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THE INFLUENCE OF NATURAL SELECTION ON THE INCIDENCE OF LEPROSY[1]

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INTRODUCTION

The application of the laws of natural selection to the study of the behavior of diseases that wax and wane has been sadly neglected in medicine. Topley and Wilson (21) quote Andrewes, with full approval, as saying:

> Of all the teeth in the terrible comb with which Nature sorts out the inefficient, disease is one of the most formidable.

There is, however, active opposition to the introduction of natural selection as a reasonable explanation of some of the phenomena of the behavior of disease. This is curious, and seems in part due to a fear that acceptance of such a doctrine might paralyse efforts to limit the ravages of certain diseases.

Belief in the operation of natural selection does not, of course, lessen the importance of conditions such as improvement in housing,

[1] This subject was presented before the Congress of the Australasian Association for the Advancement of Science, in Sydney, on August 18, 1932. This was done with apologies for venturing into the field of evolutionary science, and with an invitation for criticism and advice from those who are expert in that field. On the other hand, it was believed that there is perhaps some advantage in having a medical man present the problem of the influence of natural selection on the course of endemic disease.

hygiene and nutrition, or of other influences such as treatment which diminish the period of infectivity of a disease. If, for example, we believe that leprosy waned in Europe because it exhausted the susceptible stock, it does not follow that public health authorities should let leprosy run its course unchecked. Yet such a consequence was actually suggested by Muir, of Calcutta, who believes that the great epidemic of bubonic plague known as the "Black Death" cleared England of leprosy by greatly reducing its population. It would be just as logical if I should suggest that his belief might be understood by health authorities as being a suggestion that leprosy might be wiped out by deliberately spreading bubonic plague.

Muir goes to considerable lengths in his opposition even to the theoretical application of natural selection to the leprosy problem. For example, he says (15):

> It has been put forward by certain writers that the relative freedom of certain countries is due to an acquired racial immunity, but there is no reason to believe that this is so. Europeans living in Eastern countries are just as liable to it as the native inhabitants and there are many instances of Europeans who have contracted it from native servants and others, even in spite of their comparatively hygienic mode of living.

The second statement, advanced in justification for the first, is just as devoid of supporting evidence as that which it is intended to uphold. The number of Europeans in India with leprosy should be easily ascertainable, and statistical evidence must be had before so sweeping a statement can be accepted. That many Europeans have contracted it, in spite of their higher standards of hygiene, is a vague statement of negligible value. If the word "many" means simply that in Muir's experience he has on some inconsiderable number of occasions found Europeans who have been infected, the evidence is unimportant. No one will deny that susceptibles still occur in European stock, or that the unfavorable conditions of the tropics will in some cases diminish the natural resistance to a point below the threshold. If "many" means a number approximating the proportion of natives infected in the same district, this statement is contradictory to the first one. The protective value of higher standards of living and hygiene is admitted by all. It therefore follows that if Europeans are "just as liable to (leprosy) as the natives" in spite of their standard of hygiene, then the natural resistance of the natives must be markedly higher than that of Europeans. For "many" we must substitute some figure. If this is small in comparison with the incidence in the natives, the evidence is unimportant. If it is large, the existence of a higher resistance in one race than the other will be evident. In the absence of any evidence of value supplied by Muir to support his contention it is worth while to seek evidence on the opposite side.

The present paper presents the argument which leads me to believe that natural selection was the major and most important influence that determined the disappearance of leprosy from Europe.

It includes some portions of a previous one (14), which has been the subject of lengthy comment by Muir (16). His criticism, though drawing attention to some real defects, shows a failure to appreciate the real foundations of my argument, and displays many misconceptions as to my statements and object. In the present paper I have made some corrections, have defended some statements and conclusions to which Muir objects, and have added a discussion of the Black Death hypothesis. I have abbreviated the evidence in support of my premises (which, of course, are the foundations of my argument) since much of that given in the previous paper would appear obvious. I am anxious, however, to obtain what has not yet been supplied, namely, criticism from someone familiar with the laws of natural selection. I shall welcome any correction, even if it means the abandonment of my belief.

