morphological elements of the blood were altered except by a slight leucocytosis. If the inoculated substance, however, be very concentrated in the solution, some inflammatory œdema is produced at the point of inoculation, and lasts some days.

The animals vaccinated with small doses on one occasion only, or with the minimum killing dose divided into two or three times, and injected subcutaneously at intervals of two days, show the utmost indifference to the subcutaneous and intraperitoneal injections of a great quantity of virulent culture, while healthy animals of the same weight but not vaccinated treated with the same quantity of culture die in twenty-four hours after the injection in the peritoneum, and some days after the subcutaneous injection. In these experiments we have preferred the injection into the peritoneum both for vaccinated and non-vaccinated animals.

The virulent plague bacillus causes different morbid processes according to the place where the injection is made. If into the peritoneum there is an extremely rapid septicæmia (less than twenty-four hours) in the subcutaneous injection, there is a polyadenitis very much like the natural infection in man, and the animal dies in a week.

If the injection is made in the peritoneum with the attenuative culture, or if the animal is one less liable to plague, then, owing perhaps to a bactericidal action of the peritoneum, we find at first only a slight peritonitis, but a few days later the remaining living bacteria cause the characteristic polyadenitis, and the animal dies. The period between the slight peritonitis and the polyadenitis is five or ten days.

Peritoneal are preferable to subcutaneous injections because they cause an infection which is surely mortal, and so they render it possible to ascertain in less than twenty-four hours the virulence of a culture. We can be sure of the immunity conferred by the vaccination if the animal vaccinated and infected go beyond the tenth day. Ours did not show any morbid phenomenon after five weeks from the infection, and the microscopic and bacterioscopic examination of those killed after two weeks did not show any plague bacillus in the blood, the spleen, or in the lymphatic glands.

The vaccinated animals are immune from the infection of plague for at least five weeks from the last vaccination. From the animals vaccinated with the minimum lethal doses, divided and inoculated on three occasions at intervals of two days, we obtained after fourteen days a serum with decidedly preventive and curative properties. We have made experiments on rats and mice with the serum of mice or rabbits, and we ascertained that both have the same curative efficacy; 1.0 c.cm. of serum is enough to prevent peritoneal infection, and with the same quantity a rat weighing 180 to 200 g. injected in the peritoneum with a great quantity—4 to 5 platinum needlefuls—of virulent culture is cured. The curative injection of the serum was tested also after injection through the alimentary canal.

We put in a cage seven small mice (mus musculus), and gave them milk in which a virulent culture was dissolved. Three of them died after three days, and in their blood plague bacilli were found; the other four were severely ill with the characteristic symptoms. We injected in them 0.33 c.cm. serum from a vaccinated rabbit, and all survived. At the present moment we are vaccinating a horse to obtain a curative serum.

Our substance can be regarded as harmless for man, because, when inoculated under the skin in doses of 5 mg. dissolved in sterilised alkalised water it causes only a slight local œdema lasting twenty-four hours. The body temperature is, during the first hours, slightly under the normal; then there is slight fever; the urine is normal; a little prostration and uneasiness is felt. We have inoculated it under the skin of our arms and have besides vaccinated four other persons.

We have already made experiments on more than 120 mice and rats, 30 rabbits, and 15 guinea-pigs. We are certain of the preventive action of our vaccine, that it is free from bacteria, and that its action in animals is very rapid. The vaccine is quite harmless on man, and as the morbid phenomena of the plague in man and in animals are similar we think that its use would be followed by the same effects in man as in animals.

The advantages to be obtained owing to the possibility of working with a substance free from bacteria, dried and dosable, is clear. If we shall be able to prove that the horse by this method gives a serum with curative properties, it will then be easy everywhere and without any danger to prepare it more quickly than by means of virulent cultures.

The cultures of the plague bacilli we owe to Professor Lukianow in the first place, and later to Professor Gabritchewski.

REFERENCES.

