonstrated in the affected lymphatic glands which are enlarged, congested and soft. They are also found in the inflammatory fluid in the tissues surrounding the primary lesions, though from secondary infection, other organisms, such as streptothrices, may be found.

The liver usually shows cloudy swelling, areas of fatty degeneration and even necrosis in fatal cases, while the spleen may show enlargement and congestion. The kidneys also show cloudy swelling, and numerous organisms may be found in the adrenals as well as in other organs. Myocarditis may occur as a complication, and bronchitis and bronchopneumonia may be met with.

The blood shows a polymorphonuclear leucocytosis during the fever and an eosinophilia during the later stages. A secondary anaemia is usual. A weakly positive Wassermann reaction may occur, and immune bodies may be demonstrated after the attack.

The urine usually contains albumin and may also show the organisms.

Demonstration of the organisms is best by Adachi's method which consists of fixation for 30 to 60 seconds in a 1 per cent solution of osmic acid in 0.5 per cent corrosive sublimate solution and staining with Giemsa's solution, to 10 c.c. of the diluted stain of which a drop of 1 per cent alkaline potassium carbonate solution is added. Tribondeau's modification of Fontana's stain may also be used.
TYPES OF SPIROCHÆTAL INFECTIONS.

INFECTIOUS JAUNDICE.

This is an acute infectious disease, caused by a spirochæte, *Leptospira icterohæmorragiae*, and running a short febrile course associated with jaundice, from hepatic involvement.

The disease is most common in Japan and is also met with in Egypt where it assumes epidemic prevalence. Cases occur in Europe in the Balkans, and West Africa is an endemic zone. Recently, cases have been reported from the Andamans. Leptospirosis occurs as a natural infection in

![Image of Leptospira icterohæmorragiae](image)

**Fig. 13.**

*Leptospira icterohæmorragiae.*

(× 3,000) (after Noguchi).

rats and mice in whom the disease apparently spreads by contamination, since the organisms are excreted in the urine. Apart from man, the disease may cause severe epidemics in hounds. The organisms have been found in water and have been found to be pathogenic. Transmission occurs probably by contamination. The leptospiræ have been differentiated into a separate genus by Noguchi who has demonstrated the small elementary coils in the organism, besides the larger waves. The organism exhibits marked motility and flexibility, and during progressive movement it presents a hook-like curve at one end while the rest of the body
is held rigid, the hook apparently acting as a propeller to direct the parasite forwards. Sometimes both ends are curved, and forms described as S forms and C forms may be met with in rotatory movement. Sometimes the organism may appear as a rapidly whirling dot, and Noguchi has drawn attention to the appearance under the dark-ground illumination when the organism appears like a moving chain of cocci, the small dots representing the minute primary coils. The organisms can be cultured on Ringer's solution to three parts of which one part of serum agar has been added. They are found only in scanty numbers in the blood, but inoculated into guinea-pigs, they can easily be demonstrated. In guinea-pigs the organism causes severe jaundice with rise of temperature ending fatally after a rapid course. The leptospirae are found in numbers in the blood and in all the organs, particularly the liver where they can be demonstrated by Levaditi's method.

In man there is an early enlargement of the liver where the most important lesions are met with. There is at first a diffuse necrosis showing itself as an early swelling of the cells which becomes more marked in the centre. The nuclear changes of necrosis, such as karyolysis and pyknosis, are met with. Later on, fibrous overgrowth from reactive changes occurs. The small bile ducts are found distended with pigment. Compensatory hypertrophy of some cells are also met with. Cellular infiltration may be marked in the later stages as in subacute liver atrophy. Fatty degeneration may be met with, but this is not so marked as in yellow fever, or in acute yellow atrophy. The jaundice is the result of this necrosis of the liver cells and not from any obstructive lesion.

The spleen is sometimes enlarged and in a condition of acute hyperplasia. Hyperæmia of the pulp and areas of hæmorrhage are generally present. Swelling of the lymphatic glands may be met with showing hyperplastic changes.

The kidneys show cloudy swelling and occasionally hæmorrhages. Bile-staining is usual. An interstitial nephritis of the acute type with cædema and inflammatory
infiltration of the interstitial tissue has been occasionally met with. The stomach shows areas of submucous haemorrhage and ecchymosis. A diphtheritic colitis has been described. Haemorrhages have been met with in all the internal organs and into serous membranes. The external features are those of a severe jaundice, with cutaneous petechiae. Ædema of the legs may be met with.

The blood shows a marked secondary anæmia with a fall in the number of red blood cells and the amount of haemoglobin. The blood platelets are said to be diminished. The bone marrow may show reactive changes.

The urine contains albumin and casts, is highly acid and high coloured. Leptospiræ may be demonstrated under the dark-ground illumination.

YAWS.

A specific infective granuloma somewhat resembling syphilis due to infection with a spirochæte, Treponema pertenue, and characterized by the successive development of cutaneous nodules as well as lesions in bones in the late stages.

The disease is generally limited to a tropical belt near the equator and even in these regions has a tendency to affect primitive tribes. It occurs in parts of Africa, in the south of India, in Ceylon, in the Malay States and in the Pacific Islands.

The causative organism, Treponema pertenue, was described in 1905 by Castellani in the same year that Schaudinn described Treponema pallida of syphilis. It is a delicate spirochæte about 18μ in length on an average and has 6 to 20 waves or primary spirals which are rather closely wound together. During movement, secondary waves may be formed which, however, are much larger. The primary coils are not, however, so closely wound as in the genus Leptospiræ. The ends are pointed and of extreme tenuity, but whether they can be regarded as flagella is doubtful. They possess no central axial filament such as is met with in the sub-order of
Spirochætes nor a wavy crest such as is found in the Cristospira. The organism is generally indistinguishable by its morphological characters from T. pallida of syphilis, and, by many observers, is regarded as a variant with marked dermotrophic properties. It is found in the tissues in and around the lesion as well as in the blood, in scanty numbers, and in the late stages, in the viscera. It is easily stained by Giemsa's stain or by Tribondeau's modification of Fontana's stain. Cultivation may be carried out by Noguchi's method in ascitic fluid with rabbit's kidney, under strict anaerobiosis, as with the organism of syphilis.

![Image of spirochætes](image)

**Fig. 14.**

*Treponema pallida* (× 3,000) (after Noguchi).

Generally it is possible to differentiate three distinct stages of the disease, the primary stage being the stage following the inoculation. The secondary stage corresponds to the period where the generalized nodular eruption occurs, while a tertiary stage where bone lesions occur is also recognized. Unlike syphilis, sexual contact is not the common mode of infection for which a breach of surface is essential. The infection is also not known to be hereditary, the cases in children being due to infection after birth. Contact is an important mode of infection, and some abrasion on an exposed part of the body may show the primary lesion which may start at the site of a pre-existing ulcer. A child may infect its mother from close contact. There is a belief that flies may
transmit the infection, and this has been experimentally demonstrated, the flies however acting as mere mechanical carriers. Overcrowding and insanitary surroundings predispose to infection. Experimentally, the infection can be transmitted to monkeys by inoculation under the skin of the eyebrow, after which a primary lesion develops. It consists of an acuminate papule which increases in size, crusts over and forms a yellowish tumour very similar to the lesion met with in man.

In man the primary lesion or yaw chancre generally occurs in the lower limb or in any exposed part of the body. A mother suckling an infected baby may show a primary lesion on the nipple. It has the appearance of a vegetating nodule which falls off after a time and leaves a chronic ulcer. There is very little induration. Often, it is not possible to trace the occurrence of this primary sore which may be unnoticeable. In other cases, the secondary eruptions spring up before the subsidence of the primary sore.

Generally the primary sore subsides and after an interval of one to three months the secondary nodules come up. An early lymphadenitis sometimes occurs after the primary lesion. The secondary eruption consists of acuminate papules surrounded by zones of congestion. Each papule is formed under the superficial keratinized layers of the skin which is raised up and later on gives way in irregular fissures, through which the serum escapes and forms a yellow scab on the surface. The yaw gradually increases in size and forms an irregular fungiform mass somewhat resembling a raspberry, and hence the name frambesia is sometimes applied to the disease. Sometimes the eruption is circinate in shape with central healing. Very often the larger nodules are surrounded by a crop of smaller nodules. The nodules have a tendency to occur on the limbs and at muco-cutaneous junctions. They come up in succession all through this secondary stage which may last for about two to three years. After lasting a variable period, the yaw gradually shrinks in size, the crust which dries up becomes brownish in colour, gradually falls off and
reveals a scar instead of the original bleeding granuloma. Very often the primary lesion persists during this stage, but in most cases it is absorbed. Associated with and sometimes preceding the secondary eruption, desquamation of the skin is at times present. In the palms and soles, owing to the thickness of the superficial layers of the epidermis, the yaw breaks through much more slowly and leaves irregular pits after healing, giving rise to a curious condition called 'Crab Yaws.'

Histologically the yaw, whether primary or secondary, is a granuloma which commences in the superficies of the Malpighian layer of the epidermis. There is a marked proliferation of the layer so that the papillary down-growths of the skin become prominent and spread deep in club-shaped masses. Later, the epithelial cells degenerate and are replaced by masses of granulation tissue. With increase in size, the layers of keratinized epithelium are pressed upon and raised up forming the early acuminate papule. It will thus be seen that the essential lesion starts within the layers of the epidermis, the spirochætes multiplying in the prickle cells of the Malpighian layer. This is somewhat different from the lesion met with in syphilis where the reaction starts first in the corium and the spirochætes are found in the deep layers of the skin. With increase in size of this granuloma, the keratinized layers of skin give way as mentioned and a scab is formed on the surface consisting of coagulated serum and fibrin. Endarteritis, so prominent in syphilis, is not a marked feature. The granuloma is gradually absorbed with the subsidence of the inflammatory reaction and a dense mass of cicatricial tissue forms at the site.

During what may be called the tertiary stage of the disease, deep irregular ulcers may be met with, some of which are due to the persistence of the secondary nodules which ulcerate. The fingers and toes are particularly affected and a dactylitis may be met with, as in syphilis, due to a diffuse osteomyelitis of the phalanges. Deformity and contracture of the fingers may follow. Chronic periostitis of the tibia or a
more diffuse osteitis with sabre-shaped deformity has also been described. A rarefying osteitis occurring in multiple areas and tending to implicate the interior of bone has also been described. While tertiary visceral lesions are rare, aortitis and aortic aneurysms have been described. Involvement of the mucous membranes has been till recently regarded as rare in yaws; but there is reason to believe that the disease called 'gangosa,' which is a form of severe ulcerative rhinopharyngitis involving the nasal mucosa, septum and palate, is only a late manifestation of yaws. Similarly, osteophytic growths on either side of the nose affecting the nasal process of the superior maxillae from a chronic periostitis labelled 'goundou' are now regarded as a tertiary feature of yaws. Epiphysitis may occur in yaws as in syphilis; but the phalanges and metacarpals are more often involved. Juxta-articular nodules of fibrous tissue which sometimes occur as a condition affecting the whole body are now classed as a yaw manifestation. Unlike syphilis, however, nervous lesions like locomotor ataxia and general paralysis are not met with; but on the whole the relation between these two diseases is extraordinarily close.

The blood, as in syphilis, shows a positive Wassermann reaction. The question of cross immunity between syphilis and yaws is not settled.

**SEVEN-DAY FEVER OF JAPAN.**

This is an acute infection with a mild course which occurs in Japan.

The disease occurs during the autumn. The seven-day fever of Indian ports is regarded by Rogers as the same disease.

The infective agent has been proved by Japanese observers to be *Leptospira hebdomedalis*, an organism that appears to be very closely allied to *L. icterohaemorrhagiae* of Weil's disease. Differentiation is possible only by serological reactions. It can be recovered from the blood of patients
during the first six or seven days of the disease and can be cultured from the blood. It is also excreted in the urine during convalescence. The field mouse appears to be the natural reservoir of infection.

Experimentally the disease can be transmitted to guinea-pigs in whom the disease is reproduced in a fatal form. The lesions met with in guinea-pigs are cloudy swelling, fatty degeneration and focal necrosis in the liver, congestion and hyperplasia of the spleen. Petechial haemorrhages are not so common nor is jaundice an important feature. This serves as an important point of distinction from experimental Weil's disease. The leptospiรฉร can be demonstrated from the liver by Levaditi's method.

The disease has no pathologic anatomy since it is not fatal.

The blood contains spiroch kształcidal substances at the end of the first week.
CHAPTER III.

TYPES OF INFECTIONS WITH FILTERABLE VIRUSES.

YELLOW FEVER.

This is an acute infection characterized by severe toxic jaundice with multiple haemorrhages, running a short febrile course, the infective agent being suspected to be a filterable virus, while the insect transmitter is definitely known to be a mosquito.

The disease is endemic in certain regions of Central America and the west coast of Africa and sometimes assumes epidemic proportions. Cases occur commonly in seaport towns and sometimes in ships. It has a tendency to limit itself to localities probably owing to the habits of the mosquito transmitter, Aedes argenteus also called Stegomyia fasciata. Thus, the disease cannot spread in localities where the insect transmitter is absent, even though direct infection is possible under experimental conditions. Another important feature of its epidemic prevalence is that temperatures lower than 24°C. prevent the spread of the disease, apparently a factor depending on the development of the infective organism in the mosquito. The infective stage of the disease is only during the first three days and, since mosquitoes are not found infected in nature, they must receive the infection during this short period. The question of susceptibility of the host is also of great importance since the disease disappears for long periods in endemic zones, the immigrants, however, catching the infection. 'Larval' forms of the disease possibly exist, particularly in children, giving rise to no clinical symptoms, and these serve to keep the mosquitoes infected, though the question of chronic 'human
carriers' of the organism has not been fully decided. However, infected mosquitoes retain their infectivity throughout life, but do not transmit the infection to the larvæ.

With regard to the infective organism, the virus of yellow fever, Noguchi's claim that *Leptospira icteroides* a small spirochæte, is the infective agent, has not been proved, this organism being regarded as identical with *Leptospira icterohæmorrhagiae* of infective jaundice. All attempts to cultivate Noguchi's spirochæte from the African cases have so far failed. On the other hand, a virus which is a filter-passér in its human stage is now suspected to be the causative agent. The disease has been experimentally reproduced in monkeys by inoculation with the blood of infected individuals and from them the disease has been again transmitted. Mosquitoes infected experimentally can also transmit the disease to monkeys, but only after an incubation period of 12 days, during which the mosquitoes are non-infective, the virus probably undergoing some cycle of development in the mosquito. Guinea-pigs are refractory, and this is of value in differentiating the condition from Weil's disease to which guinea-pigs are susceptible. The virus is apparently contained in the blood which is highly infective, but loses its infectivity if heated to 55°C. for 10 minutes. A cell-free filtrate from the blood is also infective, showing that the virus is a filter-passér. The changes met with are mostly degenerative, and inflammatory reaction is slight.

The pathological lesions met with in yellow fever are most marked in the liver, which bears the brunt of the toxæmia which affects also the kidneys and spleen, while severe jaundice and cutaneous hæmorrhages characterize the visible external features.

The liver is usually of a yellow colour described as that of 'box-wood,' and shows a fine mottling on the surface from the blood vessels standing out in contrast. It is usually normal in size, firm, and preserves its shape. The capsule is usually transparent and shows the yellow colour of the parenchyma, but is also yellow from bile staining. On section,
the appearance is that of a fatty liver, the yellow colour of the lobules being demarcated by the blood vessels which, however, are not congested. The cut surface is greasy and may show oil globules. Areas may show dark red patches of haemorrhage. If the fatty change is advanced the organ is flabby and friable. Microscopically, the most important feature is the marked necrotic change affecting the middle zone of the lobule, 'mid-zonal' necrosis. But in the later stage the change spreads from the middle zone to the centre of the lobule and towards the portal tract so that the whole lobule is involved. The central and peripheral cells may be comparatively less affected. Towards the periphery of the necrotic areas, the liver cells may show marked eosinophilic staining, this being preceded by a hyaline change. It has been suggested that this eosinophilic change is analogous to the accumulation of acidophile granules in cells met with in 'virus' disease. The nuclear changes of necrosis, such as pyknosis and karyolysis, are most marked in the middle zone, while extensive fatty degeneration also occurs, the fat appearing as small droplets inside the cells. Congestion is slight, but areas of haemorrhage into necrotic zones may be met with. The Kupffer cells, as a rule, show marked hyperplasia and this probably accounts for the jaundice, since these are the cells that manufacture bile pigment. Later the endothelial cells show slight degenerative changes. Fatty degeneration of the capillary endothelium occurs and accounts for the haemorrhages.

The kidneys are generally enlarged and reddish in colour with an admixture of yellow from bile staining. Underneath the capsule are small haemorrhages. The capsule strips with ease and leaves a bulging, smooth surface, yellowish red in colour, showing prominent blood vessels. On section, the cortex is swollen and there may be small red dots indicating points of haemorrhage. The distinction between cortex and medulla is well marked, but the vascular striations are indistinct in the cortex owing to swelling. Yellow streaks of fat may be met with. Microscopically, the appearance of the kidney is what has been described as acute tubular nephritis,
the condition being, however, an acute degenerative change affecting the tubules and not involving the glomeruli, the toxic 'nephrosis' of German authors. The epithelium shows all gradations between fatty degeneration and necrosis ending in desquamation and resulting in the formation of casts in the tubules. Acidophile necrotic cells may be met with in the kidneys. Some of these casts are albuminous, others undergo calcification, and the presence of these lime casts has been regarded as characteristic. Hämorrhages may be present into the tubules. The epithelial cells may be found loaded with small droplets of fat in frozen sections.

The spleen is generally normal in size, but is somewhat congested and microscopically shows characteristic hyperplasia of the endothelial cells of the lymph nodes leaving the lymph sinuses unaffected. The lymphoid cells are scanty and the follicles are consequently atrophied. Later, these enlarged endothelial cells are set free into the sinuses and degenerate, becoming hyaline and granular and showing mitotic figures. Thus, the toxic action is on the parenchyma of the liver and kidneys and on the endothelium of the spleen and the capillaries.

The stomach shows capillary hämorrhages into the mucous membrane besides a marked congestion and swelling. The contents are usually black in colour and consist of altered blood which, when vomited up, forms the characteristic 'black vomit' of the disease. The duodenum shows marked congestion and petechial hämorrhages more constantly than the stomach, but the rest of the intestines are negative, except that altered blood may be present in the lumen. The brain and the membranes show congestion, besides points of hämorrhage. The adrenals are described as showing fatty changes.

Externally, the skin shows irregular areas of ecchymosis and petechial hämorrhages. There is a diffuse bile staining not only of the skin and mucous membranes, but of all the internal organs. The jaundice is now regarded as toxic and not hämolytic. The blood, as in all cases of jaundice, is fluid
and does not readily coagulate. There is no constant blood picture, but a slight polymorphonuclear leucocytosis is described. The urine generally contains large amounts of albumin which increases with the course of the disease. Bile stained casts may be present. Sometimes anuria may occur.

A very high degree of immunity exists after infection and consequently convalescent serum is of great protective value.

**Dengue.**

An infection spread by mosquitoes manifesting itself as a short biphasic fever with a cutaneous rash, and generally running a mild course.

It generally occurs in the tropics and subtropics where it assumes epidemic prevalence, though sporadic cases do occur. There is a tendency to occur in pandemic waves at intervals of five or six years. The disease is transmitted by the common banded mosquito, *Aedes argenteus*, also called *Stegomyia fasciata*. The causative organism is generally regarded as a filterable virus, and the disease can be transmitted from man to man by injection of the filtered blood. In animals, such as guinea-pigs, though they may retain the infection, the clinical features of the disease do not develop. Their blood, however, remains infective after inoculation and from them the disease can be transmitted experimentally to human beings. The virus occurs in the blood only in the early stages of the disease, and is not generally found after the third day after infection. In mosquitoes, the infection develops after a long incubation period of two weeks. The organism is introduced into the blood of the host directly by the mosquito and so far as evidence goes there is no other mode of infection, since the virus is not found in the excreta. The incubation period in man is short, unlike in the mosquito, and is usually about 4 to 7 days. The occurrence of leptospiræ in cases of dengue has been described, but so far the evidence is not conclusive. Recent workers have distinctly failed to find this organism
which has been experimentally proved incapable of surviving in the stomach of the sandfly.

The mortality is very low and does not occur apart from complications such as pneumonia. Inflammatory changes in joints, such as arthritis and synovitis, are sometimes met with. The skin may show septic secondary infections apart from the characteristic eruption.

The blood shows a distinct leucopenia which affects mostly the polymorphonuclear cells. There is a relative monocytosis which is more prominent than in sandfly fever. Immune bodies exist in the blood for a variable time after the attack. The mononuclear increase subsides rapidly. A yellow coloration of the serum has been noted.

**Phlebotomus Fever.**

This is a short fever transmitted by sandflies of the genus *Phlebotomus*.

The disease is mostly confined to tropical and subtropical countries and is generally sporadic in places where the infected transmitter exists. Occasionally it may assume epidemic prevalence. The infection exhibits resemblances to dengue; but the skin rashes of dengue are absent. The seasonal occurrence coincides with the season when *Phlebotomus papatassi* are met with. Kligler mentions the occurrence of rash caused by the bite of the sandflies, the fever following subsequently. The infective organism is now believed to be a filterable virus since the disease can be transmitted to volunteers by injection of filtered plasma. The blood is, however, infective only during the first forty-eight hours and, as with dengue, laboratory animals are susceptible. Claims have been made that a leptospira is the causal organism and a leptospira resembling *L. icterohaemorrhagiae* has been described; but the difficulty is in deciding whether this organism has been found in real cases of phlebotomus fever or in cases of mild infectious jaundice which are definitely leptospiral. The disease can be experimentally transmitted by direct inoculation from case to case
if the blood is taken on the first day. Female phlebotomi alone carry the infection by feeding on man and after an incubation period of seven days they become infective. The infective stage is, however, quite short and lasts only for a few days, unlike the mosquito in dengue which remains infective throughout its life.

As the infection is quite mild and of short duration, no distinct pathological lesions exist. Immunity probably exists, but is of short duration. The blood shows a distinct leucopenia with relative mononucleosis. Kligler has noted that the serum may show a yellow coloration, but jaundice is absent.
CHAPTER IV.

TYPES OF INFECTIONS ASSOCIATED WITH RICKETTSIA.

THE TYPHUS GROUP.

UNDER this group may be included those fevers that go under the name of Typhus, Tropical Typhus, Rocky Mountain fever, Tsutsugamushi disease and Trench fever, all of which are regarded as infections of rodents transmitted generally by acarinae. Occasionally man gets the infection as an accident and epidemics arise from acclimatization of the infective agent to the human host.

TYPHUS FEVER.

This is a type of infective fever that occurs in epidemic form in famine-stricken areas, in armies and in jails. It generally runs an acute course lasting for about a fortnight and is characterized by a punctate cutaneous rash and a continuous fever terminating by a crisis.

The disease is spread by lice. It occurred in Central Europe during the Balkan War and is endemic there even now. It was much commoner during the Great War and occurred in Russia and in Persia. An organism that is met with in the blood is Bacillus typhus exanthemetic and is probably a secondary invader. The organism that is now regarded as closely associated with the disease, if not the actual causative agent, is Rickettsia prowazekii. This organism is found in lice removed from typhus cases. Here it occurs in the columnar epithelial cells of the intestine where it is met with in innumerable numbers. Short coccoid forms about 0.5 in size are met with, sometimes two together in dumb-bell shapes. Longer forms
TYPES OF INFECTIONS ASSOCIATED WITH RICKETTSIAE.

about 1.5 to 2μ in length are common while occasionally bacillary and filamentous forms are met with. The question whether the organism is allied to the bacilli or to the filterable viruses is not settled. It develops in the mid-gut of infected lice, and in about a week after feeding the lice are infective. Other rickettsia bodies occur in lice—Rickettsia quintana of trench fever and Rickettsia rochalima. The organism has been grown in tissue culture by Wolbach and his co-workers. In cases of typhus, the organism has been demonstrated in the endothelial cells of the blood vessels of the skin and brain and more particularly in the rash. It has also been described in the miliary nodules in the liver and spleen.

The disease can be experimentally transmitted to monkeys and guinea-pigs by injection of the blood of patients. Whatever the nature of the infective agent, it is found in the blood and organs of man and animals during the acute phase. It is also present in the alimentary canal of lice which have been fed on patients. The louse is experimentally capable of transmitting the infection in about 6 days after feeding. The infective agent is present in the blood, in the plasma free from cells, and also in the blood platelets.

While sporadic forms of the disease occur, the disease assumes epidemic form during the cold season in Europe, particularly Russia. Mild cases, described in the United States as Brill's disease, are probably sporadic cases of typhus. It is possible that Marseilles fever and similar mild fevers in the Mediterranean are cases of typhus. Similar mild cases conveyed by ticks called tick-typhus are reported in India by Megaw. These mild types are not, however, so infective.
It is believed that the louse is the sole transmitter, infection occurring either by the bite or by contamination of the excreta of lice which are infective. Both body louse and head louse transmit the infection.

The pathological lesions met with are mostly those of an acute infection, with certain special features.

Externally there may be small petechiae, the characteristic cutaneous rash generally having faded leaving behind, however, brownish spots. Sometimes small raised nodules may be met with. Microscopically, the eruption starts as a hyperplasia of the endothelial cells of the walls of small arterioles and capillaries followed by a necrosis of the endothelial cells with infiltration of lymphoid and mononuclear cells around the vessels. Thrombosis of the vessels may be met with.

Similar petechiae are met with in all serous membranes and even the solid organs may show hæmorrhages under the capsule. Hæmorrhages may be met with from the mucous membranes of the stomach or intestine. Similar hæmorrhages may be met with in the bladder.

Respiratory complications are often met with in typhus and so bronchitis and broncho-pneumonia are common. The larynx may show ulceration. Gangrene and abscess of the lung may be met with as a termination of the pneumonic process.

The blood is fluid and does not readily coagulate. The heart may show cloudy swelling and dilatation may be met with from acute myocarditis. Thrombosis of the femoral vein and œdema of the leg may be present. Arterial thrombosis may be present as in typhoid fever from an arteritis.

Cloudy swelling of the kidneys and severe toxic degeneration of the tubules may result in the leakage of albumin. The nodules of periarterial infiltration described by Frankel may be present. The spleen is enlarged and in a state of acute hyperplasia with swelling of the lymphoid follicles. The alimentary canal, unlike typhoid fever, shows no characteristic features. Enlargement of the mesenteric
glands is uncommon. However, a parotitis may be present as in typhoid fever.

The brain may show the small miliary nodules described by Frankel. Histologically, there is necrosis of the endothelium of the small blood vessels followed by thrombosis. These Frankel’s nodules are met with in and around the aqueduct of Sylvius and at the base of the brain. The Rickettsia can be demonstrated in these nodules in the cells.

The blood shows a moderate leucocytosis affecting the polymorphs. The blood presents a peculiar feature in its ability to agglutinate suspensions of *Bacillus proteus* × 19 and this property is made use of in diagnosis in what has been called the Weil-Felix reaction. A high titre of agglutination is obtained and dilutions of 1 in 80 to 1 in 100 of the serum give definite macroscopic clumping of the organisms.

**Rocky Mountain Fever.**

A specific infective fever transmitted by ticks and bearing resemblances to typhus, Rocky Mountain fever is characterized by a specific capillary endangitis, which forms the essential lesion.

The disease is mostly localized to the states of America adjoining the Rocky Mountains. It is possible that the ‘tick-typhus’ described by Megaw as occurring in the Himalayan slopes are really cases of Rocky Mountain fever. The tick transmitter is *Dermocenter venustus*—the wood tick—the transmission occurring by the bite, and possibly when ticks are crushed into the skin. The infective virus is transmitted from the tick to the larvae, to the imago and adult and from this to the third generation. Possibly rabbits which harbour the ticks are natural reservoirs of infection.

The infective agent is found in the red blood cells and in the tissues, but is not filterable. It probably undergoes a cycle of development in the tick since they are infective only after a period after feeding. The disease can be experimentally
transmitted to guinea-pigs. A micro-organism first described by Ricketts has been found in the blood of infected individuals as well as in infected lice. The organisms occur as small coccoid bodies occurring in pairs and varying in size from 0.2 to 1 μ and are lanceolate in shape. It is called *Dermacentroxenus rickettsi* and often exhibits pleomorphism, rod-shaped forms being met with. Three definite morphological types are described by Wolbach, intracellular rod-like forms without granules only present in ticks, small rod-shaped forms with chromatic granules in the blood vessels and lanceolate diplococcal forms found in ticks and in the blood and tissues of infected individuals.

The lesions met with in Rocky Mountain fever bear marked resemblances to those met with in typhus since the vascular reaction is common to both. The brain and spinal cord are, however, not so commonly affected and there is a greater tendency to haemorrhage and gangrene. The blood shows a similar Weil-Felix reaction.

The characteristic feature is the involvement of the scrotum with marked haemorrhage into the tunica vaginalis, and into the testes, and into the ovaries and tubes in the female. Gangrene of the scrotum is sometimes met with. Microscopically, the small arteries of the skin are affected. There is a marked early proliferation followed by degeneration of the endothelial cells of the intima. A marked infiltration of the intima with mononuclear phagocytic cells is present. The media is also infiltrated. The diplococcal forms of *D. rickettsia* are met with in the cells. A thrombosis of the vessels is a usual feature. The capillaries and the veins are also affected in a similar manner. Perivascular polymorphonuclear infiltration occurs only in the later stages. This endangitis appears to be toxic and similar to the endothelial degenerations met with in 'virus' diseases.

Apart from the skin, the capillaries, the arteries and veins of the testes, ovaries and other organs show a similar reaction. The peripheral blood vessels are, however, mostly affected.
Types of Infections Associated with Rickettsiae.

Dull red macules—the rash of Rocky Mountain fever—and petechiae and ecchymosis may also be met with at autopsy.

Internally, petechiae may be met with in the serous membranes. The heart may show cloudy swelling. A broncho-pneumonia is met with or a lobar pneumonia may occur, both as complications. There is a marked enlargement of the spleen as in all acute infections. The condition is one of acute hyperplasia affecting mostly the endothelial cells. Phagocytosis may be present. The liver shows cloudy swelling and focal necrosis. Fatty degeneration may be met with. The kidneys show congestion. The muscles may show the vascular lesions.

