A Paper

ON

BRITISH DISCOVERIES IN TROPICAL MEDICINE DURING THE LAST HUNDRED YEARS *

BY

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For the state of knowledge, in the earlier days of the last century, of diseases peculiar to warm climates we must look to the writings of those excellent clinicians in the service of the army of the Honourable East India Company.†

THE "SOWERS"

The reign of these sowers, as we may with justification term them, extended over some forty years, from 1830 to 1870, so that we can still turn with pleasure and profit to the writings of Sir T. Ranald Martin, F.R.S. (1793-1874), a surgeon on the Bengal medical establishment of the Company. He is chiefly known for his edition of James Johnson's book on the *Influence of Tropical Climates in producing the Acute Endemic Diseases of Europeans* (1861). This book, which, as Balfour remarks, is too fond of calomel, gives an accurate idea of the state of medical knowledge at that particular time. Sir James Annesley, who flourished from 1780 to 1847, produced one of the most remarkable and beautifully illustrated of medical works in his *Researches into the Cause, Nature, and Treatment of the more Prevalent Diseases of India and of Warm Climates Generally* (1828). For accuracy of clinical observation this work has rarely been surpassed, and one still recognizes the characteristic lesions of amoebic and bacillary dysentery, though these two diseases are inextricably confounded in the absence of accurate aetiological knowledge of what he so aptly terms "intertropical diseases."

Among the sowers of modern knowledge we must surely include Sir George Ballingall (1780-1855), mainly because he appears to have been the first to differentiate on clinical grounds the two forms of dysentery. A somewhat similar work was the publication, in 1832, of William Twining's (1790-1835) *Clinical Illustrations of the More Important Diseases of Bengal*. The memory of Charles Morehead (1807-82) will chiefly be revered for his pioneer work in medical education in India. His book *Researches upon the Diseases of India* was regarded as a standard work, and he deserves our gratitude for his scathing condemnation of the abuse of mercury in the treatment of fevers. The labours of Norman Chevers (1818-86) in the cause of "medical jurisprudence in India" also deserve notice.

Into this period steps the imposing figure of David Livingstone (1813-73), who shares with Stanley the honour of opening up the Dark Continent with all its peculiar maladies to the gaze of the white man. The public are apt to regard him more as an explorer and missionary than as having the role of a pioneer in tropical medicine, but in his travels, published in 1857, he gives an accurate description of the tsetse fly, or *Glossina morsitans*, ascribing the diseases with which it is associated to poisons injected by its sting.

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† Balfour, A.: *Trans. Roy. Soc. Trop. Med. and Hyg.*, 1925, xix, No. 4, 189.

THE "TILLERS"

The sun of enlightenment, heralded by the discoveries of Pasteur and Koch, shed its rays across the world and began to illuminate the next three decades. This we can regard as the age of the "tillers," for surely the harvest was plentiful, but the labourers few.

These were pioneers working amidst the unhealthy climates and in conditions of indescribable difficulty, isolated from that scientific collaboration which is so invaluable to research. Among them was the great Timothy Richard Lewis (1841-86), a Welshman who had a distinguished career in London and Aberdeen before entering the Army Medical Service in India. By his discovery of the rat trypanosome and of the *Filaria sanguinis hominis* he has a claim to be regarded, as Dobell has styled him, the "Godfather of Tropical Medicine." He was certainly the "Godparent of Tropical Helminthology." Bracketed with him is the name of D. D. Cunningham (1843-1914), who will also go down to history, for it is now realized that Cunningham first found and accurately described *Entamoeba coli* and two small flagellate protozoa of the intestine. He undertook amongst other things a most painstaking examination of the organisms found in the air and published an illustrated monograph in 1872. Although he did not work in the Tropics the name of Thomas Spencer Cobbold (1828-86) must be mentioned in association with these tropical parasitologists. It was Cobbold's task to collate the material collected in the tropical field and to systematize tropical helminthology. It was Cobbold, too, who corresponded with Timothy Lewis and with Joseph Bancroft and who named and described the *Filaria bancrofti* and the *Bilharzia haematobia*.