[1] Yersin and Roux. [2] *Annales de l'Institut Pasteur*, 1895-97. [3] *Deut. med. Woch.*, No. 10. 1897. [4] Hammarsten, *Zeit. f. physiol. Chemie*, 1894, Bd. xix. [5] *Deut. med. Woch.*, April 8th, 1897. [6] On the toxic qualities of this substance we must repeat here what we have already published in the *Deut. med. Woch.*, April 8th, 1897, namely, that they may vary very much with the age and virulence of the culture from which the substance is taken, and mode of preparation. In two preparations we obtained a vaccine which was more poisonous than that we are now preparing, and the lethal doses given in our first publication (which referred only to two preparations) differ from those that we now give, and which we have ascertained with greater precision.

THE MICROBIAL ORIGIN OF BALDNESS.

SABOURAUD'S RESEARCHES INTO THE RELATIONS BETWEEN SEBORRHŒA, ALOPECIA AREATA, AND BALDNESS.[1]

By L. WICKHAM, M.D.,
Formerly Chef de Clinique in the Saint Louis Hospital, Paris.

I.

DR. SABOURAUD, a former pupil of the Pasteur Institute, the scientific value of whose work on ringworm [2] is already well known, has just completed some very interesting researches at the St. Louis Hospital on seborrhœa, alopecia areata, the falling out of hair, and baldness. Such diseases as seborrhœa, alopecia areata, ringworm, and baldness do not at first sight appear to have much in common, and the conjunction of their names in the title of a single work must appear very curious. The reader will, however, soon understand the relations between the facts regarding them.

After four years devoted to the mycological and therapeutical study of tinea tonsurans, and after trying in succession all the remedies devised for its cure, Sabouraud came to the conclusion that no antiseptic treatment is absolutely efficacious in the case of a tinea fungus which has invaded the hair as far as the root. This is due to the inaccessibility of the root to antiseptics owing to the narrowness and depth of the hair follicle, which prevent the diffusion of all the therapeutic agents which have been employed. He has furthermore become convinced that if, as appears in favus, one could make a complete series of epilations without breaking the hairs, tinea tonsurans would be rapidly cured. But the diseased hairs break off close to the surface, and so it is necessary to take care to enucleate them by working somehow from below, by the root or even the follicle, killing the latter "temporarily." Following out this line of argument and applying it to alopecia areata, Sabouraud came to the conclusion that if the loss of hair in this disease is due to microbial intoxication, the toxins of the micro-organisms would be capable of inducing alopecia. It would then be possible to use them to produce a temporarily bald area at any desired spot, and so to cause a spontaneous falling out of the tinea-infected hairs, which are too fragile to be removed by epilation. These ingenious but logical conclusions led their author into a new series of researches occupying three years. All that follows is simple to explain, and can be summed up in a few words, but it will be easy to read between the lines the amount of patient labour which Sabouraud has had to carry out.

II.

These ideas seemed at first very pretentious, requiring as they did for their verification nothing less than the discovery of the microbe of alopecia areata. The first research consisted in the most careful clinical study of the disease, having for its objects the determination of (1) the possibility of a microbic origin of alopecia areata, (2) the exact spot at which the micro-organism, if it existed, was to be looked for.

This preliminary study showed that alopecia areata started from a central point, and that the baldness spread from this point by creeping in every direction along its circumference, in the manner of a spot of oil in a fabric. It showed furthermore that the most pathologically active zone of the patch is situated at its confines, and that it is in this circumferential zone that the infected and broken hairs are found in the