The blood shows a slight leucocytosis. A marked mononucleosis may be met with. There is a degree of haemolytic anaemia and this accounts for the jaundice that is present.

The urine is high coloured and contains albumin and sometimes casts.

The Tsutsugamushi Disease.

This is a form of infective fever transmitted by a hairy mite and characterized by a local lesion and regional lymphadenitis as well as an exanthema.

The disease occurs in Japan and is often called Japanese river fever since it has a tendency to occur during periodic floods. The insect vector of infection is a hairy mite called tsutsugamushi and is the six-legged larval form of Trombicula akamushi, the infection following the bite of infected larval mites. Other mites of the genus Trombicula have also been implicated. Human infection appears to be accidental. Rodents are the natural hosts.

The infective virus is present in the blood and the enlarged lymphatic glands corresponding to the site of infection. In the blood it is present in the cells and not in the filtrate. Micro-organisms have been described and Rickettsia-like bodies have been met with in the mononuclear cells of the glands and in the infected wound. Coccoid forms
about 0.3 to 1.5μ in size have been found and similar bodies have also been described in infected mites. The name *R. nipponica* has been suggested by Sellards.

The primary lesion consists of an area of necrosis in the skin at the site of the bite followed by slight induration. Later, a small blister is formed which ruptures and leaves a small ulcer which crusts over and has slightly thickened and clear cut walls. Healing occurs gradually towards the end of the fever. Microscopically, there is an area of necrosis corresponding to the bite and this is surrounded by an area of cell infiltration and engorgement. The cells met with are plasma cells and mononuclears. The infiltration is diffuse. There is an associated lymphangitis in the lymphatics leading from the ulcer which stand out as red lines. An acute lymphadenitis is also present, with marked enlargement of the affected gland, which becomes soft and smooth with a tense capsule showing a bulging greyish-white cut surface often with specks of haemorrhage. Histologically, there is an acute lymphadenitis with swelling and shedding of the endothelial cells, followed in the late stages by infiltration and fibrosis with formation of giant cells. Necrotic foci may be occasionally met with. The neighbouring lymph nodes may be secondarily involved.

The spleen is soft and enlarged and shows hyperplasia with necrotic foci. The liver may show cloudy swelling, and similar changes may be met with in the heart and kidneys. The bone marrow shows necrotic foci and is usually red. The lungs may show bronchitis or congestion. Bronchopneumonia may be met with as a complication.

The blood shows a marked leucopenia. Slight anaemia may be met with. Immune bodies exist in the blood, but the immunity is neither marked nor lasting. The Weil-Felix reaction is negative.

**Trench Fever.**

This is an infective fever, transmitted by the louse, that occurred in epidemic form in the armies during the Great
War in Europe, though sporadic forms of the disease occurred in the tropics in Mesopotamia and Egypt.

The insect transmitter is the ordinary body louse. The virus is present in the blood, in the red blood cells and leucocytes and is not present in the filtered serum, since the virus is not a filter-passer. Experimentally it has been found that lice become infective after feeding, in a variable period after five days, indicating a development in lice. The infection probably occurs by inoculation of infected excreta of the louse when it is crushed into the skin, either through abraded skin or through the lesions caused by the louse in the skin.

In the intestinal contents of infected lice, small round or oval bodies 0.3 to 0.5μ in size have been found. These bodies are regarded as Rickettsia forms and the name Rickettsia quintana has been applied. Unlike the rickettsia of typhus these are not found inside the cells. Similar rickettsia are found in uninfected lice called R. pediculi and the two organisms have been regarded as identical and derived probably from some source of infection. An important feature is that the intestinal contents of lice with rickettsia have been found infective, while lice without such rickettsia are not infective. The causal relationship between the rickettsia and the disease has not been settled, but the evidence is suggestive.

The pathological anatomy is uncertain since the disease is not fatal. An enlargement of the spleen occurs as in all acute infections. A toxic myocarditis has been described. The blood shows a leucocytosis mostly affecting the polymorphonuclear cells. The urine contains a trace of albumin.

Immunity exists for a period that is variable. The Weil-Felix reaction is negative.
CHAPTER V.

TYPES OF INFECTIONS WITH FUNGI.

MYCETOMA.

THIS is the name given to a clinical condition rather than a pathological entity. A disease caused by fungi either of the Actinomyces or the Maduromyces groups, mycetoma is a condition generally occurring in the foot which becomes enlarged, swollen, boggy and nodular and riddled with sinuses. The term 'mycetoma' means a fungus tumour.

A similar condition may rarely occur in the hand but other situations are rare.

The fungus is easily demonstrated in diseased tissue as granules or dense felted masses. The colour of the granules has been hitherto the basis of all classifications and black, white, yellow and red mycetomas have been described, but modern experimental work seems to indicate that the colour of the fungus is a mere physical variation that could be brought about in the same species by varying cultural conditions. A correct classification based on the species of the causative fungus is yet to come.

It has been found that mycetoma may be due to two main groups of fungi. The first is the Actinomyces group in which the mycelial threads are thin and filamentous, the septa are indistinct if at all present, the cell walls are not easily demarcated, and chlamydomspores, which are simple septal thickenings of the hyphae, are absent. In this group are included a number of species of organisms which are mostly parasitic in animals, sometimes in man. The mycelium is a fine network with numerous branches, with radiating threads ending in prominent club-shaped terminations like a ray fish; hence the name 'ray fungus.' The specialized
spores, or conidia, are formed by portions of the filaments which break off. The fungus forms dense granules which are mostly coloured. Two main sub-heads of this wide group are: (1) the Nocardia, which are aerobic, and (2) the Cohn streptothrix, which are anaerobic.

The group Maduromycoses, on the other hand, is made up of fungi with a mycelium in which the threads are much stouter and segmented, with well defined walls and chlamydospores. These have been classified into two large sub-groups of which the first include the common madurella and the indiella belonging to the Fungi Imperfecti, and the second, the aspergilli, the sterigmatocystis and the penicillium groups, belonging to the Ascomycetes. They are subdivided again into black, white, yellow and red varieties.

The fungi can be demonstrated in diseased tissue if the granules are taken out and squeezed on to a microscope slide. Sections of tissue may also show the fungi. For cultural purposes the granules should be washed in saline free of all infective organisms and heated to 56°C. to kill any secondary organisms. The granules may be then implanted into Sabouraud's maltose agar, the ideal cultural medium. The material should if possible be removed from unopened sinuses to obviate secondary infection. The growth is necessarily slow and takes two to three weeks.

The fungus gains entrance to the deeper tissues through some abrasion in the skin possibly due to a scratch or a prick while walking barefoot. The type of inflammatory reaction is peculiar in that it allows the fungi to make its way into the tissues causing progressive destruction and decay of tissue. The tissue reaction consists of an attempt at encapsulation—a type which is found in most fungal infections. This is, to some extent, similar to the type of reaction met with in other infective granuloma since endarteritis obliterans and encapsulation are attempts to destroy the infected tissue in toto. In mycetoma, this causes extensive destructive lesions and marked fibroid thickening since the fungus is exceedingly resistant.
Fig. 17. Mycetoma.
Actinomyces.

Maduromyces.
The early lesions are localized nodules of dense fibrous tissue containing the grains of the fungi which are the essential elements of a mycetoma. The sole of the foot is the usual site, but any part of the body may be the site for a mycetoma which literally means a fungus tumour.

From the encapsuled nodules, sinuses burrow their way in different directions, some coming out on the surface as small nodular elevations with tiny tracts inside. They may make their way into the deeper structures, disorganize muscles, ligaments and tendons, while in bone they cause a rarefying osteitis. The sinuses communicate with one another and lead into cavities in which the coloured grains may be found imbedded in a mass of cell debris. The whole tissue becomes dense, elastic and tough owing to the formation of dense fibrous tissue. The natural configuration of the part is lost, and when it affects the foot, the sole of the foot becomes thickened and hypertrophied, assuming a padded appearance. Nodules and sinuses are found on the dorsum discharging

**FIG. 19.**

Mycetoma (x 225) showing the edge of the fungus. Note the giant cells and the endothelial hyperplasia around. The cells are polymorphs and lymphocytes.
thin sanious pus containing the granules. A lymphadenitis of the regional glands is usual though there are no features of a general infection. Occasionally the lymphatic glands may themselves contain the fungus.

Fungi belonging to the Actinomyces group are sometimes obtained from cases of typical mycetoma and it should be recognized that this condition is not uncommonly due to infection with this group which causes a wide variety of lesions in cattle as well as in human beings in Europe. The lesions are quite similar, but occasionally tumour-like nodules develop. The lesions caused by the actinomyces may occur in a variety of situations other than the foot. Thus, cases have been described in the jaw, in the breast, in the arm, and in the sacral region.

Microscopically, the well-developed mycetoma granules consist of a dense felt-work of the mycelium surrounded by a
mass of inflammatory cells mostly polymorphs, while there are a few endothelial cells and lymphocytes, a reaction which, at this stage, is somewhat different from that of tubercle. In fact they are more like encapsuled abscesses containing the fungus. The surrounding tissue shows infiltration with polymorphs, lymphocytes, numbers of plasma cells and occasionally giant cells. Endarteritis obliterans of vessels is sometimes met with and dense infiltration with plasma cells may be another feature.

The earliest noticeable lesions, however, are different and consist of foci of infiltration with lymphoid cells and mononuclear cells with occasional foreign body giant cells. The polymorphonuclear reaction appears to be the result of secondary infection. The early nodules are surrounded by dense whorls of fibrous tissue and this, together with the lymphoid cells and giant cells, may present an appearance not unlike a tubercle; but in the later stages with the growth of the fungus this appearance is lost and small abscess surrounding the fungi form the characteristic microscopic feature.

Cells containing eosinophilic or fuchsinophile granules are generally met with in the neighbourhood and these appear to be derived from plasma cells. At first these fuchsinophile granules are small, later the whole cell may be converted into one eosinophilic body; unlike the ray fungus, the mycelium does not present any radiating hyphae and no tissue reaction in the shape of club-shaped pink staining structures are met with at the periphery of the fungus. Occasionally the peripheral part of the fungus may present a thickened edge somewhat like that of a dense capsule.

**Rhinosporidiosis.**

This is a chronic infection affecting the mucous membrane of the nose, characterized by the formation of a raspberry-like polypoid mass of minute cystic growth. The infective organism, *Rhinosporidium seeberi*, is now definitely classed as a fungus.
The disease occurs in parts of India as Madras and in the small state of Cochin where this type of nasal polypus is fairly frequent. Similar polypoid growths are rarely met with in the conjunctivæ, lachrymal sac, in the soft palate and on the genitalia. A very similar condition has been described in the horse. The infective agent was formerly regarded as a protozoon and was relegated to the class Cnidosporidia which are amoeboid protozoa with a vegetative spore-forming phase. Ashworth has recently pointed out that the parasite is a fungus. In its early stages it is a rounded body inside the connective tissue. It has a small vesicular nucleus and the whole structure is surrounded by an envelope of chitin which gradually becomes thicker so as to resemble a resistant cyst or a spore. The cell, about 8µ in size, gradually increases in size till it assumes the appearance of a large cyst, when the nucleus undergoes rapid division so that a number of nuclei are formed. In the later stages, the protoplasm gradually collects round these nuclei to form a number of small cellular structures, so that in the final stage, the appearance is that
of a cyst, or sporangium with a dense, resistant, thick wall, with a number of small spore-like cells inside. In the fully developed cyst or sporangium, the central cells are the most mature and show well developed vesicular nuclei, while the peripheral ones are small and immature. The ripe sporangia burst and the cells are often set free into the surrounding tissues where they repeat the cycle. The resultant polypoid growth is a raspberry-like pinkish tumour showing a variable number of glistening minute cyst-like bodies on the surface and deep inside the mass. The infection is exceedingly chronic since the surrounding tissues are infected. The mode of infection is not known, but the sporangia rupture through the mucosa and the spores are passed out in the nasal secretion.
Fig. 23. *Entamoeba histolytica* (× 2,000) showing character of pseudopodia.
CHAPTER VI.

TYPES OF PROTOZOAL INFECTIONS.

AMOEBIASIS.

Under the term amœbiasis are included pathological conditions occurring in man caused by a parasitic protozoon, *Entamoeba histolytica*. The usual habitat of the parasite is the large intestine, where it causes ulceration giving rise to the clinical symptoms of dysentery or of diarrhoea; the parasite may make its way through the portal vein to the liver causing a type of abscess of the liver. Rarely abscess of the brain, of the lung or of the spleen may occur.

*Entamoeba histolytica* is a parasite that is found in the mucous membrane of the colon in man. The active forms are rounded, motile, refractile protozoa, 20 to 30µ in diameter, the ectoplasm being quite clear and well demarcated from the endoplasm which is finely granular and may contain ingested red blood cells, and sometimes food vacuoles. Bacteria, other vegetable organisms, or starch granules are not found in the endoplasm. The nucleus is rounded and is on one side and is not visible in the actively motile forms. Staining with iron-hæmatoxyl or Mann's stain brings out the nuclear structure. It is about 4 to 7µ in diameter and its chromatin is arranged in a 'ring' of fine granules on the inner surface of the nuclear membrane. There is a very small central karyosome with a very clear space around it—a nuclear halo. The rest of the nuclear structure is clear and shows no dots of chromatin. The normal habitat is the mucosa of the colon where the parasite lives in the tissues and multiples by binary fission. 'Cysts,' or resistant forms, are formed, when the environment becomes unfavourable, and are passed out in the faeces and
infect other individuals. They are rounded clear refractile bodies with a definite cell wall. They are variable in size ranging from 6 to 14μ. At the commencement of encystment the amoeba divides into a smaller type, a minuta phase, and then forms a cyst wall so that early cysts are uninucleate. Later, the nucleus divides into two and then into four so that the mature cysts are quadrinucleate when passed in the motion. The cyst contains besides the nuclei one or two brightly refractile bodies called chromatid bodies which take a deep stain in stained preparations. A small granule of glycogen is also generally found. Supernucleate cysts containing 8 nuclei may occur.

Pathogenic rôle of Entamoeba histolytica.—The normal habitat of *E. histolytica* is the mucosa of the colon where it lives at the expense of the tissue cells causing ulceration of the mucosa, by means of a proteolytic ferment which dissolves the cells; hence the name ‘histolytica.’ Under natural conditions of parasitism, a balance is maintained between the parasite and the human host so that the ulcers heal by the regeneration of tissue and symptoms are not apparent, only cysts being passed in the stools. This is the commonest form of amœbic infection met with, and the host is only a ‘carrier.’ The general health is maintained though, occasionally, vague symptoms may be met with. When, however, the parasites are more active or there is a diminution of the resistance of the host, there is extensive destruction of tissue which the regenerative process cannot cope with, and the host goes down with an attack of dysentery, and passes blood and mucus in the motion. In the mucus, numerous motile vegetative forms of *E. histolytica* may be met with, since the normal process of encystment is interfered with. More often the patient gets an attack of diarrhoea where the motions contain numbers of amœbae. Occasionally the amœbae may pass through the submucosa into the branches of the portal vein to the liver where they cause a similar reaction. In the earlier stages of parasitism in the liver, the tissue becomes engorged and is in a condition of active hyperæmia giving
rise to the condition called amoebic hepatitis. In other cases there is a histolysis of tissue causing an area of colliquative necrosis of the liver cells forming, what has been called, a tropical 'abscess' of the liver. Sometimes the amöebæ may be carried to other and distant organs giving rise to 'abscesses' of the brain, spleen, etc. 'Abscess' of the lung may also occur by spread from the liver through the diaphragm, besides the hæmatogenous route. With regard to the infection of the host, it must be understood that the active free-living forms that are passed in the dysenteric stool are not the infective forms. The latter are the quadrinucleate cysts that are passed in the carrier stage and in chronic dysentery. When the cysts are swallowed, their walls are dissolved and four little amöebæ are set free and make their way into the wall of the large intestine, where they live as obligatory parasites. Encystment occurs only in the faeces and not in the tissues of the host, whereas the free-living forms are met with in the tissues. Thus, it becomes obvious that the carrier stage is much more important from the point of view of infection since the motile vegetative forms met with in dysentery are not themselves infective. The commonest source of infection is infected drinking water in which the cysts survive for 2 to 3 weeks. Flies have also been proved to transmit the disease by infecting food, since the cysts have been found to pass through the alimentary canal of the fly unaltered. Excreta used as manure may also transmit the infection, since vegetables are likely to be contaminated. It has been found that mere infection of the host is not generally followed by dysentery. For the production of clinical symptoms, some alteration of the state of balance between the parasite and the host is essential. Lowered vitality, irritable food, strain, inanition, all these have been blamed for setting up the attack, but possibly it may be some alteration in the pH of the intestine that is the exciting factor. The reason for the incidence of secondary amoebiasis, such as abscess of the liver, is not clear, since liver abscess has a geographical distribution of its own and is not found commonly in women.
and children, unlike dysentery. Alcoholic excess is, however, believed to give rise to a condition in the liver which predisposes to abscess formation. The healthy liver has probably some powers of destroying amœbae.

Amœbic ulceration of the intestine.—This is met with in the large intestine, the small intestine being very rarely affected. Ulceration may be present throughout the whole length of the large intestine, but the parts of the colon where there is comparative stasis are most affected. Thus, the cæcum, hepatic flexure, splenic flexure, and particularly the sigmoid and also the rectum are common sites. Rarely, ulceration of the cæcum may spread to the appendix. The earliest amœbic lesions met with in autopsies are minute yellow nodules with yellow specks of ulceration. It is believed that minute yellow nodules without breach of surface are the earliest lesions, since the amœbae apparently make their way to the deeper layers through the crypts of Lieberkühn causing small areas of coagulation necrosis in the submucosa. Minute thrombi form in the capillaries and a small area of mucosa undergoes necrosis. The amœbic ulcer thus formed increases in size by the spread of the necrotic process. At first oval in shape, along the length of the gut, the ulcers may later on become irregular. The commonest type of amœbic lesion is a large irregular ulcer covered by grey necrotic slough with undermined edges and a sloughing base. Since the necrotic process extends deep and spreads in the submucosa as a result of the proteolytic activity of the amœba, the ulcer extends in size and depth in the deeper layers. Thus, the breach of surface in the mucosa may be small compared with the extent of the ulcer below, so that these ulcers have been described as ‘flask-shaped’ on vertical section. The floor of the ulcer may be formed by the muscle coat or even by the serosa, and is generally covered, especially at its centre, by dark friable hair-like mass of slough. The surrounding mucosa does not show any inflammatory reaction, in uncomplicated cases, but is generally òedematous and boggy. The neighbouring ulcers may communicate by irregular
Fig. 24. Slide P. 931. Acute amoebic dysentery.
Section of the intestine showing amœbae in submucosa. Note the œdema of the submucosa, the comparatively slight cellular reaction.
Subacute Amoebic Dysentery.
TYPES OF PROTOZOAL INFECTIONS.

undermined channels. The small blood vessels are generally involved in the necrotic process and this accounts for the haemorrhage that is usually met with in the dysenteric stool. In hyperacute infections, large areas of mucosa may become gangrenous, and tags of mucous membrane may be found hanging loose into the lumen of the gut. The process may extend into the deeper coats and perforation and peritoneal adhesions may be met with. In chronic cases the margins of the ulcer are clear-cut and sharp, and the ulcers have a punched-out appearance. Sometimes the whole of the sigmoid may be studded with small clear-cut ulcers giving a honeycombed appearance to the mucous membrane. The wall of the intestine is very much thickened in these chronic cases from the formation of fibrous tissue, the result of healing. Sacculation may occur and pigmented scars are a common feature. The peritoneal coat may be thickened and plastic adhesions are common.

Histologically, the reaction is one of necrosis of tissue rather than inflammatory in type. The whole mucosa and submucosa become converted into a greyish gelatinous mass in which the nuclei of the cells are no longer visible or show pyknotic changes. Small blood vessels in places are filled with pale thrombi and surrounded by perivascular cuffs of lymphoid cells and mononuclear cells. Infiltration with polymorphs may occur towards the surface from secondary infection. The amebae are generally found in the deeper layers, as rounded or oval masses, stained blue when stained with haematoxylin and eosin. The central endoplasm is much more deeply stained than the outer ectoplasm, but the boundary zone is not well defined. The nuclei are not well stained in ordinary sections and this serves to distinguish the organism from the large mononuclear macrophage cells and the nerve cells of the plexus of Auerbach that are met with in these situations, and in which clear structural details are well brought out. During the stages of healing, large ulcers are bridged over by granulation tissue which later on contracts and forms dense fibrous tissue. Atrophy
of the wall of the gut is met with in extensive ulcerations and possibly from general malnutrition.

Amoebic hepatitis, hepatic abscess.—The amebæ have been met with in the branches of the portal vein in histological sections, and presumably make their way to the liver and cause a tissue reaction analogous to that met with in the intestine. Rarely, an infection may be met with by a more direct channel, an amoebic ulcer of the colon adherent to the liver extending directly into that organ. The earliest lesions

met with would appear to be small areas of focal necrosis where the liver cells break down and disintegrate forming pale granular areas. The liver is generally much congested, but whether all these areas become converted into abscesses is not certain. It is possible that the amebæ may die and the necrotic tissue absorbed. If the infection is not massive or if the resistance of the tissues is high, there is a mild grade of reactive inflammation of the liver around the necrotic

FIG. 26.

Amoebic ‘abscess’ of the liver showing the ragged wall and commencing necrotic foci in the neighbourhood.
TYPES OF PROTOZOAL INFECTIONS.

foci so that the amœbæ are destroyed giving rise clinically to pain and tenderness in the liver, hepatitis.

In other instances, the amœbæ multiply and destroy the liver cells resulting in a large area of necrosis of the liver constituting the so-called hepatic abscess. The liver cells undergo a colliquative necrosis, the amœbæ making their way between the interstices of tissue to neighbouring areas where they set up a similar reaction. The abscess cavity thus increases in size from the coalescence of necrotic foci. The cavity contains, as a rule, a viscid chocolate-coloured sticky

mass, consisting of necrotic liver cells, granules of fat, amœbæ, leucocytes, red blood cells, occasionally crystals of hæmatoidin, cholesterin and sometimes Charcot-Leyden crystals. In places this 'liver pus' may be tinged with blood or sometimes with bile. Rarely it may resemble the yellow creamy pus met with in inflammatory conditions. The so-called 'liver pus' is thus only a mass of necrotic liver tissue and not pus formed as in suppurative processes. The wall of the abscess is formed by liver tissue and there is no well-defined wall of granulation tissue. The wall, on the other hand, has a ragged appearance

FIG. 27.

(x 225) E. histolytica in the wall of the abscess causing lysis of tissue. Note the appearance of necrotic tissue.
with irregular breaking down masses of liver tissue projecting into the abscess cavity. There is usually no attempt at encapsulation, though in histological sections, the liver cells are stretched out into elongated masses arranged in layers all round the necrotic tissue. Usually small areas of pale stained tissue are met with in the neighbourhood of the abscess and these represent the areas of histolysis caused by the living amœbæ which have made their way into the tissues. The sinusoids surrounding the abscesses are usually full of blood and the liver as a whole may be congested. The wall of the

![Image](https://via.placeholder.com/150)

**FIG. 28.**

Liver abscess (x 225). Note the compression of the liver cells which form the capsule and the slight inflammatory reaction.

abscess may be infiltrated with lymphoid cells and large mononuclear endothelial cells and a slight fibroblastic reaction may be met with in chronic cases, but infiltration with polymorphs, or other signs of active inflammatory reaction are generally not met with in uncomplicated cases. In histological sections, the entamœbæ may be demonstrated as darkly stained oval masses, both in the wall of the abscess, as well as in the neighbouring foci in the liver. In the pus itself, it is difficult to demonstrate the amœbæ, but a scraping of the wall of the abscess is generally sufficient for this purpose.
After aspiration of the abscess, the amœbæ often appear in the pus in 4 to 5 days. Rarely, the abscess may become infected with ordinary pyogenic organisms and a typical inflammatory abscess may result. In rare cases when the amœbæ get destroyed by the tissues, encystment of the abscess may occur as a part of the mechanism of defence, by the formation of a dense wall of fibrous tissue, the whole abscess becomes encapsuled, the pus becomes converted into a dense cheesy mass which may later on undergo calcification, and the abscess cavity shrivels up into a nodular mass.
THE AMOEBAE LIVING IN MAN.

Usually amoebic abscesses are single, but less commonly they are multiple. The right lobe is more commonly affected and of that, the right upper quadrant. The abscess may spread towards the surface, infect the peritoneum or spread up the diaphragm to the pleura and the corresponding lung, causing an empyema and pulmonary abscess. An abscess of the left lobe may point in front and give rise to errors in diagnosis.

Amoebic abscess of the lungs.—These are most often secondary to hepatic abscesses, the pus making its way through the diaphragm and infecting the lung direct. The pleural cavity is either shut off by adhesions or an empyema may form. The abscess often ruptures into a bronchus and the pus is expectorated. Rarely, primary abscess of the lung may occur from haematogenous spread from the bowel. Fibrosis of the lung is the result in cases of natural cure following erosion into a bronchus.

Amoebic abscess of the brain.—This occurs as a complication of generalized amoebiasis, particularly hepatic abscess. The amoebae may settle in any part of the brain and cause a similar reaction. The abscess is usually of small size and amoebae may be demonstrated in the wall.

Amoebic abscess of the spleen.—This has also been described as a consequence of spread of infection from ulcers in the splenic flexure.

THE AMOEBAE LIVING IN MAN.

The amoebae living in man are of 4 different genera. There are, however, 6 species.

These are: 1. Entamoeba histolytica.
2. Entamoeba coli.
3. Entamoeba gingivalis.
4. Dientamoeba fragilis.
5. Endolimax nana.
6. Iodameba butschlii.

Of these, all except E. histolytica are harmless commensals.
1. *E. histolytica*.—The morphology of *Entamoeba histolytica* has already been described.

2. *Entamoeba coli*.—This is the large common amoeba that is met with in the faeces. It shows great resemblances to *E. histolytica*. Both belong to the genus *Entamoeba*, and both are characterized by the same type of nuclear apparatus and are about the same size, 20 to 40μ in diameter. The chromatin of the nuclear apparatus is, however, made up of larger beads arranged inside the nuclear membrane, the karyosome is larger and eccentric in position, and not central, and there is no clear halo between the karyosome and the nuclear membrane. The parasite lives upon the bacteria and other vegetable matter in the colon and consequently the protoplasm is granular and vacuolated and contains ingested bacteria, starch granules, vegetable matter and fungi. There are no red blood cells as in *E. histolytica*, since the parasite lives on the contents of the colon and not on the tissues of the host. Multiplication appears by binary fission. In fresh specimens, the motility is sluggish unlike *E. histolytica* which exhibits active motility when examined.

*Entamoeba coli* (x 2,000). Note the lack of differentiation of the protoplasm as well as the ingested material.
FIG. 31.

The amoebæ of man. (By kind permission of Professor Dobell.)

THE AMOEBAE LIVING IN MAN. 75
soon after being passed out in the faeces. Later, however, *E. histolytica* swells up and dies, its protoplasm becomes invaded by bacteria and other organisms and comes to assume an appearance not unlike that of *E. coli*. As regards motility, there is little in the way of progression, *E. coli* merely changing its shape forming dome-shaped pseudopodia unlike *E. histolytica* which streams across the field of the microscope throwing out finger-like narrow pseudopodia. Precystic forms are smaller as in *E. histolytica*, but the cysts are slightly larger than those of *E. histolytica*, and when mature, contain 8 nuclei formed by successive division. The cysts always contain glycogen in the early stages but not in the mature types. Sometimes, supernucleate cysts containing 16 nuclei may occur. Chromatid bodies are absent as a rule and, when present, are in the shape of sheaves of pointed spicules. The cysts measure, as a rule, from 15 to 20μ. They are passed in the faeces and infect other individuals when swallowed.

3. *Entamoeba gingivalis.*—This is the common amœba met with in the mouth and was at one time thought to be the cause of pyorrhœa alveolaris. It varies from 10 to 25μ in diameter and is thus smaller than the other types of entamoebae. The nucleus is ‘ring’ shaped and is true to type though small, being 2.5 to 3μ in size. The protoplasm contains food vacuoles besides greenish refractile bodies and numerous bacteria. In its clear refractile pseudopodia and well-defined ectoplasm, the parasite resembles *E. histolytica*. The life history of this amœba has not been fully worked out. In its habits and mode of life, it resembles *E. coli*.

4. *Dientamoeba fragilis.*—This is the smallest and the least common of the amœbæ of the human intestine according to Dobell. It measures from 3.5 to 12μ in diameter, is generally binucleate with the nuclei about 2μ in size, vesicular, with delicate nuclear membranes, and central clusters of chromatin. From the karyosome of the nuclear apparatus fine threads of linin radiate towards fine granules inside
the nuclear membrane. The ectoplasm is clear and well
demarcated from the granular endoplasm which contains
food vacuoles and bacteria. Division occurs probably by
binary fission. The amoebae are extremely fragile, and
derenerate rapidly to cystic forms.

5. Endolimax nana.—This is the commonest amoeba
met with in the intestine of man. Like E. coli, it lives
inside the lumen of the gut and does not feed on the tissues.
It is a small amoeba measuring from 6 to 12μ in diameter,
commonly 8μ. The motility is sluggish and the endoplasm
is scanty. It is usually present in large numbers. The
nucleus is not visible in fresh specimens, but staining shows a
vesicular nucleus 1 to 3μ in size. The chromatin is all clumped
together in one irregular karyosome, which is eccentric in
position, and there are other smaller granules which are
connected to it. There is a clear ectoplasm and a finely
granular endoplasm containing food vacuoles and bacteria.
Cysts have a characteristic appearance since they are oval
and not rounded, with very thin walls so that they are not
visible in unstained preparations. Iodine, however, shows up
the cysts as greenish oval bodies which contain one, two, or in
the mature cysts, four nuclei. The cysts measure from 7 to
9μ in length and usually contain volutin granules which are
very refractile. Sometimes, supernucleate cysts containing
8 nuclei may be met with.