VARIATIONS IN SUSCEPTIBILITY TO DISEASE

Certain infectious diseases are checked and limited by artificial immunization, as for example small-pox and typhoid fever. Improvement of water supply and sewage disposal has eliminated others. Syphilis has been definitely diminished by increased efficiency of treatment. But other diseases have nearly or quite died out from certain races without the intervention of scientific measures, though these same infections remain virulent to races which are new to them. The virulence of tubercle bacilli in the average European on the one hand, and in the Senegalese (21) or Australian aboriginal on the other varies greatly. The mortality from measles in a European community is insignificant in comparison with its plague-like ravages among previously sheltered islanders. Without going here into the question of environment, nutrition and hygiene, it may be said that the Senegalese exposed to tuberculosis is much more likely to contract it than is the average European; and, once infected, is much less likely to survive the infection, even under the best of circumstances.

The most remarkable instance is afforded by leprosy. This was common among Europeans between 500 and 1200 A.D. except in Scandinavia and certain other communities beyond the sphere of Roman colonization. The first leper house in England was in use in 600 A.D. (10), and there were many between 1000 and 1300 A.D. The disease was introduced into Scandinavia from England by the Vikings in Saxon times, but as shown by the establishment of the

first leper house (12) it was 1000 A.D. before it assumed the importance which it has reached in England 400 years previously. It is significant that leprosy has only recently died out in the Shetlands, and it still survives, though moribund, in Norway.

Leprosy has persisted in the East, but even in India and China its incidence today is not nearly so heavy as it is when first introduced among virgin races like Pacific Islanders or Australian aboriginals. It was brought into Victoria by Chinese during the days of Gold Rush (20), but not a single European case was observed though housing, hygiene and nutrition were certainly bad under gold-rush conditions. But when it was introduced into Northern Australia—again by Chinese—it affected the aboriginals in large numbers (2). It can flourish in temperate and cold climates, as in England and Norway, so tropical conditions are not essential to its spread. Why, then, did it fail to cause epidemics in London, Paris, Hamburg and other European cities where lepers reside without any restriction? According to Darier (4) there are more than 150 lepers domiciled in Paris.

PREVIOUS HYPOTHESES OF THE DISAPPEARANCE OF LEPROSY FROM EUROPE

Two main reasons have hitherto been advanced to explain the disappearance of leprosy from Europe. These are: (1) the supposed efficacy of the mediaeval regulations against leprosy, and (2) the improved housing, hygiene and nutrition of the modern European. Another reason that has been advanced is (3) the influence of the great epidemic of bubonic plague, the Black Death.

1. MEDIAEVAL REGULATIONS

Belief in the efficacy of these regulations became general when leprosy was shown to be an infectious disease. In those days there was much more faith in isolation as a means of controlling infectious diseases than exists today. Later examination of the value of these regulations for the conduct of lepers has reduced faith in their efficacy to the vanishing point. Hutchinson (7) and Liveling (13) long since ridiculed the idea, and had Virchow in support (18). Cabanes' account (1) shows that the leper houses provided charity and shelter for the lepers without segregating them, and makes it still more difficult to credit the regulations with any real force as preventive measures.

Rogers and Muir (18), who formerly expressed belief in isolation of leprosy, have now withdrawn their support (15, 19). They follow the lead of others in pointing out that fear of isolation causes concealment of the cases, thus leaving them a source of infection for a greater time than is the case when there is no fear of segregation. If the powers of modern science, with early diagnosis, are useless even with the added force of hopeful treatment, how can we credit the absurdly inadequate mediaeval regulations with any real effect in the eradication of leprosy from Europe, especially when there was no hope of cure to induce disclosure of the condition?