form of clubs. Careful study of patches of lupus leads to the conclusion that their centres are smooth, healed, and appear to present no visible alteration of the mouths of the hair follicles, while the active peripheral zones show considerable dilatation of the pilosebaceous orifices. All this local evolution goes to support the arguments founded upon numerous examples of epidemics in favour of the microbial origin of alopecia areata. But more than this, the local development indicates that the micro-organism resides in the active peripheral zone, and more exactly in the dilated orifices of the hair follicles. These views are borne out by histological facts. Fortune favoured M. Sabouraud by providing him with invaluable histological material from the body of a hospital patient who was suffering at the same time from a skin affection and alopecia areata. M. Sabouraud was thus able to see clearly in his histological specimens that a constant small bacillus was to be found infesting the upper part of the hair sac. He was further able to discover that the orifices of the follicles were filled with a fatty substance which could be squeezed out on pressure, and which he called the "seborrhœic cocoon." Now in this seborrhœic cocoon can be found, surrounded by a crowd of other microbes, the same organism which has been demonstrated in the histological sections. It remained to isolate this bacillus, to cultivate it, and to demonstrate that it is the actual cause of alopecia areata.

The essential part of the research had, in fact, still to be undertaken, and in carrying it out the author's patience was put to a severe test. The bacillus had to be isolated from the crowd of microbes found in cultures of the seborrhœic cocoon taken *en masse*. There is present under such circumstances practically the whole dermatological flora studied by Unna. It was necessary to discover a medium which should have the power of destroying all micro-organisms except the one in question; which should, in other words, allow the alopecia bacillus to grow while proving unadapted to the life of all other microbes of the seborrhœic exudate. After a long series of attempts M. Sabouraud has achieved the desired result. It consists of a very acid culture medium, of which the ingredients are the following:

Peptone ...	...	20 grammes
Glycerine ...	...	20 ,,
Acetic acid	...	5 drops
Water ...	...	1,000 grammes
Gelose ...	...	13 ,,

With this medium one obtains in many of the tubes, in the midst of the other colonies, one or two pure cultures from the beginning, which are visible on the third to the fourth day, the temperature being 35° C. They show as pointed mounds, the colour of which is dirty white on media containing glycerine, a very characteristic brick-red on glycerine media. There still, however, remains a microbe which continues more persistently than any of the others; it is a white coccus, quite characteristic in appearance, and suspected by Sabouraud of playing some part in the genesis of alopecia. This organism must be got rid of, and the author effects this by a novel and ingenious method—the use of immunised gelose. By using in the preparation of the gelose a liquid in which the white coccus has been cultivated a medium is obtained which gives from the first abundant and definitely isolated cultures of the bacillus already mentioned. The same result can be obtained in another way by a slow sterilisation; a temperature of 65° C. for ten minutes kills the white coccus but spares the bacillus. The latter has thus been isolated and cultivated, but it remains to be proved whether or no it is the cause of alopecia areata.

A series of experiments were now made with a view to reproducing alopecia areata in animals. Certain results were obtained, some rabbits being caused experimentally to lose their hair in bald patches, but some desiderata still prevent M. Sabouraud from pronouncing definitely and formally declaring the bacillus to be the microbe of the disease. The question is, however, not far from solution.

III.

In all this there has been so far no question of either seborrhœa or baldness; we shall now see, however, that these subjects are intimately allied to those we have already discussed. From the time when Sabouraud first discovered and investigated the bacillus of the "seborrhœic cocoon" in alopecia areata he was struck by its resemblance to the microbe studied by Unna and described by Hodara as the bacillus of acne. This involved the necessity of examining this acne bacillus anew, and Sabouraud soon saw (1) that Hodara's bacillus is not that of acne, since it is found not only in the comedones, but in every form of oily seborrhœa, in the course of which the comedones of acne seem to be no more than an epiphenomenon resulting from local symbiosis; and (2) that his bacillus of the seborrhœic cocoon and Hodara's so-called acne-bacillus are certainly identical. This latter conclusion naturally made Sabouraud hesitate in his idea that his microbe was that of alopecia areata, for up till then there had not appeared to be the slightest connection between this disease and seborrhœa. Nothing discouraged, he returned to the study of his microbe, and endeavoured to ascertain all the localities in which it was possible to detect it. A series of researches was thus undertaken which resulted eventually in the demonstration of the microbial nature of baldness. A preliminary study of seborrhœa in the hairy scalp revealed (1) that the bacillus of the brick-red cultures from alopecia areata is also present in the seborrhœic plugs of the mouths of the hair and sebaceous follicles in seborrhœa, that it is there present in considerable quantity, and that it certainly is the cause of seborrhœa, (2) that consequently seborrhœa and alopecia areata have a common origin from the same micro-organism. Finally, having studied the obvious relations existing between seborrhœa and the habitual falling out of hair, Sabouraud came to the conclusion that the disseminated loss of hair in seborrhœa was the prelude of baldness. The histology of bald scalps shows that the mechanism of the process leading to baldness is as follows: Whenever the specific bacillus of seborrhœa invades a follicle, it produces around it, and especially at its base, around the hair papilla, an afflux of wandering cells. The papilla gradually atrophies, producing as it does so a hair which is progressively more and more frail and devoid of pigment. Finally it dies, and the dead hair is expelled. In this seborrhœic infection of the hairy scalp the colonies of bacilli are enormously abundant; the sebum, which is effused on the surface of the skin in the form of an apparently homogeneous crust, is composed of an infinite number of seborrhœic plugs turned out of the follicles, and each of these plugs contains the bacillus in millions.