6. Iodamœba butschlii.—This amoeba is well known by
its characteristic ‘Iodine cysts.’ The amoeba itself is about
9 to 13μ in diameter and is generally like E. coli with
sluggish motility. The nucleus is vesicular and all the
chromatin is in a large central karyosome around which are
a number of granules arranged in a ring. The granules are
stained feebly with haematoxylin. The amoeba lives in the
intestine and forms thick walled cysts, each of which contains
a large mass of glycogen besides a few volutin granules.
Usually, the cysts are uninucleate with the chromatin
aggregated at one pole, and all the granules at another,
giving rise to a ‘signet ring’ appearance of the nuclei.
CHAPTER VII.

TYPES OF PROTOZOAL INFECTIONS.

LEISHMANIASIS.

Infections with small oval or rounded parasites, the most rudimentary of the hæmoflagellata called leishmania, at least three separate clinical conditions exist called Kala-azar, Oriental sore and Espundia.

Kala-azar.—This is a form of irregular tropical fever characterized by marked enlargement of the spleen and a profound anæmia due to infection with protozoal parasites called Leishmania donovani.

The disease is found in many parts of India, China and in the Mediterranean coasts of Europe and also in parts of Africa. It is a disease of localities and endemic areas remain infective for long periods. The Indian type is a disease that affects young adults, is commoner in males and is more frequent in districts with a heavy rainfall and a rather temperate climate. It sets in during the cold or rainy seasons. The Mediterranean type affects usually infants and children and is called Infantile kala-azar, but the clinical features are similar and the parasites appear to be morphologically similar, though some authorities call it Leishmania infantum. Moreover, in these regions the disease occurs in dogs, and is possibly transmitted by the dog flea.

The parasites, first described by Leishman and Donovan, are small oval bodies about 2 to 4μ in length and 1.5 to 2μ in breadth and are the most undeveloped of the hæmoflagellata, the flagellate phase occurring only outside the body. The cytoplasm of the parasite is usually stained a pale blue with Leishman's stain and shows two masses of chromatin, one of which is larger, rounded or oval and forms the nucleus,
LEISHMANIASIS.

while the other, generally elongated, more deeply stained, rod shaped, or oval and set at an angle to the nucleus, forms the k inetoplast. Sometimes a small vacuole can be demonstrated in relation to the kinetoplast. The parasites are usually found inside the endothelial cells in the internal organs, where they undergo division by longitudinal fission, to form numerous small leishmania lying in clusters, inside the endothelial cells, which become enormously enlarged and very often disintegrate. Sometimes, in the spleen, the parasites may assume elongated cigar-shaped or 'spindle shaped' forms. In other instances degenerate coccoid forms may occur, especially after death. Very similar parasites which are morphologically indistinguishable are Leishmania tropica, which causes a granulomatous ulcer on the skin called oriental sore and Leishmania americana, which causes a type of ulcerative rhino-pharyngitis, besides cutaneous ulcers. The disease occurs in South America where it is called Espundia.

Outside the body, the parasite can be cultivated in NNN medium which is a modified form of blood agar. The parasite multiplies in the water of condensation of this medium, becomes larger in size and develops an anterior flagellum from a small rounded granule in the kinetoplast called the blepharoplast. The parasite gradually becomes ovoid, then pyriform, then spindle-shaped, and grows in size till it is about 14 to 20μ in length and about 2μ in breadth. It has now the typical leptomonad form, with a large macro-nucleus and a kinetoplast consisting of three elements, from one of which, called the blepharoplast, a rod-like structure, called the rhizoplast, arises and passes forward through the anterior end of the parasite as a free flagellum. Between the blepharoplast and the parabasal body is a vacuole which can be made out even in the leishmania stage. In cultures, these flagellate forms appear on the third day, and owing to repeated longitudinal division, clusters of these appear with the flagella grouped together in the centre. Such multiplication forms are usually more slender and slightly smaller than the mature flagellates which occur singly. Development occurs
only at low temperatures of about 22°C. 'O' forms have been described as resistant forms occurring in culture, a sort of cystic stage, which, according to Row, is the most infective. The flagellate forms are not easily inoculable into laboratory animals while the leishmania forms are the most infective. The infection can be transmitted into monkeys by massive injections into the peritoneum, of infected splenic tissue. Recently it has been found that the Chinese hamster, a small rodent about the size of a mouse, is extremely susceptible to infection. In this animal, in whom infection occurs even through the gastro-intestinal tract, the development

FIG. 32.
Enlarged spleen in kala-azar showing the marked thickening of the capsule and the swelling of the pulp.

of the parasite in the reticulo-endothelial system can be demonstrated.

The mode of transmission of kala-azar is even now unknown. There are two chief views regarding the mode of spread. One is that some blood-sucking insect is the vector. It was put forward that the bed bug was the transmitter since the flagellate phase was found to be developed in the midgut of the bug. With regard to another blood-sucking insect the sandfly, *Phlebotomus argentipes*, more convincing evidence is brought forward to show that not only is there a
development of a flagellate phase, but salivary infection with the parasite occurs, though all attempts at experimental transmission by sandfly bites have failed. However, infection occurs if the flagellate forms in the sandfly are injected. So it is argued that the disease is transmitted when sandflies are crushed on the skin. The flagellate leptomonads are also essentially parasitic in insects where development occurs in the posterior station and cystic forms are passed in the

\[ \text{FIG. 33.} \]

Enlarged liver in kala-azar showing the swelling of the cut surface, faeces, transmission occurring by contamination. The question that has been raised is, whether kala-azar in man is an insect leptomoniasis, or whether the human types are different. The second theory that has been put forward is that the resistant forms of the parasite are passed in the faeces and urine of kala-azar patients and that infection occurs by contamination. In favour of this, is the occasional occurrence of parasites in the urine and faeces, though experimental
transmission has hitherto failed. The occurrence of intestinal lesions in kala-azar and the existence of a resistant phase, which has been put forward, together with the endemicity of the disease, lend some support to this theory.

The pathological lesions in kala-azar are generally distinctive.

The spleen is markedly enlarged and is in a stage of chronic hyperplasia. The capsule is generally thickened in chronic cases. It may show marked perisplenitis. The edges are generally thin and sharp, the organ is usually firm and on section presents a deep red, or a violet red, or plum colour, from hyperplasia of the pulp and engorgement of the sinuses. In chronic cases, as with all chronic hyperplasias, there may be marked fibrosis and the trabeculae may be enlarged and prominent. Infarcts may sometimes be present. Histologically, in sections stained with Leishman’s stain, the parasites may be found in numbers in the endothelial cells of the sinuses and in the mononuclear cells lying free. Dilatation of the venous sinuses and engorgement may be met with. Blood vessels may show parasites inside the endothelial lining and sometimes in the lumen, which may be stuffed with mononuclear cells containing parasites. Degenerative changes, however, are extremely rapid owing to post-mortem decomposition, and the parasites can be well demonstrated only soon after death.

The liver is generally enlarged, firm, brownish in colour or sometimes mottled. Histologically, it can be made out that the enlargement is due to a swelling of the endothelial cells lining the capillaries which are full of parasites. The parasites are never found in the hepatic cells, but only in the Kupffer cells and the mononuclear wandering cells. In a small proportion of cases, cirrhotic changes mostly of a multilobular type have been noticed. The bone marrow shows parasites both in the endothelial cells and the mononuclear cells. Parasites may also be found in the endothelial cells of the blood vessels, in the kidney, in the testis, in the adrenal and in other organs.
Fig. 34. 1. *Leishmania donovani* inside an endothelial cell from the spleen.
2. *Leishmania donovani* inside a mononuclear leucocyte.
3 and 5. Early flagellate forms in rosettes in culture.
4. Flagellate forms fully developed and single in culture.
6. Free forms from a ruptured endothelial cell.
7. Flagellate forms after division.
The large intestines may show inflammatory changes extending to actual ulceration giving rise to the clinical features of dysentery. The parasites may rarely be found deep in the ulcers, in the endothelial cells. Occasionally amœbic dysentery may be met with as a complication.

Among general features are a hyperpigmentation of the skin, trophic changes affecting the hair and nails, extreme general emaciation and œdema of the extremities.

The blood usually shows a severe anæmia with a marked fall in the number of red blood cells and a proportionate reduction in the haemoglobin. There is a severe leucopenia quite out of proportion to the anæmia, so that the proportion of leucocytes to the red blood cells ranges from 1 in 2,000 to 1 in 4,000, instead of the normal ratio of about 1 to 600. The polymorphonuclear cells are markedly diminished and so are the eosinophiles, while there is a relative increase in the number of mononuclear cells. Septic complications, such as pneumonia or cancrum oris, may, however, set up a reactive leucocytosis. In severe cases, the parasites may be encountered in the blood in the mononuclear cells, if a careful search is made in a number of slides and if care is taken to take smears with a definite leucocytic edge. Parasites may, however, be much more frequently obtained by culture from peripheral blood, though, for obvious reasons, cultures are more certain if the intact endothelial cells are obtained by puncture of the spleen, liver or bone marrow during life. The easiest mode of demonstration is by puncture of the liver or spleen.

Oriental sore.—This is a form of cutaneous leishmaniasis due to infection with Leishmania tropica.

The parasite is morphologically similar to Leishmania donovani and is found in the endothelial cells in the cutaneous lesions. Visceral lesions, however, do not occur. In cultures, the parasites are much more hardy than Leishmania donovani, since growth occurs even with bacterial contamination. The geographical distribution of this disease is quite
different from that of kala-azar, being common in the Mediterranean coast of Africa, in Mesopotamia, Arabia and Upper India. The disease occurs in dogs in endemic areas. Transmission of the disease is now believed to be by means of the sandfly, since sandflies are found infected in nature with a similar leptomonad, and it has been found possible to transmit the disease experimentally by crushing the sandflies on to the skin in individuals living miles away from the endemic zone. Sergents Ed. and Et. proved the insect transmission by inoculating the material of ground-up sandflies.

**Fig. 35.**

Oriental sore (x 225). Note the endothelial cells and lymphocytes that make up the granuloma. The granularity of the protoplasm is due to the presence of parasites which are not visible under the low magnification.

Infection with leptomonads of sandflies has been followed by lesions very like oriental sore, the question being whether this is only a leptomoniasis or oriental sore. The relation between the natural leptomonads of insects and *Leishmania tropica* has yet to be settled.

The pathological lesion consists at first of a papular elevation generally situated on exposed parts, such as the face, arms and legs. This gradually increases in size, is surrounded by a zone of congestion and gradually gets covered
by a layer of scales which becomes converted into a scab and finally into a crust. This falls off exposing an ulcer, with irregular sharp margins, which is extremely chronic and indolent. It is generally about an inch in diameter. The base usually shows exuberant granulations. Secondary sores may start in the neighbouring skin. Healing is extremely slow, and occurs, after repeated scabbing, by the formation of granulation tissue which finally leaves a depressed cicatrix. Varying sizes from small papules to large open sores may be met with. The sores are curiously distributed on the limbs and on exposed parts, especially on the dorsal surface. Histologically, Adler has shown, in experimental cutaneous leishmaniasis, that the lesion starts in the endothelial cells of the capillaries. These cells become distended with multiplying leishmania. Probably the same origin occurs in man. The lesion first consists of granuloma which infiltrates the dermis so that the normal structures are replaced by a granulation tissue consisting mostly of small round cells, endothelial cells and plasma cells. The parasites may be found in sections in the endothelial cells and lying free. The epithelium may show proliferative changes as in all chronic cicatrizing ulcers. Endarteritis may be met with. Giant cell formation is described to occur, but is rare. In some cases, the lesion assumes the form of a papillomatous tumour involving a large area of skin. In others, the growth does not ulcerate and resembles a keloid.

A form of multiple tumour-like nodules somewhat resembling the appearance of nodular leprosy has also been described under the term 'dermal leishmanoid,' but here the infection is with Leishmania donovani occurring as a complication of kala-azar.

Espundia.—This type of leishmaniasis is particularly common in South and Central America and parts of Africa. The causative agent is a leishmania which is morphologically similar to L. tropica. Direct inoculation is a possible mode of transmission, but some biting insect is suspected to carry the infection, as with oriental sore. The disease
has also been regarded as an accidental infection of man with a natural leptomonad of insects.

The occurrence of a primary lesion on the skin has been described and the lesions of the mucous membranes are regarded as secondary; but generally both cutaneous ulcers and mucous lesions are met with together. The cutaneous ulcers resemble those of oriental sore. The lesions in the mucous membrane start very often in the nose, mouth, or palate as irregular granulomatous ulcers which extend gradually, involve the nasal septum and cartilages and give rise to extreme deformity. The larynx and pharynx are involved, the condition being extremely progressive and chronic. There is no visceralization, but the internal organs may show amyloid degeneration and chronic ulceration. The espundial lesion consists, histologically, of a granulomatous ulcer with large aggregations of endothelial cells, mononuclear cells, plasma cells and lymphocytes. The parasites can be demonstrated inside the endothelial cells.

**Trypanosomiasis.**

These are disease processes caused by infection with highly developed flagellate protozoa, the trypanosomes. Some species are extensively parasitic in the lower animals, to many of whom they are normally adapted. Wild animals harbour trypanosomes without any untoward effect while domestic animals are very susceptible to infection. Probably the same biological maladjustment holds in human trypanosomiasis.

The trypanosomes that are pathogenic to man are three in number, *Trypanosoma gambiense* and *Trypanosoma rhodesiense* which cause the sleeping sickness of Africa, and *Trypanosoma cruzi* which causes the varying clinical types of American trypanosomiasis.

*African trypanosomiasis.*—This type of trypanosomal infection, which is found in Central Africa and West Africa, is characterized by an early lymphatic infection with polyadenitis, febrile reaction and occasional hæmic infection,
followed by a stage of mental lethargy and torpor from cerebral localization.

The disease is confined to Tropical Africa and two types exist depending on the species of the infecting organism. The type due to *Trypanosoma gambiense* occurs in the west coast of Africa, in Senegambia, the Congo and Uganda, while the type due to *Trypanosoma rhodesiense* occurs in Rhodesia. Whole communities may be infected by *T. gambiense* in hyperendemic zones where the disease often spreads in large epidemics. There is a tendency to spread along watercourses and the courses of rivers. The disease affects all races, all ages and both sexes. The Rhodesian type is much more irregular in its distribution, and does not assume epidemic spread though the disease itself may be more virulent.

The causal organism, the trypanosome, is the most highly developed of the haemoflagellata, of which the most primitive and rudimentary are the leishmania which are small oval protozoa, each with a central nucleus, the rudiment of the locomotory organ, the flagellum existing as a small thread or rod inside the protoplasm. This rod is the rhizoplast which arises from a granule, the blepharoplast, which is in relation to a parabasal body, the whole constituting the kinetoplast, the structure from which the flagellum arises and which controls the movements of the flagellum. The next higher in the order of development is the leptomonad which is more ovoid or fusiform in shape and exhibits a free flagellum projecting from the anterior end by the growth of the rhizoplast. The crithidia are the next in type and each exhibits an undulating membrane which is attached by its shorter margin to the parasite, while its wavy border projects free and contains the flagellum within its fold. This undulating membrane arises as a thin fold of protoplasm from the kinetoplast and extends to the anterior end of the parasite where the flagellum projects free. In the trypanosomes which are elongated, fusiform or spindle-shaped flagellata, the flagellum generally arises from a blepharoplast at the posterior extremity, so that the undulating membrane is well developed.
and extends from one pole of the organism to another, while the flagellum projects forwards through the free end of the undulating membrane as a whip-like filament at the anterior extremity. Between the blepharoplast and the parabasal body, a vacuole can be made out, all of these structures probably representing one unit. The organisms are variable in size measuring 18 to 30µ in length, by 1 to 3µ in breadth, and sometimes show cytoplasmic granules. After division long slender forms may be met with, while short stumpy forms occur before division. Division is usually by longitudinal fission commencing at the kinetoplast, followed by division of the trophonucleus, and then of the body. The Rhodesian type is usually indistinguishable from the Gambiense type morphologically. The two trypanosomes exhibit differences in pathogenicity to lower animals. Experimental infections with *T. rhodesiense* run a more rapid course and are fatal to laboratory animals which are rather refractory to *T. gambiense*. With the latter, infection, if once established, runs a more chronic course. Their serological behaviour also serves for differentiation. The organisms can be cultured in NNN medium and its modifications.
Fig. 37. *Trypanosoma gambiense.*
The disease is transmitted to man by the bite of the tsetse fly, *Glossina palpalis* being the insect vector of *T. gambiense*, while *Glossina morsitans* is the insect vector of *T. rhodesiense*. In the body of the fly the trypanosomes undergo development only in a small proportion of cases since subsequent feeds have a tendency to kill the trypanosomes. Development is more rapid at a high temperature. In the body of the fly, by a process of repeated division, a number of long slender forms are produced. The gut seems to be the reservoir of these slender forms. They work their way to the anterior part of the gut along the proventriculus, to the hypopharynx and the salivary glands where the trypanosomes assume the crithidial phase, the undulating membrane being very short and arising in front of the nucleus, while the body becomes more stumpy. The infection is thus transmitted by the bite of the insect, the crithidial forms assuming the trypanosome shape before infection. These young forms which arise after the cycle of development are called the metacyclic forms and are the most infective. Recently, however, it has been found that direct mechanical transmission can and does occur in a large number of cases, the fly acting as a mechanical agent without any cycle of development. Transmission by the genitalia has been hypothecated and, experimentally, blood introduced into the vagina has been found to be infective, but direct sexual transmission has not been proved.

Introduced into the body, it appears probable that infection occurs through the lymphatic system, since early lymphatic enlargement and enlargement of the spleen occur and the parasites are easily demonstrated in the lymphatic glands. In *T. gambiense* infections the trypanosomes are met with in the blood in scanty numbers. Recently Peruzzi has conclusively proved, in experimental trypanosomiasis in monkeys, that the morbid anatomy is always the same with local reactions depending on the number of parasites. He has demonstrated the existence of a leishmania phase in the myocardium and in the internal organs in *T. gambiense*
infections in monkeys. The trypanosomes collect in the heart muscle where they pass through a phase of multiplication in the muscle fibres, causing a trypanosomal myocarditis. There is reason to believe that a similar cycle occurs in man in African trypanosomiasis, since many observers have described forms without flagella in the blood and in the internal organs. Wenyon has questioned the occurrence of this latent phase, since he regards these forms as merely degenerate types. However, the analogy with *T. cruzi*, which exhibits such a definite phase in its life cycle, suggests that this phase is probable in the African types. In the later stages, the trypanosomes are found in the cerebrospinal fluid where they exhibit extreme pleomorphism, long, short, multinucleate and multilflagellate forms being met with. They are found also in the brain tissue both in the grey matter and in the vessels, and are directly responsible for the symptoms.

The essential pathological lesions met with are those of early lymphatic enlargement together with a chronic hyperplasia of the spleen. The blood contains only scanty numbers of parasites. With infection of the meninges, the features are those of a lymphangitis affecting the brain and its membranes. The cerebrospinal fluid increases in amount, becomes cloudy, not only from cellular exudate, but from the presence of parasites. The lesion in the brain is a meningo-encephalitis. Marked involvement of the small arteries occurs, followed by lymphocytic cuffing such as is met with in most forms of encephalitis. The perivascular infiltration consists of lymphoid cells, mononuclear cells, large neurophages and cells containing hyaline fuchsin bodies. Proliferation of the endothelial cells of the capillaries is also met with. This reaction is found in the brain and meninges while the cord is comparatively free. Changes occur in the choroid plexus, in which massing of trypanosomes may be met with when they penetrate the vessels and enter the cerebrospinal fluid. Peruzzi's researches in monkeys show that a similar granulomatous process occurs
TRYPANOSOMIASIS.

in many internal organs besides the heart and the brain. He found lesions in the serosa, in the kidneys and the liver.

The blood generally shows a marked anaemia. Clumping of the red blood cells is another feature, due to the presence of agglutinating substances affecting the red blood cells. The infecting trypanosomes are a variable feature, being more commonly met with in Rhodesiense infections.

The lymphatic glands in the neck, the axillæ, in the mesenteric nodes and in the retroperitoneal tissues are all enlarged and congested. On section, they are soft and pink in colour and may show areas of haemorrhage. Microscopically, trypanosomes may be met with inside the glands in the early stages. There is a marked hyperplasia of the lymphoid tissue and the endothelial cells of the germ centres may show mitotic figures. In the late stages, the inflammatory reaction subsides, the glands undergo fibrosis and become hard and shotty. This lymphoid hyperplasia is widespread in trypanosomiasis and may affect the follicles of the intestine and the Peyer's patches.

Rhodesian type of African trypanosomiasis.—A point of great importance with regard to Trypanosoma rhodesiense, the cause of this type of the disease, is the question of its identity with T. brucei which is found as a natural infection in wild game in Rhodesia. Bruce regards the two trypanosomes as identical and considers that wild game form a reservoir of the infective agent of human trypanosomiasis. Duke's experiment with two cow-boys in an area which was experimentally depopulated for five years is held to indicate that the flies have some other source of infection besides man, since the boys caught the infection in this human experiment. Taute and the German school of workers hold that the animal trypanosomes, though morphologically similar to the human type, are quite distinct. He failed to infect himself and more than a hundred volunteers with T. brucei, a proved pathogenic strain to domestic animals being used.
AMERICAN Trypanosomiasis. Chagas' Disease.

This condition is characterized by varying types of clinical manifestations depending on the localization of the infecting organism, *T. cruzi*.

The insect transmitter is *Triatoma megista*, a kind of flying bug with biting habits. The disease occurs in Brazil and in other parts of South America and was first properly described by Chagas. Children are more often affected while infection of adults is rare.

The infective organism, *T. cruzi*, is a stumpy thick trypanosome about 20μ in length and 3μ in thickness exhibiting two forms in the peripheral blood, a short thick form, and a narrow slender form. Morphological differences exist between this type and the human trypanosomes of Africa. The parabasal body is large and oval, the undulating membrane, in its free end, is only slightly curved, and the body as a whole is more short and stumpy.

The life cycle shows a distinct leishmanial phase in the internal organs, the parasites, after entering the blood, migrating towards the viscera, particularly the heart, where they enter the endothelial cells and parenchymatous cells, round up, lose the undulating membrane and flagella and assume the typical leishmanial phase, with a rounded macronucleus and a rod-shaped kinetoplast. By repeated binary fission, a number of such forms appear in the cell which becomes enormously distended. The parasites then become oval or fusiform, the rhizoplast grows forwards as a flagellum while a short undulating membrane develops, the leishmania thus assuming the crithidial phase. After this, young trypanosomes are formed, while the cell ruptures and liberates these young forms into the circulation.

In *Triatoma megista*, development occurs in the mid-gut, the so-called posterior station, where they assume the crithidial phase, the infective metacyclic trypanosomes being passed in the faeces. Chagas postulates infection of the salivary glands and saliva as in *Glossina palpalis*. The
CHAGAS' DISEASE.

armadillo appears to be a reservoir of infection and is found infected in nature in a large proportion of cases, and since the bugs live in the burrows of the armadillo, infection can easily occur.

The pathological lesions met with are somewhat similar, though involvement of the central nervous system is not so common. The lymph glands are generally enlarged and congested and may show haemorrhages. There is a marked enlargement of the spleen due to hyperplasia and congestion. The liver shows enlargement and fatty change. A marked goitrous condition of the thyroid is described by Chagas and forms the basis of the myxoedematous type of the disease; but since endemic goitre is met with in these situations, the question has been raised whether this thyroid involvement is really due to the trypanosomal infection. In such types, the subcutaneous tissues are thickened and myxomatous while atrophy of the hair and sweat glands may be met with. Effusions into the pleural cavity and pericardium are usually present, while subpleural ecchymosis may occur. The heart may show marked dilatation while the myocardium is pale and shows fatty and sometimes fibroid change. Microscopically, this is found to be due to the presence of the developing parasites, the affected muscle fibres being converted into pseudocysts. The meninges may show congestion and the cerebrospinal fluid may be cloudy. Microscopically the parasites may be demonstrated in many of the organs such as the adrenal, the thyroid, the testis, but mostly in muscle fibres of the skeletal muscle and the plain muscle of the intestine besides the cardiac muscle. The adrenals are often involved, and this seems to be the basis of the pigmentation that is met with. The blood shows no obvious features. The trypanosomes are generally scanty, so that injection into a guinea-pig is made use of, for diagnostic purposes.
CHAPTER VIII.

TYPES OF PROTOZOAL INFECTIONS.

Giardiasis.

This is a condition of infestation of the intestinal tract with a flagellate, *Giardia intestinalis*, resulting in chronic catarrh and enteritis.

The parasite, *Giardia intestinalis*, is a highly developed flagellate with eight flagella, an octomitus. It is about 10 to 18 μ in length, is symmetrical in shape, and has a characteristic appearance from the presence of two vesicular nuclei with well-marked nucleoli, one on either side of the body. It is pyriform in shape, the posterior end being narrow and curved dorsally. The ventral surface is slightly concave while the dorsal is convex. Four pairs of flagella arise in relation to the nuclei from blepharoplasts near the anterior end. These flagella have a peculiar arrangement giving the organism a resemblance to a face. This appearance has been aptly compared by Dobell to that of a pear with an oval slice cut out from one side. The two topmost flagella project free one on either side of the nuclei while the next two arise from marginal blepharoplasts and project lower down. The next two curve down from the middle line, and project across the body of the parasite, while the last two project free from the posterior extremity. Two supporting rods or axostyles extend from above downwards. Multiplication occurs by binary fission, while oval cysts with thick walls are formed in the lower ileum and are passed out in the faeces. The flagellates live in the duodenum and small intestine, as far down as the ilio-caecal valve. They absorb nutrition from the intestine by applying themselves by their ventral sucker-like surface to the mucosa. A catarrhal enteritis is the lesion that is commonly met with.
The giardia has to be carefully distinguished from two other harmless commensals that are occasionally met with in the intestine. One is *Trichomonas hominis*, a flagellate about 10 to 15μ in size. The body is pyriform with a narrow posterior end. There is a single oval nucleus at the anterior end in relation to which is a group of blepharoplasts from which three flagella arise, pass forwards and show extreme motility. There is a definite undulating membrane on the dorsal surface extending from the anterior to the posterior end, as well as a supporting axostyle. A small anterior slit represents the mouth which is on the ventral side. The cytoplasm shows a number of food vacuoles. Degenerate amœboid forms may, sometimes, be met with.

The other flagellate that is sometimes met with is *Chilomastix mesnili*, a pear-shaped organism with a more pointed posterior extremity which is often found attached to some fixed material, while the rest of the organism exhibits marked side to side movement, especially during feeding. There is a well-developed mouth with lips extending down from the
anterior end. The nucleus is oval and vesicular and situated at the anterior end, where, from a group of blepharoplasts, three flagella pass forwards while another flagellum passes down into the mouth cavity, between the lips. Supporting fibres exist for the lips. During feeding, the anterior flagella can be seen to sweep the food material into the large mouth while the oral flagellum passes them on to the body cavity. A number of food vacuoles are found in the body cavity.
CHAPTER IX.

TYPES OF PROTOZOA\(\text{L}\) INFECTIONS.

MALARIA.

An infection with protozoal parasites called plasmodia which live on the red blood cells, malaria is characterized clinically by fevers of different types depending on the species of parasite. The parasites belong to the class of sporozoa, or spore-forming protozoa, which undergo asexual multiplication or schizogony alternating with a sexual cycle, or sporogony, where spores are formed. The plasmodia are parasites of the blood and hence belong to the sub-order hemosporidia. The asexual cycle occurs in man while the sexual cycle occurs in the anopheles mosquito.

Landmarks in the history of the disease are, the discovery of the parasite by Laveran and the description of the asexual cycle by Golgi, while the tentative hypothesis of mosquito transmission, put forward by Manson, was established by the brilliant work of Ross who traced out the life cycle in the mosquito. Man gets the infection by the bite of the anopheles mosquito, in the stomach of which the parasites undergo sporogony. The fevers may be of an intermittent type occurring every fourth day, or they may be intermittent and tertian, or remittent and continuous depending on the species of parasite. Three well-defined species of parasites are known to infect man, \textit{Plasmodium falciparum}, the parasite of quotidian fever, \textit{Plasmodium vivax}, the parasite of tertian fever, and \textit{Plasmodium malariae}, the parasite of quartan fever.

Malaria occurs in tropical and subtropical regions and sometimes even in temperate climates. Though the mosquito is the transmitting agent and infected mosquitoes retain
their infectivity throughout life, the human reservoir, in endemic areas, is an important source of malaria. Whole communities may be infected and may show an enlargement of the spleen as the only obvious feature of infection. Thus, those acclimatized may function as human 'carriers' of the parasites and, by means of the anopheles, serve to pass on virulent malaria to fresh arrivals.

The cycle in man.—The infective spores, or sporozoites which are injected by the mosquito, are small sickle-shaped parasites 10 to 12µ in length by 1 to 2µ in width. They make their way through the salivary secretion into the puncture caused by the bite. They then enter the blood stream, work their way towards the red blood cells, which they penetrate by boring through the limiting membrane. Generally, only one parasite is found inside each red blood cell where it rounds up and becomes converted into an amœboid ring, the haemamoeba, which, in its growing stage, is called a trophozoite. The trophozoite, in its early stage, is a small rounded body, about 2µ in diameter, exhibiting active amœboid movement. Sometimes the parasite may be met with on the surface or on one side of the red blood cell, 'accolé' forms. It lives at the expense of the red blood cell which gradually becomes paler in colour from the absorption of the haemoglobin. The parasite elaborates a pigment of its own and this appears, inside the growing trophozoite, as fine granules of brownish pigment. In preparations stained with Leishman's stain, the young trophozoite has a signet-ring appearance in its early stage, with a red dot on one side formed by the chromatin of the nucleus, a large central vacuole and a thin rim of protoplasm stained blue.

