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RECENT RESEARCHES INTO THE EPIDEMIOLOGY OF MALTA FEVER.[1]

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IN this place it is not necessary to go into any detail in regard to the history or symptoms of this fever, but a few introductory words will not be amiss.

Malta fever, as you are all aware, is a disease of long duration, averaging four months, but in some cases dragging out its weary length for one, two, or even three years. The temperature-curve is characterised by extreme irregularity, fresh exacerbations of fever being frequent. Another prominent feature of this fever is the presence of symptoms of a rheumatic or neuralgic character. Few marked cases pass through their course without the occurrence of painful and swollen joints or neuritis in various nerves, which combine with the prolonged temperature to bring the patient to a condition of extreme anæmia and debility from which recovery to health is slow.

I think I have said enough of the nature of this fever to impress upon those of you who are not familiar with it the importance and severe nature of the disease under discussion.

Historical.—Let me say a word in regard to the history of

[1] A paper read before the Epidemiological Society, February 15th, 1907.

Malta fever. This fever has naturally been chiefly worked at by Army medical officers who have come in contact with it among the garrisons in Malta, Gibraltar, Cyprus, or at Netley Hospital. Those interested in its history should read the old accounts of it by Marston in 1863 and Veale in 1881. At that time it was generally considered to be malarious in origin, and was usually returned as remittent fever; but the most severe cases were often returned as enteric, and the very mild as febricula or simple continued fever. In 1887 the specific micro-organism, the *Micrococcus melitensis*, was discovered, which effectually separated it from other continued fevers; and it found a place in the third edition of the "Nomenclature of Diseases," published in 1896. In 1904, as the incidence of this fever among the garrison of Malta had increased to a marked extent, the Royal Society, at the request of the Admiralty, War Office and Colonial Office, undertook its further investigation, and sent out a small Commission to Malta for that purpose. This Commission has been at work during the summers of 1904, 1905, and 1906, and the Royal Society has already published seven volumes of reports. It is a summary of the work done by this Commission which forms the subject of this paper.

Geographical Distribution.—In regard to the geographical distribution of this fever a few words will suffice. One curious thing is that it has almost or quite disappeared of late years from Gibraltar, where some years ago it was very prevalent. In the Mediterranean it undoubtedly occurs in such places as Tunis, Algiers and Alexandria, as well as in Malta. It also occurs in such widely separated places as South Africa, India, China, the Philippine Islands and America. It has, therefore, a world-wide distribution, although nowhere does it seem to occur in such numbers as in Malta.

In regard to other etiological factors, such as the influence of age and sex, of occupation, length of residence, climatic conditions, &c., I must refer you to the reports, where the matters are entered into very fully. Permit me, however, to glance briefly at one or two points which I consider of interest.

Social Position.—Here we come against a curious fact, and one which it was impossible to explain until lately. It may be stated, broadly, that the better the social position the more the liability to this disease. Officers and their wives and families, living in large, airy and clean houses, suffer more frequently than the men in their more crowded barrack-rooms. In fact, the risk of the military and naval officer to take this fever is more than three times as great as in the case of the men.

This higher incidence among the officers cannot be explained by sanitary conditions, by convection of the disease by mosquitoes, or by inhalation of infected dust, or any of the theories usually held, as the officer is, if anything, less exposed to these influences than the men.

Climatic Conditions.—The climate of Malta, as you are aware, is extremely hot and dusty from about the middle of June to the middle of October, while the winter months are correspondingly bleak and wet. Now, although the number of cases of Malta fever do show a marked increase in summer, yet it is a disease which is prevalent all the year round, one-third as many cases occurring in the coldest and rainiest months as in the hottest and dustiest. Another fact of interest is that if we study the incidence of Malta fever in individual years we are struck by its irregularity, a large number of cases suddenly appearing in February or December, or other of the cold and rainy months. It was found difficult to reconcile these facts with mosquito or dust theories of propagation.

Distribution of Malta Fever among the Civil Population.—Until recently it was supposed by many of us that this fever was restricted to the inhabitants of the cities surrounding the Grand Harbour. This was in the days when the theory was held that the virus was carried in sewer air or other foul gases. As the Grand Harbour in those days was a huge cesspool, the drainage of the cities falling into it, there was some excuse for a belief in the theory. Malta fever is now known to occur in every part of Malta, and, in fact, the very general distribution of the fever is very striking. It is not the cities round the harbours which are struck most heavily, some of the inland towns and villages showing a much greater incidence.