Topley and Wilson (21) gave as a considered opinion:

> If isolation removed from the community the whole, or even the great majority of infected individuals it might be expected to exert a considerable influence on the prevalence of an infective disease. But if the ratio of latent or atypical infections to clinically recognizable cases is high, we cannot hope to effect any marked reduction in the morbidity rate by removing to hospital those cases which exhibit the typical stigmata of the disease . . . It is interesting to find that the expectations based on bacteriological and experimental findings are borne out by administrative experience . . . The value of the isolation hospital must apparently be judged by the benefit which it confers on the sick within its walls; for it would seem to have little effect on the health of the community as a whole.

These authors do not, it is true, apply these findings to leprosy, but the wording of this quotation could not have been made more applicable to leprosy if it had been specially designed for that purpose.

It seems only fair, then, in considering the eradication of leprosy from Europe to dismiss the influence of mediaeval regulations as negligible. However, this does not mean that isolation practiced with modern knowledge, especially by a strong government upon a docile native population in small communities such as islands, and aided by modern treatment, is incapable of modifying the ravages of the disease. But in India Muir finds it worse than useless, and in parts of the world like Central Africa it is impossible.

2. IMPROVEMENT IN LIVING CONDITIONS

It is well to admit at once that improvement in housing, hygiene and nutrition is a potent factor in diminishing the ravages of an infection like leprosy in the generation to which they apply. But it is quite another thing to believe this influence capable of eradicating

it. The converse may be true, viz.: Europeans living under conditions which to them are unnatural and unfavorable, as in the tropics, may show less resistance to leprosy than do their brothers in Europe. But there is significance in the figures for the French convicts in New Caledonia (18):

> The reported rates per mille were 200 in 1899, 82.1 (or, if half the suspected cases are included, 119) per mille in 1905, and 57.1 in 1909 (Ortholan). In 1914 (Leboeuf) the rate had fallen to 26.6 per mille in the natives, and was 12.4 per mille among the Europeans, being twice as high in the European convicts as in the free population.

Even under severe penal conditions, among convicts almost certainly deteriorated by excesses, the tropical climate, and probably by disease, the incidence (in 1914) was but half that among the natives, and only a fraction of that among the natives fifteen years before.

The incidence in India today is nothing like that in New Caledonia when leprosy was first introduced there, or that in the Sandwich Isles (8) and in Nauru (5). It is questionable, in spite of Muir's protest, whether the standard of hygiene and nutrition of the masses in India is higher than that of the average Pacific Islander. It seems, therefore, that the Indian today has a higher average resistance than the Polynesian.

It is when we examine the living conditions in England and France during the period of decline of leprosy that we find the strongest evidence that this factor cannot explain the disappearance of the disease. In England this was during the 13th, 14th and 15th centuries, but it was not until the late Tudor period that conditions improved to a degree that would seem to justify a belief in the efficacy of this factor. In France, even up to the time of the Revolution (1789), the peasants lived under conditions of misery, overcrowding and squalor that can only be regarded as tending to favor rather than eradicate leprosy. Yet centuries before the revolution the disease had disappeared from France, except in Brittany. This, however, could still have provided a focus for re-infection, if the rest of the population had been susceptible.

Regarding the conditions in England between 1400 and 1600 A.D. (3, 11) one finds such passages as this:

> The narrow unhealthy homes of all classes of the people, the filthy neglected streets, the abundance of stale fish that was eaten, the scanty variety of the vegetables that were consumed.[2]

These conditions, described as typical of the century or so which followed the Black Death in spite of increased wages occasioned by the diminution of population that it caused, cannot have tended to eliminate leprosy.

Moreover, the improvement in living conditions that came gradually after the 15th century reached Scandinavia almost as soon as England and France, yet leprosy still lingers in Norway, 400 years after it died out in the other countries. Are we to contend seriously that the conditions of life among even the most ignorant of the Norwegian population, right up to 1900, was so inferior to those existing among the other peoples between 1300 and 1500 as to explain the survival in Scandinavia? Without denying the beneficial action of improved hygiene and nutrition, this influence cannot be credited with being the sole cause or even the main factor in the disappearance of leprosy from England and France.