In hairy scalps which have been once invaded, the microbial infection remains endemic and settled so that a hair once shed is never renewed. Furthermore the permanent effusion of this germ-bearing sebum infects one by one the follicles which have remained sterile. In this way ordinary baldness is little by little established; the progressive sclerosis of all the elements of the hair follicle brings with it considerable changes of form. The whole part of the follicle invaded by the bacterial colony becomes hollow and broken up by narrow diaphragms which render the seat of infection inaccessible to external antisepsis. But the incredible abundance and absolute purity of the infection persist even when the baldness is finally and definitely established. Even at this terminal stage in its evolution, ordinary baldness remains the most abundantly and most purely microbic malady known in the skin.

Such are the conclusions to which clinical and histological results lead the author, but a further difficulty has to be cleared up. It is that at the moment of infection the bacterial colony does not invade the hair papilla, but remains in the upper third of the follicle. By what mechanism can the colony exert its influence upon the papilla? One can only admit an action at a distance, and this remains to be proved. Sabouraud, thinking then that this distant action was effected by the toxins of the micro-organism, devised and carried out the following experiment, which is conclusive, and practically seals this chapter on the microbial nature of baldness. He made a cultivation on a liquid medium, and having filtered it through porcelain, inoculated the filtrate deeply under the skin and into the muscular tissues of a rabbit. The rabbit at once commenced to shed its fur, and within forty days from the date of inoculation general alopecia was established. This experiment is of the greatest value as showing that the toxin of the bacillus of seborrhœic plugs is so specific and individual that when inoculated into the heart of the system it retains its elective and exclusive action on the papillæ of the cutaneous hairs.

This is the exact point at which Sabouraud leaves us for the moment; but he promises us before long another memoir containing the results of experiments not yet completed. If we retrace the ground covered by this analysis we find (1) that the microbial origin of baldness is certain; (2) that the micro-organism of baldness is the same as that of seborrhœa; (3) that it is identical with that of the seborrhœic plugs of the orifices of the hair follicles in alopecia areata.

To render the whole work complete, to prove that these results are definitely allied to each other, it would suffice if the following could be added to the third conclusion: The bacillus which is the cause of both seborrhœa and loss of hair acts according to its greater or less virulence under varying conditions in a manner either violent and fulminating, producing what has hitherto been known as alopecia areata, or moderately gentle, giving rise to that progressive loss of hair which in ten or twenty years ends in baldness. This last deduction Sabouraud does not give, in spite of certain favourable experiments. For prudence sake he does not wish to state it yet, because he has till now perhaps been unable to produce in an animal the true patch of alopecia areata, that is to say, the typical disease with the club-shaped hairs. There is probably, however, but a shade of difference to overcome, and we are convinced that after what has gone before Sabouraud's last scruples will soon prove to be baseless. Thus from this work, besides all the other discoveries which it comprises, we hope to see arise at the same time the key to the much-sought solution of the problem of alopecia areata in the definitely and finally established discovery of the microbe of the disease.

