muscular fibres in the stroma, and to the formation of fibrous connective tissue, and this may in some instances extend through the substance of the gland.

The inference, therefore, from the case I have related is that these structural changes in the enlarged prostate eighteen days after bilateral castration are preliminary to the ultimate atrophy of the glandular tubules and to the conversion of the prostate into a small, firm, and fibrous mass, containing only remnants of the tubules, and but few traces of its muscular fibres.

Changes similar in many respects to those described above as occurring after castration in man take place in the prostate of a dog after double castration. Thus in June, 1890, I castrated, while residing in Paris, a hound 3 to 4 years old, and three weeks (twenty-one days) after the animal was killed. In the gland, which was obviously small for so large

Fig. 3.—Section of prostate of full-grown dog twenty-one days after bilateral castration $\times 50$. (a) Contracted tubules lined by low cubical or flattened epithelial cells; (b) stroma composed chiefly of fibrous connective tissue.

a dog, the tubules were much reduced in size and number, and the intervening tissue was relatively increased. In many of the tubules the epithelial cells filled the lumen, and these cells were of irregular shape and size. In others the tall and slender columnar cells had given place to a single layer of small cubical or flattened cells enclosing a very narrow fissure-like lumen. In parts of the stroma the muscle fibres had to a great extent disappeared, their place being taken by connective tissue cells; in others, where the tubules had in great measure disappeared, the stroma consisted of fibrous connective tissue with hardly any traces of unstriated muscle fibres.¹

Thus the changes that arise after castration in a man with enlarged prostate are similar to those which follow castration in a dog, and no doubt the ultimate result is the same in each. The gland, whether enlarged or normal, undergoes certain degenerative changes after removal of the testicles which lead to its conversion into a small, tough and fibrous mass in which there are only remains of the glandular tubules and ducts.²

With regard to the enlargement of the prostate gland I published a paper in the *Journal of Anatomy and Physiology*, 1890, vol. xxiv, from which the following conclusions are taken:

1. That enlargement or hypertrophy of the prostate gland results from a growth of the gland tubules with their associated muscle so as to form new gland substance closely resembling that of the normal gland. This constitutes the first or glandular stage.

2. That after a variable time degenerative changes set in which ultimately convert the new tissue into a mass of more or less dense fibrous connective tissue containing only the

atrophied remains of the glandular and muscular elements. This constitutes the second or fibrous stage.

When this second or fibrous stage has been reached throughout the gland, as occasionally happens, I apprehend that castration would not cause any very marked diminution in size of the enlarged prostate and, therefore, it must not be supposed that dwindling of the enlarged gland will invariably result after castration, though this may be the usual result.

THE MILROY LECTURES ON THE NATURAL HISTORY AND AFFINITIES OF RHEUMATIC FEVER.

*Delivered before the Royal College of Physicians of London,
March, 1895.*

By ARTHUR NEWSHOLME, M.D.LOND., M.R.C.P.,
Medical Officer of Health for Brighton.

[ABSTRACT.]

LECTURE III.

INFLUENCE OF TEMPERATURE.

THE marked preference of rheumatic fever for the winter season was shared by infective diseases like small-pox, measles, whooping-cough, etc. This seasonal incidence was explicable as due to the effect of climatic influences on the life-history of the specific micro-organism, or to their effect on the receptivity of the community.

A comparison of the curve of mean annual temperature at Greenwich with that of hospital cases of rheumatic fever in London showed that in the epidemic years 1866 and in 1868-9, the mean temperature was 1 to 5 per cent. above the mean for the whole period 1866-93; in the epidemic years 1874-5 the mean temperature was at the mean line. In 1879 low rheumatic fever corresponded with a low mean temperature; and in 1884 and 1893 there was again an association of high mean temperature and excessive rheumatic fever. The curves of mean temperatures for the first and fourth quarters of the year showed that higher temperatures usually coincided with excessive rheumatic fever, though there did not appear to be any definite proportion between the two.