As the parasite grows, the protoplasm becomes more plentiful and the parasite assumes an amœboid shape and the vacuole becomes comparatively small and irregular. The pigment now appears as small irregular granules scattered about diffusely in the protoplasm. In tertian and subtertian infections, the infected red blood cell shows small dots, red in colour, scattered about in its protoplasm, probably as a
result of degenerative changes in the protoplasm. With the growth in size of the trophozoite, the chromatin becomes larger, and with the cessation of growth, the chromatin begins to divide into a number of irregular masses, and at this stage the parasite is called a schizont. It is about 8 to 9μ in size. With the commencement of schizogony, all growth ceases, and depending on the species of parasites, a variable number of small bodies are formed inside each infected red blood cell. The chromatin first divides into a number of smaller granules, after which the protoplasm also divides into spherical or oval masses round each granule of chromatin, forming what are called merozoites. The enlarged and now completely de-haemoglobinized red blood cell shows, in its centre, a mass of pigment formed by the parasite. Around this is a cluster of merozoites arranged in one or two rows or sometimes irregularly, according to the species of parasite. In tertian infections, the merozoites are 16 to 24 in number arranged either in two rows or irregularly, giving rise to an appearance somewhat like a rosette. The corpuscle now bursts and liberates the merozoites into the blood stream. The whole process takes place in tertian infections in 48 hours, in quartan infections in 72 hours while subtertian parasites have a life cycle in man varying between 24 and 48 hours. With the rupture of the red blood cell, the pigment clumps are also liberated and are engulfed by mononuclear leucocytes in the blood. The liberated merozoites adhere to the red blood cells, then make their way inside the cells and repeat the process of schizogony. The malarial paroxysm, or ague, occurs coincidently with the rupture of the distended red blood cells, possibly as a result of protein shock from the sudden rupture of a large number of red blood cells, and the setting free of a large number of merozoites and pigment into the blood.

Thus, it is easy to understand that with the tertian parasite with a life cycle of 48 hours, the paroxysm of rigor and fever is intermittent and occurs every other day, while the quartan parasite, with its 72-hour life cycle, causes paroxysmal fever
Fig. 1-7. Development of *P. falciparum*.—1. Multiple infection of a red blood cell with early ring forms; note one 'accolé' form. 2. Larger rings. 3. Larger forms met with in the splenic vein; note the pigment and Maurer's dots. 4. Dividing form from a cerebral capillary. 5. Complete division; 'bunch of grapes' appearance. 6. Female crescent. 7. Male crescent.


FIG. 39. The malarial parasites.
MALARIA.

101

occurring every fourth day. The subtertian, with its life cycle varying between 24 and 48 hours, causes continuous remittent or irregular fever, the patient getting rigors with the varying periods of schizogony. Schizogony and infection of fresh red blood cells thus go on with increasing severity, till the reactive forces of the body are brought into play. There is, then, an increase in the number of mononuclear leucocytes in the blood to deal with the merozoites. During these later stages of infection, along with schizonts for the purpose of schizogony, sporonts or gametocytes are formed for sexual multiplication. These gametocytes, which are formed in a similar manner from the trophozoites, are larger in size than the mature trophozoites, less actively amœboid, have no ring stage in their early growing forms, are circular in shape and have no vacuole, while the hæmazoin pigment is much more prominent and diffusely scattered through the parasite, whereas in the mature schizont this pigment collects towards the centre of the parasite. The male gametocyte, or microgametocyte, is usually smaller than the female which is the macrogametocyte. The protoplasm of the former is of a lighter blue, the chromatin is diffuse and central, while the hæmozoin pigment is in the form of thin rods. The female is more coarsely pigmented, its protoplasm is a deeper blue and the chromatin is more compact and situated on one side. Thus, on the whole, the female, though larger, is more compact and brighter coloured than the male. A gametocyte may sometimes be found inside a corpuscle side by side with a growing or dividing schizont, as a result of double infection, and this fact has lead to an erroneous idea of parthenogenesis.

The mosquito cycle.—The further development of the gametocytes occurs in the stomach of the mosquito when it has ingested the blood of an infected individual. Maturation of the gametocytes occurs by the shedding of polar bodies from the nuclear chromatin, followed by escape from the infected red blood cell. In all forms, after maturation, the male gametocyte becomes extremely active, throws out a number of flagella-like vibratile bodies, somewhat like spermatozoa,
but pointed at both ends. The process starts by the successive division of the nucleus resulting in the formation of 5 to 8 chromatin threads which are then thrown out of the cell, each with a thin investing covering of protoplasm.

These flagella-like bodies break away from the remains of the cell and, by their vigorous motility, approach the female, or macrogamete, which is a comparatively quiescent body, rounded in shape, and formed after extrusion of the polar bodies from the macrogametocyte. The nucleus of the macrogamete by this time comes to assume a position underneath the surface. One flagella-like body, or microgamete, as it is now called, succeeds in effecting an entrance into the macrogamete near a small protrusion caused by the nucleus of the latter. The male pronucleus now fuses with the female pronucleus and the macrogamete is now called a zygote, in other words, a fertilized ovum. One, and only one, microgamete can effect an entrance into the macrogamete, though a number of microgametes may be seen surrounding the female. The process has been observed in all its details first by MacCallum in *Plasmodium falciparum*. The early stages of the formation of the flagella-like microgametes can easily be observed on a cooled slide, if a drop of blood containing gametocytes is examined, some 25 minutes after exposure to air. After fertilization, the zygote, or oökinete, as it is called, becomes oval in shape and later elongated, forming what is called, the travelling vermicule, which makes its way by worm-like movements to the midgut, where it burrows its way through the epithelium into the musculo-elastic layer. Here it rounds up and encysts. The whole process is complete in about two days. The oöcyst increases in size, its nucleus undergoes repeated division, the protoplasm becomes converted into a mesh-work of threads, finally breaking up into innumerable spindle-shaped, thin, crescentic sporozoites, each with a tiny nucleus. The oöcysts are found as globular rounded masses on the outer surface of the midgut. They contain hundreds of sporozoites which are liberated into the body cavity by rupture of the cyst wall. Each sporozoite is an elongated
sickle-shaped body, about 12μ in length by 1 to 2μ in thickness. The sporozoites make their way by their own motility to all parts of the body, but mostly to the salivary glands of the mosquito, and from there, to the salivary secretion, whence the infection is transmitted to man. This development occurs only in certain species of mosquito of the genus 'anopheles,' of which many types are known to harbour the parasite. When the temperature falls below 16° C., this development does not occur.

A comparative study of the parasites.—The early ring stages of the parasites are almost alike, but even here a careful study will bring out many distinguishing features. Thus, the ring stage of *P. falciparum* is extremely small, about 1 to 1.5μ in diameter, multiple infection of the red cell is common and many rings show a double chromatin mass. The number of infected cells are also numerous and generally all the parasites are at the ring stage in one slide. ‘Accolé’ forms, where the ring appears as a small arc on the margin of the red blood cell without any vacuole, but only a dot of chromatin, are quite common in this type. The benign tertian ring is generally larger, about 3μ in size, and shows quite early an increase in size of the red blood cell, besides changes in the staining reaction. Multiple infection is not quite so common, and the ring sometimes assumes irregular shapes owing to the extreme amoeboid activity of the parasites. The quartan ring, though slightly smaller, is more prominent owing to a slightly, thicker rim of protoplasm. Hæmozoin pigment appears in this form in very early stages, since the quartan is the most pigmented form of the parasite.

The full-grown trophozoite stage of *P. falciparum* is found only in the internal organs and is only very rarely found in the blood. The affected red blood cell is not markedly enlarged, but large irregular brick red dots appear in the protoplasm called Maurer’s dots. *P. vivax* shows extreme variability in shape in the trophozoite stage so that many different forms are met with in the same blood. Sometimes, irregular filamentous forms may be met with. In all these types the
affected red blood cell is generally enlarged, the protoplasm is pale, and there occur in the protoplasm small pink staining dots called Schüffner's dots. The growing trophozoite of *P. malariae* does not cause any marked enlargement of the affected red blood cell and Schüffner's dots are absent, but the pigment is more prominent and in the form of coarse rods or dots.

The dividing forms, or schizonts, are generally met with only in the spleen and the internal organs in *P. falciparum*. The schizont is about 5μ in size, slightly more than half the size of a red blood cell. The merozoites are small, less than 1μ in size, and vary from 8 to 24 in number. The chromatin is eccentric in position and the merozoites are so small that the dividing form looks like a bunch of grapes. With *P. vivax*, the schizont is quite large, almost fills up the enlarged corpuscle, the merozoites are large, about 2μ in size and about 14 to 24 in number, arranged irregularly, or in two rows somewhat like a rosette, around an eccentric mass of yellowish brown pigment. The quartan parasite, in the fully mature schizont stage, is about 6μ in size, and fills only two-thirds of the cytoplasm of the infected cell. The merozoites number from 6 to 12, and in the mature forms are arranged round a dark cluster of pigment in one row like a daisy. The merozoites are oval and much smaller than those of *P. vivax*.

The gametocytes of the subtertian parasite are crescentic in shape, sometimes showing a thin rim, on the concave edge, which represents the border of the dehaemoglobinized red blood cell. They are about 9 to 14μ by 2 to 3μ in size, the female being longer, more slender, with more compact chromatin and pigment, and stained a deeper blue than the male. The gametocytes of the benign tertian parasites are large, about 13 to 16μ in diameter in the male, and 8 to 11μ in diameter in the female, are rounded in shape, and exhibit the same differences between the male and the female. The quartan gametocytes are smaller, but much more pigmented, and show somewhat similar staining reactions, the chromatin being compact and bright red and eccentric in position in
the female, while it appears as a diffuse oval band in the male, the protoplasm of the former being blue while the latter takes a pale bluish green stain.

Comparative features of the malarial parasites.

<table>
<thead>
<tr>
<th></th>
<th>P. vivax</th>
<th>P. malaria</th>
<th>P. falciparum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fever.</strong></td>
<td>Tertian</td>
<td>Quartan</td>
<td>Quotidian</td>
</tr>
<tr>
<td><strong>Length of cycle.</strong></td>
<td>48 hours</td>
<td>72 hours</td>
<td>24 to 48 hours</td>
</tr>
<tr>
<td><strong>Stages in peripheral blood.</strong></td>
<td>All.</td>
<td>All.</td>
<td>No segmenting stages.</td>
</tr>
<tr>
<td><strong>Number in infected red cell.</strong></td>
<td>Usually one.</td>
<td>Usually one.</td>
<td>Often two or more.</td>
</tr>
<tr>
<td><strong>Motility.</strong></td>
<td>Actively amœboid</td>
<td>Sluggish</td>
<td>Actively amœboid.</td>
</tr>
<tr>
<td><strong>Size of infected cell.</strong></td>
<td>Larger.</td>
<td>Normal.</td>
<td>Normal.</td>
</tr>
<tr>
<td><strong>Colour of infected cell.</strong></td>
<td>Schüffner's dots</td>
<td>None.</td>
<td>Maurer's dots.</td>
</tr>
<tr>
<td><strong>Pigment.</strong></td>
<td>Short rods, very motile.</td>
<td>Large rods, or granules, slightly motile.</td>
<td>Small grains, feebly motile, scanty.</td>
</tr>
<tr>
<td><strong>Number of merozoites.</strong></td>
<td>14 to 24</td>
<td>6 to 12</td>
<td>8 to 24</td>
</tr>
<tr>
<td><strong>Arrangement of merozoites.</strong></td>
<td>'Rosette' with two rows or irregularly spherical or ovoid.</td>
<td>'Daisy' with one row and central pigment sometimes irregular.</td>
<td>'Cluster of grapes.'</td>
</tr>
<tr>
<td><strong>Gametocytes.</strong></td>
<td>Spherical or ovoid.</td>
<td>Spherical or ovoid.</td>
<td>Crescentic.</td>
</tr>
</tbody>
</table>

The pathological lesions met with are the result of an overgrowth and increased activity of the reticulo-endothelial system, causing changes in the spleen, the liver, bone marrow and other organs, all depending on the presence of the parasite.

The spleen in malaria.—In acute malaria, when the patient has died, whether from acute subtertian fever or severe tertian infection, the condition of the spleen is one of acute hyperplasia, such as is met with in acute infections, and differently called acute splenitis, or septic spleen. The
FIG. 40

The spleen in acute malaria.
enlargement is moderate. The capsule is rather tense and shiny and slate grey in colour from the colour of the pulp underneath. The organ is soft and flabby and cuts with unusual ease, exposing a dark tarry surface which bulges out, owing to the hyperplasia and softening of the pulp. The pulp is dark grey, or even black in colour and is so softened that it can be scraped off. In some cases it is almost diffusent. The Malpighian bodies are generally not visible and the trabeculae are obscured by the swelling of the reticulum. Microscopically, the endothelial cells contain parasites and a varying amount of pigment. The parasites are found inside red blood cells in varying stages of disintegration. Some are found lying free in the sinuses and many inside large mononuclear endothelial cells that line the sinuses. Many are phagocytosed by the pulp cells. The parasites appear as small rounded vacuoles, each with a blob of pigment. In sections stained by Leishman’s stain the blue protoplasm of the parasites can be made out with a red chromatin mass, only if the autopsy has been carried out immediately after death. After death the chromatin first disappears and this is followed by a disappearance of the protoplasm of the parasite, so that only granules of pigment are found in ordinary autopsy conditions. The pigment is almost universally distributed throughout the spleen, and appears in fine black dots somewhat smaller in size than blood platelets. It is also found inside the parasites as well as lying free and inside cells.

In chronic malaria, the spleen is very much enlarged and corresponds to the ague-cake of the old tropical clinicians. It may reach down below the umbilicus, and shows well-defined notches. The edges are thickened and rounded. The capsule is thickened and opaque or even hyaline. It may show areas of perisplenitis and may be adherent to structures in the neighbourhood. In some cases, owing to the retraction of the fibrous tissue, the capsule may be wrinkled. The organ is hard, tough, and cuts with difficulty. On section, the cut surface is flat or concave from retraction of the fibrous
tissue. The colour is generally slate grey, or even dark grey, from deposit of pigment. The trabeculae can be made out as greyish white bands of tissue, traversing the organ irregularly and breaking it up into areas of variable size. Histologically, the pigment occurs in irregular large blocks, in addition to finer granules lying inside the phagocytic splenocytes. The Malpighian bodies do not contain pigment. Yellow granules of haemosiderin are also usually present. The trabeculae may show marked fibrosis and hyaline change.

The liver is frequently enlarged, and is firmer than normal in chronic cases. The usual reddish tinge of the organ is lost in a shade of grey, somewhat like the colour of lead. This colouration is, however, not so marked as that of the spleen. The organ preserves its shape, the capsule may show thickening in places, in chronic types. On section, there may be more resistance than normal owing to slight cirrhotic changes which accompany the deposition of pigment. In some cases this cirrhotic change may be marked and causes a contraction of the organ, but a hobnailed appearance is not met with.
Histologically, the enlargement is due, not so much to the congestion, as to a stuffing of the capillaries with mononuclear cells containing pigment, as well as to a hyperplasia of the Kupffer cells lining the capillaries. These become loaded with small granules of pigment probably derived from the breaking down of individual parasites. While the pigment deposits are not so numerous as in the spleen, they are much more definite in the liver, and are practically confined to the Kupffer cell system and the circulating cells and do not affect the hepatic cells. Thus, a histological diagnosis of malaria can be made with much more certainty by examining sections of the liver rather than those of the spleen which normally contain irregular blocks of blood pigment. If the autopsy is done sufficiently early, in addition to granules of pigment which represent individual parasites, the parasites themselves with their blue protoplasm and red chromatin can be made out, in sections stained with Leishman's stain. Apart from these coccoid granules of pigment representing degenerate parasites, irregular clumps of pigment may be met with either lying free or inside endothelial cells. Fine golden yellow dust-like
granules of hæmosiderin may also be met with in the liver cells, and derived from the hæmoglobin. Fatty degeneration of the liver cells may be met with in acute cases, while in chronic cases atrophy of the liver cells is more usual.

The intestines may not show any lesions except in subtertian infections, where punctiform hæmorrhages into the mucosa, or more profuse hæmorrhage into the lumen of the intestines may be met with. The mucous membrane may be markedly bile stained. Histologically, the parasites may be found blocking the small capillaries of the villi. These lesions obviously account for the choleraic, dysenteric and diarrhoeic types.

The brain, in subtertian malaria, may show punctiform hæmorrhages in the semi-oval centre and the corpus callosum, while, in other cases, there may be no obvious naked-eye changes except congestion of the pia-arachnoid. Sometimes, the colour may be that of a smoky grey from the pigmentation. Microscopically, however, embolic blockage of the small capillaries by plugs of agglutinated red blood cells, some containing parasites, are the lesions met with in 'cerebral malaria.' Periarterial areas of gliosis due to hæmorrhage

FIG. 43.
Section of brain (× 600) showing cerebral capillary blocked by parasites.
MALARIA.

may be met with such as found in cerebral vascular lesions. Small nodular elevations, due to reactive glial changes round capillaries containing parasites, have been described under the term, malarial granuloma. Apart from actual blockage, capillaries containing parasites which look like small vacuoles each with a granule of pigment inside red blood cells, are quite common features. The parasites are easily demonstrated in smears taken from the white matter where the capillaries often appear intact. The importance of brain smears in the diagnosis of cerebral malaria cannot be overemphasized. It is possible in places where no facilities exist for the preparation of pathological sections, and is a procedure of as great importance as taking a spleen smear.

The bone marrow is usually red and congested, and may show clumps of pigment inside the marrow cells. The heart muscle usually shows cloudy swelling; but fatty degeneration may be met with in subtertian infection. The kidneys also show cloudy swelling and a true nephritis is occasionally met with in quartan infections. The adrenals may show parasites. A reduction of the lipoids in the cortex is another feature.

Among general features, a pigmentation of the skin is noticeable and, sometimes, emaciation is present. Externally, the anaemia, the icteroid tinge of the sclera and the pigmentation of the skin which is met with in chronic cases, are the usual features. Edema of the legs may be met with, in long standing anaemia. A general anasarca is sometimes met with especially in quartan infections, and nephritis is the probable cause.

The blood shows a marked secondary anaemia due to the enormous destruction of the red blood cells by parasites, and probably from the increased phagocytic activity of the spleen pulp. That the malarial anaemia is haemolytic is shown by the fact that there is an indirect positive Van den Berg's reaction in the blood. The bilirubin may be so marked as to colour the conjunctiva yellow. The reduction in the number of the red blood cells is most marked during the first few bouts of fever, while during the apyrexial stages, active regeneration
Takes place. Changes in the shape of the red blood cells, such as anisocytosis and poikilocytosis, occur, while punctate basophilic stippling and alteration in the staining reaction are also met with. Microcytes and megalocytes, stained a faint bluish pink, are met with, while nucleated red blood cells are rare. There is a reduction in the haemoglobin which is more marked than the fall in the number of red blood cells and there is a reduction in the total volume of the circulating blood. There is a well-marked leucopenia affecting especially the polymorphonuclears. This becomes evident in a few hours from the commencement of the attack, so that the normal ratio of 1 to 600 between leucocytes and red blood cells falls to about 1 in 900. There is, however, a marked relative increase in the number of mononuclear cells to about 15 per cent. Some of the large mononuclear leucocytes may contain granules of haemoglobin pigment, a feature of great diagnostic value. Granules, stained a faint crimson, sometimes appear in the mononuclear leucocytes, and should not be confused with granules of pigment which are yellowish brown in colour. Besides the mononuclears, Türcck's irritation leucocytes are sometimes met with in malarial blood. These are mononuclear cells with basophilic protoplasm stained a dark blue and a nucleus stained a uniform dark purple with Leishman's stain. Another cell that is sometimes met with is the plasma cell which, however, though very similar, has a cart-wheel-like nucleus showing distinct nucleoli. The malarial parasites are usually met with after a careful examination, when a thin, stained film is examined, but if they are scanty, the thick film method should be used, where, after a thick film is made, it is dehemoglobinized in water before staining, so that the parasites stand out more clearly against a colourless background. The malarial parasite may be cultured from the peripheral blood in obscure cases. Row draws the finger blood into a small sterilized tube from which after defibrination a drop or two are transferred into a flat-bottomed tube which is kept in a larger tube like an ordinary potato tube. Anaerobiosis is secured by a little pyrogallic
acid in the larger tube which is kept hermetically sealed by a rubber cork.

Another change, met with in malaria, is an increased excretion of urobilin in the faeces, owing to the hæmolysis. A trace of albumin in the urine is met with after the attack. There is a constant excretion of urobilin in the urine which lasts for some time after the attack.

**Blackwater fever.**

This is a form of hæmoglobinuric fever associated with hæmolytic jaundice.

It is most common in certain parts of Africa, in the southern States of America, in parts of India, and in the Mediterranean coast of Europe in those areas where virulent subtertian type of malaria is endemic. In Africa the European settlers are attacked, while in India, it attacks settlers in the Dooars in Bengal and the Agency tracts in Madras where whole communities are infected with subtertian malaria, but very few develop blackwater fever. New arrivals get the disease after a residence of one to two years. The immunity of local residents may be more apparent than real, the symptoms being so mild that the condition may be overlooked.

The etiology of blackwater fever has long been the subject of great interest since so many different views are held. But the general trend of opinion now is that massive infection with the subtertian parasite of malaria, *Plasmodium falciparum*, is an essential factor in the incidence of blackwater fever. The parasites can usually be demonstrated in the early stages of the disease, though they are not easily found in the later stages. In favour of the malarial origin of blackwater fever are, that the geographical distribution of blackwater fever coincides with that of subtertian malaria, that antimalarial measures have distinct effect in diminishing the incidence of blackwater fever, and that the disease attacks people who have at one time or other suffered from subtertian malaria. An important factor in regard to the etiology is the tendency of quinine to precipitate an attack. Though

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it is now almost certain that malarial infection is the essential predisposing cause, the exact mechanism of hæmolysis, or why it occurs, is not understood. Whether it is due to some altered resistance in the red blood cells to osmotic tension, an undue fragility of the red blood cells, or whether there is some change in the osmotic tension of the plasmodium itself favouring hæmolysis, has not been decided. In paroxysmal hæmoglobinuria, the effect of sudden lowering of temperature in inducing hæmolysis is well known. Possibly, a similar state of affairs occurs in blackwater fever, since there are cases on record where the hæmoglobinuria started after a sudden change in the environment. Chills are believed to predispose to hæmoglobinuria in such cases. The mechanism of hæmoglobinuria is also of interest. It is believed that there is always a degree of hæmoglobinæmia present, and that, when the concentration of hæmoglobin rises above the renal threshold, hæmoglobinuria results. Christophers, however, holds that the hæmoglobinæmia and the hæmoglobinuria are almost coincident, depending on the sudden lysis of the red blood cells that occurs. A contraction of the spleen often occurs in blackwater fever and this has been interpreted as coincident with the liberation of hæmolytic substances. A hæmolytic substance is believed to exist in the blood; but the difficulty is to explain its sudden liberation. The kidney has been regarded as the seat of the hæmolysis, the whole mechanism being considered as the manifestation of anaphylaxis.

The blood shows a marked oligocythaemia from the lytic effect on the cells. Though the parasites are not readily demonstrable during the well-developed stage of the disease, they may often be found in the early stages. Their absence during the well-developed phase is apparently due to the enormous destruction of the red blood cells containing the parasites. Whether the cells that contain the parasite are particularly prone to hæmolysis is a moot point. However, pigmented mononuclears, another important evidence of malaria, can be demonstrated in all the stages
of the disease. During the stage of recovery, regenerative changes in the red blood cells, evidenced by basophilic stippling, are present. As in malaria, a mononuclear increase occurs. Bilirubin is present in the blood from the hæmolysis, and this accounts for the jaundice that is met with.

The urine shows hæmoglobin in varying amounts, and various shades of red colouration, ranging from dark brownish red to pale red, may be met with during the progress of the disease. Spectroscopically, the absorption spectra of oxy-hæmoglobin and methæmoglobin are present. No bile pigment is present, though urobilin is invariably excreted in excess, being derived from the blood pigment. This feature is met with in most hæmolytic conditions including malaria. The urine is usually highly acid. There is a marked deposit of sediment consisting of hæmoglobin and casts. Albumin is always present in large amounts, but red blood cells are not usual.

The spleen is generally enlarged, and shows marked pigmentation. Microscopically, grains of dark brown malarial pigment inside the endothelial cells are usual. The liver generally shows malarial pigmentation and microscopic features of malaria. The general features of autopsy are those of malaria. There is a marked hæmosiderosis in all the organs, most marked in the liver. The kidneys show hæmoglobin casts in the tubules besides degenerative changes in the epithelium.

**Sarcosporidiosis.**

This is an exceedingly rare condition in man, but is more common among animals, where the causative organisms are localized in the muscles and give rise to characteristic white, thin-walled, oval, cysts called Miescher's tubes. The tubes, when examined microscopically, are found to be divided by a number of thin septa into compartments, the more mature of which contain a number of sickle-shaped 'spores' which are closely packed together.
Man gets the infection by eating meat containing the tubes. The cycle of development is not clear. In the lower animals the parasite is said to pass through an amœboid stage in the intestine, followed by encystment in the muscles. In man, the muscles of the heart, larynx and the pectoral group have been involved.

The life history has not been fully worked up and the systematic position of the parasite is uncertain.

It is provisionally classed as a sporozoon.
CHAPTER X.

TYPES OF PROTOZOAL INFECTIONS.

BALANTIDIOSIS.

These are infections of the intestinal tract with a protozoan, *Balantidium coli*, and are characterized clinically by diarrhoea and dysentery.

The infection occurs in many parts of the world, and is not confined to the tropics.

The parasite belongs to the class of Ciliophora, the most highly developed of the protozoa. It is an actively motile organism, oval in shape, and shows extreme variability in size. Commonly it is about 60 to 70μ in length and 40μ in width. The anterior end of the body shows a tubular depression, leading to a narrow cytostome or mouth, through which food material is swept into the body of the parasite by circumoral cilia. The outer surface of the body is thickened to form a periplast from which row upon row of countless, short, vibratile cilia project free, and serve for the motility of the parasite. The ciliary motion is in even sequence like that of a row of oars in the old Viking ships. In the middle of the protoplasm is a large kidney-shaped nucleus, the trophonucleus, and close to it is a small kinetonucleus. The protoplasm contains a number of food vacuoles; but besides these, there are two
contractile vacuoles which are excretory in function, the excretory material being shot out of the body by periodic collapse of the vacuoles after distension. At the posterior extremity is a rudimentary hypostome.

The normal host is the pig, to whose intestine the parasite is adapted, existing there as a harmless commensal. In man, in a proportion of cases, no symptoms are caused even though the parasite, like *E. histolytica*, lives on the mucous membrane, cysts being passed out normally in faeces. This condition of parasitism may, however, be upset by some other cause, when severe symptoms are caused. The parasite burrows into the mucous membrane causing lesions, varying from chronic catarrh to widespread ulceration. The ulcers have blackish necrotic slough in the centre and resemble the ulcers met with in amœbic infections. Microscopically, in the early stages, the parasites may be met with deep in
the submucosa without extensive ulceration, the parasites, apparently, making their way between the cells causing only minute lesions. In the submucosa, marked eosinophilic infiltration, oedema and necrotic changes are generally met with, while occasionally polymorphonuclear infiltration suggests secondary infection. Hæmorrhages may sometimes be met with. However, cases are met with where, with the presence of numbers of organisms in the submucosa, remarkably little cellular or necrotic changes are observed. Unlike *E. histolytica*, no proteolytic ferment is formed by these parasites. The occurrence of these protozoa in the mesenteric nodes has been reported.

The diarrhœic and dysenteric features met with are obviously the result of the catarrh and the ulcerative lesions met with.
CHAPTER XI.

DISEASES OF UNKNOWN OR INDEFINITE CAUSATION.

THE BERIBERI GROUP.

Under this group of diseases, clinical types exist, exhibiting differences from each other, but characterized by the presence of changes in the peripheral nerves, and cardiac degeneration often ending in sudden death. These are variously called Beriberi, Ship Beriberi, Infantile Beriberi and Epidemic Dropsy, the term Beriberi being used to include two types, the wet and the dry forms. The exact relationships of all these diseases to each other have not been completely settled.

Beriberi.—This is a disease of unknown causation occurring in certain restricted areas in the tropics and characterized by a form of peripheral neuritis and, in some cases, by an acute cardiac dilatation and oedema.

Beriberi is endemic in parts of Japan, in Java and in Brazil, while occasional cases crop up in India, China and the Malay peninsula. Two types of the disease exist, the wet type, characterized by oedema and cardiac dilatation, called Beriberi, and the dry type, where an atrophic type of peripheral neuritis occurs, which was formerly called Barbiers. It is now believed that these are only two stages, or at most, two types of the same condition. Both sexes, all classes and ages are affected, though a type called Infantile Beriberi exists which shows some distinct features. A seasonal relationship to the rice crop has been claimed. There is a tendency to occur in armies, camps, jails and asylums. Another type of the disease exists, called Ship Beriberi, on
THE BERIBERI GROUP.

board ship, in tropical regions affecting both Europeans and Asiatics.

Etiology of beriberi.—This is still an unsolved problem, and various conflicting theories are held, each more or less based on some experimental and clinical evidence.

Until recently the great majority of observers were inclined to regard this condition as a nutritional disorder, resulting from the deficiency in the food of an essential food factor, a vitamin. Experimentally, Eijkmann found that fowls fed on a diet which contained a deficiency of this vitamin developed symptoms of peripheral neuritis. This vitamin has therefore been called, the anti-neuritic vitamin, or vitamin B, and beriberi has been believed to be the result of a want of this anti-neuritic vitamin in the diet. It has been pointed out that beriberi is a disease which occurs mostly in people whose staple food is rice, or some rice product, and that when the rice is polished during the course of milling, the outer layer, which contains the anti-neuritic factor, is removed, so that polished rice is the important factor in its causation. Parboiled rice in which the outer layer is adherent has been held not to cause beriberi. In support of this hypothesis are the human experiments of Fraser and Stanton who fed nearly 300 Javanese coolies, divided into two batches, on two different diets, the first of which mainly consisted of white rice. The result was that 20 cases of beriberi occurred in the first group. Strong and Crowell conducted similar experiments on prisoners in the Manila Jail and symptoms resembling beriberi were reported in groups where white rice was the main article of the diet. However, it must be pointed out that these experiments were carried out in an endemic zone and that in none of them the complete picture of beriberi resulted. It has also been argued in favour of this theory that beriberi can be rapidly cured by a supply of the extract of rice polishings, in fact, the anti-neuritic vitamin. McCarrison has pointed out, however, that experimental avian polyneuritis is different from beriberi in that there is an atrophy of the heart in the former while dilatation of the heart occurs in
true beriberi. He holds, that for the production of true beriberi in pigeons, *Beriberi columbarum*, as different from polyneuritis, besides the deficiency of vitamin in the diet, some intestinal or metabolic toxin is essential, the vitamin deficiency being regarded as the negative factor, while the toxic substance is the positive agent.