Henry Vandyke Carter (1831-97), who eventually became deputy surgeon general in the Indian Medical Service, was the first to find the relapsing fever spirochaete in India, and proved the three types of malaria parasite in that country shortly after Laveran's discovery. In Sir Joseph Fayrer (1824-1907) we can study the career of one who devoted himself mainly to the clinical medicine of India and to a study of the poisonous snakes. His great monograph on the *Thanatophidia of India* with its beautiful illustrations still remains a standard work on the subject. Closely associated with him was George Lamb (1869-1911), a man of brilliant attainments who devoted himself mainly to the toxicology of snake viruses. As a pioneer entomologist G. M. J. Giles (1853-1916) must be mentioned. He did much for the study of mosquitos in India when this subject was barely appreciated. Andrew Davidson (1836-1918) certainly belongs to this period, and his name should be held in greater honour than has been so in the past. Long before Manson had returned to England from China, Davidson's name was known in connexion with tropical medicine. He was the author of two standard works—*Geographical Pathology and Hygiene and Diseases of Warm Climates* (1893). J. E. Dutton (1877-1905) was mainly known as a research worker of the modern school. He went out to Central Africa as the representative of the Liverpool School of Tropical Medicine. On the Gambia he described and named the *Trypanosoma gambiense*, and later, with J. L. Todd, did his great work on African tick fever, to which he ultimately succumbed in his thirtieth year.

MANSON AND OTHERS

It is necessary to leave out a number of workers, but among those who reaped and profited by the labours of the earlier pioneers we can mention a number of household names. It is almost superfluous to describe the career of Sir Patrick Manson (1844-1922). He has been well known, and justly so, as the "Father of Modern Tropical Medicine." Coming early in the field, he made

his mark as a pioneer investigator, as a clinician, and as the founder of a school of tropical medicine. Working in Amoy, China, he discovered first the periodicity of *Filaria bancrofti* (1877), then part of the life-cycle in the mosquito, (1878), and he was the first to associate the transmission of disease with a winged insect. We may note that he found the eggs of *Paragonimus* in the sputum, *Sparganum mansoni*, and *Tinea imbricata*. He described sprue, became a great practitioner in Hong-Kong, and founded the school of medicine there which has now become a University. Returning to England, he was instrumental in describing several new species of filaria. He confirmed the development of the guinea-worm in cyclops, foreshadowed the life-history of the malaria parasite, and eventually, at the climax of his career, founded and conducted the London School of Tropical Medicine. We may regard his career as the culminating point of the foundation of tropical medicine.

Almost in the same breath, and out of a pious regard for historical truth, I must refer to two great laymen who helped to make the foundations of British tropical medicine more secure. The first is the great statesman Joseph Chamberlain, at one period Secretary of State for the Colonies. Without his aid Manson could not have founded the London School of Tropical Medicine; nor without the name of Chamberlain could he have obtained that influence he ultimately wielded so successfully. The other is Sir Alfred Jones, a prominent Liverpool merchant, much interested in the Elder Dempster Line and in the development of the Colonial Empire. I knew him as a boy, and well remember the sensation that was caused by his introduction of the banana to the dinner table of the citizens of Liverpool. And so it came about that Alfred Jones laid the foundation of the sister school of the Liverpool School of Tropical Medicine. Sir Ronald Ross, a contemporary and associate of Manson, must be well known to all for his historic researches on malaria and for his many activities in various aspects of this disease. He was the original professor of tropical medicine in the Liverpool School, which he joined in 1899.