The temperature of the earth 4 feet deep, so far as records were available, showed a much closer relationship than that of the air. The earth temperatures taken at Regent's Park since 1871 (records missing for 1877-9) showed that in 1871-4 inclusive the mean earth temperature of the year was always at or above 50° F., a temperature which was not again reached except in 1884 and 1893, which were also epidemic years. The maximum and minimum earth temperatures give similar indications. During the period in which comparison was possible in London, epidemics of rheumatic fever occurred only when the mean temperature of the soil was exceptionally high, that is, over 50° F., and the greatest epidemics occurred when the mean temperature had been thus high for two or more years in succession.

INFLUENCE OF RAINFALL.

The relationship between damp air and damp soil and the prevalence of rheumatism being almost accepted as axiomatic in medicine, rainfall might be expected to exercise a great influence in increasing rheumatism. The observations of writers on this point were hopelessly at variance. The Collective Investigation Committee of the British Medical Association reported that most cases began in damp or wet, or cold and cloudy weather; and Dr. Gabbett, from an examination of the London Hospital statistics, thought that rheumatic fever tended to vary directly with the rainfall. On the other hand, Hirsch, Edlelsen, and Longstaff, among others, had found that the amount of rheumatic fever was more or less inversely with the rainfall.

Comparing the yearly and quarterly rainfall at Greenwich with the hospital incidence of rheumatic fever, it was found that a heavy rainfall was usually associated with a low amount of rheumatic fever, and a light rainfall with excessive rheumatic fever, though no exact proportion was observable be-

¹ In one of the experiments made by White of Philadelphia, reported in the *BRITISH MEDICAL JOURNAL* of September, 1893, in which the dog was castrated seventeen days previously, there were apparently no atrophic changes in the prostate gland.

² I have, in the *Journal of Anatomy and Physiology*, vols. xxiii and xxviii, published a detailed account of the prostate gland as it is found in castrated animals and in eunuchoid persons respectively.

tween the two. In provincial towns the results were somewhat contradictory. It was highly probable that, as at Glasgow, a deficiency of rainfall for several years favoured the prevalence of rheumatic fever much more than a shorter deficiency.

INFLUENCE OF GROUND WATER.

An almost unbroken series of weekly observations of well levels at the Lewes Road Well, Brighton, since 1867, existed. Although pumping goes on there, this had increased of late years, and the curves showed the influence of seasonal and climatic factors, with but little disturbance. There was no connection between great or small range of ground-water level and excess of rheumatic fever. It appeared to be simply a question of level. The years of highest level of ground water never had excessive rheumatic fever, and the years of lowest level nearly always had excess of rheumatic fever. The same relationship between low ground water and excessive rheumatic fever was seen at Croydon.

In London the years noted in the 1885 report of a Committee of the Royal Meteorological Society as years of "marked low water" were nearly always associated with excessive rheumatic fever; and the years of "exceptionally high water" were never so associated. Collateral evidence reaching up to the present date from wells in the vicinity of London confirmed this result. Thus, comparing a well at Barley in Herts with those at Croydon and Brighton, low well levels found in the former in 1871-72 were not seen in the latter. There was an epidemic of rheumatic fever in London, none in Brighton or Croydon. The low levels and epidemic of 1874-75 were common to all. The effect of deficient rainfall on the ground-water level in the absence of artificial obstructions to its outflow varied in time and extent with the character of the subsoil. Thus in 1871 there was a greater deficiency of rainfall in Brighton than in Greenwich and Herts, but there was an epidemic of rheumatic fever in London and none in Brighton. The drought in London, from the tenth to the twenty-fourth week of 1893, did not produce a prompt effect in increasing the weekly admissions for rheumatic fever to Guy's Hospital. The number of admissions in the first quarter was 25, in the second 24, in the third 42, in the fourth 39. From a careful examination of the evidence it was concluded that the effect of deficient rainfall took time to develop, and that it was exerted as the result of its effect on the subsoil, this effect usually showing itself by a marked lowering of the ground water. The low ground water must be regarded as an index of certain conditions of dryness and temperature of the subsoil which favoured the growth of the micro-organism of rheumatic fever. This being so, low ground water, when unaccompanied by the required conditions of temperature, etc., might be unassociated with an increase of rheumatic fever, though conversely a high ground water was never found accompanying excessive rheumatic fever.