The rice intoxication theory of beriberi was first put forward by Braddon, who noted the association between rice and beriberi and concluded that some toxin in rice is responsible for the symptoms. Recently claims have been made by Acton and Chopra, that rice, during storage, gets infected with some spore-forming bacteria, with the result that different toxins are formed on rice, one of which acting on the nerves causes the neuritis while the other causes cardiac dilatation and oedema. The occurrence of polyneuritis in general, dependent on a large group of exogenous poisons which are ingested, such as lead, arsenic or alcohol, and the existence of intoxications, such as lathyrisis and botulism from toxic substances in food material, suggest that a similar condition may possibly hold good in beriberi. It is also pointed out that, with regard to the human experiments, the test diets showed not only a lack of vitamin B, but other factors; and the only conclusions that could be drawn from these experiments are that disease processes were more commonly met with in groups of people kept in an ill-regulated diet. It is even open to question whether the disease produced was beriberi.

On the other hand, a theory has been put forward that the disease is an acute infection. The occurrence of cases affecting members of the same family, the occurrence of cases transmitted by an affected individual on his arrival in a healthy household, away from an endemic zone, which have been reported, and the occasional occurrence of ship beriberi, are all brought forward as evidence in favour of an infectious factor. It is pointed out that cases occurred in British troops in Mesopotamia, where rice was not a factor in the diet. The relationship with epidemic dropsy which resembles an
acute infection is held in favour of this view. The outbreak among the medical students in Vizagapatam hostel which was investigated by Kamath is suggestive, since the disease died down with change of residence, without any change in the diet.

The pathological lesions met with in beriberi are three, the neuritis, the oedema and the cardiac degeneration.

With regard to the neuritis, marked degenerative changes have been described in the peripheral nerve endings, less marked in the peripheral nerves and in the cord. Microscopically, Wallerian degeneration has been described side by side with regenerative changes. Chromatolytic changes have been noted in the ganglion cells and the cells of the spinal cord, but are of doubtful significance. Degenerative changes have also been described in the nuclei of the vagi and in the fibres of the vagi, but such changes are difficult to demonstrate. The sympathetic fibres are also said to be degenerated.

The heart presents a striking feature at autopsy. The pericardium is generally distended with fluid, but often shows the heart wall bulging through. The heart is markedly dilated, and still more commonly, distended with blood. This is more marked on the right side, the right auricle being turgid, while the veins that open into it are also engorged. The wall of the right ventricle is firm and thick, but it is doubtful if this is a true hypertrophy. The cavity is markedly dilated and is filled with red blood clot. The tricuspid ring is also dilated, often admitting four fingers or more. In contrast to this marked dilatation on the right side, the left side may show no enlargement and this is in consonance with the other systemic changes of tricuspid regurgitation and failure of the right heart. The features of passive congestion and oedema of the lung may also be present. Microscopically, the heart muscle may show fatty change, but an interstitial oedema and an intracellular oedema are interesting features. Mebius has pointed out that the longitudinal striation is distinct while the transverse striation is lost.
Wenckebach has pointed out that there are no inflammatory changes in the cardiac muscle, and there is a pseudohypertrophic swelling of the muscle followed by öedema. It is put forward that the muscles are the largest water reservoirs of the body and that the condition of the heart muscle in beriberi showing increased conductivity with the electrocardiograph is analogous to the condition met with in an experimentally water swollen heart. The vagal factor is regarded as negligible. Fragmentation and segmentation of the muscle fibres are also met with, but are of no significance.

The öedema of beriberi manifests itself in serous effusions such as hydrothorax, hydropericardium, ascitis and general anasarca. The subcutaneous and subperitoneal öedema and the öedema between the muscle fibres is much more than the slight öedema of the liver, spleen and kidneys. Mebius holds, that this öedema can explain all the symptoms of beriberi, the sensory disturbance being due to the öedematous condition of the skin, the loss of tendon reflexes, to the swelling of the sensory nerve endings, while the cardiac features are regarded as due to the water retention in the muscle. Wenckebach argues, that just as the thickness of the heart muscle is due to water retention, so also the changes in the peripheral nerves and central nervous system arise from a similar factor. Subcutaneous öedema may not be marked, but öedema may be present in the deep tissues in the retroperitoneal tissues and in the organs.

Of the internal organs, the liver often shows marked venous congestion and consequent enlargement. It may present a typical nutmeg appearance with a tense capsule and a swelling cut surface. The spleen is also congested and rather more firm than normal. The kidneys are usually dark purple in colour and show marked congestion, with a dripping cut surface showing dark red vascular markings. Petechiae may sometimes be met with, but are more common in epidemic dropsy. The stomach shows intense congestion and sometimes ecchymosis. This may be equally marked in the
duodenum, though there is nothing to suggest that primary duodenitis exists, as put forward by Hamilton Wright. I have found intense congestion and ecchymosis in the mucosa of the intestine. But it cannot be denied that the changes met with in the gastro-intestinal tract suggest a possible localization there, since they are more marked than would be accounted for by the venous stasis. Óedema of the gall bladder is a feature to which attention has been drawn recently. It is out of proportion to the general anasarca. It affects only the outer wall and not the mucosa. The adrenal is often found enlarged.

Parenchymatous degeneration and hyaline change have been described in muscles. Sometimes, fatty degeneration may be met with. The muscle fibres are often swollen, microscopically, and there is reason to believe that an intercellular Óedema exists.

The blood shows no obvious features except a variable anaemia.

*Infantile beriberi.*—This is a type of the disease that occurs in infants, particularly breast-fed babies, and there seems to be a definite association with beriberi in the mother. Sometimes, however, the mother may show very slight features of the disease while successive infants are attacked. The disease is very often more acute than the adult type, the sudden cardiac dilatation resulting in the restlessness, cyanosis and Óedema that are met with. Gastro-intestinal features are more common at the commencement with vomiting and abdominal pain. The disease runs a very rapid course like an acute infection. A paralysis of the left vocal chord is said to be responsible for the altered voice that is met with.

The pathological anatomy is that of an acute cardiac failure involving only the right side of the heart. Thus the right auricle and ventricle may be turgid and the cavities dilated. There is marked stagnation of blood on the venous side. Changes have also been described in the peripheral nerves and nerve endings, but are slight.
The most striking feature of the condition is the improvement that occurs, when the child is put on a diet containing extract of rice polishings, or even yeast preparations, such as toddy, which are rich in vitamin B. This fact has been interpreted to mean that a vitamin deficiency is the cause, but the improvement met with might equally be due to absence of the mother's milk, which might contain a toxic or infective factor.

Ship beriberi.—This is a type of beriberi that occurs on board ship. It is met with most commonly in ships in tropical waters and is also found in Swedish and Norwegian steamers, in recent years. The features are those of oedema of the legs, sometimes all over the body, followed by cardiac dilatation and a tendency to sudden death occurring often in epidemic form on the high seas. According to the vitamin deficiency hypothesis, the cause is the low vitamin B content of the diet, since bread baked from white flour is largely used. It has been noted that the features of neuritis are absent and the disease has been regarded as allied to scurvy. Intoxication or some infective agent cannot be excluded.

Epidemic dropsy.—This is a condition that is closely allied to beriberi if not identical with it. It occurs in outbreaks, very often of sudden onset, with features of gastro-intestinal derangement, fever, with an occasional rash, marked oedema, cardiac manifestations, a tendency to haemorrhages and a variable neuritis. The disease occurs in India, particularly in Calcutta, but outbreaks occur in Mauritius. Megaw holds that the disease affects only rice eaters. The disease is different in many features from war oedema. Megaw implicates parboiled rice which has been stored as containing a toxic factor which is responsible. A seasonal relationship with the rice crop is also brought forward. In its tendency to haemorrhages and in the gastro-intestinal features of onset, together with the frequency of glaucoma, the disease presents differences from beriberi. In the tendency to oedema and sudden death from cardiac failure and the variable neuritis, the disease is strikingly like beriberi. It has been put forward,
that the disease is an acute infection, and its sudden outbreaks, fever and gastro-intestinal features are certainly suggestive. There is no association with the defective nutrition in the diet, since the disease affects even the well-to-do classes and occurs in sudden outbreaks, so that the question of vitamin deficiency is not of much importance. On the other hand, the association with beriberi seems so close as to suggest that a similar etiological factor might operate in the latter condition. It may be mentioned, however, that Veddor holds that while beriberi is due to one type of vitamin deficiency, lack of another vitamin is possibly responsible for epidemic dropsy and allied conditions.

The only striking difference that may be present at autopsy is the tendency to petechial haemorrhages into the serous membranes, and diffuse haemorrhage into the stomach, the lungs and the rectum. It is also interesting to note that the marked congestion of the stomach and duodenum that is met with in this disease is similar to the condition that is sometimes met with in beriberi.

PELLAGRA.

This is a disease of indefinite causation characterized by a cutaneous rash, together with gastro-intestinal and nervous features.

The term 'PELLAGRA' itself means 'rough skin,' and this forms the most striking feature of the disease which shows also a combined degeneration of the spinal cord. The disease is endemic in the Mediterranean coast of Europe, particularly in Italy, Spain and Roumania. Rarely, occasional cases are met with all over the world. It is a disease which exhibits marked seasonal variations.

The exact etiological factor that operates in the production of this spinal sclerosis is not well understood. Lombroso was the first to implicate a toxic factor in maize as the underlying cause. He regarded the condition as an intoxication from diseased maize or diseased corn. This theory, which is called the 'Ziest' doctrine, has many adherents
even now. They hold that pellagra is much more common among people who eat maize, and that maize during storage gets overgrown with fungi, with the result that poisonous products are produced. Some experimental evidence is advanced in support of this view, since disease conditions resembling pellagra were produced by using an extract of diseased maize. This theory, however, cannot explain the sporadic cases met with in different parts of the world, though even here the Ziests bring forward that flour made from corn cannot entirely be ruled out. The Ziests point out that pellagra became prevalent in Europe only after introduction of maize as the staple article of food. It is also advanced by others that the maize is decomposed in the alimentary canal and that poisonous bases are formed which act on the nervous system, a theory which is difficult to prove.

Pellagra has also been regarded as an acute infectious disease. Sambon held that it was a protozoal infection and even implicated midges as the transmitting agents. Goldberger's experiments, however, are against this view. He failed to infect himself as well as volunteers by ingestion of the epidermal scales and cutaneous secretions of pellagrins for a long period.

The theory of food deficiency is the one that is favoured by many modern workers. They hold that pellagra is due to absence of a factor in the food. This factor, the pellagra-preventing factor, or the P. P. factor, is particularly deficient in maize and, according to these workers, the apparent association with maize is capable of this explanation. Goldberger has brought forward some experimental evidence in favour of this view. The test diet consisted of a food deficient in proteins, and in half the number of persons experimented on, a cutaneous lesion was produced which was regarded as similar to pellagra. In experiments on rats and dogs, a disease similar to pellagra has also been produced by omitting this P. P. factor. It was put forward that this P. P. factor was associated with, what has been termed, biological protein, that is, the protein that is available for assimilation.
containing the essential amino-acids, tryptophane and lysin. If the biological value of the protein was deficient it was found that pellagra resulted. Recently Goldberger has put forward that this P. P. factor is allied to vitamin B, and is closely associated with vitamin B, and that all foods containing vitamin B contain this P. P. factor.

The disease has been divided into various stages. A prodromal stage is followed by a stage of gastro-intestinal disturbance during which the cutaneous lesions, which affect the exposed parts of the body, occur. These are characterized by periodic recurrence ending in pigmentation. This stage is followed by a stage of nervous involvement characterized by nervous features and mental features from cerebral involvement.

The lesions met with in pellagra are varied. Externally, the features are those of a chronic cachexia with wasting and anæmia. The cutaneous lesions which are sharply demarcated present shiny atrophied skin with raised margins, surrounded by areas of pigmentation. Internally, the heart is shrunken, with a wrinkled epicardium, a gelatinous serous change in the fat, and a rich chestnut brown colour of the heart muscle, a condition of brown atrophy. Slight atrophic changes may be met with in the liver. Sometimes fatty infiltration may be met with. The spleen may also be in a condition of atrophy with a shrunken capsule, well marked trabeculæ and scanty pulp. The kidneys may also take part in the atrophy, but more often chronic fibroid changes may be met with. Very often the great vessels may show atheroma. The mucous membrane of the intestine may show marked atrophy, and thinning and atrophy of the lymphoid follicles have been described. Sometimes, ulceration may be met with, particularly in the terminal coils of the intestine. Microscopically, the atrophy is most marked in the muscle coat and appears to be a part of the general atrophy that is usual. The pancreas also shows atrophy.

The lesions met with in the spinal cord consist of a central neuritis with swelling of the cells, disappearance of the
Nissl granules, and lateral displacement of the nuclei. Retrograde cell changes of a similar nature are found in the cerebral cortex. There is increased lipoid material throughout the central nervous system. Thickening and hyalinisation of the vessels of the brain and cord are also met with. Degeneration of the dorsal and lateral columns is found in the dorsal and cervical regions. Changes in the sympathetic nervous system have been described by Roaf who holds that the skin lesions are the result of the affection of the sympathetic nervous system. Fragility of bone is a constant feature due to an osteoporosis affecting the shaft. A fibrosis of the thyroid has been described.

Microscopically the cutaneous lesion in pellagra consists of an atrophy of the superficial layers of the skin with overgrowth of the deeper layers and inflammatory changes affecting the corium. The Malpighian papillae are lost.

The blood shows a moderate secondary anaemia which has no characteristic feature. A trace of albumin may be noticed in the urine.

Sprue.

A clinical condition characterized by a chronic diarrhoea, a superficial desquamation of the tongue and mouth, and a pernicious type of anaemia, sprue has been regarded as a morbid entity.

The disease is found mostly in tropical countries, notably China, India and Ceylon and has a regional distribution even there; but there is reason to believe that the condition described by Gee in Europe in children, called celiac disease, is very similar to sprue. The disease is met with more often in women and mostly in adults. It frequently follows parturition in women. It is said to follow bacillary dysentery and amoebic dysentery, but whether the condition is then one of sprue or of chronic dysentery is not quite clear. There are instances of the disease affecting families. The reason would appear to be one of environment, rather than a real familial spread. Residence in the endemic area would appear to be essential.
Regarding causative factors, sprue has been first attributed by Kohlbrugge to infection with the thrush fungus, Monilia albicans, which he found in the tongue, intestinal mucosa and the faeces in large numbers in cases of sprue. Manson-Bahr found similar elements of mycelia in the intestine and deep in the tongue. Similar fungi were however found in the stools of normal individuals. It has been pointed out that it is not possible to produce the symptoms of sprue by feeding experiments with monilia though it is toxic when injected into guinea-pigs. Ashford put forward that the monilia of sprue belonged to a different species. He regards sprue as a mycosis superimposed on a state of deficiency of certain essential food elements. Recently, claims have been made that the disease has been reproduced in China, in white mice and monkeys, by feeding them on cultures of the monilia. Ashford’s claims of a complement fixation reaction, with cultures of monilia as the antigen, have so far not been confirmed. It is also pointed out that experimental moniliasis in guinea-pigs and septicæmia in rabbits by intraperitoneal injections of massive doses of living monilia are not equivalent to tropical sprue in man.

Vitamin deficiency has been regarded as a causative factor, since the lesions met with in man bear some resemblance to lesions described by McCarrison in pigeons when they were fed on a diet deficient in vitamins. But it is also objected that the lesions observed, as a result of deficiency of vitamin C, were inflammatory and degenerative changes in the alimentary canal resembling dysentery rather than sprue.

The familial and regional distribution suggest an infective factor. Mackie and Fairley, working in Bombay, have found that the intestinal flora in sprue are similar to those found in post-dysenteric conditions such as are met with after Flexner infections. Fairley has brought forward a pleomorphic organism resembling B. mallei as the probable infective agent. The reputed occurrence of sprue after dysentery raises the question whether we are dealing with a definite morbid
entity. The occurrence of cases of indigenous sprue in Europe, reported by competent observers, also raises the question whether we are dealing with a symptom-complex, since there are no definite pathological criteria for the purpose of diagnosis.

The parathyroids present no abnormality in sprue though a parathyroid defect was considered by Scott who found a low ionic calcium in the blood. The pancreatic functions are normal though a pancreatic defect has been suspected.

The clinical features of gaseous acid diarrhoea, with pale abundant frothy stools, together with the gaseous distension of the abdomen, and the good effect of milk treatment suggest that the monilia may have at least some part in producing the symptoms.

The lesions found in sprue cannot be regarded as distinctive, except for the condition of the tongue which shows a type of atrophic glossitis, a condition that is also met with in pernicious anaemia, a disease which resembles sprue in some respects. The tongue may show a diffuse inflammation of the fungiform papillae, later on followed by atrophy. Yellow aphthae may be found in the early stages. Later, the tongue has a glazed appearance from atrophy of both fungiform and filiform papillae, so that the superficial epithelium is thinned and fissures appear. Microscopically, inflammatory infiltration may be noticed and sometimes fungal elements as well.

The intestines show a general atrophy of all the coats, particularly near the ileocaecal region where the gut is almost diaphanous and distended. This has been described as a specific atrophy, but is probably due to gaseous distension. Fairley lays a good deal of stress in this 'atrophic enteritis' which, however, is an appearance met with in chronic inanition. He regards this condition as a specific enteritis due to the action of a specific virus. The bowel may be congested and may show a catarrhal enteritis of the terminal coils of the ileum which, again, has no distinctive features. Actual ulceration has been described in a few cases and sometimes petechiae. Microscopically, there is an atrophy of all the
coats besides an atrophy and shrinkage of the villi which has been called a withering of the villi, probably a post-mortem change. Inflammatory changes in the submucosa have also been described and sometimes actual ulceration. Deposits of haemosiderin may occur. Manson-Bahr describes extensive ulcerative lesions in the intestine with erosion of the villi and glands, sometimes total destruction, with the formation of small cysts and even submucous abscesses followed by pigmentation and fibrosis, lesions very like chronic dysentery. Enlargement and thickening of the mesenteric glands have also been described. Micro-organisms, such as streptococci and B. welchii, have been cultured, but since they are normally present in the intestine they are of no significance. The absence of a definite morphological picture and lack of correspondence between the features described by different writers raise the question whether, under this heading, two different conditions are being dealt with, one a syndrome called sprue and the other a chronic post-dysenteric diarrhoea.

The whole body is generally wasted, the subcutaneous fat is almost absent, and the muscles are also atrophied. The heart is generally in a condition of brown atrophy. All the viscera show atrophy probably from starvation. The liver is also atrophied and this has been regarded as a specific atrophy due to defective absorption of fat from the intestine. Fibrotic changes have been described in the pancreas but are not common. Microscopically, the liver may show fatty degeneration and deposits of haemosiderin. The spleen is generally atrophied and may show hyaline change which, however, is not characteristic. The bone marrow usually shows aplasia, or gelatinous degeneration, but may sometimes show an erythroblastic reaction in the earlier stages.

The blood picture may be that of a secondary aplastic anæmia with a high colour index or that of a megalocytic anæmia resembling pernicious anæmia, depending on the reaction of the bone marrow. Poikilocytes, macrocytes and rarely polychromes are met with, while normoblasts are very rare. There is a leucopenia with relative lymphocytosis.
There are no remissions as in pernicious anaemia. A positive indirect Van den Bergh’s reaction for bilirubin is usually present. The blood calcium is reduced below 9.5 mg.

The pale colour of the faeces, evident only in the later stages, is due to the conversion of the bile pigment into colourless leucobilirubin. Fat is usually in excess since it is not absorbed. This is also from the nature of the diet which is mostly milk. Fatty acid crystals are usually in excess of neutral fat, unlike the condition in pancreatic disease.

**Infantile Cirrhosis.**

This is a form of cirrhosis of the liver met with in some districts in India, affecting only infants.

The disease is common in Calcutta, Bombay and Madras, cases generally coming from rural areas though sometimes originate in the towns themselves. Brahman children are more often affected and a striking feature of the disease is the tendency to affect children of the same mother. It is not strictly congenital though it is difficult to decide whether there is a congenital predisposition. The disease commences very early in life, very often six months after birth, and does not affect children over two years of age. The causative factor is still unknown. Malaria, kala-azar, syphilis and other specific infections play no part in its etiology. The disease has no relation with the infantile forms of kala-azar met with in the Mediterranean. The tendency to affect the children of the same mother leads to the suspicion of some anti-natal cause acting slowly after birth. It has also been argued that the disease is due to some toxin excreted in the mother’s milk. The toxic and microbic origin of cirrhosis in general, which is now regarded as the result of mild inflammatory changes, suggests that a similar condition might operate in infantile cirrhosis, especially as the condition called Hanot’s cirrhosis, which is an almost analogous disease occurring in young adults, is being regarded as the result of angiocholitis. The occurrence of biliary cirrhosis apart from obstruction or inflammatory changes in the bile ducts is improbable and
the same argument would hold in infantile cirrhosis. The most reasonable idea appears to be that the condition is the result of a mild angiocholitis, an ascending infection from the duodenum, the infective agent causing a mild duodenitis. This would explain the onset with gastro-intestinal features and the probable association with the mother's milk. The histological resemblance to syphilitic cirrhosis suggests, however, that it may be due to a poison carried by the umbilical vein as in congenital syphilis, an umbilical vein cirrhosis.

The features are those of a chronic, insidious, progressive cirrhosis with enlargement of the liver, with early jaundice, gastro-intestinal disturbances and a low febrile course ending in ascites often terminating fatally.

The morbid pathology of the disease has been carefully described by Gibbons in the 'Scientific Memoirs.' The liver is uniformly enlarged, dark brown in colour, the surface having a moróçco-leather appearance from the fine cirrhosis that is present. On section, thin fibrous bands can be made out in between the lobules resulting in increased consistence of the liver. Histologically, the appearance suggests a pericellular cirrhosis, since the fibrous tissue is found between the

**FIG. 47.**

Infantile cirrhosis (x 50) showing the irregular monolobular arrangement of fibrous tissue.
individual cells. This, however, is not so uniform as in congenital syphilis since there is a tendency to a more monolobular distribution, so that the cirrhosis is really a combination of monolobular and pericellular types. Periportal fibrous formation is not marked. The fibrous tissue, at first young and cellular and consisting of small round cells and fibroblasts, in the later stages becomes converted into the adult type of dense fibrous strands giving rise to the characteristic appearance on the surface. New bile duct formation occurs as in

all forms of cirrhosis and proliferating bile canaliculi are noticeable features. Ascites is common. The spleen may show slight enlargement. Catarrhal changes may be met with in the gastro-intestinal tract, especially in the small intestine. Externally, jaundice may be a marked feature and oedema of the legs may be present.

**INGUINAL GRANULOMA.**

This is a condition affecting particularly the inguinal region and external genitalia, characterized by the formation
of a granulomatous ulcer on the skin with a tendency to cicatrization.

The disease is found in many tropical countries, such as parts of India and China. It occurs also in South America and parts of Australia and Africa.

The etiological agent has not been definitely determined. Spirochætes have been found, but they are probably

![Image of Inguinal Granuloma](image)

**Fig. 49.**

Inguinal granuloma ($\times$ 225) showing the commencement of the growth in the corium and the atrophy of the surface epithelium.

saprophytic organisms similar to *S. refringens* met with commonly in ulcerative lesions. A bacterium, called *Calymmatobacterium granulomatis*, was described by Donovan; but the etiological relationship is not proved. This organism is an oval or fusiform coco-bacillus about 1.5 to 2μ in length and is found in clusters inside the mononuclear cells. The association of this bacillus with this condition seems
to be rather close, but experimental inoculations have been so far negative.

The lesion first commences in the groin or in the genitalia, and is definitely associated with sexual contact. At first nodular, the surface gradually becomes thin and moist and breaks down, leaving a raised, irregular, granulomatous mass which extends in circumference, spread also occurring by contact on the opposite side. The process is extremely chronic and lasts years so that with peripheral extension, central healing and cicatrization may be met with. The skin in the neighbourhood may be thickened and corrugated. The disease has a tendency to spread, involving successive parts of the genitalia and even involving the perineum and rectum. The lymphatics leading from the mass are involved and a lymphadenitis of the inguinal glands is usual. Owing to extensive cicatrization and ulceration, the urinary passages may be involved and fistulae and stricture may result, followed by ascending infections of the urinary tract. Histologically, in the earlier stages, there is a marked down-growth of papillae, so that the earlier changes are found in the connective tissue of the corium in between the papillae. The epithelium is thus raised up as a nodule. The change in the corium consists of an infiltration, with lymphoid cells, plasma cells and endothelial cells. The epidermis over these areas show at first deficient keratinisation, then gradually swells up and undergoes degeneration, resulting in softening and ulceration. The chronic inflammatory reaction spreads down into the deeper tissues, so that in the later stages the structure is that of a chronic granulomatous ulcer consisting predominantly of plasma cells, lymphoid cells, capillary buds, endothelial cells and fibroblasts. Polymorphonuclear cells are also met with probably from secondary infection. Giant cell formation is not a feature. In the deeper tissues there are clusters of plasma cells and round cells around the small arteries, an appearance that is practically indistinguishable from syphilitic inflammation. The endothelial cells lining the vessels may also show proliferation.
CHAPTER XII.

TYPES OF HELMINTHIC INFESTATIONS: 
TREMATODE INFESTATIONS.

SCHISTOSOMIASIS.

THIS is a condition resulting from the infestation of man by a group of parasitic trematodes belonging to the genus Schistosoma.

There are three important varieties, Schistosomum haematobium which infests the urinary system of man, Schistosomum mansoni which inhabits the intestine, and Schistosomum japonicum which causes widespread changes, most marked in the liver and spleen.

Urinary schistosomiasis.—A chronic disease endemic in Egypt and the coasts of Africa, this is characterized by hæmaturia and cystitis due to papillomatous growths in the urinary tract, from infestation of the pelvic veins with the trematode, Schistosomum haematobium.

The parasite is a flat trematode, the male and female being generally found together, the slender filiform female being enclosed in a canal formed by the enfolding of the flat leaf-like body of the male. The male is about 1 to 1.5 cm. in length and 1 mm. broad, and is a flat leaf-like worm with its body curled upon itself. The narrow anterior end carries two suckers, a terminal oral sucker carrying the mouth, and a larger stalked ventral sucker which is prehensile in function and is situated on one side just a little below the oral sucker. The posterior end is attenuated and rounded as in most trematodes. In the genus Schistosomum the body, which is widest at its middle, is curled on itself to form a gynæcophoric canal, so called since it serves for enclosing the female. The
outer surface of the body is roughly tuberculated in *S. haematobium*. Two thin longitudinal canals at either side form the excretory vessels, and the excretory pore is dorsal and terminal. The alimentary canal consists of a short oesophagus commencing at the oral sucker and bifurcating opposite the ventral sucker to form two intestinal cæca, which pass backwards on either side and unite half-way down to a single tube which ends at the posterior extremity. The testes are four or five in number and lie dorsal to the ventral sucker. From the testes a number of vasa efferentia unite to form the vesiculae seminalis which opens by a short duct at the genital pore just below the ventral sucker. There are two oesophageal ganglia which encircle the oesophagus and from which two nerve cords proceed down, one ventral and the other dorsal.

The female is long and filiform, about 2 cm. in length and 0·25 mm. in breadth and is generally found with its middle half inside the canal of the male, while its anterior and posterior ends are projecting free. There are a number of anal papillæ at the posterior end. The suckers are similar, but smaller, the oral being slightly the larger. At the commencement of the posterior half of the worm, an elongated solid organ can

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*Fig. 50.* Schistosomum *haematobium.*
*Fig. 51.* Schistosomum *japonicum.*
be made out to be the ovary, from which an oviduct passes forward to where the vitelline ducts open into it. The posterior part of the worm is filled by the yolk glands, while the uterus, an elongated tube, extends forward from the ovary to open at the genital pore just behind the ventral sucker.

The ova are oval and show a distinct terminal spine. They are yellowish in colour and measure 160μ by 60μ. Inside the shell is an embryo or miracidium surrounded by a vitelline membrane.

The paired worms, which inhabit the larger branches of the mesenteric vein near the bladder, make their way against the blood stream as far up as possible, when the female, for oviposition, leaves the male and travels still further up the vein till the lumen is so narrowed that further progress is impossible. The ova are then deposited with spines in the direction of the blood current, so that when the worm withdraws itself, the spines are driven through the thin walls, and the ova escape by penetrating through the mucosa causing a certain amount of haemorrhage into the bladder. In cases where the ova do not escape into the bladder, the miracidium dies, the shell shrinks and undergoes calcification. From the urine, the ova escape into the water where owing to diminished osmotic tension the shell bursts and liberates the now ciliated miracidium which swims about actively in the water. In structure it is oblong and, with the exception of a terminal anterior blunt extremity, is completely covered with cilia. There is a primitive alimentary canal surrounding which are a number of embryonic germ cells and posteriorly are excretory tubules surrounded by large flame-shaped cells which are excretory in function. The active miracidia make their way by penetration into the antennae of various species of fresh water snails of the genus Bulinus, or Physopsis, where the next cycle of development takes place. Here they shed their cilia and encyst, forming sporocysts and daughter sporocysts which make their way into the liver and hermaphrodite gland, where they develop into tailed embryos called cercaridæ. These have an ovoid body and a bifid tail.
The complete development takes place in six weeks. The cercariae then burst through the cyst wall and make their way into the water.

Each cercaria has a well defined oral sucker with a number of papillae. The ventral sucker is small and inconspicuous and lies near the posterior end of the body. The outer surface is covered by fine spines. There are six flame cells in the body forming the excretory system. The tail is tapering and forked at the extremity. These cercariae are just visible to the naked eye and move about with the tail in front. They attach themselves to the skin of the host, usually man, monkeys or rodents. They penetrate the skin, gradually increase in size, enter the venous system possibly by the bloodstream or by the lymphatics and attain maturity in the portal vein in about six weeks.