In Charles Wilberforce Daniels (1862-1927) Manson discovered a capable and well-equipped first lieutenant, who, after performing original work in Fiji and in British Guiana, was instrumental in confirming Ross's malaria researches in 1899. Daniels was a great teacher and inspirer. He taught me the elements of tropical medicine, and in consequence I hold him in reverence as a reaper of the tropical harvest. Major-General Sir David Bruce (1855-1931) and Lieutenant-General Sir William Leishman (1865-1926) were both officers of great distinction, and their names and their work will for ever illuminate the records of the Army Medical Service. The reader will have no difficulty in recognizing the vital nature of their work in undulant fever, trypanosomiasis, relapsing fever, and kala-azar, which appear in the historical portions of this paper. They constituted a necessary corollary of the work of Patrick Manson and they reaped a harvest such as will never be seen again. Sir William Simpson (1855-1931) and Sir Andrew Balfour (1873-1931) can suitably be mentioned together. Although neither contributed materially to the science of tropical medicine, they reaped to the full the results of their predecessors and may be said to have laid the foundations of tropical hygiene. Only now is the real value of Simpson's pioneer efforts in tropical Africa being fully appreciated, and Andrew Balfour will ever be remembered as the pioneer of hygiene in the Sudan, as the first director of the new London School of Tropical Medicine, and as a great apostle of his cult.

Thus my brief survey of the great workers in British tropical medicine draws to a close. The present may be called the age of the gleaners. The seed sown in the

past century has grown into a great tree whose limbs, stretching out in all directions, have borne a bounteous crop, but there are still some plums left in the uppermost branches for energetic gleaners of the present day.

MALARIA

It was not till 1894 that interest was aroused by Manson regarding the full life-history of the malaria parasite. Observing that "flagellation" of the crescent form of the subtertian parasite took place not in the circulating blood but only on withdrawal from the body, he enunciated his famous "mosquito-malaria hypothesis." From 1895 to 1898 Ronald Ross hammered out the probable life-history of the malaria parasite of man, again by analogy, by working on the cycle of development of the plasmodia of birds, *Plasmodium praecox*, in culicine mosquitos, and he also traced part of the cycle of the human malaria parasite to dapple-winged (that is, anopheline) mosquitos. Finally, he established that the mosquito not only removed the parasites from the blood but also transplanted them as sporozoites into their new host. But it now appears that an English-born American citizen in the person of A. F. A. King (1841-1914) wrote a very able paper as far back as 1883 in which he set forth his views on the transmission of malaria by mosquitos and adduced no fewer than nineteen reasons in support of his theory. After the scientific establishment of the mosquito transmission of malaria, there were other pieces of constructive work performed by British pioneers.

The public soon demanded visible and ocular proof that malaria could be disseminated by mosquitos and, *per contra*, prevented by their exclusion. Hence on behalf of the Colonial Office and of the London School of Tropical Medicine, Manson organized two experiments which would dispose for good and all of any objections which might have been advanced against this work. A special mosquito-proof hut was devised and erected in one of the most malarious localities in the Roman Campagna, and in it Dr. Carmichael Low, the late Dr. L. W. Sambon, and Mr. E. Terzi lived for three months without contracting the disease. Whilst this experiment was in progress, mosquitos fed in Rome on patients suffering from benign tertian malaria were forwarded in suitable cages to the London School of Tropical Medicine, and on their arrival were set to bite Dr. P. Thurnburn Manson (Manson's eldest son) and Mr. George Warren. In due course both these volunteers contracted malaria, and the characteristic parasites were demonstrated in their blood. The mosquito-malaria theory was thus proven as far as scientific proof could be obtained—a theory was transferred from the realm of fancy into that of fact, and a glorious page in British medicine was thus completed.

The practical application of all this work was undertaken by the pioneer efforts of Ronald Ross himself in Nigeria in 1899-1900. The measures he then devised for the extermination of anopheles mosquitos in a malarial locality proved the basis of all future anti-malaria work and led to the brilliant results obtained by Sir Malcolm Watson in the Malay States. J. W. W. Stephens contributed considerably to our knowledge of what might be termed the new malaria by the discovery in 1922 of a new species of parasite—*Plasmodium ovale*—which, though having affinities with the quartan parasite, is nevertheless but feebly pathogenic for man. Recently (1931) this discovery has been amply confirmed by S. P. James and P. G. Shute at Horton Mental Asylum in this country.