The foreign returns from Munich and Berlin agree with those already stated in that high ground water is never accompanied or immediately followed by high rheumatic-fever prevalence.

LECTURE IV.

The clinical features of rheumatic fever confirmed the view that it was a specific febrile disease. 1. The mode of onset, including in a large proportion of cases throat symptoms. 2. The progress of the disease, which was fairly definite in the absence of complications. 3. The tendency to relapse was shared by the specific disease erysipelas, and in a somewhat less degree by pneumonia, influenza, enteric fever, diphtheria, and even scarlet fever. 4. The liability to later attacks was another point of resemblance to erysipelas. There is a scale of immunity by one attack, from erysipelas and rheumatic fever at one end to small-pox at the other end. Third attacks of scarlet fever were known. 5. The influence of the personal equation varied greatly in different infective diseases. In small-pox it was very slight; in diphtheria and enteric fever it was great; in rheumatic fever and erysipelas it was greater still. Hay fever might be regarded as the type of a local infective disease in which a special personal proclivity or anatomical peculiarity was required for the production of the disease. Rheumatic fever might be regarded as the type of a septicæmic disease in which a

similar proclivity or peculiarity was required. 6. The method of infection in rheumatic fever was probably by the naso-pharynx. 7. The degree of infectiousness. There was a scale of decreasing infectiousness from small-pox to erysipelas, in which not only abraded surface, but also a personal predisposition was necessary, and to rheumatic fever, in which the degree of infectiousness was unknown. In rheumatic fever the chief seat of multiplication of the specific contagium was in the affected joints; it was deeply buried, and it was possible that it pays for its hardihood in invading the system by securing a sepulture in its cells. 8. The fact that the joints were the seat of the trouble favoured the infective theory, the "vessels of the synovia of the joints appearing to have some special proclivity to form a nidus for the wandering germs of disease" (Payne). The specific action of salicin and salicylic acid was an additional argument in favour of its specific febrile character, being comparable to that of quinine in malaria, and of salts of mercury and iodides in syphilis.

The bacteriological investigations of Cornil and Babes, Wilson, Mantle, Petrone, Popoff, Birch-Hirschfeld, Triboulet, Sahli, Sacaze, Leyden, etc., were then described, none of them containing conclusive proof of the pathogenic relationships of the organisms described. In malaria the inoculation of the blood of a patient had produced malaria in another. In rheumatic fever this evidence was still wanting, though two cases of congenital rheumatic fever described by Pocock and Schäfer came near to demonstrating this point. It was still doubtful whether comparative pathology would help. The disease described as rheumatism by veterinary authors was probably not true rheumatic fever. Many such cases were really septicæmia, especially the arthritis of calves traceable to infection from the umbilicus (MacFadyean).

DIRECT EVIDENCE OF INFECTIVE CHARACTER.

Dr. Fiessinger had described an outbreak in a village of about 500 houses. Out of a total of 21 cases, 10 occurred in 12 houses, namely, 4 in one house, 2 in the same room (at intervals of a year and in members of different families). Edlefsen, at Kiel, had described 728 cases, in which the proportion was 100 houses for 148 cases, namely, 2 cases in one house, 100 times; 3 cases, 27 times; 4 cases, 5 times; 5 cases, 5 times; 6 cases, once; and 7 cases, once. Similar instances had been described by others.

Cases had been described by Drs. Mantle, Dalton, and others, which appeared to be only explicable on the supposition of direct personal infection or of indirect infection, which clung about certain houses, as did diphtheria. Malaria was the type of an endemic non-infectious disease. It sometimes, however, became epidemic or even pandemic, the pandemics corresponding in time with increase of sickness in the endemic foci. This did not necessarily imply the acquirement of the quality of infectiousness. It might simply be that the local conditions had become more favourable to the growth of the plasmodium of malaria. Whether the same applied to rheumatic fever, and each case implying that a saprophytic organism, never previously parasitic, had become so, or whether there was an alternation between parasitic and saprophytic life, as in yellow fever, cholera, and enteric fever, and possibly, also, in diphtheria, tetanus, and tuberculosis, was doubtful.