It is evident, then, that the incidence of Malta fever cannot depend upon sanitary conditions, since the greatest variety exists, from the paved, drained, swept Valletta, to the inland towns and villages where the most insanitary conditions prevail. It cannot depend on the water supply, since there is often a larger number of cases in towns with an excellent supply of pure water than in towns which depend for their supply on shallow wells. The cause must be sought in some condition which affects all classes and all conditions.

Distribution among the Garrison.—Next I would draw your attention to the prevalence of this disease among our soldiers and sailors in Malta, in order to impress upon you the importance of

this disease to the State. Among the soldiers, who average, as a rule, about 8,000, there is an average yearly incidence of 37·6 per 1,000, or 312 admissions to hospital every year for Malta fever. Among the sailors there is an incidence of 28·55 per 1,000, or about the same number of admissions to hospital as among the soldiers.

Now as the average duration of this disease may be put down at four months, it means that 624 soldiers and sailors are in hospital 120 days, which makes 74,880 days of illness. What an amount of personal suffering and loss to the State this sickness and invaliding entail it is impossible to estimate, but the mere pecuniary loss must be very considerable.

Study of the Micro-organism which causes Malta Fever.—It is evident from the foregoing account that little light has been thrown on the etiology of this disease by a study of sanitary conditions, effect of climate, age and sex, length of residence, occupation, food or water supply, &c. It is therefore necessary to turn to the laboratory to see if anything can be discovered from a study of the micro-organism which causes the disease. The *Micrococcus melitensis* has been described so often that it is not necessary for me to do so. Suffice it to say that it is very minute, that it grows outside the body on artificial media, and that it can be distinguished from other micro-organisms by suitable tests.

The members of the Commission entrusted with the laboratory work set themselves to study how this micro-organism leaves the body, how it behaves outside the body, and how it is able to again gain entrance to the body.

How does the Micrococcus melitensis *Leave the Body ?*—It is important, of course, to find out how a parasite leaves the body, as this may throw light on the mode of infection. Many experiments were made to try to discover it in the expired air, in the saliva, expectoration, sweat and scrapings of skin of patients, and finally it was decided that the principal path by which this micro-organism leaves the body is by way of the urine. It is true it also leaves the body in small numbers by way of the blood, by the agency of mosquitoes and other biting insects, and this led to the idea that infection might take place in this way. The urine sometimes contains the Micrococci in enormous numbers, but as a rule they are scarce, ranging from three or four to as many hundreds per cubic centimetre. The Commission examined several thousand samples and found the micrococcus in 10 per cent. This excretion of the

parasite in the urine, taken in conjunction with its resistance to drying, was looked upon by the Commission as a very probable factor in the spread of the disease, and many experiments were made on this hypothesis.

Life of the Micrococcus melitensis *Outside the Body. Vitality of the Micrococcus.*—Many experiments were made by the Commission, the results of which went to show that this micro-organism is fairly resistant to external influences. It can exist in a dry condition in dust or clothing for two to three months. It lives in tap-water or sea-water for about one month. Even in urine which has decomposed and become markedly alkaline it can live for a week. Exposure to direct sunlight kills it in a few hours.

Habitat of the Micrococcus Outside the Human Body.—Many attempts were made to discover this parasite outside the body. As the theories in vogue named insanitary conditions, sewer air, dust from infected places, the water of the harbour, &c., as causing this fever, diligent search was made in every likely place to discover this microbe, but up to the present with no success.

How does the Micrococcus Gain Entrance to the Body?—It is on finding the correct answer to this question that the success of an investigation such as this probably hangs. Does the parasite gain entrance by way of the alimentary canal, by the lungs, through mucous membranes, or through the skin? In other words, is it conveyed from the sick to the healthy by means of food or drink, by contaminated dust, or by blood-sucking insects?

In trying to find out a means of stamping out a disease, it is important to try to narrow down the paths of infection. As long as yellow fever was thought to be spread by contact, infected clothes, food, water, &c., nothing could be done. As soon as it was discovered that it was spread by a particular species of mosquito the problem of prevention was simple. In the same way in Malta fever: if it can be spread by contact, contamination of food or water, by the inhalation of dust, sewer air, &c., it will be impossible to do more than recommend the ordinary established rule of hygiene. But, on the other hand, if the mode of spread can be narrowed down to some one path, then stamping out the disease becomes possible. Let me, then, shortly discuss the experiments made by the Commission to solve this question.