TRYPANOSOMIASIS AND LEISHMANIASIS

In 1891 the first patient suffering from "negro lethargy" was sent to the London Hospital under Sir Stephen Mackenzie. His blood was studied by Patrick Manson, who found the *Filaria perstans* in this as in other

cases, so that he came to associate the presence of this parasite with the disease. Five years later David Bruce and his gallant wife went to Zululand, and after two years of isolation they discovered the *Trypanosoma brucei* and proved its transmission through *Glossina morsitans*. In 1901 Forde showed J. E. Dutton what was thought to be a filaria in the blood of a European on the Gambia, but Dutton instantly recognized it as a trypanosome, though neither of them associated it with sleeping sickness. In 1903 A. Castellani and later David Bruce, by the discovery of the trypanosome in the cerebro-spinal fluid, definitely clinched the association of the trypanosome with the disease. Later (1903), Bruce, Nabarro, and Greig definitely found that the disease was spread by *Glossina palpalis*, in which fly the trypanosome underwent development. In 1910 J. W. W. Stephens and H. B. Fantham found a new species of trypanosome (*T. rhodesiense*) in patients from the Luangwa Valley, N. Rhodesia, and in 1912 A. Kinghorn and W. Yorke showed that it was transmitted by *Glossina morsitans*.

Kala-azar is the visceral infection with *Leishmania* and is a widespread disease accompanied by a high mortality. Attention was first drawn to it by the epidemic in Assam in 1875, which decimated the inhabitants of the Garo Hills. In 1900 Sir William Leishman found the parasites in films made from the spleen of a soldier who died in Netley Hospital from a chronic fever contracted in Dum-Dum, an unhealthy station in Bengal, where kala-azar is not infrequent amongst Europeans. Leishman was apparently so careful that he did not publish his discovery till 1903, when he considered that these bodies represented a degeneration of some form of trypanosome. In July of that year Donovan observed the same parasite in a blood smear obtained by splenic puncture during life, whilst in 1904 S. R. Christophers published a valuable report on the morphology of the parasite and a commentary on the disease. In the same year Sir Leonard Rogers published his observations on the development of what he called the Cunningham-Leishman-Donovan bodies into flagellated organisms in citrated splenic blood, and in 1915 Rogers introduced treatment by intravenous injection of tartar emetic, following the lead given by Vianna in Brazil. The transmission of kala-azar has now been proved, principally by British workers—Christophers, Shortt, Knowles, Napier, Barraud, Lloyd, and Smith—to take place in the sandfly *Phlebotomus*, and quite recently this has been proved to be true for the Mediterranean form in Malta by S. Alder and O. Theodor (1932).

In 1885 D. D. Cunningham apparently first described the parasites of Oriental sore. They were curious organisms in the mononuclear cells derived from the sores. That this infection is disseminated by the agency of some small biting fly was first adumbrated by C. M. Wenyon, who suggested that the sandfly (*Phlebotomus*) was the possible vector in Baghdad, and he found that 6 per cent. of these insects caught in Aleppo had a flagellate of the *leptomonas* type in their intestinal canal.

YELLOW FEVER AND RELAPSING FEVER

The transmission of yellow fever through a mosquito was first foreshadowed by C. J. Finlay in 1891. This pioneer, despite the Christian names of Carlos Juan, was, it seems, of British stock. Sir Rubert Boyce first drew attention to the existence and deadly nature of yellow fever in West Africa, and pointed out that this area was a secondary endemic centre in addition to the more extensive and notorious range in South America. Several British investigators have fallen victims to "yellow jack" during their unselfish labours. We may mention Walter Myers (1873-1901), Adrian Stokes (1928), and A. Young (1928). It was Stokes who first demonstrated the ultra-microscopic nature of the yellow fever virus and its communicability

to *Macacus* monkeys, an observation which has been the basis of all the more recent researches on this historic disease. As regards the prophylaxis, the work of E. E. Hindle must be mentioned, especially in respect of the toxicity of the virus and the immunity which can be produced in monkeys by the injection of attenuated preparations.