Pathological changes produced in the tissues of the host.—The most important and characteristic changes occur in the bladder, where the earliest lesions noticed are small papular elevations surrounded by zones of hyperaemia. These are found on the posterior wall and are due to the deposition of ova in the bladder wall. Sometimes, there is a uniform thickening of the mucous membrane, while in other instances the nodules may be confined to the trigone. In any case, there is increased vascularity and hyperplasia of the mucosa. The ova make their way by eroding through the centre of the nodules, causing an intense local reaction and a general catarrh of the mucosa. In chronic cases, the entire mucous membrane may have a granular appearance and show ‘sandy patches’ from the presence of numerous calcified ova in the submucosa. Later, this may undergo so much thickening that the bladder may be converted into an almost solid organ. In other cases, the bladder may show villous, branching, papillomatous masses caused by the irritation produced by the ova and even a true malignant condition may supervene from chronic irritation.

Histologically, the reaction is the same as met with in parasitic infestations, namely, a local cluster of eosinophiles
and small round cells. The ova induce a non-suppurative inflammatory reaction. The ulceration is believed to be due to secondary infection. There is no breach of surface. The ova make their way to the surface between the glandular crypts causing marked inflammatory reaction. At first the ova are surrounded by fibroblasts and foreign body giant cells forming a granuloma. Sometimes small abscesses form in the submucosa round calcified ova, or worms. These are at first not septic, but later on become secondarily infected. Even then, eosinophile infiltrations may be marked though polymorphs are quite numerous.

Small mucoid retention cysts are met with in the ureter, sometimes causing obstruction to the lumen. Besides these, a diffuse infiltration of the mucosa or more localized 'sandy patches,' similar to the changes found in the bladder, may be met with. This is most marked near the lower end.

In the kidney, small aseptic abscesses surrounding ova may occasionally be met with in schistosomum infestations, showing, histologically, clusters of eosinophiles and mononuclear cells. As result of obstruction to the lumen of the ureter, dilatation of the ureter followed by hydronephrosis may occur, and this may lead to renal insufficiency. Septic infection may supervene and pyelitis and pyonephrosis with extensive destruction of kidney tissue may cause death.

The prostate and urethra may be involved causing perirenal fistula. Lymphatic obstruction may follow and may cause an elephantoid condition of the scrotum and perineum. Edema and elephantoid thickening of the penis may occur, and in the female papillomatous nodules and ulceration may occur in the vagina and cervix. Calculi formation may result, the ova forming nuclei for the stones. The rectum may be involved in the process, and ulceration may sometimes occur apart from infections with S. mansoni. In heavily infested individuals, the ova may be found in all the internal organs, such as the lungs and liver and even in the brain and spinal cord.
TREMATODE INFESTATIONS.

The blood generally shows a well defined eosinophilia as in most parasitic infestations. The urine shows microscopically the terminal spined ova besides large numbers of red blood cells from haemorrhage. The ova, if few, are found in the last few drops of urine.

Immunity reactions occur in schistosomiasis. Fairley has devised a complement deviation reaction on the lines of the Bordet-Gengou reaction, by using an extract of the liver of infected Planorbis as the antigen. This reaction is successful in 90 per cent of cases. An intradermal reaction has also been recently described. The cuti reaction is positive in the whole group.

**Intestinal schistosomiasis.**—This is a chronic disease caused by the infestation of the mesenteric veins by *Schistosomum mansoni* causing dysenteric symptoms with the passage of ova in the faeces. Sometimes a fine cirrhosis of the liver is present.

The parasite resembles *S. hæmatobium* in its general appearance, the essential difference being in the shape of the ova which have a lateral, instead of a terminal spine. The male is slightly smaller than that of *S. hæmatobium*, and its cuticle is more roughly tuberculated. Minor differences in structure are that the intestinal caeca unite together in the anterior half to form one long tube, that the ovary in the female is in the anterior half so that the uterus is much reduced in size and contains only two or three ova, and that the male has 8 to 9 testes. The lateral spined ova are generally coloured dark by the faeces. They measure 140 to 150µ by 60 to 70µ. The intermediate host is not a snail, but a mollusc of the genus Planorbis. The cercariae are shorter and thinner and differ slightly in structure. The manner in which infection occurs is the same in both species, but the normal site of election of the worms is the mesenteric vein instead of the pelvic veins. The branches of the portal vein may also harbour the parasites, and so the lesions met with are in the large intestine and the liver, while those of the *S. hæmatobium* are in the bladder.
The pathological lesions met with are variable depending on the site of election of the parasites. Thus in some cases the lesions are confined to the intestine while in others visceral manifestations are more important.

The lesions met with in the large intestine are of five types. There is a diffuse infiltration of the colon with ova giving rise to a diffuse thickening and where the ova are calcified a 'sandy patch' appearance may be present. The whole mucous membrane looks thickened, yellowish in colour and in places shows hæmorrhagic foci besides a diffuse catarrh. The catarrh and hæmorrhages give rise to the dysenteric symptoms. The large intestine may be studded with adeno-papillomata, most marked in the rectum, giving rise to a condition of colitis polyposa. These adenomatous masses may prolapse through the anus appearing like hæmorrhoids. Pericolic nodules may sometimes be met with, similar to the condition in experimentally infected monkeys. The polyloid masses may result in intussusception. The papillomatous masses may drop off and leave multiple, oval, punched-out ulcers resembling dysenteric ulcers caused by entamæbæ.

Microscopically, there is a diffuse infiltration of the submucosa with clusters of ova surrounded by masses of eosinophile cells. The type of inflammatory reaction is a chronic proliferative type characterized by giant cells, fibroblasts, endothelial cells and eosinophiles forming a granuloma. The presence of the worm itself produces no inflammatory changes in the vessel walls. These are the result of the deposition of ova in the tissues. In the papillomatous forms there is extensive proliferation of the mucosal glands, besides a general thickening of the mucous membrane.

In the liver, the earliest lesions give rise to a slight enlargement from commencing periportal infiltration round numerous ova, which are found in the portal vein and the periportal tissues. This is followed, in the later stages, by a curious form of 'pipe-stem' cirrhosis, apparently due to the distribution of fibrous tissue around the larger branches of the
portal vein. There is an associated perihepatitis without much shrinkage. Irregular scars may be present on the capsule, but a hobnailed appearance is not met with. On section, there are irregular bands of fibrous tissue distributed round the medium-sized branches of the portal vein dividing up the liver into lobules. The causation of the cirrhosis is believed to be the mechanical irritation induced by the ova and not toxic absorption. Microscopically, the fibrous tissue is seen to be distributed round innumerable lateral spined ova around the portal tracts. It is at first a young, cellular, vascular tissue, but later becomes dense and avascular. In the early stages nodules of young cellular tissue are found round small areas of focal necrosis surrounding the ova. The cell reaction is eosinophilic in the early stages. In the fibrous bands, new bile-duct formation is a prominent feature as in all types of cirrhosis. Clusters of granules of dark pigment in the Kupffer cells are a prominent feature.

The mesenteric glands are usually enlarged and fibrotic, and marked splenic enlargement, possibly from toxic absorption, is also a feature of the visceral types. The spleen is in a condition of chronic hyperplasia. Pigment may be found in the endothelial cells of the pulp. Rarely a pneumatic condition of the lungs from deposition of the ova may be met with.

Immune substances occur in the blood. A precipitin reaction has recently been devised for intestinal schistosomiasis.

**Asiatic Schistosomiasis.**—A chronic condition met with in parts of Asia, particularly Japan, China and the Philippines, due to infestation of man with *S. japonicum* which causes widespread lesions in the liver, the spleen and the intestines often resulting in ascites.

The mode of entrance of the parasite to the human host is similar, the cercariae penetrating the skin of the hosts, mostly paddy cultivators, since the intermediate host, the snail, *Blandfordia nosophora*, is found in the fields. The adult forms of the parasite live in the branches of the mesenteric veins and the portal vein. The parasites themselves are
SCHISTOSOMIASIS.

slightly smaller in size than *S. haematobium*, the male being 9 mm. and the female 12 mm. in length, while they are slightly thicker in their middle. The ventral sucker is funnel-shaped and short, while the outer cuticle is smooth and not tuberculated. The gynæcephoric canal is well formed, the oesophagus has two lateral bulbs and the intestinal cæca unite at the posterior end. There are six to eight testes. The uterus of the female is a long tube and may contain 50 to 300 ova. The ova are small, measure 75μ by 45μ and have a more rounded oval shell than those of the other species. There is a blunt rudimentary spine, a mere cuticular prominence which is laterally placed. The miracidia are smaller in size and the intermediary host is a small snail, *Blandfordia nosophora*. The fork-tailed cercariae are smaller in size and have a well developed oral sucker.

The pathology of the lesions differ somewhat owing to the widespread nature of the changes and the toxicity of the worm. The cercariae produce a local papular eruption at the point of entry, sometimes, a foreign body reaction. From the tissues, they get into the circulation, and curiously enough, make their way into the lung as with many nematodes. From the lungs they burrow their way through the mediastinum and diaphragm into the liver, in the portal tracts of which development takes place till the worms attain maturity. They then travel down in pairs to the mesenteric veins, against the blood stream until a small venule gets distended by the worms. A large number of ova are then deposited by the female, so that the venule ruptures, after which the paired worms withdraw. The ova make their way through the mucosa into the intestine and are expelled in the faeces. Many ova are driven up by the blood stream into the portal tracts of the liver and there deposited in the periportal spaces. Toxic features, from absorption of toxic material formed by the worms, are very common in this type of schistosomiasis.

The liver shows in the earlier stages focal areas of necrosis with collections of round cells. Later, connective tissue proliferation occurs, dividing up the liver tissue into irregular
lobules giving rise to typical multilobular cirrhosis with, in addition, clusters of ova in the fibrous tissue. Pigment granules are also met with in the Kupffer cells. In the intestine, there is a diffuse infiltration of the submucosa followed by superficial necrosis.

The retroperitoneal glands show chronic lymphadenitis from the presence of ova. Splenic enlargement is the rule. There is a chronic hyperplasia from toxic absorption and possibly from the portal cirrhosis. Embolic lesions may result from the entrance of ova into the circulation. Thickening of the pia-arachnoid may cause cerebral symptoms. Ascites occurs generally from cirrhosis of the liver and chronic peritonitis. The bladder is unaffected.

Mixed schistosomiasis.—In Egypt, urinary infestations with *S. hematobium* and intestinal infestations with *S. mansoni* may coexist, the terminal spined ova of the former being found in the urine, while the lateral spined ova of the latter are passed in the motions. The pathological lesions met with show a complicated picture.

**Clonorchiasis.**

Infestations of the liver and sometimes of the pancreas are met with in man with the small trematode *Clonorchis sinensis*.

The disease occurs in parts of Japan and China and rarely in India. The parasite, *Clonorchis sinensis*, is met with in the bile ducts of man as a small fluke with a smooth external surface, about 10 to 20 mm. in length and about 4 mm. wide. It is narrow and pointed at its anterior end and gradually tapering at its posterior. It has a brownish-red pigmented body. There is a terminal oral sucker which serves as the mouth, while the acetabulum, or ventral sucker, which is prehensile in function, is situated somewhat below at the commencement of the lower three-fourths of the body. There is a bilobate ovary in the middle line, and two branched testes are placed one behind the other. The vitelline glands are small and not well developed and situated on either side of
the body. The egg is small, oval, about 30μ in size, and on one side, which is the narrower, is a lid or operculum which is lifted when the embryo escapes. Inside the egg is a ciliated embryo called a miracidium. The normal host of this parasite appears to be the dog or cat and human infection is only an accident.

Development, outside the body, occurs in a mollusc, *Bythinia striatula*, which is the intermediary host. Inside the body of this mollusc, cystic structures called sporocysts are formed, from which larval cercariae escape into the water, undergo another encystment in another intermediary host, very often some fresh water fish, from which the infection is transmitted to man. In the duodenum of man, the small flukes make their way into the bile ducts and undergo development.

The pathological lesions produced by the parasites are chiefly in the liver, where they cause marked dilatation of the walls of the bile ducts, and form many irregular ‘burrows’ or channels into the surrounding tissues. Sometimes large cavities are formed. The liver may contain a number of these flukes. The organ is much enlarged, the enlargement
being due to the dilatation of the ducts and the fibrous changes induced around the walls. The liver cells in the neighbourhood may undergo atrophy, and in the later stages, the whole organ may be shrunken from fibrosis. The parasite may, in a similar manner, cause dilatation of the pancreatic duct resulting in an enlargement of the organ and fibrotic changes. In some cases the flukes are found in the intestine. Marked enlargement of the spleen, probably from toxic absorption, is usual.

The peritoneal cavity contains fluid in the later stages, both from portal obstruction and from the chronic peritonitis set up. Externally, jaundice is a marked feature, apart from the anaemia and sometimes the general anasarca, that may be met with.

**Intestinal Distomiasis.**

The most important trematode parasite that is met with in the intestine is *Fasciolopsis buski* also called *Distoma buski.*

The infestation is widely distributed in the tropics but is most common in China and parts of India. The hog appears to be the natural reservoir of infection. The parasite is much more commonly met with in man than *Fasciola hepatica* the common and cosmopolitan fluke that infests the liver and biliary passages of sheep, causing sheep-rot.

The fluke is about 30 mm. in length, about 12 mm. wide at its middle, and has gradually tapering extremities so as to resemble in appearance a small leaf. It has a fleshy colour when alive, and is variable in size depending on the contractility of the body. The oral sucker is terminal while the acetabulum, or ventral sucker, is slightly below. The alimentary canal is simple, and consists of two intestinal cæca which unite together, at the anterior end, to form a muscular pharynx. There are two testes, one behind the other, showing dichotomous branching. The small ovary, situated at about the centre, is connected to a centrally placed shell gland into which the numerous vitelline glands, which are situated on either side along the free borders of the parasite, open.
the shell gland commences a tortuous tube, the uterus, which is situated on the anterior half of the body. The genital opening is close to the oral sucker. The eggs have each a thin transparent shell measuring about 30μ by 80μ, and are operculated and contain a number of yolk cells besides an ovum.

According to Clayton Lane, the full life history has not been worked out. A cercarial stage possibly exists in some fresh-water snails.

![Diagram of the life cycle of Fasciolopsis buski](image)

**Fig. 53. Fasciolopsis buski.**

The pathological features are those of intestinal catarrh, the presence of the parasite causing diarrhoea. Anaemia is another feature that is met with. In the later stages, a condition of cachexia results from cardiac and renal involvement. Ascitis and oedema of the legs may occur.

**Paragonimiasis.**

This is an infestation with the parasitic trematode, *Paragonimus ringeri*, most often of the respiratory tract of man.

The disease is very common in Japan, Korea, and the Philippines. The parasite is a trematode, about 8 mm. in
length, almost oval in shape, with a thick almost rounded body somewhat like a lens. The cuticle is covered with spines. The oral sucker is terminal and situated at the apex of a conical projection which is at the anterior end. There is a large acetabulum, or ventral sucker, which serves for attachment, situated at about the middle of the body. As with most flukes, the parasite is hermaphrodite, and contains the two branched testes posterior to the uterus, which is on one side, while the ovary is on the opposite side. The genital pore opens just below the acetabulum. The intestine is simple and consists of two blind intestinal caeca which unite in front and open into the pharynx. The yolk glands, or vitellaria, are well developed and extend on either side so as to cover the intestines. The ova are oval, about 60 to 70µ in size, and operculated.

The habitat of the fluke is the tissue of the lungs, though occasionally, other situations are affected. The ova are expelled in the sputum, and in water, undergo development so that in each a ciliated miracidium is formed. This escapes and enters the body cavity of certain molluscs of the species Meliana where it undergoes encystment and forms cercariae, which, again, enter the body of certain freshwater crabs, Potamen dehani, in the liver of which they undergo encystment. The second intermediary host may occasionally be a cray-fish. From these hosts the parasites find their way into the intestine of man when the crabs are eaten raw or partly cooked. From the intestine, the young flukes work their way through the diaphragm, enter the pleural cavity and lungs, where they attain maturity.

The lesions met with are mostly in the lung, where the parasite forms 'burrows,' or irregular tracts surrounded by thickened and fibrosed lung tissue. Sometimes cystic cavities
of variable size and of a slate-grey colour are met with. The flukes may be found inside the burrows as well as the cavities, in the mucoid and cellular debris, which have a characteristic rusty-brown appearance. The small blood vessels are eroded, and this accounts for the haemoptysis which forms the most important clinical feature. The cavities may be filled with blood and granular debris, in which the ova are found in numbers. They may communicate with bronchi and may really form a type of bronchiectasis. Microscopically, the walls of the cavities may be infiltrated with ova. The cells that are present show a predominance of eosinophiles and mast cells. Pneumonic consolidation may sometimes be met with as a complication. In other types fibrosis of the lung may follow. Abscess formation may occur.

Similar cystic lesions may be met with in the brain, and sometimes the lesions may be met with in the liver, spleen and intestines, which are all affected. Intestinal infection is responsible for a number of features. Extensive ulcerative lesions resembling amœbic ulcers may be met with, and the ova are passed out in the faeces. Chronic lymphadenitis may cause enlargement of the glands. Chronic epididymitis and prostatic enlargement has been described. Externally chronic indolent cicatrizing ulcers may be met with.

The sputum is usually rusty and viscid and contains numerous characteristic pale yellow, oval, large, operculated ova.
CHAPTER XIII.

TYPES OF HELMINTHIC INFESTATIONS: CESTODE INFESTATIONS.

HYMENOLEPIASIS.

This is a type of intestinal infestation with a cestode parasite, the dwarf tapeworm, *Hymenolepis nana*.

The parasite is a cosmopolitan cestode in the tropics, found most frequently in children. As with all cestodes, the worm has a head, a neck, and a number of segments called proglottides, the whole forming a colony or strobilus. The head, which is called the scolex, has a hemispherical projection called a rostellum with a number of hooklets, about 25 in number, arranged in a single row all round. There are four suckers, or cup-shaped depressions, arranged round the head. These are for the purpose of absorption of nutritive fluid from the mucous membrane, while the hooklets anchor the parasite to the intestine. Neither mouth nor alimentary canal is present, as in all cestodes. There are 100 to 200 segments or proglottides, the more mature of which are the most terminal while the immature ones are small and nearer the head. Longitudinal excretory canals run on either side of each proglottis which also contains flame-shaped excretory cells. Each proglottis is a hermaphrodite unit containing both the testes and the ovaries. The testes are three in number and consist of a number of small tubes which unite to form a vas deferens opening on one side, while the paired ovaries unite to form a single tube, the oviduct, which passes on to a median tube, the uterus, which contains lateral branches. The genital opening is common and is situated on one side of the proglottis near the anterior end. The proglottides are short, but broad throughout the posterior
ones being larger in size. The eggs are oval, about 40 µ in size, and have two distinct shells, one outer being thin and large, while the inner, which is much smaller, has two small projections at each pole. Inside this is the six-hooked or hexacanth embryo. The eggs are extremely transparent and form characteristic structures.
The habitat of the worm is the small intestine, where the parasite undergoes maturity. Fertilization occurs by one segment fertilizing a near neighbour. The ripe segments are cast off and undergo disintegration in the faeces, so that the eggs are set free in the faeces. The exact life cycle is not clear, but on analogy with the hymenolepis of the rat it is believed that when the eggs are swallowed the larva are liberated and enter the villi of the small intestine, where they assume an elongated cystic phase, the cercocystis. The cysts then burst through, the immature worms are liberated into the intestine, where they attach themselves to the mucosa and attain maturity. The peculiarity of this life cycle is that this is the only type of cestode infestation, where no intermediate host is necessary for the development of the larval stage, both stages being probably passed in the intestine of man.

The lesions depend on the presence of large numbers of parasites which usually occurs. The presence of these parasites induces a catarrhal enteritis with colicky pain and features of gastro-intestinal disturbance. Grassi has described areas of hæmorrhage, congestion, and excessive secretion of mucus, in experimental infestations in rats. In human cases, especially in children, toxic absorption is marked and results in various nervous phenomena.

**Intestinal Tæniasis.**

Under this term are included intestinal infestations of man with the common tapeworms or cestodes, *Tænia solium* and *Tænia saginata*.

*T. solium* is the tapeworm that is generally present all over the world since the intermediate host is the pig. It is not found among Mohammedans. The worm is generally 2 to 3 meters in length, has a well developed head, a neck and a number of proglottides forming a strobilus or colony. The head, which is extremely small, has a well developed pigmented rostellum with a double row of hooklets 25 to 50 in number. There are four round suckers. The mature proglottides are
twice as long as they are broad, each has a marginal genital pore with thick lips, while the uterus has seven to ten lateral branches. The eggs are oval, about 30 to 50μ in size and have two coverings, an inner radially striated membrane, and an outer thin shell. Inside the egg is a hexacanth embryo.

![Diagrammatic structure of a proglottis of a tapeworm.](image)  

Ex. cl., excretory canal; T., testes; Ut., uterus; Ov., ovary; S.G., shell gland; Vt.G. vitelline gland; Vt.D., vitelline duct; R.S., receptaculum seminis; Va., vagina; G.P., genital pore; C., cirrus. V.D., vas deferens; N.C. nerve cords.  

(The partly after Rivas.)

The habitat of the worm is the small intestine of man where it attaches itself, by means of its hooklets, to the mucous membrane, absorbs nourishment and attains maturity. The fertilized proglottides are passed out in the faeces, where they
disintegrate and liberate the eggs which are ingested by the pig. Inside the body of the pig, the larvæ are liberated, make their way through the wall of the intestine into the blood stream and are carried to the muscles, where they lose their hooks and form cysts called cysticerci, through the walls of which in each the head of the larva, the scolex, invaginates itself. These cysticerci which are called 'cysticerci cellulosi,' are met with as small glistening white bodies in the muscles of the pig, 'measly pork.' Rarely man himself may act as the intermediary host and cysticerci have been found in the muscles of the chest, tongue, eye, or sometimes in the internal viscera. Rarely the brain may be involved. When 'measly pork' is eaten by man, the cysticercus is dissolved by the gastric juice, the scolex evaginates itself and is set free in the intestine where it attaches itself to the wall and the whole life cycle is repeated.

The lesions met with are mostly intestinal, where chronic catarrh may result from the presence of the worm. Anæmia is sometimes met with. In those rare cases of human infestation during the larval stage, cysticerci have been met with in different organs. They are small cysts varying in size from a pin's head to a pea. Microscopically they show a laminated wall of chitin with an invaginated scolex on one side carrying hooklets.

**Hydatid Disease.**

This is a condition where man becomes the intermediary host of a type of cestode, *Echinococcus granulosus*, so that the larval stage is passed in man, resulting in the formation of parasitic cysts in different parts of the body.

The disease is met with most commonly in Australia, the Argentine Republic and New Zealand, while occasionally cases occur in many tropical and subtropical countries. The infection occurs in man mostly through drinking water contaminated with the excreta of dogs which harbour the adult forms of the parasites. Close association with dogs also favours the incidence, since direct transference of infection
may occur from licking hands and feet. Vegetables may be infected. Wolves and jackals may harbour the adult worm. Besides man, cattle and sheep may serve as intermediary host.

The parasite, *Echinococcus granulosus*, is a small tapeworm with a head, a neck and only 3 or 4 segments of which the last one is sexually mature and generally full of ova. The whole worm measures about 3 to 4 mm. in length. The small scolex has a rostellum with two rows of hooklets and there are 4 suckers. The ova are ovoid in shape and each contains a six-hooked embryo. When swallowed the shell is digested by the gastric juice after which the larva penetrates the wall of the intestine, enters the branches of the portal vein and is carried to the liver where encystment occurs in a large proportion of cases. Occasionally, other organs may be involved. It forms a bladder-like mass, the hydatid cyst, in which the invaginated scolex can be made out. The cyst increases in size very slowly, development taking often months or years before it becomes clinically noticeable. Due to pressure and irritation a fibrous outer wall is developed from the surrounding tissue. Inside this wall of fibrous tissue, the cyst proper itself consists of two walls, an outer consisting of laminated chitinous material called the ectocyst, and an inner wall called the endocyst made up of the true germinal layer, from which a number of scolices can be seen to project inwards. Each consists of an invaginated head, neck and hooklets enclosed in a small bladder. More often, these scolices arise from endogenous papillary processes called brood-capsules.

![Fig. 57. Echinococcus granulosus.](image)
has pointed out that the brood-capsules arise just as the scolices, by a multiplication of the germinal epithelium to form a nodule, which becomes vacuolated to form a small vesicle which increases in size and becomes pedunculated and is sometimes set free. The scolices develop inside the brood-capsules as small buds which gradually undergo differentiation and develop rostella and hooklets, while each head becomes invaginated. Apart from this, however, the germinal layer may form small secondary cysts, called daughter cysts, in which also scolices may arise. The daughter cysts are supposed to arise when the mother membranes—the walls of the original cyst—undergo degeneration from pressure of the surrounding tissue. The cyst thus formed contains clear watery fluid in which the daughter cysts are afloat. This fluid contains innumerable such scolices besides a trace of glucose, chlorides and calcium salts. It contains no
It is highly toxic when injected into the tissues and is responsible for the severe symptoms that occur when rupture of the cyst takes place. Recently it has been put forward that these toxic symptoms are really anaphylactoid in nature. Apart from the ordinary endogenous type of development that has been described, another type of development may occur. This is an exogenous type due to the protrusion of the germinal layer through the outer walls to form daughter cysts, in the surrounding tissue, which later break away and form the starting point of similar processes—

![Image of hydatid fluid showing scolices in the invaginated head and hooklets inside the small bladder-like cysts.]

what has been called by Barnett a malignant transformation. The exogenous development may sometimes result in a multilocular cyst from the degeneration of the surrounding tissue. However formed, the cysts may occasionally terminate by absorption of fluid, degeneration and death of the germinal epithelium with calcification of the outer fibrous layer. Others however, increase in size and burst into surrounding tissue and cause death from severe shock; or the scolices may be implanted into the peritoneum and
form the starting point of numerous other cysts, secondary echinococcosis.

![Diagram](image)

**FIG. 60.**

I. Schema of a hydatid cyst showing development of brood-capsules with scolices.
II. Hydatid cyst showing development of daughter cysts.
III. Development of scolices from the germinal layer showing invagination.
   (Partly after Dew.)

Rupture into a vein and embolism has been described and sudden death may occur, a metastatic echinococcosis.
CHAPTER XIV.

TYPES OF HELMINTHIC INFESTATIONS: NEMATODE INFESTATIONS.

FILARIASIS.

Under this term are included various disease conditions caused by nematode parasites which invade the tissues and live in the lymphatics. The embryos, called microfilariae, are often met with in the blood where they apparently live for long periods.

The filaria that is of great pathological importance is *Filaria bancrofti* which causes a whole series of morbid conditions. The embryos of this species are called *Microfilaria bancrofti*. Other microfilariae that are met with in the blood are *M. loa*, *M. perstans*, *M. ozzardi*. The adult filariae are thin thread-like worms, the male measuring about 40 mm. in length and only 0.1 mm. in thickness, while the female is about double the length and thickness of the male. The worms have each a simple unarmed head with two rows of circumoral papillae. The cuticle is transversely striated. The tail of the male is twisted forward in a sharp curve and possesses two unequal spicules and a variable number of caudal papillae. The tail of the female is blunt and rounded. The whole of the body cavity of the female is filled by the uterine tubes, the vagina opening near the anterior extremity. The worm is viviparous, the embryo being contained in a thin membrane which gradually elongates to form a sheath for the microfilaria. The adult worms are found, if carefully looked for, in intricately coiled masses inside the lymphatic glands, in the deep lymphatics, in lymphatic cysts, and in filarial abscesses.
The cycle in man.—Invasion of the human host occurs by the bite of the *Aedes* or the Culex mosquito *Aedes varigatus*, or *Culex fatigans*. The larvæ make their way from the proboscis of the mosquito, penetrate the skin of the host in the neighbourhood of the puncture, and make their way through the lymphatics of the skin to the regional lymphatic nodes. Development is difficult until the larvæ can make their way into the larger lymphatics where they increase in size, and mature into adult types. The adult worms can be found in the lymphatic glands at this stage. The female gets fertilized in the larger lymphatics, and sets free a stream of embryos which make their way into the circulation through the thoracic duct. In cases where the thoracic duct or its main branches, or the regional nodes containing the worms

![Diagram of nematodes](image-url)

*Fig. 61.*

1. Microfilaria bancrofti.
2. Microfilaria loa.

(Drawn from microphotographs, × 600.)
are blocked by inflammatory changes set up by the worms or their products, the microfilariae cannot make their way into the general circulation and are not found in the blood. Such lymphatic obstruction, however, is not found in every case of filarial disease and microfilariae are generally found in numbers in the blood in infected individuals who may not, all, clinically show any other evidence of the disease. The worm lives in the large lymphatics of the pelvis, inguinal, or femoral regions and sends forth a constant stream of microfilariae into the blood.

Microfilaria bancrofti as it is found in the blood, is a small wriggling worm, about 300μ long and 7μ in width, enclosed in a thin transparent envelope which prevents any progressive movement. An anterior spicule can be demonstrated in stained specimens, and this serves for the purpose of penetration and rupture of the sheath when the microfilaria is ingested by its intermediate host, the mosquito. As seen under the microscope, this microfilaria has a tendency to arrange itself in rounded curves unlike the allied form, M. loa, which is arranged in more irregular waves. Stained specimens show the parasites as having a more or less rounded anterior extremity and a somewhat pointed tail. The protoplasm is uniformly granular, except for a tail spot and a large V spot, respectively near the caudal and cephalic third of the parasite. Identification of species depends on the situation of these spots and on the granularity of the cephalic and caudal extremity. A circular mouth-like structure covers the cephalic end. The outer coat is a musculo-cutaneous layer which is transversely striated. The granularity of the parasite is due to the presence of a column of cells which extends throughout the length of the worm. Near the middle, the granules are collected together to form an elongated organ. The V spot at the anterior third would appear to be an excretory vesicle, while the tail spot corresponds to the cloaca and the genital cells. The column of cells does not extend right down to the tail in this species, unlike M. loa. The sheath of the microfilaria is considerably
longer than the worm itself, but is almost of the same width. As with the malarial parasite, infection of the mosquito is by way of ingested blood from an infected person, and it would appear that the microfilariae found in the blood are for the purpose of completing the cycle, since no further development occurs in man. Interesting features of the habits of the microfilaria are its nocturnal periodicity, when the blood becomes flooded with the parasites, and its comparative absence during the day. This appears to be an adaptation to the habits of its intermediate host, the mosquito, and serves for the purpose of transmitting the infection when the mosquitoes are most active. It has been found that during the day, the microfilariae retire to the internal organs, mostly the lungs, the large arteries, the heart, the kidneys, and other organs. Another interesting feature is, that this nocturnal periodicity is absent in Fiji and other places, where the intermediate host, Aedes varigatus, is an active feeder both during day and night. It has been argued that filarial periodicity is dependent on a cyclical parturition of the worm, the microfilaria in the blood being destroyed in the internal organs during the day. Against this view, it has been pointed out that there is no evidence of any tissue reaction in the viscera, that would follow such massive destruction of microfilariae.