It might be that in non-epidemic years of rheumatic fever its micro-organisms were kept at bay by their natural enemies in the struggle for existence. In plant pathology there were many analogous cases. The historical potato-blight of 1845 was not a completely new disease, though it had never previously produced such ravages. So with the *Puccinia malvacearum*, a fungus attacking hollyhocks, etc., which suddenly appeared in England in 1873. In rheumatic fever the known factors favouring the growth of its micro-organisms, were a dry condition of the subsoil and an optimum temperature. The gradual spread of the disease of which evidence had been given in Norway, London, Yorkshire towns, etc., might mean gradual progression of infection, or that the necessary reaction of environment to the specific virus, always endemic in each district, occurred at different times, or that the susceptibility of entire populations varies at different times. The latter supposition was favoured by the frequent alternation of greater and less epidemics.

According to Metchnikoff, the Versaillese had an almost incredible immunity against cholera, when its vibrio was in their drinking water, owing to the absence of "favouring organisms" from their alimentary canals.

THE PERSONAL FACTOR.

Rheumatic fever was rather more common in males. The ages most prone were 15 to 45. The influence of heredity had been much exaggerated. Injury, whether due to actual mechanical causes or to former disease, as erysipelas, or caused by fatigue or exposure, had an important influence in causing rheumatic fever. Fatigue also affected the localisation of the joint affection, which was more common in the upper than the lower extremities, and in the right than the left arm. Of the influence of race and occupation there was very little evidence. Although meat food was a not infrequent cause of relapse in rheumatic fever, there was no evidence on a large scale that omnivorous or chiefly carnivorous races were more prone to rheumatic fever than vegetarians.

AFFINITIES OF RHEUMATIC FEVER.

1. *Chronic rheumatism*, so called, had been the chief cause of the erroneous conclusion that damp favours rheumatic fever.

2. *Muscular rheumatism* was probably very closely related to rheumatic fever. Distinct epidemics of it had occurred both in this country and abroad.

3. *Chorea* had a remarkable resemblance in seasonal incidence to rheumatic fever (Lewis). Dr. Newsholme had found a similar resemblance in the annual curves. This did not necessarily imply an identical infection any more than in the allied case of erysipelas. The sex incidence of chorea was very different from that of rheumatic fever, the two sexes being attacked in nearly equal numbers in the latter case, and three times as many females as males in the former case.

4. *Epidemic cerebro-spinal meningitis* presented many points of analogy. Both occurred in irregular epidemics, but rheumatic fever did not entirely disappear in the intervals, as epidemic meningitis appeared to do. Joint symptoms were common in the latter disease. In neither was there clear evidence of personal infection. In both it appeared to be rather a question of infection of the place than of the person.

5. *Erysipelas* and rheumatic fever resembled each other in many clinical respects, as already indicated. Dr. Longstaff had shown the resemblance between the annual curves of the two diseases in England. The resemblance was even more strikingly shown in the curve of notified cases in Norway. There was this peculiarity about the Norwegian curves: comparatively large epidemics of rheumatic fever accompanied comparatively small epidemics of erysipelas, and *vice versa*. The smaller epidemics of erysipelas in Norway were the more fatal, and probably this was also true for rheumatic fever. The same inverse relationship between the magnitude of epidemics of rheumatic fever and erysipelas corresponding in point of time was seen in Berlin. The seasonal incidence of rheumatic fever and erysipelas were identical in Norway. The age incidence of the two diseases was practically identical. Thus:

	Under 15.	Over 15.
Erysipelas percentage 1887-91	15.1	84.9 (based on 43,537 cases)
Rheumatic fever p.c. 1865-91	15.3	84.7 (based on 62,834 cases)

6. *Puerperal fever* shows similar annual curves to those of rheumatic fever and erysipelas. This did not necessarily or probably mean identity of virus. It was furthermore evident that the view that want of antiseptic care alone accounted for puerperal fever was not tenable unless it were imagined that in England and in Prussia there was in years of excessive mortality from puerperal fever a conspiracy of carelessness. The explanation of the epidemic prevalence of erysipelas and puerperal fever, as well as of rheumatic fever, lay in the favouring influence of a dry and warm subsoil on the specific contagia of the three diseases.