The main work of British investigators has centred round the Central African, or tick-borne, form of relapsing fever. P. H. Ross and A. D. Milne, in 1904, and later J. E. Dutton and J. L. Todd, discovered the spirochaete in the blood of natives suffering from the disease, and it was due to this infection that Dutton lost his life; but this last pair of investigators, working on the Congo, proved definitely that the spirochaete was conveyed by the bite of a tick—*Ornithodoros moubata*—and, moreover, that the parasite could pass into the egg and so to the nymph and to the mature tick of the succeeding generation. In 1907 F. P. Mackie recorded an outbreak of relapsing fever in India in which lice—*Pediculus humanus*—served as transmitting agents.

BERI-BERI AND AMOEBIASIS

The pioneer observations of C. Eijkman, in 1897, on the production of polyneuritis in fowls by the administration of polished rice led to the classical experiments of H. Fraser and A. T. Stanton in 1909. In this work they were aided by W. L. Braddon, to whom a share of credit in the foundation of the modern knowledge of avitaminosis is due. These observers noted that in a gang of Javanese coolies, whose main diet was white, or polished, rice, beri-beri was of frequent occurrence till rations of unpolished or parboiled rice were substituted. The idea that the absence of a particular factor in the diet could generate something positive in the production of disease was an entirely new conception in medical science. Fraser and Stanton further showed that the antineuritic element is located in the pericarp of rice, in the aleurone layer, and in the embryo of the grain; that it is soluble in water and alcohol and is readily destroyed by a temperature of 130° C.; and that the amount of phosphorus in any given sample of rice is an indication of its safety. This work led up to the discovery by C. Funk at the Lister Institute in 1912 of those mysterious substances known as vitamins.

The organism we now know as *Entamoeba histolytica* was discovered in 1873. It now seems clear that the animalcules seen by D. D. Cunningham (1871) and Timothy Lewis in non-dysenteric stools were *Entamoeba coli*. For the painstaking researches which eventually culminated in the differentiation on morphological grounds of these two species of amoeba we are indebted to some extent to C. M. Wenyon. This was not the only difficulty to be overcome; there were several more, including the separation of the other non-pathogenic species of amoeba which inhabit the intestinal canal of man, and for the solution of the problem we can thank Wenyon and C. Dobell. The remarkable advances in the treatment of intestinal amoebiasis are mainly due to British workers. The older pioneers had been in the habit of treating chronic forms of dysentery with powdered ipecacuanha, and we find Manson in his practice in Hong-Kong, from 1883 onwards, firmly convinced of the specificity of this remedy in certain cases. But the exact action of ipecacuanha on the dysentery amoebae was not appreciated or understood. From 1917 onwards emetine, the alkaloid of ipecacuanha, had been recommended for the treatment of dysentery, but special attention was drawn to this drug by the experiments of Vedder in 1910, to the fact that it was without any visible action on the dysentery bacilli, but would kill saprophytic amoebae in 1 in 100,000.

In 1912 L. Rogers experimented with solutions of emetine hydrochloride and found that a similar strength rendered the *Entamoeba histolytica* inactive and apparently killed this organism. He then treated a series of cases of severe dysentery with hypodermic injections of emetine hydrochloride, with rapid improvement in the symptoms and disappearance of the amoebae from the stools. During the last twenty years there has been ample opportunity of assessing the value of Rogers's original discovery, and it can be affirmed that emetine still remains one of the most remarkable specifics in treatment. In the chronic stages of the disease, when the cysts of *E. histolytica* are present in the faeces, emetine proved less efficacious. In 1915 A. G. Dumez prepared the double iodide of bismuth and emetine known as emetine-bismuthous iodide. This was introduced into practice by H. H. Dale in 1916 and tried out in a series of chronic cases, and is undoubtedly successful in bringing about a permanent cure.