3. THE BLACK DEATH

The third hypothesis to be advanced, that of the Black Death, is really only a variant of that of improved living conditions. When Muir ascribed to this epidemic a dominant share in the elimination of leprosy from England, he implied that its influence is more important than the evolutionary one, if it does not exclude it. His belief is based on the considerations:

(a) That leprosy does not spread rapidly in sparse populations, and that the Black Death killed off 50 per cent of the inhabitants of England, thereby making the population sparse to a degree that prevented the spread of leprosy.

(b) That as the result of scarcity of labor wages rose considerably and better conditions obtained for the remaining population.

Examining the first ground, the statement that leprosy does not spread rapidly in sparse populations may be true of some communities in India today. However, leprosy did spread in the sparse population of Britain when the disease was introduced by the Romans. Leprosy does spread, and alarmingly, in the sparse aboriginal

[2] The full quotation from Cunningham, together with other authorities, is given in my previous paper.

population of Northern Australia today (2). But we are not concerned with the rapidity of *spread* of leprosy. Our concern is its *survival* in sparse populations, such as those of Cornwall and Scotland in 1400 A.D. on the one hand, and that of depopulated England after the Black Death on the other hand.

Does Muir mean that the Black Death spared Scotland and Norway, while it ravaged England and France? We know it did not spare the former countries. If, then, sparseness of population due to the plague had any considerable share in the elimination of leprosy from England and France, it is necessary to explain why this did not occur in the still more sparse populations of Scotland and Norway.

Let us assume, for the sake of argument, that it could be allowed that Cornwall, the Hebrides and Shetland were spared.[3] On the depopulation theory it would then become necessary to imagine that these parts of Britain were more thickly populated after the Black Death than the rest of England, if as claimed by Muir the latter was freed from the infection by reason of the sparseness of population. The only other alternative seems to be that such sparseness occasioned by the ravages of a pestilence can eliminate leprosy—though Muir says that in Nauru one favored the spread—while an even greater sparseness due to other causes cannot do so.

It is a fact that for centuries after the plague Cornwall remained sparsely populated in comparison with the rest of England, which by the end of the 17th century had much more than regained its previous density of population. Yet Cornwall continued to produce cases of leprosy until the end of the 18th century, though its inhabitants lived under much the same conditions as those in other parts of rural England. Moreover, Cornwall in the west and Scotland in the north provided foci of infection with a disease which utterly

[3] The commonly held supposition that Cornwall was spared this pestilence is shown to be incorrect by Gasquet's book, "The Black Death", which gives ample evidence that Cornwall was badly striken:

> The diocese of Exeter, comprising the two counties of Devon and Cornwall, was stricken by the disease apparently about the same time as the county of Somerset . . . The number of institutions [of new abbots] in each month of the year points to the conclusion that the disease lingered somewhat longer in these counties than elsewhere. (Page 100).
>
> A bundle of accounts for the Duchy of Lancaster gives a good idea of the effect of the pestilence of Cornwall . . . . Besides numerous holdings and hundreds of acres, represented as in hand and producing nothing, entire hamlets are named as having been depopulated. (Page 200).

failed to re-establish itself in the more thickly populated parts, while demonstrating its capacity to spread in spite of the general standard of hygiene and nutrition of the time. England proper, according to the Black Death hypothesis, must have provided conditions more favorable to it than Cornwall and Scotland. These facts must be reconciled with the depopulation hypothesis if it is to stand as more valid than that of natural selection. On the other hand, the facts present no difficulties under the latter theory.

It would appear, then, that if reduction of population by the Black Death contributed to the result it was mainly in the capacity of handmaid to natural selection, by reducing the volume of stock from which the susceptibles had to be purged.