By Contact.—This is important, as questions of segregation, evacuation and disinfection of barracks depend on this mode of infection. Experiments were made by placing monkeys in more or less intimate contact, and it was found that if the contact was

quite intimate infection does take place. If, on the other hand, the contact is less intimate, so that contamination of the food by infected urine was prevented, infection did not take place. It was concluded that monkeys probably took the disease by having their food contaminated by the urine of their sick neighbours, and that therefore contact resolved itself into a feeding experiment. As it is very unlikely that man has his food so grossly contaminated as in the case of the monkey, it is improbable that infection takes place, except very rarely, in this way.

In regard to this question of conveyance by contact, there is one argument against it which seems to me unanswerable, and that is that thousands of cases of Malta fever have been invalided home to England and treated in our naval and military hospitals, without, as far as I am aware, a single case of the fever arising among the patients, orderlies, or nursing sisters. We may, therefore, conclude that contact with Malta fever patients, or the handling of infective clothing or discharges, is not the path by which the Micrococcus gains entrance to the body.

By Dust Contaminated by the Micrococcus melitensis.—For some time it was considered probable that this would prove to be the common method of infection. The fact that the Micrococcus withstands drying for a long time, the dusty nature of Malta, and the probability that gross contamination of the surface of the soil takes place by infective discharges, rendered this view likely.

Experiments were made to put the theory to the test. Dust was artificially contaminated with Micrococci and blown about a room in which monkeys were confined, or blown into their nostrils or throat. Several of these experiments were successful. It was therefore proved that dust artificially contaminated with *Micrococcus melitensis* could give rise to the disease. This, however, was no proof that this mode of infection occurs in Nature. The artificially-contaminated dust contained myriads of Micrococci. Under natural conditions they could seldom be numerous, and the powerful Maltese sunlight would tend to kill them off rapidly. The dust blown about by the wind must also dilute the Micrococci to an enormous extent, so that it is only possible to conceive of a Micrococcus here and there in a vast quantity of dust. Experiments were therefore made with dust contaminated with urine, in order more closely to resemble natural conditions. The Commission made many experiments on these lines, but in no case with a successful result. Dust collected from suspicious places and blown about the cages, sprinkled on food or injected under the skin, also gave negative results. The

conclusion was therefore come to that conveyance of the infective germ by means of contaminated dust could only rarely, if ever, give rise to the disease.

By Way of the Alimentary Canal.—As it is most important to ascertain, without the shadow of a doubt, whether an infective micro-organism can enter by way of the alimentary canal, many feeding experiments were made. It had long been known that the smallest quantity of the Micrococci introduced under the skin, or applied to a scratch, would give rise to the disease in man and monkeys, but some previous work had cast doubts on infection by the mouth.

I need not bring the details of these experiments before you, but will only state that it has been abundantly proved that Malta fever can be conveyed to healthy animals by way of the alimentary canal. Even a single drink of fluid containing few Micrococci almost certainly gives rise to the disease.

By Mosquitoes or other Biting Flies.—As already mentioned, the theory had been advanced that Malta fever, like yellow fever and plague, might be conveyed by blood-sucking insects. The fact that the Micrococci are frequently found in the peripheral blood, although, it must be confessed, in very small numbers, gave some colour to the belief. The Commission, therefore, fully investigated this question and made numerous experiments with the different species of mosquitoes found in Malta, and also with other blood-sucking insects.

The results went to show that this mode of conveyance of the Micrococci from sick to healthy animals, if not absolutely negatived, can only be of the rarest occurrence.

Up to this point, then, the Commission had shown, by experiment, that the most probable way the Micrococcus gained an entrance to the body was by the alimentary canal, and therefore by some infected food or drink. There was no evidence that contact, inhalation of infective dust, or mosquitoes, play any prominent *rôle*. But, on the other hand, the epidemiologists could see no reason for suspecting the water supply or any particular food-stuff.