CHOLERA, PLAGUE, AND UNDULANT FEVER

In this terrible scourge of cholera, whose visitations yearly demand a colossal toll amongst the myriads of religious devotees in India, British writers have played a not ignoble part. It was by John Snow (1813-58), a man who had never lived or worked in the Tropics, that the dissemination of this infection was traced to water supply. Everyone has heard of the story of the Broad Street pump and his observations on the spread of cholera in London in 1854, and it was these facts which were so clearly substantiated by the work of Koch in the Hamburg epidemic of 1892. As regards the pathology of cholera and the part played by carriers in the spread of epidemics, we are indebted to the work of E. W. D. Greig (1914). The treatment of cholera has been much improved by the work of Sir L. Rogers (1908-11). Believing that collapse in cholera was due to the excessive loss of chlorides from the blood stream, he introduced the method of treating cholera by intravenous injection of hypertonic saline solution. It is claimed that since the introduction of his method the mortality from this disease has been much reduced. Rogers has further placed his method on a scientific basis by introducing a special method for estimating the specific gravity of the blood in cholera. The use of Haffkine's prophylactic of killed cholera vibrios which have been grown to great virulence has done much to protect the individual against acquiring the disease. The statistics obtained in the Balkan war of 1913, in Batavia in 1915 and 1916, and during the course of the great war have done much to confirm the early impressions of the value of Haffkine's inoculation.

It was J. Ashburton Thompson who from 1900 to 1906, by his observations on plague in Sydney and by his very careful analysis of the epidemiological facts observed in the Sydney outbreak, first reached the conclusion that plague in rats always preceded plague in man, and that infection was transferred from rat to rat and from rat to man by means of the flea and in no other way. He did this after the German and the first Indian Plague Commissions had decided against this theory. The work of Glen Liston (1905) and the Report of the second Indian Plague Commission (1906-8) amply confirmed these observations and gave due credit to Thompson's originality. The exact method of multiplication of the plague bacillus in the flea and the conditions governing the transmission of the bacillus by that insect were worked out in a very fine and precarious piece of research by C. J. Martin and A. W. Bacot in 1911. The part played by the rat-flea (*X. cheopis*) in plague has naturally stirred the entomologists to study the morphology of these insects closely. In 1914 C. Röthschild and K. Jordan described the rat-

fleas of India as belonging to three closely allied species, *Xenopsylla cheopis*, *braziliensis*, and *astia*. It soon became apparent from the work of F. Hirst and F. W. Cragg that the last-named species is either unsuitable for the conveyance of the plague bacillus or it is unable to effect it, so that its presence as the common ectoparasite of the rat in India and Ceylon probably explains the absence of plague in districts where the appropriate rats are common.

Undulant fever was previously termed Malta fever. Marston, who personally suffered from the disease in 1859, first gave an accurate account of its clinical history under the term "Mediterranean remittent or gastric remittent fever." In 1886 David Bruce was the first to recognize and to demonstrate in the spleen of ten fatal cases of undulant fever the specific microbe, which he named *Micrococcus melitensis*. In 1905 Bruce and his wife, together with Zammit, discovered that the goat in the island of Malta was the source of the infection of undulant fever, and were able to lay down the measures for the control of this disease which have proved so eminently successful. The recent history of undulant fever, especially the serological diagnosis and the treatment of the disease, has been much illuminated by the late Sir P. W. Bassett-Smith (1861-1927). The association between *Brucella abortus* in cows' milk and a type of undulant fever in man, now known as abortus fever, was made by L. E. W. Bevan in 1922, and the main conclusions he arrived at have since been found to be correct.