The second ground advanced is that better conditions of hygiene and nutrition obtained after the plague. But even if they were really better, they were still shockingly bad, as is shown by Cunningham's description. It must be admitted that they were no better than those in Cornwall at the time, and yet with ever improving conditions Cornwall remained infected for three centuries. They were incomparably worse than those which failed to eliminate leprosy from Scandinavia during the 19th century.

If by some extraordinary antagonism the Black Death was responsible for stamping out leprosy, the race would have remained as susceptible as before. Reintroduction of leprosy from Scotland and Cornwall in the 16th and 17th centuries, and from the East in modern times would have caused a new endemic. This has not resulted (4). Clearly, plague as a disease does not act in antagonism to leprosy since India, where plague continues to the present day, is also one of the modern strongholds of leprosy.

All considerations of the depopulation hypothesis lead us to an impasse or an absurdity if used to the exclusion of natural selection. It seems obvious that we have to seek for another and more potent influence than that of improved hygiene and nutrition to explain the disappearance of leprosy from Europe.

ELEVATION OF RACIAL RESISTANCE BY ELIMINATION OF SUSCEPTIBLES

This influence was first advanced in 1873 by Liveing (13), who maintained that leprosy died out because it had killed off the susceptible stock in the population. Sporadic attempts to revive Liveing's application of the theory of natural selection have since been made,

but until the trust in the isolation measure declined they failed to attract much attention. Jadassohn (9) considers at length the history of leprosy for evidence for and against the existence of racial predisposition.[4] Though obviously searching for proof of some such theory, he is unable to express conviction. It is impossible to arrive at a definite conclusion on this basis because of the difficulty of separating the effects of natural selection from those of improved nutrition.

However, the laws of natural selection are now firmly established, justifying one in using them as a basis for deduction. It is hoped to show that, as a result of the operation of these laws, the effect of saturation of the population by a disease like leprosy must be the gradual raising of the resistance of the later representatives of the race. Two premises are necessary:

1. That, apart from deterioration occasioned by unfavorable influences, variations exist in the degree of natural resistance (or, conversely, in the degree of natural susceptibility) to leprosy and to other diseases of chronic infective origin, even in races to whom the disease has not yet been introduced.

2. That such natural resistance (and, conversely, susceptibility) is a characteristic of the kind which is transmissible to descendants, but is not necessarily transmitted to all progeny in the same degree.

The truth of these premises is self evident from analogy with the results obtained in animal herds by Topley and Wilson (21). There is no reason to believe that mankind differs from other animals as a herd upon which natural selection can operate, or leprosy from other infections in the elimination of susceptibles. There is some degree of natural resistance to infection with any and every microorganism; otherwise man's body would be simply a culture medium on which the bacteria would grow until the nutriment was exhausted. Further, this natural resistance is present, in some degree at least, in all men of all generations. Therefore, it is an innate heritable quality and belongs to the category of Darwinian characteristics. All such characteristics, like tallness, skin color, etc., are variable. It would be as absurd to say that all men have the same degree of natural resistance to any infection as to say that all are equally tall. It matters not whether this natural resistance is the same as, or different from, the capacity to react in an allergic fashion (9), since it

[4] Much detail and quotation from Jadassohn is given in my previous article, loc. cit.

is admitted that this capacity for allergic resistance (*Allergisierbarkeit* of Jadassohn) is an hereditary characteristic (Török [22]).

Illustration of the first premise is available in actual life in the history of the outbreak of leprosy in Nauru as described by Dew (5). Here, in a small homogeneous population, occurred an almost incredibly severe epidemic. The incidence was extremely high, 30 per cent of the inhabitants being infected. In 90 per cent the form was mixed or anesthetic, forms which are generally admitted to occur in those possessing a relatively higher resistance. Therefore, in this virgin population we have a large majority whose resistance is high enough to prevent the infection; some in whom resistance, though insufficient to protect against infection, is able to prevent the disease assuming its worst form; and finally a small minority whose resistance is so low that the severe nodular type of the disease develops.