The cycle in the mosquito.—The microfilaria, when ingested along with the blood, penetrates the sheath by means of the spicule, and makes its way, in about 24 hours, through the wall of the stomach into the muscles of the thorax, where it increases rapidly in size, becomes more rounded and stumpy by the absorption of its tail, and develops a mouth and a double bulbbed oesophagus, while the tail spot becomes converted into the anal aperture and the anterior V spot develops into an excretory pore. The worm then increases in length, migrates slowly through the muscles of the thorax where it lies at the base of the proboscis by about the 20th day. During this time, the worm has developed a well-marked alimentary canal and peculiar caudal papillae to assist its
Filaria makes its way through the proboscis, penetrates a thin membrane at its tip and enters the human host at a point in the neighbourhood of the puncture.

The pathological lesions in filarial disease are three: lymphangitis, lymphangiectasis from lymphatic obstruction, and elephantiasis due to a combination of lymphangitis and lymphatic obstruction.

Filarial lymphangitis.—This makes its appearance soon after the bite of the infected mosquito. The bite may not, however, be noticed in many cases. The affected lymphatics are congested and swollen and stand out as irregular bright red lines. The skin may show a diffuse erythema while the inflammatory swelling and redness spread to the neighbouring
soft tissues, but marked oedema is not a feature at the commencement. This superficial radicular lymphangitis is often accompanied by a tubular lymphangitis affecting the deeper lymphatics. Histologically, there is a marked reaction on the part of the eosinophiles and exudation and congestion of the vessels are present. The affected lymphatics show catarrhal swelling of the endothelium with some desquamation. The skin over the affected part is generally healthy except for the erythema, but in chronic cases impetiginous inflammation may be present. This primary lymphangitis may be mild and not noticeable and may subside without leaving any trace. In other cases the condition may become chronic, as a result of repeated attacks of inflammation, the exact cause of which is obscure. It seems that the repeated attacks are due to trauma caused by the worms or possibly to toxins excreted. Others believe that these are really due to secondary streptococcal infections. The affected lymphatics become thicker and stand out as cords. Microscopically, there is an endo- and a peri-lymphangitis of the proliferative type so that the lumen of the vessel is often obstructed and fibrous transformation results. In many cases the adult worms have been found inside these thickened trunks, some lying in cyst-like dilatations while others are calcified. The attacks of lymphangitis of whatever type are often accompanied by sudden severe febrile reactions which, however, subside equally suddenly somewhat after the manner of a malarial paroxysm.

An acute lymphadenitis of the regional glands often accompanies these attacks of lymphangitis. The glands in the early stages show a soft swelling, sometimes terminating in suppuration involving the surrounding tissues. In other cases, the glands become large, hard masses which microscopically show marked overgrowth of fibrous tissue and atrophy of the lymphoid elements. The cell reaction is eosinophilic as in all parasitic infestations, but besides these cells which are found in clusters around parasites or their products, mononuclear cells and rarely giant cells may be met
with. In some instances, the dead worms may be found in sections inside the gland.

Filarial abscess may occur either in the affected glands from an attack of lymphadenitis or lymphangitis owing to the severity of the reaction. More often this is the result of the death of the worm. Secondary infections may possibly play a part, though sometimes the abscess may be sterile.

Filarial orchitis, epididymitis and funiculitis are all the result of local lymphangitis affecting these parts. Very often the presence of the worm can be demonstrated in sections. The testis and epididymis are swollen, tense and congested in the early stages, and there may be severe febrile reactions with rigor as in lymphangitis elsewhere. When the reaction subsides, it leaves behind a condition of chronic thickening and enlargement of the affected tissues from fibrous overgrowth. Repeated attacks may be followed by dense fibrosis and atrophy of the testis may occur.

A lymphangitis affecting the synovial membrane may result in synovitis, but this is much more commonly the result
of invasion of the worm into the tissues of the joint. Arthritis and its consequences sometimes follow, leading to ankylosis of the joint.

_Filarial lymphangiectasis._—This is the most important pathological feature of filarial disease apart from the lymphangitis. It is caused either by the presence of the parent worm in the deeper lymphatics and the consequent reactive changes induced, or possibly by the irritation caused by the toxic products excreted by the worm, in all cases eventuating in lymphatic obstruction. Whatever may be the mechanism of its production, obliteration of the lymphatic channels or similar changes in the deep lymphatic glands, or in the thoracic duct are met with. Obstructive changes may, in many cases, be made out on careful dissection in the ramifications of the receptaculum chyli. The pelvic or inguinal groups may be involved in other cases. The result of such fibrotic changes in the lymphatics or in the glands is the production of lymphatic varices. These varicose lymphatics may be met with most commonly in the inguinal groups. The spermatic cord, the scrotum, the retroperitoneal tissues and the abdominal walls show a similar lymphatic involvement. In all cases the affected lymphatics become very much dilated and tortuous, their walls undergo fibrosis and lose their elasticity. On the scrotum, the affected lymphatics may be found as vesicular dilatations on a thickened and fibrosed integument. In the abdomen, they form large masses in the retroperitoneal tissues and in the pelvis. Microscopically there is overgrowth of fibrous tissue in the wall of the affected vessels which are very much dilated, so that they appear like veins. The dilated lymphatics may in some cases undergo suppuration from secondary infection, or from the presence of the worms, giving rise to severe septic lymphangitis, and lymphangiectatic abscess.

Chyluria is a common condition that is met with in filarial disease, as a result of deep lymphatic obstruction in the pelvis, so that the lymphatics of the bladder or the pelvis of the kidney rupture through the mucous membrane, so that
the urine becomes pale or milky white in colour, through admixture with chyle. Sometimes blood may be present. The urine contains fat in extremely fine subdivision which can only be made out in many cases under darkground illumination, as small rounded particles exhibiting Brownian movement. Occasionally, some larger globules may be met with if the urine is kept and the surface layer examined. Staining with Sudan III may be of use for the demonstration of the fat. Besides these fat globules, red blood cells, leucocytes, granular cell debris and sometimes microfilariae, may be met with. The urine may undergo spontaneous coagulation and in most cases the fat, though difficult to demonstrate under the microscope, may be extracted out with ether. The urine if kept, separates into three layers, the top layer containing the fat, the middle layer the white coagulum, while the lowermost layer contains the deposit.

Lymph scrotum is an associated condition of lymphangiectasis affecting the scrotum followed by rupture of the small varicose lymphatics on the surface. The rupture may result from mechanical trauma or overdistension and an unhealthy or thinned epidermis. The lymph escapes from the surface as a persistent oozing, a condition of lymphorrhagia. The skin becomes sodden and unhealthy and secondary infection may occur. Effusion into the tunica vaginalis is a usual accompaniment.

Chylocele, or chylous effusion into the tunica vaginalis, may occur in filarial disease, apart from simple hydrocele, and is the result of a rupture of dilated deep lymphatics. Very often the fluid contains numerous microfilariae. A condition of lymphorrhagia may occur into the intestine from involvement of the lymphatics and give rise to chylous diarrhoea. Chylous ascites may occur from rupture of the abdominal or pelvic lymphatics, the peritoneal cavity containing chylous fluid.

Elephantiasis.—This is a condition affecting the skin and subcutaneous tissues, occurring in filarial disease, the result of repeated attacks of lymphangitis, in areas of lymph stasis
NEMATODE INFESTATIONS.

and lymphangiectasis. The skin becomes markedly thickened, the normal papillae very much hypertrophied, often standing out as warty masses, while the subcutaneous tissues show extensive œdema and fibrosis. The legs are most often affected, while the scrotum, penis and the female genitalia are commonly involved. The arms are rarely affected while occasionally other situations are involved. The condition is associated with repeated attacks of lymphangitis. Very often microfilariae are absent in the blood, since the parent worms

![Elephantoid tissue showing dilatation of cutaneous lymphatics and perilymphatic infiltration. The muscle bundles of the dartos are also shown.](fig_64.jpg)

are blocked off from the general circulation. The worms can, however, be met with in the deep lymphatics of the affected part. The skin shows besides the hypertrophied thickening, marked exaggeration of the normal folds. In some cases, nodular tumour-like masses, some of which look like the pedunculated fibromata of molluscum fibrosum, may be met with. The surface of the skin may be in a sodden eczematous state. When the condition affects the scrotum there is enormous enlargement, so that the patient is unable to move
about. The spermatic cord and testes are often lost inside the mass. The repeated attacks of lymphangitis are associated with fever and rigor. Often the cause of this inflammation, which might be erysipelas in type, is obscure. It has been regarded as being due to secondary streptococcal infection. On the other hand, the presence of the parent worms

![Image](image.jpg)

**FIG. 65.**

Elephantoid skin showing the thin papilliform outgrowths as well as a more nodal thickening.

in the deep tissues suggests that the condition may be in some way connected with that factor. Possibly microfilariae are expelled into the connective tissue, instead of into the blood stream and cause lymphangitis when they burst through their sheath.
Microscopically the skin shows marked thickening and hypertrophy of the papillae. Under the skin, the lymphatics which are normally inconspicuous can be made out as irregular slits running between bundles of fibrous tissue. Their presence in numbers under the skin indicates an extreme dilatation of the cutaneous lymphatics. Well-marked evidence of chronic inflammatory changes is invariably present, the lymphatics being surrounded by clusters of lymphoid cells and plasma cells, the appearance being very suggestive of the perivascular cuffing met with in syphilis, only here affecting the dilated lymphatics. Fibrous tissue overgrowth is also another marked feature. In the scrotum, there are round bundles of hypertrophied dartos muscle just under the skin, and the lymphatic spaces in between these muscle bundles also show dilatation. The deeper tissues are very loose and show oedema from lymph stasis, but even here the perilymphangitic clusters of cells are present. The worms may sometimes be met with in sections. The dilated lymphatics do not appear as wide vessels, but as mere longitudinal slits owing to the compression by the fibrous tissue.

Blood changes in filarial disease.—An eosinophilia is usual in filarial infestations and occurs even quite early in the disease. A mononuclear increase has been described. For the demonstration of microfilaria in the blood, a large drop of blood should be taken on a slide and spread out under a round cover slip which should be ringed round with vaseline. For study of the structure, however, a large drop should be spread out to form a small circle so as to get an even thick film. After the blood has been dried by waving over a flame, the slide should be immersed in water for a few minutes to dehæmaglobinize the red blood cells, after which it should be stained with Leishman’s stain. An ordinary thin film may also be of value.

Dracontiasis.

This is a condition caused by infestation of the subcutaneous tissues with a long filarial nematode, Dracunculus medinensis.
The infestation is found in parts of India, in New Guinea, in Persia, Turkestan and Africa, and in parts of America. The parasite, *Dracunculus medinensis*, also called *Filaria medinensis*, is a long string-like white worm, the female of which is the one that is commonly found, the male being very very rarely met with. Extreme variation in length is met with. According to Ewart the female is on an average 90 cm. in length and 1.5 mm. in thickness and is generally found in the tissues of man just under the skin where it can be made out as a long coiled cord. In structure the worm has a curved pointed hook-like posterior extremity which serves for attachment to the tissues. Externally, it is smooth with no striations. Inside the musculocutaneous layer throughout the length of the worm is the large tubular uterus which contains a number of embryos. The vaginal opening is supposed to be at the anterior extremity close to the buccal cavity. The buccal cavity has 6 lips.

The situation of the worm is just under the skin for the purpose of expelling the embryos into the water. The worm makes its way, by an unerring instinct, to those parts of the body which are likely to come into contact with water. Thus it is generally found in the lower limbs. Arrived under the skin, the worm burrows through and raises a blister by the injection of a toxic secretion. This ruptures and leaves an open sore, from the centre of which the head end may occasionally protrude. When the skin is brought into contact with water, the worm expels a portion of its uterine tube through an aperture near the mouth, possibly the vagina. This appears as a thin delicate membranous tube, which ruptures and expels a white fluid in which hundreds of embryos are present. These embryos are flattened worms, each about twice the size and thickness of a microfilaria. Each has a long attenuated tail, a round head and an alimentary canal with a bulbed oesophagus. They become extremely active when brought into contact with water and swim about with lashing movements of their tails. During the normal life cycle, they are ingested by a fresh water crustacean,
Cyclops quadricornis, in the body cavity of which they undergo successive moultings. They then make their way in the drinking water into the body of the host. The infected cyclops is killed by the hydrochloric acid of the gastric juice, while the contained larvæ are liberated and find their way into the subcutaneous tissues.

The lesions met with in man are the result of the wandering habits of the parasite. In the great majority of cases the worms reach the surface and pierce the integument. During this stage, the toxin excreted causes general hæmic eosinophilia, cutaneous urticaria and, in some cases, constitutional features. In other cases, the worms fail to reach the surface and die giving rise to abscesses in the tissues. Very often
the abscesses are sterile; but, in other instances, secondary streptococcal infection occurs. On the other hand, the worm may undergo complete calcification after death, so that irregular coiled calcified masses are found in unusual situations. Occasionally the worms may give rise to a marked foreign

![Fig. 67.](image)

Cyst of fibrous tissue formed round a guinea-worm. Note the portion of the worm protruding.

body reaction and may be encapsuled by dense masses of fibrous tissue showing histologically, well-marked giant cell formation. Cyst formation around a worm may sometimes be met with. During the migration of the worms, they may penetrate joint cavities and set up severe arthritis, resulting
in ankylosis. Apart from arthritis, synovitis may sometimes be met with. Diffuse spreading cellulitis, from rupture of the worm from trauma, may sometimes be met with.

**Loaiasis.**

This is a type of filariasis due to infestation of the connective tissues with a filaria called *Loa loa*.

The disease is practically confined to West Africa, particularly the coasts.

The adult worms are filiform thin hair-like parasites, found in the connective tissues where they give rise to localized swellings. The male is about 30 mm. in length and about 0.3 mm. in thickness, while the female is about twice the length and about 0.5 mm. in thickness. This species is characterized by the presence of round smooth cuticular prominences or bosses giving the outer surface a tuberculated appearance. The mouth is simple and unarmed. The alimentary canal is simple. The tail of the male is curved. There are two unequal spicules and a number of papillae. In the female the vagina opens near the anterior end. The embryos are contained in thin oval sheaths which gradually elongate when they are expelled from the uterus. *Microfilaria loa* is a sheathed worm very similar in its appearance to *M. bancrofti* and is found in the blood. Minor differences in structure are that the column of cells extends to the tip of the tail which is generally acutely flexed in *M. loa*. The body itself is more irregularly sinuous than that of the *M. bancrofti*. Fulleborn has pointed out that the first genital cell is much more conspicuous.

The microfilariae are met with in the blood in large numbers during the day while they disappear into the internal organs at night—the exact opposite of what prevails with *M. bancrofti*. The insect transmitter is *Chrysops dimidiata*, a blood-sucking fly with diurnal habits, in the thoracic muscles of which the larvae undergo development in a similar manner to that of *M. bancrofti* in the muscles of the mosquito.
Once the larva are injected into the tissues they increase in size, development taking years to complete. The habitat of the worm is the subcutaneous tissues where the migratory habits of the worm give rise to the pathological effects.

During its wanderings it generally gives rise to transient swellings in various parts of the body. These are called Calabar swellings and consist of smooth localized areas of swollen skin and subcutaneous tissue, each showing an erythematous flush. They disappear in the course of a few days and are believed to be due to the irritation caused by the worms or expelled microfilariae, which have been demonstrated in the puncture fluid. They are also regarded as dermal and subdermal reactions to toxins excreted by the worms. In some cases definite inflammatory changes affecting the muscles and fasciae are met with, sometimes resulting in abscesses. In some cases, the worms may actually be seen in the subcutaneous tissue, especially over bony prominences. These Calabar swellings occur on the fingers, eyelids and in areas of loose skin.

Onchocerciasis.

These are filarial infestations where the infesting parasite, Onchocerca volvulus, forms localized subcutaneous fibroid nodules in different situations.

The disease is found in parts of Africa in the Congo and more rarely in parts of South America.

Onchocerca volvulus is a thin filiform worm, the female of which is considerably longer than the male being about 40 cm. in length, while the male is hardly 40 mm. long. The worms are found intricately coiled up in tumour-like masses surrounded by dense walls of fibrous tissue. The microfilariae occur in the blood only in small numbers while they are more commonly met with in the subcutaneous tissue. Blacklock has recently implicated Simulium damnosum as the possible vector, since the worm undergoes a cycle of development in this fly similar to the cycle of the filaria in the mosquito.
The lesions caused by the parasite consist of tumours which occur in lax tissue in the folds of skin, the axillæ and popliteal region, in the back of the neck and other situations. They sometimes occur over bony prominences as well. On section, the wall is composed of dense strands of fibrous tissue while towards the centre the worms lie in tubular canals surrounded by a looser meshwork of fibrous tissue. The sexual aperture of the males and females are left free in little cystic cavities containing mucoid material. The microfilariae occur in the surrounding tissues causing small subcutaneous nodules and papules. Sometimes they may be met with in perfectly healthy skin. Very often only the larvae are found since the parent worm takes a very long time, often years, to develop. The blood shows a constant eosinophilia.
CHAPTER XV.

TYPES OF HELMINTHIC INFESTATIONS: NEMATODE INFESTATION.

Ankylostomiasis.

Under this term may be included the severe anaemias commonly met with in the tropics due to intestinal infestation with small nematode parasites called Ancylostomes.

The disease is extremely common in all tropical countries, especially Asia and Africa, where whole communities are infested, some harbouring the parasite without any marked ill-health while the others show severe anaemia. The parasite nematode is either Ancylostoma duodenale or a very similar worm called Necator americanus though sometimes Ancylostoma braziliense, a slightly smaller parasite of dogs and cats, is met with in the human intestine. *A. duodenale* is a small white or pinkish-white nematode, the male of which is about 9 mm. in length while the female is about 10 to 13 mm. The head end of the parasite shows a well-developed buccal capsule with four well-developed hooks by which the worm attaches itself to the mucous membrane of the intestine and absorbs blood. The opening of the mouth is directed towards the dorsal surface. There are two glands in the head which secrete some anticoagulant. The necator, a smaller worm, has no hooks at the cephalic extremity, but two semilunar plates which serve a similar function. It possesses a dorsal conical tooth in addition. The cuticle in both species is smooth and the whole body is occupied by the reproductive organs, the alimentary canal being rudimentary. The male has got a well-developed caudal bursa from which two fine spicules project. In the necator the caudal bursa is slightly different in structure and this, together with the
presence of two curves in the body, one dorsal near the cephalic end and the other ventral below, serve to distinguish this species from the ancylostome which is often comma-shaped. The vagina of the female is situated at the commencement of the posterior third of the body, so that the paired worms which are sometimes met with look like the Greek letter γ.

The normal habitat of the worm is the jejunum where, after attaining maturity, the fertilized female lays a stream of eggs which are passed out in the faeces. The eggs have a characteristic thin shell and a transparent appearance, are oval in shape and contain four or eight well-developed segments, the whole measuring about 70μ by 40μ. The eggs, when passed out in the faeces, are hatched and set free active embryos each with a double bulbed oesophagus and a rudimentary intestine. These are called the rhabditiform larvae and are extremely active and voracious feeders. After two successive molts they become the infective larvae which make their way from moist earth into the tissues of the man by boring
ANCYLOSTOMIASIS.

183

their way through the skin of the leg. They find their way into the blood stream and are carried to the capillaries of the lung and, after another moult, work their way through the alveoli and the bronchi into the oesophagus and the stomach arriving in the intestine where, after moulting again, mature forms attach themselves to the mucosa. The passage through the lung is regarded as enabling the parasite to acquire the power to resist the acid secretion of the gastric juice. In the mucous membrane, the worm absorbs blood and lives on the tissue juices, so that they are often reddish in colour from contained blood. They cause a severe anaemia not only by the absorption of blood from the host, but by the action of a haemolysin which is injected through the puncture of the wound.

The pathological lesions met with in ancylostomiasis depend on the severity of the infestation. The jejunum may show a number of these parasites attached to the mucosa. There are small areas of submucous haemorrhage around the puncture. Bleeding points may rarely be met with in the mucosa where the worms have fallen off. Sometimes no obvious lesions are met with. The mucous membrane is generally pale and in severe cases increased secretion of mucous together with a thin atrophied pale mucosa suggests chronic catarrh. The pallor may be present throughout the intestine.

The heart may show dilatation from myocardial degeneration and a patchy distribution of fat may be met with under

FIG. 69.
Ancylostomes fixed to the mucosa of the jejunum.
the endocardium similar to what is met with in pernicious anæmia. The muscle is pale and may show streaks of yellow from fatty infiltration. Effusions in the pericardium are quite common and so also is pleural effusion. Microscopically, fatty degeneration is generally met with and can be demonstrated by staining frozen sections with Sudan III, while in some cases atrophy of the fibres is met with.

Externally, the pallor may be a noticeable feature, while cedema is generally present in the legs. The puffiness of the eye-lids and face, the flabby pale condition of the muscles, the pallor of the lips and mucous membrane of the mouth and the white conjunctivæ form important features.

The lungs may show hypostatic congestion and sometimes cedema. Bronchitis may sometimes be present.

The liver is pale brown in colour and on section may show irregular yellow greasy spots of fatty change. In advanced cases a diffuse fatty degeneration may be met with. The lobular markings are indistinct and the vessels empty.

The spleen may show no obvious features but microscopically hæmosiderin pigment may be present. The peritoneal cavity may contain thin serous fluid. The peritoneum itself is pale and may show thickening, while the serous coat of the intestine is white and thickened. The stomach may be in a state of atonic dilatation, and chronic atrophic catarrh is a noticeable feature, the mucous membrane being pale and thin and covered with adherent mucus. There is some cédema of the mesenteric tissue, and the retroperitoneal glands and mesenteric glands are enlarged, soft and swollen.

The kidneys are pale in colour, but may show no other obvious feature.

The blood usually shows a marked secondary anæmia with a low colour index. There is an increase in the total volume of blood as demonstrated by Boycott. There is a marked fall in the percentage of the hæmoglobin and this is much more marked than the fall in the number of red blood cells. In advanced cases the red blood cell count may fall to 2 millions. Anisocytosis and poikilocytosis are well-marked features,
while polychromes are very common; occasionally normoblasts and megaloblasts are met with. Microcytes are said to be extremely common. There is a well-developed eosinophilia. The anæmia is the result of a number of factors. The minute oozing of blood from the punctures made by the worm, the blood absorbed by the worm, the hæmolytic toxin injected by the worm, all have a share in its production. Experimentally hæmolytic substances have been extracted from the worm.

The catarrh of the small intestine that is set up by these multiple small lesions in the mucosa no doubt interferes with proper assimilation and is in the main responsible for the gastro-intestinal disturbances.

The hæmic eosinophilia is no doubt co-related with the clusters of the eosinophiles that are found at the site of the puncture in the jejunum and the eosinophilic response that is met with in the bone-marrow which may also show an erythroblastic reaction.

An ancylostome dermatitis is sometimes met with in the legs often between the toes as localized red swellings of variable size. This is believed to be due to the reaction induced by the penetration of the larva through the skin. Sometimes a definite vesicular eruption is met with. Microscopically there is a localized inflammation where clusters of eosinophiles are characteristic features.

**ASCARIASIS.**

This is the commonest helminthic infestation that is met with generally in tropical countries, the parasite being *Ascaris lumbricoides*, the ordinary round-worm.

It is cosmopolitan in its distribution and is found infesting not only man, but pigs and monkeys and sometimes dogs and sheep. The normal habitat is the small intestine but the parasite may be met with in a variety of situations owing to its migratory habits.

The worms are about 20 to 40 cm. in length, the male being slightly smaller. The mouth is simple, and has three prominent
lips; there is an oesophagus with a single bulb surrounded by the nerve ring. The male has a tail with a well-marked ventral curve and two spicules, while caudal papillae are present in both sexes. The eggs are oval with an inner clear shell which is colourless, while the outer shell is coarsely tuberculated and stained with bile. Inside is the ovum which appears as a single granular cell. The eggs measure about $70\mu$ by $45\mu$ and various types are met with in the faeces. Some long and oval with coarsely granular contents are unfertilized.

When the eggs are passed out in the motion segmentation occurs and the coiled embryos can be seen if the eggs are kept moist and warm. When the eggs are accidentally swallowed the larvæ are set free in the stomach. From there they undergo a curious life cycle which has been recently traced out experimentally in rodents. The larvæ make their way from the stomach into the liver and bore their way into the lung where they may set up inflammatory changes. Some change would appear to take place in the lung, after which the larvæ

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**FIG. 70.**

Ova of *A. lumbricoides* ($\times 50$) showing the developing larvæ in artificial culture.
work their way up the trachea and down the oesophagus and finally make their way into the intestine by about the tenth day, after which they attain maturity, and eggs are passed out in the faeces.

The lesions met with are varied. In the earlier stages of infestation it is easily explained, with the new knowledge of the life cycle, how inflammatory changes varying from mild bronchitis to broncho-pneumonia may be met with. This is quite common in children and very often the underlying cause may be overlooked. Gastro-intestinal features varying from mild gastric catarrh to severe irregular diarrhoea may be met with. The wandering habits of the parasite are responsible for many obstructive lesions. They make their way into the glottis and cause laryngeal obstruction. A number of worms may be coiled together in a mass and cause intestinal obstruction. They may make their way into the bile duct and cause obstructive jaundice or into the pancreatic duct and cause pancreatic obstruction. Besides these lesions they make their way into the appendix and cause appendicitis. They may penetrate the wall of the bowel and cause peritonitis. In other instances an abscess may result around a worm in the tissues or in the internal organs. This very often follows death of the worm. Possibly from the absorption of toxic products excreted by the worms, cutaneous lesions, such as urticarial rashes and small papules, may be met with in children. Nervous phenomena are also attributed to toxic absorption, but may possibly be the result of sympathetic stimulation and reflex irritation of the nervous system.

The blood shows an eosinophilia as in all parasitic infestations.
CHAPTER XVI.

TYPES OF INJURY.

Snake Poisoning.

Snakes are reptiles belonging to the sub-order Ophida, most members of which group secrete poisonous principles in their salivary secretions which, when injected into the tissues by the bite, cause severe toxic features often ending in death.

The degree of toxicity of the poison or venom varies within wide limits; but poisonous principles are almost invariably present in all snakes in the saliva. In some the toxicity is to a great extent nullified by the absence of specialized fangs for the purpose of injecting the venom. Toxic effects are also not manifest if the fangs that are present are situated far back in the mouth. Snakes with anterior fangs are thus more poisonous. Such snakes belong to two great families, the Colubridae, and the Viperidæ. The Colubrid has an elongated oval head, round pupils, grooved teeth, which form the fangs, and a long pointed tail. The Viper has a triangular head, elliptical pupils, specialized canalized teeth called fangs and a short rounded and stumpy tail. These two families are again divided, the Colubridae including the Elapinæ or the land snakes and cobras and the Hydrophinae which are water snakes. The Viperidæ include the Crotalinae which are pitted vipers, having a small pit in front of the eyes, and the Viperinae, the pitless vipers, which have no similar depression. The further differentiation is based on the study of the dentition. In general, the head has two laterally placed eyes and nostrils, with a characteristic groove on the middle line under the chin, while in the so-called
poisonous species long curved teeth with grooves or canals situated anteriorly form the poison fangs. The body is covered with scales which are coloured on the dorsal surface and shows characteristic markings.

Snake venom is regarded as a specialized salivary secretion from modified salivary glands situated in the upper jaw. During the act of biting there is a contraction of the gland either through muscular action or compression of the jaw and the secretion is expelled through ducts and passes along the fangs into the bite. All bites are not invariably infective, since the venom may not be expelled from lack of sufficient compression or from lack of penetration. The venom itself contains nucleoprotein substances and albumoses which are toxic. The neurotoxic element is more marked with Colubridae, whereas Viperidae secrete cytolytic and haemolytic toxic principles which are less stable. Besides these, proteolytic elements are present.

The lesions met within man differ, to a very great extent, depending on the character of the snake, since the nature of the venom is so different in the two main types.

The lesions caused by the Colubridae show a certain degree of congestion and oedema at the site of the bite. The local features, however, are not marked, since the toxin enters the circulation and acts mainly by paralyzing the respiratory centre and affecting the motor neurones. Marked degenerative changes in the motor neurones at the base of the brain in the basal ganglia are met with. The nerve cells in the cranial nerve nuclei are affected. The toxin appears to be fixed to the nerve cells so that the effects once started gradually increase. Histologically swelling and chromatolytic changes in the nerve cells are met with, sometimes pyknotic nuclei. Acton and Harvey have described granular cell inclusions like Negri bodies. It would appear as if there is an early excitation of the nerve cells in some types followed by degeneration. This would explain the occurrence of convulsions followed by varying grades of paresis and paralysis. The involvement of the respiratory centre causes paralysis of
respiration often ending in death. Some types are more prone to affect the anterior horn cells of the spinal cord.