FILARIASIS AND BILHARZIASIS

The subject of filariasis is the corner-stone of tropical medicine. The *Filaria sanguinis hominis*, to use its ancient terminology, was originally described in Havana by Demarquay in 1863 in a case of chylous hydrocele; but Timothy Lewis in Calcutta appears to have been the first to observe the larval nematode in the blood stream in 1870, and again in 1872. It was about this time that modern tropical medicine was born. It was Lewis's work that made such a momentous impression on Manson. In 1875 Patrick Manson in Amoy, China, not only confirmed Lewis's discovery, but in 1877 stumbled upon the periodicity—the swarming of these parasites in the night blood. In the next year, following the line of argument he had amplified as the result of these observations, he was able to trace the development of the embryo filaria in the thorax of the mosquito, which he, at that time, regarded in the light of a nurse to her unwilling charge. The adult filaria, now known as *Filaria bancrofti*, was found in 1876 by Dr. Joseph Bancroft in Brisbane and independently by T. Lewis in Calcutta. The actual time-cycle development of the filaria in the mosquito was worked out first by Dr. Carmichael Low in 1900 on material sent to Manson by Thomas Bancroft, the son of Joseph aforementioned. About this time S. P. James, working in India independently on these same lines, was able to confirm this observation. Patrick Manson's observations on three other species of human filariae—*Filaria ozzardi*, *Loa loa*, and *Acanthocheilonema perstans*—were made during the years 1891-7, and his predictions regarding their respective life-histories have turned out to be remarkably correct.

Bilharziasis has been known to exist in Egypt since the earliest times. In 1851 Bilharz originally discovered the parasite in Egypt, and the parasite was accurately described and named *Bilharzia haematobia* by Spencer Cobbold in 1859. The parasite was rediscovered by Harley in Natal in 1864, and its characteristic eggs demonstrated in the urine. The life-history of this parasite outside the human body and its method of transference from one man to another had long been a subject for speculation. Manson

had always stressed in early editions of *Tropical Diseases* that the life-history would in the main be analogous to that of the liver-fluke, *Fasciola hepatica*, whose cycle in a pond snail—*L. truncatula*—had first been worked at by Thomas in 1883. The first inkling of the true life-history was afforded by Ogata in 1914 for the allied species *Bilharzia japonica*, which was afterwards confirmed by R. T. Leiper and E. L. Atkinson. In 1915 R. T. Leiper, in Egypt, not only discovered the life-history of this parasite in the freshwater snail *Bullinus contortus*, but was also able to separate the intestinal form of bilharzia—*B. mansoni*, of which the lateral-spined eggs occurring in the faeces had been recognized in 1903 by Manson, and which was found to possess a distinct morphology and to develop independently in a snail belonging to a different genus, *Planorbis*. The method of successful treatment by means of continued injections of antimony tartrate in increasing strength we owe to J. B. Christopherson, who worked it out in Khartum in 1917, and it has hardly been improved upon up to the present day.

COUGH IN CHILDHOOD *

BY

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The symptomatology of diseases in childhood is rendered difficult by the absence of accurate self-expression on the part of the patient; in consequence, any symptom which can be carefully described by other observers must be regarded as of very great value. It is probable that in this fact lies the reason for "cough" being one of the commonest complaints made by parents on behalf of their children, and the frequency of this symptom justifies a more detailed analysis than is usually made in the standard textbooks. It will probably serve to introduce the subject in a more orderly manner if a definition of "cough" is first attempted, followed by a brief summary of the modern views on the physiology of the condition.