Infection by Means of Goats' Milk.—At last a discovery was made which threw a flood of light on the obscurities and seemed to explain the epidemiological features of the disease. This was the remarkable discovery that the goats in Malta act as the reservoir of the virus of this fever. The discovery came about in this way. In an investigation of this sort it is part of the work to examine the various surrounding animals to find out if any of them are suscep-

tible to the disease. The monkey was the only animal which was known to take the disease naturally, although some of the laboratory animals, such as the rabbit and guinea-pig, could be made to take the infection by various expedients, such as, for example, intracerebral inoculation. In this way the goat came under observation. The goat is very much in evidence in Malta and supplies practically all the milk used. Flocks of them wander about the streets from morning till night and are milked as required at the customers' doors. It must be confessed the Commission had little hope that an examination of these animals would yield anything. As a matter of routine several goats were inoculated with the Micrococcus and the result watched. There was no rise of temperature, no sign of ill-health in any way, but in a week or two the blood was found to be capable of agglutinating the specific micro-organism. Even then, the goat seemed such an unlikely subject for Malta fever, the observation was in danger of lapsing. Nothing more was done for several months, when by accident the matter came up again, and it was decided to repeat the inoculation experiments. A small herd was procured for the purpose, and, as an ordinary precautionary measure, their blood was examined before inoculation. Much to the surprise of the Commission, several of them were found to react naturally to the agglutination test, and this led to the examination and the discovery of the *Micrococcus melitensis* in the blood, urine and milk. Some thousands of goats in Malta were then examined, and the epoch-making discovery was made that 50 per cent. of the goats in Malta responded to the agglutination test, and that actually 10 per cent. of them were secreting the Micrococci in their milk. Thus the long and tedious investigation of this fever was beginning to bear fruit. Monkeys fed on milk from an affected goat, even for one day, almost invariably took the disease. At this time, curiously enough, an important experiment on the drinking of goats' milk by man took place accidentally. This is the case of the s.s. "Joshua Nicholson," which has been fully described by Staff-Surgeon Clayton, R.N., in vol. vii. of the Reports of the Commission. Shortly, the story is as follows: In 1905 the s.s. "Joshua Nicholson" shipped sixty-five goats at Malta for export to America. The milk was drunk in large quantities by the captain and the crew, with the result that practically everyone who drank the milk was struck down by Malta fever. There is no need for me to go into the details, as these can be read in the report. I may add, however, that sixty of the goats (five having died) on arrival in America were examined and thirty-two

found to give the agglutination reaction, while the *Micrococcus melitensis* itself was isolated from the milk of several of them.

This epidemic of Malta fever on board the "Joshua Nicholson" furnishes, in my opinion, the clearest proof possible of the connection of Malta fever in man with the Maltese goat.

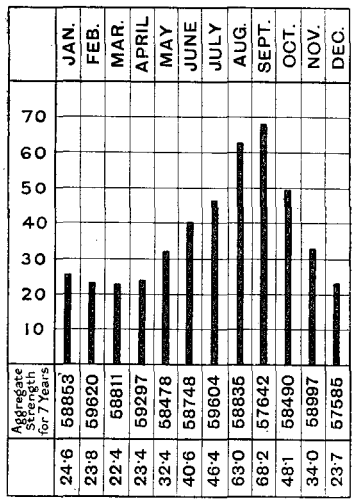
Another proof of this connection is given by Major Horrocks, R.A.M.C., the Sanitary Officer at Gibraltar, and published in vol. v. of the Reports. Twenty years ago Malta fever was very common in Gibraltar, but since that time the incidence has gradually lessened, until it finally disappeared completely in 1904. Horrocks has made the curious and important observation that this disappearance of Malta fever from Gibraltar is associated with the disappearance of the Maltese goat. He says that in 1883 practically all the goats on the Rock were Maltese, and at that time regular shipments of goats from Malta to Gibraltar took place. *Pari passu* with the withdrawal of grazing passes, and the increase in the cost of shipment, the importation of goats from Malta ceased, and goat-keepers replaced their stock partly by importation of Spanish goats and partly by breeding.

Here, then, at last, has been discovered a mode of infection which explains many of the curious features in the epidemiology of Malta fever—the irregular seasonal prevalence, the number of cases which occur during the winter months, when there are no mosquitoes and little dust. It is true there are more cases in summer, but this may be explained by the temperature being more favourable for the multiplication of the Micrococcus in milk that has been set aside, and to the fact that more milk and cream is used for fruit, in ice-creams, &c. It explains the liability of the officer to attack being three times as great as in the case of the private soldier, since the former consumes much more milk in various ways than the latter. It also explains the isolated epidemics which sometimes occur at any season of the year in institutions or in messes, such as that published by Dr. Johnstone in vol. ii. of the Reports of the Commission, where a sergeants' mess was severely struck, while the men living in the vicinity escaped.