7. *Malaria*.—The belief in the substitution of rheumatism for malaria was very general, but it was without foundation. The conditions of soil producing rheumatic fever and malaria appeared to be almost exactly opposed to each other. The seasonal distribution of the two diseases was dissimilar.

SUMMARY.

At intervals of a few years epidemics of rheumatic fever

occurred, occasionally pandemics, especially in 1868, in 1874-75, and in 1884. These epidemics occurred in or following years of sparse rainfall. This produced its effect by its influence in causing a warm and dry subsoil, usually with an exceptionally low ground water. Rheumatic fever was essentially a soil disease, having close relationships with erysipelas and other septicæmic diseases. Whether it was alternately parasitic and saprophytic or each case implied a fresh infection from the soil was doubtful.

Prophylaxis.—A careful distinction should be drawn between a dry soil due to hot seasons and the same when due to improved drainage of the soil, removal of mill-ponds, etc. A further confusion between dry soils and dry houses must be avoided. The entrance of ground air under houses should be carefully avoided.

Need for Further Investigation.—It was not creditable to this country that so few continuous ground-water observations were being made. The information as to cases of rheumatic fever was most defective. There was nothing in this country corresponding to the weekly returns from the Berlin Statistical Bureau of admissions to the chief general hospitals during the preceding week. It could hardly be expected that the General Register Office, hampered by an economical Treasury, would undertake this at present. It was suggested that the Royal College of Physicians might undertake to collect weekly or monthly the admissions to the London general hospitals, classified according to disease. Such material after a few years would be invaluable for medical and hygienic purposes.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

THROAT AFFECTIONS IN INFLUENZA.

MR. TERRY, in the *BRITISH MEDICAL JOURNAL* of March 9th, draws attention to the throat symptoms he has observed in the recent epidemic of influenza. I have noticed that in at least 50 per cent. of influenza cases the cough commences as soon as the joint pains disappear, and that this cough is due to an inflamed and elongated uvula, and in many cases enlarged tonsils, in five cases of a distinct follicular character; but unlike Mr. Terry's cases the patients have occasionally complained of pain on swallowing. In very few cases were the glands in the neck either enlarged or tender.

The first few cases I observed resisted the usual gargles, and were not relieved by painting with iron, but were quite well in a few days after gargling with salicylate of sodium 3j, glycerine 3j, aqua rosæ ad 3vj. In no cases have I noticed any marked tongue symptoms.

New Cross Road, S.E. W. T. B. DONNELLY, M.B., B.S. Durh.

I READ with considerable interest the observations of Dr. Terry on the connection between inflammatory conditions of the throat and influenza. For several times have I noticed the uvula, faucial arch, and tonsils severely inflamed in cases of influenza, but thinking that such conditions were merely accidental complications I took no further note. However, I am now convinced that there exists a close relationship between the two affections.

I have a painful recollection of the first time I noticed the above-mentioned throat symptoms in influenza, as I myself was the patient in whom they occurred. The course, symptoms, and signs of the palatal and tonsillar inflammation were precisely the same as mentioned by Dr. Terry. A few peculiar points I, however, noticed: First, that although both tonsils were inflamed, one was always worse than the other. Secondly, that the severity of the inflammation changed day by day from one to the other as long as the temperature remained up. Thirdly, that keeping the mouth as aseptic as possible, along with frequently washing the tonsils with astringent and antiseptic gargles, did not do the slightest good, the soft palate and tonsils remaining persistently inflamed till the temperature fell to normal. Since my own case I have seen