A cough is a modified expiration of an explosive character designed essentially to remove a foreign body from the mucous membrane of the respiratory tract.¹ Coughing may be voluntary or it may be purely an involuntary reflex act. Usually it is a mixture of the two: a reflex act reinforced by volition.² Thus, even in the voluntary act, there is a reflex element, and it is therefore important to consider the possible sites where the primary stimulus may arise. Broadly speaking, the afferent portion of the reflex arc runs in the glossopharyngeal nerve from the upper parts of the respiratory tract and in the vagus from the lower parts. A great deal of work has been carried out in recent years on the relative sensitivity of the various zones, and it seems conclusive that there are definite areas in the pharynx and in the region of the larynx which are more sensitive than others. The region of the bifurcation of the trachea is also much more sensitive than the rest of this structure, and as the respiratory mucous membrane is traced further and further down the bronchi sensitivity gradually disappears. The lung parenchyma is probably almost completely insensitive, although the evidence is a little contradictory. Perhaps the difficulties here can be explained, as Chevalier Jackson has suggested,² on the grounds that "tolerance" is very quickly established in the bronchial system, and after a foreign body has been inhaled the initial stage of coughing or choking is followed by a silent period as

long as the foreign body remains fixed. If movement occurs a new area of mucous membrane is involved, and this sets up a reflex cough, followed again by a period of silence. After pus forms, the cough reappears because fresh areas are stimulated by the inflammatory process. Here again there are difficulties, but, according to the same authority, in any inflammatory condition of the lungs or bronchi the sensitivity of the mucous membrane seems to be diminished. With diminished sensitivity of the smaller bronchi and absolute insensitivity of the lung parenchyma, it is not surprising that in lobar pneumonia, for example, very little cough may be present; this disease, especially in childhood, may pass almost unnoticed, so little is there to direct attention to the lungs. Pleural involvement leads to the classical restrained type of cough, since the pleura is another area from which the cough reflex may be initiated. It should also be noted that, experimentally, there appears to be a strong reflex connexion between the nasal mucous membrane and the bronchial motor system, so that cough may be initiated by the effect of irritant gases in the nose. Similarly, cough may be produced experimentally by certain forms of stimulus applied to the oesophagus or stomach, probably because of the common vagal nerve supply.

It follows from this brief summary of the origin of the cough reflex that the upper part of the respiratory tract down to the level of the bifurcation of the trachea is of very much more importance than the portions of the respiratory apparatus below this point, and that, especially in childhood, coughs have much less to do with the "chest" than is commonly imagined. It is not an exaggeration to say that the vast majority of coughs in childhood are characterized by a complete absence of physical signs on examination of the chest.

CAUSATION

In considering the possible causes of cough in childhood it will be convenient to proceed anatomically from the upper regions of the respiratory tract downwards, adding comments on special features as the long list of possibilities is set out.

Inflammation of the Nose and Nasopharynx.—Acute inflammatory conditions of the nose and nasopharynx are frequently associated with a cough, but in such instances it is almost impossible to exclude inflammation of other portions of the respiratory tract, and the cough may have a complex origin. Similarly with the difficult question of adenoid tissue in the nasopharynx, this is so frequently associated with tonsillar hypertrophy or pharyngitis that it is impossible to be certain whether adenoids alone can cause a cough. In babies with the comparatively rare condition of congenital adenoid enlargement, a cough may occur, and this, I believe, is an example of a pure "adenoid cough." A foreign body in the nostrils is said to cause a cough in some instances, but I have not yet seen an example of this. With chronic inflammation of the nose and nasopharynx, with or without "adenoids," it is quite common to see pus trickling down the posterior pharyngeal wall; cough in such cases may in part be due to the irritation of this inflammatory material in the lower parts of the pharynx. To sum up the evidence here, I should say that to attribute a cough to a purely nasal or nasopharyngeal origin is usually unwise. The possibility, however, of a cough due to an ear disease must be mentioned. Here again the exact aetiology is complicated by the concomitant tonsillitis or pharyngitis, and I have not yet seen a child with a cough which could be directly attributed to middle-ear disease alone.

Coughs of Pharyngeal Origin.—These are very common, and need little discussion. It should be remembered that a young child seldom complains of a sore throat, and

* An address to the South-West London Medical Society.