In lesions caused by Viperidae the characteristic feature is the marked predominance of the local reaction. The toxic substance is a cytolysin which has been variously called a hæmorrhagin, a hæmolysin, a leucolysin, etc. The action is on the cardiovascular system and consists essentially in a lysis of the endothelial cells resulting in hæmorrhage, together with a lysis of the red blood cells and of the leucocytes. A substance which causes intravascular coagulation is also present. As a result of the action of the cytolysin extensive hæmorrhage from mucous membranes occurs, and ecchymosis and petechial hæmorrhages in the skin and soft tissues are met with. Death generally results from cardiac failure. The local lesion consists of extensive swelling, oedema and hæmorrhage in the surrounding tissues. Gangrene of the soft tissues is a common feature and is probably the result of thrombosis. Secondary infection may occur and abscesses and cellulitis may result.

Histologically, the local lesion consists of a hæmorrhagic oedema with thrombosis of the small vessels and extensive necrosis of the cells of the affected tissue. Cloudy swelling is met within all the internal organs besides capillary hæmorrhages. A hæmorrhage into the glomeruli of the kidneys is regarded as a common feature.
APPENDIX I.

IMPORTANT LABORATORY METHODS FOR THE TROPICS.

METHODS FOR BACTERIA.

Preparation of films for examination.—A drop of the suspected material is placed on a clean slide and a thin smear is made with the platinum loop, and this is warmed gently over the flame. Simple staining is carried out after fixation, which is best effected by means of absolute alcohol or alcohol ether. Simple staining may be either by Loeffler’s methylene blue or by Nicolle’s carbol-thionin, the slide being flooded with the stain for about 3 minutes after which it is rinsed in water, dried and examined under the oil immersion lens.

Gram’s stain is essential in routine work and is important for the purpose of identification. It is a regressive stain, the aniline dye staining all the Gram-positive and Gram-negative organisms, after which the Gram-negative organisms are differentiated by treating with alcohol and counter-staining with a simple stain. The films are dried and fixed in absolute alcohol and then stained with a 1 per cent solution of methyl-violet in water for three minutes. Carbol-gentian violet in 1 per cent watery solution containing 2 gm. of carabolic acid and 10 c.c. of absolute alcohol for every 100 c.c. of water is sometimes used instead. After this preliminary over-staining the films are washed off with Gram’s iodine and flooded with this stain for two minutes and then decolourized with absolute alcohol. This decolourization is the most difficult part of the whole process since differentiation may be either more or less than is required. The films are then rapidly rinsed in water and counter-stained with a 1 per cent aqueous solution of neutral-red for about three minutes after which they are
rinsed rapidly in water, dried and examined. Gram-positive organisms are stained a blue or a black colour, while the Gram-negative organisms are stained red.

The **Ziehl-Neelsen stain** is another valuable method for differentiation of organisms and is of great importance in staining the acid-fast bacilli, such as *B. leprae*, *B. tuberculosis*, *B. smegma*, etc. The principle of the method rests on the fact that, when these organisms are stained with carbol-fuchsin, they retain the stain after treatment with acid or alcohol, this property being probably the result of the resistant waxy capsule they possess. The method is applicable not only to smears or films, but to sections. When sections, however, are fixed in formalin the staining reaction is often lost so that fixation should preferably be by means of Zenker's fluid. In formol-fixed sections preliminary treatment with a drop of weak ammonia will bring out the staining. Smears of suspected material are fixed in absolute alcohol and then flooded with carbol-fuchsin solution and steamed over a flame for about five minutes or stained in cold carbol-fuchsin in a dish for half an hour. The stain is then washed off in water, and the film decolourized with 25 per cent sulphuric acid for about 5 seconds for the tubercle bacillus, and with a weaker acid of about 5 per cent for *B. lepra*. It is washed in water and counter-stained with a simple stain, such as methylene blue, for one minute, rinsed in water, dried and examined. The tubercle bacilli and lepra bacilli are stained a bright red, while other organisms and tissues are stained blue. *Bacillus smegma* can be differentiated since it is acid-fast but not alcohol-fast.

**Methods for Spirochætes.**

Examination of fresh unstained preparations can be carried out by the dark-ground illumination, since ordinary microscopic examination of unstained specimens is of little use owing to the extreme tenuity of the organisms. The principle of this method consists in viewing the object, not by transmitted light, but by diffracted light. The waves of light
can bend round small particles and make them visible, and so illumination of the object is effected, not by a direct beam of light, but by oblique rays which cause a brilliant diffraction halo around each particle. Thus ultramicroscopic particles, which are invisible under a direct beam of light, are rendered visible by means of their ability to scatter the impinging rays. The importance of a brilliant oblique illumination of the object is thus apparent, and this is effected by means of a special condenser which shuts off all direct rays by a circular black disc on its under surface. A powerful illuminant, such as a Mazda bulb, is used and should be kept at a distance of about 16 inches away from the microscope. The condenser of the illuminant is focussed on to the centre of the plane mirror of the microscope so as to get a beam of light 2 cm. in diameter on the mirror. The sub-stage condenser should be correctly centered by focussing the small circle engraved on the top of the condenser to the middle of the field under the low power of the microscope. The next step is to adjust the mirror till there is a uniform ring of light on the upper surface of the condenser. The condenser is then lowered, and a few drops of cedar-wood oil are placed on the top of the condenser, and this is gently racked up on to the under surface of the slide, care being taken to avoid an air bubble. For this purpose it is better to arrange the slide, so that one edge of it comes into contact with the drop of oil after which the slide can be gently moved to get the central part of the field. The object may then be focussed with the low power and then with the high power. The condenser should be gently raised and lowered to get the best result. By this method both the structure and the motility of the organisms can be studied.

Fixation of films and smears is best by Dobell’s method, where the films are not allowed to dry, but fixed for half a minute in 2 per cent osmic acid vapour before staining.

Tribondeau-Fontana method of staining for spirochetes.—This method is applicable only for smears. The smear is dried and fixed with acetic acid formalin fixative which...
APPENDIX I.

consists of glacial acetic acid 1 c.c., 40 per cent formalin 2 c.c., in 100 c.c. of distilled water. Fixation is effected in 2 or 3 minutes, after which methyl alcohol is used and allowed to burn off the slide. Fixation is thus made complete. The slide is then mordanted by a 5 per cent solution of tannic acid in water and steamed for about a minute. It is then covered with Fontana's silver solution which consists of an opalescent solution of 5 per cent silver nitrate in water to which ammonia has been added drop by drop to produce a distinct opalescence caused by a fresh precipitate of silver hydroxide. The slide is again steamed and then dried. Spirochætes are stained brown.

Staining spirochætes in sections.—Levaditi's method is the method of choice. Thin pieces of tissue are fixed in 10 per cent formol saline for a day and hardened in 90 per cent alcohol for another day before washing. The tissue is then put in a 2 per cent solution of silver nitrate for four days and kept in the incubator at 37°C., after which it is washed with distilled water to remove the excess of silver. The silver is then removed by pyrogallic acid in a 3 per cent solution in 6 per cent formalin, the tissue being kept in the reducing solution for 24 hours. It is then washed again in distilled water, passed through alcohols and xylol, embedded in paraffin and thin sections cut and examined. Spirochætes are stained black and the surrounding tissues, yellowish brown.

Noguchi's method of cultivation for Treponema.—The method consists in using two tubes, the lower larger tube being completely filled with the medium into which the material from a chancre or other lesion is inoculated. This is closed by means of a cork through which passes a smaller test tube, the lower end of which is drawn out and open. In the upper tube is placed a small fragment of sterile tissue, such as rabbit’s kidney, and over this ascitic fluid is layered. This is only carried out after the lower tube has been inoculated and corked. The upper tube is then inoculated deeply with the suspected material, layered with paraffin 3 cm. thick, after
which it is plugged. The solid medium in the lower tube consists of 2 per cent nutrient agar, to two parts of which after melting at a temperature of 50°C., one part of ascitic fluid has been added. Growth occurs first in the lower tube.

_Cultivation of L. icterohaemorrhagiae._—Noguchi recommends a medium consisting of two parts of rabbit’s serum to which 6 parts of 0·9 per cent of sodium chloride solution are added together with one part of citrated rabbit’s plasma and the whole covered over with a thin layer of paraffin. The tube should be kept preferably at 33°C. The spirochætæ can be demonstrated in 2 to 3 days by withdrawing material by means of a capillary pipette. In Fletcher’s medium tap water is used instead of saline and so the medium consists of rabbit serum 1 c.c., sterile tap water 7 c.c., and 2·5 per cent agar 0·5 c.c. Growth is much more profuse.

**METHODS FOR FUNGI: MYCETOMA.**

For examination of fresh grains they may be crushed under a slide and examined without staining. Staining may, however, be carried out with a weak solution of cotton blue dissolved in lactic acid, in a watch glass. This is a selective stain for fungi. Unstained preparations will show the outer capsule, the septa and the spores better than the stained slides, since the dye will cause some swelling of the hyphæ.

Culture of the fungus should be carried out on blood agar, or gelatine, but is easiest on maltose agar. Banana gives good growth. Growth takes place best in acid media at a pH of +2, at room temperature. Primary cultures may be made in broth into which a little gelatine has been added. Subcultures may be made in Sabouraud’s medium. If the tube is rolled immediately after inoculating from the broth better results are obtained. The edge of the slope should be examined. Here the mycelium can be seen to spread out as a thin film through the whole tube. ‘Pyrex’ tubes of uniform thickness may be used and it is possible to examine the tubes directly under the microscope.
Protozoological technique is the most difficult of histological technique and requires meticulous attention to detail. Fixation should be effected with as little shrinkage and distortion as possible.

METHODS FOR PROTOZOA: RIZOPODA: ENTAMOEBA.

Two specimens should invariably be used, one of which is an emulsion of the material in saline while the other is an iodine emulsion. The saline emulsion should be very thin and should be made by placing a loopful of the faeces or a minute particle of it on a drop of saline on a slide, and thoroughly mixing up with a glass rod, after which it should be examined under a cover slip. The emulsion should be very thin. The diaphragm should be cut down to obtain critical illumination. A number of such slides should preferably be examined. The iodine method consists of emulsifying a small particle or a loopful of the faeces with a drop of Weigert's iodine solution. This consists of 1 gm. of iodine, 2 gms. of potassium iodide and 100 c.c. of water. The solution should be thoroughly mixed up with a small pointed glass rod after which the specimen should be examined under a cover slip. The nuclear structure of amœbæ and cysts is well brought out by this method.

Heidenhain's method of staining for protozoa. This is the method of choice when permanent preparations of amœbæ or other intestinal protozoa, are required. Fixation is effected by immersing the film in Schaudinn's fluid, which consists of a saturated solution of corrosive sublimate in distilled water, to one part of which half of absolute alcohol is added. The fixative may be warmed to get the best results. Fixation is generally complete in about 15 minutes after which the slides are passed through graded alcohols, starting with 50 per cent, then 70 per cent, in order to harden the film. A few crystals of iodine are added to 70 per cent alcohol to dissolve out the mercury in the film. This takes about ten minutes, after which the film is put in rectified spirit till all the brown colour is dissolved out. The film should be passed back through
graded alcohols and through distilled water before it is stained. The next stage consists in heating with a mordant, 4 per cent iron alum. The film should be left in this for six hours after which it is stained with a ripe, watery, 0·5 per cent solution of haematoxylin. This stain takes another six hours to act when the whole film is stained black. This method of staining is a regressive method with a preliminary overstaining and then differentiation with 1 per cent iron alum which dissolves out the haematoxylin. Differentiation should be watched carefully under a microscope and should be carried on till nuclear details are brought out. The film may then be washed in water and counter-stained, if necessary, before mounting. Counter-staining may be carried out by Shortt’s method. A solution of brilliant green in carbolic acid and xylol is used in the proportion of 1 gm. of brilliant green to 25 c.c. of carbolic acid and 75 c.c. of xylol. The film should be taken through graded alcohols before counter-staining. A few seconds’ staining is enough, after which the film is washed with xylol and mounted in Canada balsam. The protoplasm is stained a bright green and amœbæ and other protozoa can be spotted with ease.

*Cultivation of Entamoebæ of man.*—Boeck and Drbohlav’s medium is the one that is commonly used. It consists of two parts, a solid and a liquid, and the amœbæ grow at the junction. The liquid portion of the medium consists of Ringer’s solution, the pH of which is adjusted to 7·4 with alkali, added to which is sterile egg albumin 5 c.c. to each litre. The solid part of the medium consists of the same Ringer’s solution to one litre of which 14 gms. of agar are added. To these agar slopes 5 c.c. of the liquid medium are added and the tubes kept in an incubator at 37°. The mucus from the dysenteric stool is inoculated into the fluid portion. Growth occurs in 48 to 72 hours. The Ringer’s solution for this medium consists of sodium chloride 6 gms., and 0·1 gm. each of potassium chloride, calcium chloride and sodium bicarbonate in a litre of distilled water, the pH being adjusted after adding 5 gms. of mono-potassium phosphate to act as a buffer.
METHODS FOR PROTOZOA: MASTIGOPHORA: INTESTINAL FLAGELLATES.

The examination of fresh preparations may be carried out in a saline emulsion on a slide as for amoeba.

For staining, ordinary methods used for blood films are quite unsuitable for flagellates. In staining flagellates fixation should be carried out instantaneously so that distortion effects are minimized. Shortt’s method is rapid and easy. A thin wet film or a faecal smear is fixed by exposure to osmic acid vapour for a minute or two after which the film is dried and again fixed with methyl alcohol. After washing in water to remove the acid the film is stained by Giemsa’s stain using a 1 in 10 dilution as for blood films.

METHODS FOR PROTOZOA: MASTIGOPHORA: FLAGELLATES.

For examination of blood flagellates, such as the trypanosomes, examination of fresh blood or stained preparations may be carried out, as for the malarial parasites. Examination of fluid obtained from puncture of a gland is of greater value, since the trypanosomes are found in much greater numbers in the lymphatic glands. For permanent preparations, the iron haematoxylin method may be carried out after fixation in Schaudinn’s fluid.

For leishmania, the method of choice for demonstration is by puncture of the spleen or liver, and examination of the stained films. A much less risky procedure is the culture of the peripheral blood. Two c.c. of blood should be taken from a vein and mixed with 1 c.c. of 6 per cent citrate solution and the sediment inoculated into NNN media, in the water of condensation of which growth occurs. The same medium is used for the culture of trypanosomes.

NNN medium for the culture of leishmania.—The medium called Novy, Nicolle, and McNeal medium was first used for the culture of trypanosomes. It is made of blood agar and consists of 14 gms. of agar, 6 gms. of sodium chloride dissolved in 900 c.c. of water and steamed for two hours after
which it is poured out into test tubes after filtration. Each tube contains about 3 c.c. of medium to which, when it is cooled to 55 degrees, twenty drops of rabbit’s blood are added, the blood being drawn from a vein through a coating of melted paraffin. The tubes are rolled and incubated for twenty-four hours and the usual sterility tests carried out before inoculating with the blood or spleen-puncture fluid. Small drops of ‘sweat’ form inside the tubes and the growth occurs in this water of condensation. The cool incubator should be used and the temperature should be kept at 22 degrees centigrade.

**METHODS FOR PROTOZOA: SPOROZOA: PLASMODIA—THE MALARIAL PARASITES.**

*Preparation of a thin blood film.*—The finger-blood is generally examined for the demonstration of malarial parasites or for the differential leucocyte count. The finger should first be cleaned with rectified spirit and this should be allowed to evaporate so that the finger is perfectly clean and dry before it is pricked. The pin used should invariably be sterilized by heating over a flame. A deep prick is not necessary in the great majority of cases unless the patient is markedly anæmic. The drop that wells up should be brought into contact with the under surface of a slide. The slides should be kept in spirit in the laboratory in a closed bottle. Just before use they should be wiped dry and gently waved over a flame. The drop of blood should be on one side so that there is enough space for the smear. For spreading the smear another slide should be used, preferably with a rounded edge. This should be brought into contact with the drop edgewise and the film is spread by pushing the drop forwards along the slide, the layer of blood being in the angle between the two slides. This is a much better procedure than the practice of drawing the blood film after the slide. With a little practice a thin even film can be obtained. If it is desired to have a distinct leucocytic edge, when the smear is more than half-way through, the moving edge should suddenly be raised off the film so that
the rest of the blood is left as a distinct edge, where all the leucocytes are collected.

Preparation of a thick blood film.—Thick blood films are usually preferred for the routine demonstration of malarial parasites or if parasites are scanty. Here a large drop of blood is brought into contact with the centre of the slide, and with the rolled edge of another it is spread out to form a small circle about 1 cm. in diameter, so that the drop is evenly distributed. An apparent anomaly is that a thick film should be as thin as possible, and best results are obtained with such films. The film should be dehaemoglobinized before staining and the importance of the method lies in this, since the red blood cells are not stained while the parasites and leucocytes are well stained and clear. For dehaemoglobinization the film, after it has dried, is gently immersed in water when the haemoglobin is gradually dissolved out until the thick film becomes colourless. It is then allowed to dry and is then stained.

Unstained blood is examined for the study of motility of malarial parasites, microfilariae, etc. For this purpose a drop of blood from the finger is placed on a slide and examined under a cover slip. The cover slip should be perfectly clean and kept in a corked bottle. The proper way to use the cover slip is to keep it on the table, invert the slide containing the drop of blood and gently bring it down so that the drop of blood is brought into contact slowly with the cover slip, which becomes adherent and allows the blood to spread out. Air bubbles are thus prevented, and owing to the effect of surface tension an even distribution is obtained. The slide should then be turned back to the original position before examination. For microfilariae the blood should be taken at night. A larger drop should generally be used. In all cases, however, the slide should be carefully ringed round with vaseline to prevent coagulation. A thin, stained film should be used for the study of structure either of microfilariae or of malarial parasites.

Staining blood films.—This is preferably done by means of Leishman's stain. The stain is prepared by dissolving
0.15 gm. of the powder finely ground up in a mortar in 100 c.c. of acetone-free pure methyl alcohol. The alcohol should be gradually added to the stain while the solution is aided by grinding up the powder. The dissolved stain should be decanted and poured off and the process repeated till the whole amount is dissolved in the 100 c.c. The stain should be kept for a few days to ripen before use. The advantage with Leishman’s stain is that the methyl alcohol acts as a fixative and so no previous fixation is necessary.

The undiluted stain should be poured on to the slide, drop by drop. It is more economical to mark off with a grease pencil the portion of the slide that is to be stained. After the stain has acted for a minute it is diluted by adding twice the amount of distilled water from a drop bottle on to the slide. Care should be taken to see that the distilled water mixes well with the stain and this is carried out by gently blowing on the stain or by rocking the slide gently. A scum will at once form on the surface. The stain should not on any account be allowed to dry and to prevent this the whole slide may be covered by a Petri dish. The stain should be allowed to act for 7 minutes after which a stream of distilled water is poured on to the slide which gradually removes the stain and takes off any deposit. The stain in no case should be poured off the slide, since the scum will form a deposit on the surface. After this the slide is washed in a stream of distilled water till the film is pink in colour. If the stain has been allowed to dry or a deposit has formed, a drop of the undiluted stain should be poured on and the slide washed rapidly in water. It is dried in air and is then ready for examination.

Giemsa’s stain may also be used. This consists of 3 gms. of Azure II eosin and 0.8 gm. of Azure II dissolved in 250 c.c. of glycerine and 250 c.c. of methyl alcohol. Preliminary fixation is essential in this case. This may be effected by absolute alcohol or methyl alcohol for 10 minutes. When the film is dry, it is kept in a dish filmside downwards, but raised above the surface by two parallel rails at the bottom. The diluted stain is used, 1 c.c. of the stain being diluted with 10 c.c. of
distilled water containing a drop of 1 per cent potassium carbonate to alkalinize the stain. The stain is poured into the dish between the rails so as to form a layer beneath the slide and any deposit is thus prevented.

*Cultivation of malarial parasites.*—Thompson’s modification of Bass’s method is as follows. Ten c.c. of blood are withdrawn from a vein and placed in a test tube containing 0.1 c.c. of sterilized 50 per cent glucose solution. The blood is then defibrinated by stirring with a glass rod and the clot removed. The defibrinated blood is put into a series of small test tubes plugged with cotton-wool and covered over with rubber caps and incubated at 38°C. The red blood cells settle to the bottom and leave a clear layer of plasma above. The parasites develop in the red blood cells at the junction between the two layers.

**Methods for Protozoa:** Ciliophora: *Balantidium coli.*

Fresh preparations may be examined in warm saline emulsion as for amoeba. The cysts form characteristic structures.

For permanent preparations the iron haematoxylin method should be carried out after fixation in Schaudinn’s fluid.

**Methods for Helminths:** Trematodes.

Fresh specimens may be examined under the cover slip after preliminary washing in a test tube with saline and after all mucus has been removed with a brush.

For permanent preparations the flukes are put in saline containing an equal proportion of saturated corrosive sublimate solution. They are then transferred to iodized 70 per cent alcohol to remove the mercury and preserved in 70 per cent alcohol. For staining, a weak solution of haematoxylin may be used; but alum carmine in acetic acid forms a better stain. To make this, excess of carmine is added to a saturated solution of potassium alum in water, boiled for 15 minutes and 10 per cent glacial acetic acid added. The stain is allowed
to stand for a week and then filtered and diluted thirty times in water before staining. The flukes are kept in the stain for 24 hours after which they are differentiated in acid alcohol and then dehydrated and cleared with carbolic acid or creosote. They are then put through alcohol and xylol and mounted in balsam or cedar-wood oil.

Methods for Helminths: Cestodes.

Fresh preparations may be examined in saline after thorough cleansing.

For permanent preparations saline corrosive sublimate may be used or preferably saturated aqueous corrosive sublimate with 1 per cent glacial acetic acid, kept at a temperature of 70°C for 15 minutes. They are transferred to iodized 70 per cent alcohol and kept in 70 per cent alcohol. For staining, the same process may be carried out as for trematodes.

For sections any standard methods may be used, as for tissues.

Methods for Helminths: Nematodes.

Fresh preparations may be examined under cover slip in saline.

For fixation, Looss' method is as follows. The worms are kept in a test tube containing saline and shaken vigorously for cleansing. They are transferred to 70 per cent alcohol kept at a temperature of 70°C without boiling. This causes extension of the worms. For permanent preparations the specimens are transferred to a 5 per cent solution of glycerine in 70 per cent alcohol kept at 55°C. They are then mounted in glycerine jelly and the cover slip ringed round with Leitz' 'Deckglaskitt.'

Methods for Ova of Nematodes and Helminths.

Ancylostome ova may be concentrated by various flotation methods for facilitating examination under the microscope. Clayton Lane has devised a centrifuge by which the ova are made to float up owing to centrifugal action, and
FIG. 71.

are caught on cover slip kept on the top of the centrifuge tube. A simpler method consists in making an emulsion with saturated salt solution, in which the ova float up and are caught on a cover glass from the surface.

The demonstration of other ova may be carried out by routine examination of faecal emulsions.

For preservation of ova Langeran's lacto-phenol may be used. This consists of phenol 1 part, lactic acid 1 part, glycerine 2 parts, and water 1 part. Microscopic preparations may be ringed round with seccotine on a turntable.
APPENDIX II.

AUTOPSIES IN THE TROPICS.

The difficulty in obtaining complete post-mortem examinations in the tropics is very great, mostly owing to religious objections. The necessity of making a partial examination in cases where this can be carried out without difficulty should be borne in mind. In those cases where an autopsy is not permitted, it is possible to do a liver and a spleen puncture immediately after death so that a partial investigation is possible. This applies equally to laboratory methods which are not found feasible during life owing to the gravity of the case. Pericardial effusion may be tapped and a sample of pleural or peritoneal fluid obtained in cases where necessary for completing the diagnosis. In abdominal operations a method is described showing how a complete investigation of post-operative death can be carried out without any further external deformity than the operation wound.

Post-mortem decomposition is extremely rapid in the tropics and consequently autopsies should be carried out as soon as possible after death. This does not apply so much to places where facilities exist for refrigeration. In cases where decomposition has set in, one should be careful to allocate changes due to disease and those due to decomposition. It is a wise principle not to draw inferences from organs which are decomposed. This is particularly the case in organs like the kidneys and the brain, where, quite early, post-mortem changes give rise to marked alteration in appearance. The kidney may present a picture of acute congestion with bright cortical striations and hæmorrhage from a post-mortem change. Microscopically the beginner is very often liable to diagnose chronic parenchymatous nephritis from the appearance of
advanced tubular degeneration that is only a post-mortem change. In a similar manner the intestines may show arborescent areas of patchy congestion which are the result of hypostasis. Gaseous distension of the stomach and intestine is quite a common feature.

The preliminary cleansing of the body is of great importance in the tropics, and in cases where decomposition has started, 10 per cent formalin should be used as a deodorant. This is a better procedure than the turpentine and other essential oils that are generally recommended. When the abdomen is opened after a preliminary examination, oil of eucalyptus may be poured into the abdominal cavity to minimize the odour. The examination of the viscera should be carried out as thoroughly as possible and invariably a smear from the spleen and liver and, in cerebral cases, from the brain, should be taken and examined immediately after the autopsy is finished, for the purpose of demonstrating parasites or pigment. Intestinal lesions are quite common in the tropics and the examination of the intestines forms the most important feature of the autopsy. The intestinal contents should invariably be filtered through wire gauze to demonstrate the presence of parasites.

The active co-operation of the bacteriologist in the post-mortem room is essential, particularly in dealing with intestinal lesions, since in doubtful cases, a culture should be taken from the base of the lesion. For this purpose the intestine should be completely washed out, and the surface of the ulcer should be seared with a hot knife, and a scraping obtained after incision into the base through the necrotic debris on the surface.

The importance of routine histological examination of diseased tissues, both for the purpose of diagnosis and study, is a point that cannot be over-emphasized. Quite often unexpected aid in the diagnosis will crop up under the microscope. Slight degrees of malarial infection may be overlooked when it is occurring either as an accident or as a terminal event in other diseases.
In examination of the liver care should be taken to see that no parasites are overlooked. An examination of the brain should form an invariable feature in a complete autopsy and a microscopical examination should not be omitted. The bone marrow should not be neglected as it offers many features of interest in tropical anæmias and in parasitic diseases. Care should also be taken to look out for enlarged lymphatic glands and should they be present they must be carefully dissected out and examined microscopically for the presence of parasites or lesions.

A TECHNIQUE FOR MAKING A MORE OR LESS COMPLETE POST-MORTEM EXAMINATION THROUGH AN INCISION IN THE UPPER ABDOMEN.*

The necessity often arises in hospitals in India as well as, I dare say, in other countries for a post-mortem examination in cases where, for various reasons, a complete incision from the neck right down to the symphysis pubis is not desirable. This method has been of great value in Madras since it has enabled the surgeon after a fatal gastric case to satisfy himself as to the cause of death. The method of opening up the wound and exploring the peritoneal cavity and removing the abdominal viscera is very imperfect, since important causes of post-operative deaths, such as post-operative pneumonia, infarction and collapse of the lungs, are often missed. It is very often the case that the relations of the deceased take exception to a complete post-mortem incision disfiguring the patient, but do not mind the surgical incision. Very few have realized what a thorough examination can be made through the usual 6 inches surgical incision in the upper abdomen.

The technique I have been using is as follows. The surgical incision is slightly extended in either direction to the level of the costal margin above, and the level of the umbilicus below. The peritoneal cavity can then be thoroughly inspected if the edges of the wound are pulled back. The

* From the *Indian Journal of Medical Research*, April 1928.
level of the diaphragm is then ascertained, the appendicular region explored and the hernial sites investigated. The next procedure is to draw out all the loops of the small intestine freeing any adhesions that are present. The small intestines are then removed by severing the mesenteric attachment, after dividing the jejunum, until the ileocaecal valve is reached. The transverse colon is next separated by means of scissors from its mesocolon and the omentum until the splenic flexure is reached, when the colon can be pulled out gently by a few snips of the scissors. The hand is then passed into the abdomen and the sigmoid separated from its mesocolon and divided at its junction with the rectum. The hepatic flexure is then followed down to the caecum and by gentle traction the whole caecum and appendix with the attached ileum can be removed with a few snips of the scissors.

The spleen is then removed at this stage. The removal of the liver through the small incision offers some difficulty, but this can be overcome if the falciform ligament is incised and the liver separated from the diaphragm by a few touches of the knife till the hepatic veins are opened, when the finger is passed into the vein and by traction the rest of the diaphragmatic attachment over the bare area is separated, and the ligament that binds the left lobe to the diaphragm is also divided. The mesentery is then grasped and dissected upwards, the tail of the pancreas dissected off from the retro-peritoneal tissues and the liver, stomach, pancreas and mesentery removed en bloc. This method is necessary for the investigation of the biliary passages in cases of duodenopylorrectomy where the surgeon may inadvertently have tampered with the biliary or pancreatic ducts. It is also of value to determine whether post-operative jaundice is really the toxic effect of chloroform on the liver or whether obstruction of any type exists.

The dome of the diaphragm near the costal margin is then stabbed with the knife on one side, and the incision is extended severing the attachment of the diaphragm to the xiphoid process and passing on to the dome of the diaphragm.
on either side. In this way the pericardial cavity is left intact. The pleural cavity may be then investigated and any adhesions separated. If the knife is kept close to the costal margin the lung is not injured even if it is adherent to the diaphragm, but this can usually be seen by the laxity or otherwise of the diaphragm.

The knife is then passed into the thorax and the pericardium separated from under the sternum. The hand is then passed into the pleural cavities and any fluid withdrawn by a sponge and measured. After having freed the apices and posterior borders of the lungs the hand is then passed along the vertebral column and the finger insinuated between the oesophagus and the bone on one side and then similarly on the other side, the other hand being used. The knife is then passed over the tissues of the anterior mediastinum to the neck and with one hand holding the trachea and oesophagus an oblique incision is made through the trachea and oesophagus right down to the bone as high up as possible.

The trachea and oesophagus are then pulled down into the abdomen along with the lungs and the heart, the diaphragm cut out at its attachment to the pericardium and the whole thoracic structures removed en bloc. In this way the only structures left out are the larynx, the upper end of the oesophagus and pharynx.

Some difficulty may be encountered in removing the bladder and pelvic viscera, but this can be overcome if both hands are passed vertically down and each viscus grasped with the left hand while the knife is swept round it with the other. This procedure is facilitated by introducing the whole of the left elbow inside the abdominal cavity.