Muir, in his criticism of my previous paper, ascribes the Nauru epidemic to the depopulation of the island and the lowering of the resistance of the survivors occasioned by a visitation of influenza that killed 30 per cent of the population.[5] It is possibly true that the exceptionally heavy incidence of leprosy even for a first invasion was due to this. Possibly the diminution of resistance in the influenza survivors explains the infection of some 10 per cent more than occurred in New Caledonia.

[5] Muir says: If the happenings on this island (Nauru) were to support the hereditary selection theory we should have expected leprosy to spread in an acute form from within a short time of its introduction and that most of the cases would have been of the highly infectious, acute nodular, cutaneous type.

He evidently does not appreciate the fact that the relative proportion of resistants to susceptibles varies with different infections in a given population. We have to consider here a population virgin both to leprosy and to influenza. The proportion of resistants to susceptibles towards the two infections is shown by actual happenings to be different. The figures of the Nauru epidemic show that even in a population virgin to leprosy a large proportion have a high enough resistance to avoid infection, and that comparatively few are so susceptible that they develop the acute nodular form. There was a wide difference between the susceptibility to influenza and that to leprosy.

Muir also maintains that the occurrence of all forms in the first outbreak is "entirely against this theory", but assuredly the existence of all shades of resistance provides an excellent illustration of the soundness of my first premise. When he says that "fatality is a *sine qua non* for feasibility of this theory", it is obvious that a great deal of his antagonism is due to failure to grasp fundamental principles of the laws which govern the operation of natural selection.

CONCLUSION DRAWN

A natural capacity to resist bacterial infections is present in variable degrees in different individuals, and is transmissible by heredity. It therefore only needs the appearance of a particular infective disease, like leprosy for example, to set in motion against it the law of natural selection. Before that happens the natural capacity to resist the disease will confer no advantage to those who hold it in a high degree, and no handicap to those who possess only a modicum of it. After the disease appears, however, these conditions are important. Individuals with low resistance experience a severe form of it which kills them early. Those with high resistance escape it entirely. Between them is the group with moderate resistance who acquire the disease in a more chronic form. This cripples them, diminishes their capacity to provide for themselves and their dependents, renders them more vulnerable to other diseases, shortens their lives, and interferes with their reproduction. Their offspring, if any, are not only exposed to the infection, but simultaneously are subjected to conditions which tend to lower what natural resistance to it they possess. Consequently, the offspring of the more resistant survive in greater proportion than those of the more susceptible parents (17).

It must be remembered, however, that high resistance is not necessarily inherited, or if inherited, is not possessed in the same degree by all the offspring. There are, therefore, considerable differences in the resistance possessed by the second generation issuing from parents who escaped infection. But as generation succeeds generation the susceptible individuals are gradually weeded out, and ultimately the average resistance of the surviving stock is notably greater than that of the race before the introduction of the disease.

This is not to say that the race will have been purged of all the susceptible members. As the disease has less suitable soil to grow upon, victims become fewer and the manifestations less acute and less infective. Consequently, some susceptibles will escape because of the space factor. Nor must one imagine that the resistance is absolute, like the artificial immunity to vaccinia. A proportion of the surviving stock can be infected, especially if resistance is lowered by some adverse condition, as for example another disease toward which little resistance is possessed. Even apart from these considerations it is certain that a few throw-backs will continue to crop up

in a population which has, on the average, a high resistance to the first disease. But if these are only rare the infection, when re-introduced from elsewhere, will have the handicap of space to overcome. The disease will probably die out with those who re-introduced it, or at most find only a few victims (4).

Muir suggests that I should show that the children of leprous parents are more susceptible than those of parents who had been exposed to the infection without contracting it. At this point it is necessary once more to draw attention to certain facts:

1. That natural resistance (or susceptibility) possessed by a parent is not necessarily transmitted in the same degree to the child.

2. Natural resistance is not the only means of defense against leprosy or any other infection. The allergic defense built up by successive small inoculations insufficient to establish permanent disease (as suggested by Wade and Rodriguez) is also a factor, recognized in the case of other diseases as tuberculosis.