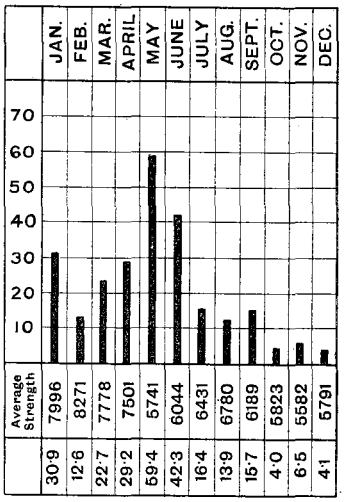
Result of Measures directed against the Use of Goats' Milk.—Preventive measures, as a result of this enquiry, were first begun in Malta in June, 1906. Of course, much opposition and prejudice were met with at first, but by dint of argument and explanation most of the regiments and military and naval hospitals agreed to banish goats' milk from their dietary. The result is very striking,

MONTHLY PREVALENCE RATIO PER 1,000 OF STRENGTH, EXPRESSED IN TERMS OF AN ANNUAL RATIO.

1899 to 1905

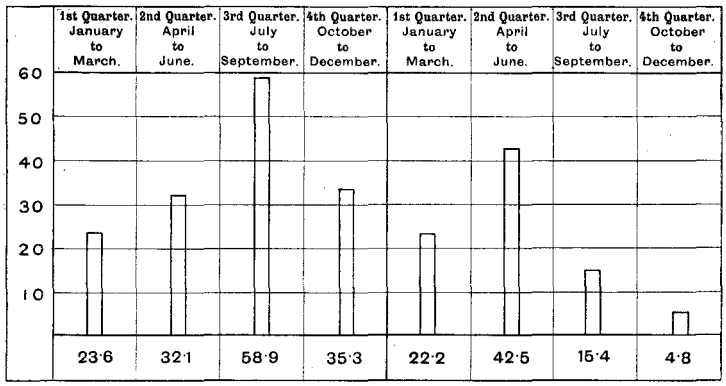


1906



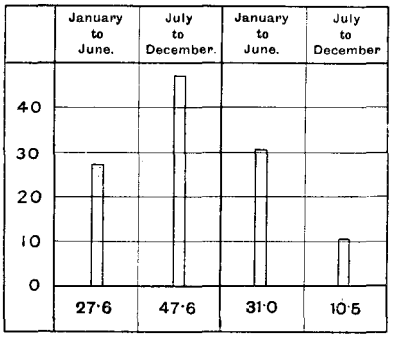
QUARTERLY PREVALENCE.

1899 to 1905 1906



HALF-YEARLY PREVALENCE.

1899 to 1905 1906



as is shown by Majors McCulloch and Weir, in the accompanying charts, which give the number of cases of Malta fever among the soldiers in the garrison before and after the preventive measures came into action.

The preventive measures, it must be repeated, only came into practical use about the beginning of July, 1906, and a remarkable diminution in the incidence is at once seen. Broadly speaking, the cases dropped to one-tenth of what would have been their normal number. It will also be noted that 1906 began badly, there being an average incidence of 31·0 per 1,000 for the first six months, against 27·6 per 1,000 for the years 1899 to 1905.

Another striking example of the benefit of this simple preventive measure is given in the case of the Royal Naval Hospital, Malta. This hospital is a fine modern building, situated in extensive grounds, surrounded on three sides by the sea, with excellent drainage and water supply, and beautifully kept. In spite of these advantages this hospital has been in bad repute for years on account of the number of cases of Malta fever which broke out among its inmates. According to Staff-Surgeon Clayton, who enters very fully into this question in his report, one-third of the cases of Malta fever which occur in the Navy can be traced to residence in this hospital. The goats supplying the hospital with milk were examined and several of them found to be excreting the Micrococcus in their milk. Goats' milk was forbidden, and from that date not a single case has occurred or can be traced to residence in this hospital.

Taking all these facts and arguments into consideration there is, I think, reasonable ground for the hope that Malta fever will now disappear from the garrison in Malta, and some 70,000 or 80,000 days of severe illness be blotted out from the yearly medical reports of the Army and Navy. This much to be desired result, which, in my opinion, must come off if the Maltese Government only take the necessary simple measures, will change Malta from one of the unhealthiest and most dangerous stations of the British Army to one of the most salubrious; and you will agree with me that the Royal Society and the members of the Commission are to be congratulated on the successful issue of the investigation.