3. Natural resistance may be lowered by the effect of other disease or malnutrition, but this acquired reduction of natural resistance is not transmitted to children.

The best fulfilment of the requirement set by Muir would be by inoculation of the children. But even if this were permissible, and if some of them developed leprosy in consequence of the inoculation, the result would be wholly inconclusive. One or both infected parents might have possessed a higher natural resistance than one or both of these who escaped infection. Factors such as the size of dose of infective material, the age when exposed, the state of general health at the time, and the existence or not of acquired allergic resistance, may have contributed to the infection of one pair and to the escape of the other. Therefore, it seems that such a demonstration could not afford convincing evidence. To get dependable evidence it is necessary to consider the results as manifested in many families after a large number of generations.

It may be held proved beyond reasonable doubt that, after a series of generations, the individuals of a family in which the majority of members have been resistant will have a notably higher average resistance to leprosy than the members of a family in which the majority have been susceptible. Moreover, the first family will be more numerous. That experimental demonstration of this in animals

is lacking does not prejudice the conclusion; experiments with other diseases afford ample proof of its accuracy.

EVIDENCE SUPPORTING THE CONCLUSION

The above constitutes the foundation of the contention that natural selection plays an important part in the disappearance of leprosy. All that is necessary now is to check the deduction drawn:

1. By experimental demonstration of the action of natural selection in raising the herd resistance to an infectious disease.

2. By demonstrating that other diseases behave in an analogous manner.

3. By showing that there is nothing in the history and behavior of leprosy which is inconsistent or incompatible with the existence and activity of the influence of natural selection.

Experimental evidence.—This is available in plenty in the herd experiments described by Topley and Wilson (21). The fact that the infection was by other organisms is of little import; we have no reason to suppose that a herd experiment upon man with leprosy would give a materially different result from one upon mice with mouse typhoid. The fact than an endemic of mouse typhoid in a herd of mice does raise the average resistance of the descendants as compared with that of their forbears is a demonstration of Nature's elimination of susceptibles from the herd.

Analogy of other diseases.—Measles affords an example. To a virgin population this is a pestilence and a disaster, but where it has long existed it causes recurring epidemics with only a comparatively low death rate, even in slum inhabitants. The great majority of moderately susceptible subjects survive measles with no injury. The natural susceptibility of their progeny, on the average, approximates that of their parents. The highly susceptible die and leave no progeny. So, gradually, the average resistance is raised though occasional susceptible throw-backs provide fatal cases in the next epidemic. The moderately susceptible stock is influenced little by selection because they survive, breed and transmit moderate susceptibility to their progeny.

With leprosy, on the contrary, the moderately susceptibles under natural conditions suffer grave permanent disability, including diminution or loss of fertility in the males. Unquestionably, this operates to the disadvantage and ultimate great diminution of the mod-

erately susceptible stock. Thus selection seems to operate more severely in leprosy than in measles.

That which happened with leprosy in the 13th and 14th centuries is apparently happening with tuberculosis today. Previously unexposed races develop this disease in larger numbers and, on the average, in more severe form than do Europeans. The mortality curve for tuberculosis had been falling steadily in Europe long before the institution of special hygienic measures, partial isolation, and better treatment.

Historical evidence.—No incident in the history of leprosy has been found inconsistent or incompatible with the action of natural selection. More, the behavior of leprosy in Europe can be explained much more satisfactorily and completely by this than by any other hypothesis.

Leprosy existed in Rome at the time of Pompey and Caesar, and the occupation and colonization of Britain and France by the Romans is an adequate explanation of its introduction into these countries. With the constant movement of troops, their transference from East to West, the settlement of veterans on the colonized lands, and the free traffic between various portions of the Roman Empire, leprosy would doubtless spread much more rapidly within the sphere of Roman occupation than beyond it. Therefore, it is reasonable to put down the date of infection of Britain at 200 or 300 A.D.

In Britain there was intense hostility between the Scots and Roman Britain, and between the Scots and Saxon England, which prevented intercourse. This explains why Scotland and outlying districts were infected later than the main population. Leprosy was known in Scotland by 950 A.D. ([10]), which was more than 300 years after the first leper house in England (600 A.D.). The infection of Norway is traced by Lie ([12]) to England, through the Vikings—i. e., in Saxon times. At any rate, the disease had attained importance there by 1000 A.D. Thus Scotland and Norway certainly were infected and saturated considerably later than England; there is no reason to suppose that Cornwall was an exception.

It apparently took about 1000 years for the susceptible stock to be eliminated from England and France. The fact that Norway has not yet been purged entirely is possible of explanation only on the ground that she is but now approaching the end of the time necessary to eliminate susceptibles from her stock by the operation

of natural selection. This also explains why Cornwall and Scotland lagged behind England in ridding themselves of infection.

As for the prevalence of leprosy in England, it is indeed questionable if it ever was as common as in some races newly infected in recent years. Muir thinks that so high an incidence would have been recorded. However, considering the lack of record of almost everything in early Saxon times, this is no evidence. As he says, many things were doubtless mistaken for leprosy, but it is equally certain that many cases of leprosy were not recognised as such. The fact remains that in a time when there was no public accommodation for the sick there occurred a remarkable innovation in the form of asylums for lepers. This shows that the public must have been thoroughly alarmed at the prevalence of the disease. Until modern times none of the other diseases that killed people inspired the idea of special accommodations.

Every village seems to have had its lepers, as indicated by the leper windows in old churches. The very horror of the disease that has been handed on through so many generations is in a way a record of the terror that it inspired; this would not have occurred as a result of the existence of a few leper cripples. In addition, there are the numerous pictures portraying the piety of various saints who displayed their heroic charity by caring for lepers. All these things show quite clearly that leprosy surpassed all other diseases as a cause of terror to the inhabitants of mediaeval Europe, and this could not have been possible unless leprosy had been common. At any rate, it is certain that leprosy was prevalent to a degree that permitted the operation of natural selection.

With the cessation of selection that occurs when a disease dies out, perhaps susceptibles will increase in proportion, and perhaps in another 1000 years Europe will have another endemic of leprosy if it has not been stamped out. If we accept the mention of leprosy in the Veda as applying to the disease we call by that name today, it is possible that the present endemic in India may be a second wave. We have yet to learn how long the wave of high resistance lasts in a race. Though the elimination of susceptibles from Europe required about a thousand years, we do not know whether after an equal or a longer time susceptibles will again become numerous enough to permit the establishment of a new endemic. However, it is a fact that if resistance and susceptibility are distributed according to Mende-

lian law, and if susceptibility or resistance to leprosy carries no other advantage or disadvantage than is implied in their names, the relative proportion of susceptibles will remain constant after cessation of selection which occurs after the disease dies out. Therefore, it appears extremely unlikely that a new endemic will be established in Europe at any time, unless that continent is inhabited by a different race.

It is to be advanced that fears that acceptance of the natural selection hypothesis will hamper efforts at the control of leprosy are baseless. We will continue to fight the disease and limit its ravages as well as we can. There is no reason for us to neglect our own generation because of what will happen in the dim future.

SUMMARY

1. By appeal to the laws of natural selection and application of the herd experiments of Topley and Wilson it has been shown that natural resistance is necessarily raised by leprosy through the elimination of the great majority of susceptibles in an infected race.

2. The behavior of leprosy in this respect has been shown to be analogous to that of other diseases, like measles and tuberculosis.

3. It has been shown that natural resistance supplies an explanation for otherwise anomalous events in the history of leprosy, events that cannot be explained satisfactorily by any other hypothesis unless it be admitted that natural selection is also in operation.

4. Natural selection was probably the dominating influence in determining the present freedom of Europe from leprosy.

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