References.

[1] Etude clinique et expérimentale sur les Origines de la Pelade, *Annales de Dermatologie*, 1896; La Seborrhée Grasse et la Pelade, *Annales de l'Institut Pasteur*, February 29th, 1897; Origine Microbienne de la Calvitie, Société Française de Dermatologie, Séance du 13 Mars, 1897. [2] Les Teignes, International Congress of Dermatology, London, 1896.

THE LUMLEIAN LECTURES

ON

SOME PROBLEMS IN CONNECTION WITH APHASIA AND OTHER SPEECH DEFECTS.

Delivered before the Royal College of Physicians, April 8th, 1897,

By H. CHARLTON BASTIAN, M.A., M.D.Lond., F.R.S.,

Censor of the College; Physician to University College Hospital and to the National Hospital for the Paralysed and Epileptic

[Abstract.]

Lecture III.

Mr. President and Gentlemen,—At the close of the last lecture I considered the different degrees of amnesia verbalis that may result from functional defects or partial lesions of the left auditory word centre. We must now consider the effects produced by more serious lesions of this centre.

(b) Effects produced by Destruction of the Left Auditory Word Centre.—Where, instead of partial or mere functional defects, we have to do with more or less complete destruction of the left auditory word centre by some organic disease a correspondingly complete word deafness is produced, so that the patient is no longer able to comprehend spoken language. Spoken words become to such a patient mere meaningless sounds. Wernicke, Déjerine, and Mirallié hold that paraphasia is the kind of speech defect resulting from destruction of the auditory word centre, and that it is invariably accompanied by alexia. In the former view Wyllie concurs.

The view that I entertained on this subject some years ago[1] were that loss of articulate speech should result from destruction of the auditory word centre, just as agraphia results from destruction of the visual word centre. Ballet[2] and Ross[3] following me expressed very similar views, though the majority have rather followed Wernicke, and regarded paraphasia as the natural accompaniment of word deafness.

Now that more cases have been observed we are in a better position for throwing light upon this point. An examination of the recorded observations in which the lesion has been limited to the hinder part of the first, and perhaps also of the second, left temporal convulsions (without perceptibly encroaching upon the visual word centre) shows surprisingly different results in regard to the nature and degree of the speech alteration met with. In some of the cases there has been aphasia; in others a more or less marked paraphasia; whilst in two or three of the cases the defect in voluntary speech has been less marked. Thus, looking to the same sixteen cases of destruction of the auditory word centre to which I previously referred[4] when speaking of the frequency with which word blindness and agraphia occur as additional symptoms, I find that what is described as "motor aphasia" existed in six of them; in six of the cases also some amount of paraphasia existed. In one case both aphasia and paraphasia are said to have existed; while in the three remaining cases voluntary speech seems to have been rather less affected.[5]

Thus it will be seen that we have all been more or less wrong; and I must confess that the revelation of these apparently contradictory results in the way of speech disturbance in association with word deafness surprised me not a little. The meaning of such remarkable variations demands a careful consideration.

The three cases last referred to in which voluntary speech has been least interfered with are, I believe, altogether exceptional. One of them is a case recorded by Claus,[6] concerning which, unfortunately, there are only a few meagre details.

The patient's hearing was good, but his intelligence weak; he understood nothing said to him, and always answered wrongly while he spoke correctly. A focus of softening was found involving the first temporal convolution except its anterior third.

It seems to be Case No. 20 in the "Table of Cases of Sensory Aphasia with Lesions and Symptoms," cited by Allen Starr,[7] and there also no further details are given. No weight, therefore, can be attached to this example, the details of which are so incomplete. The second case is one that was originally recorded by Wernicke.[8]

The patient's spontaneous speech was extremely limited, and she made frequent mistakes in words and in their pronunciation. The statement contained in Amidon's abstract that her "spontaneous speech was very good," certainly goes far beyond what there is any warrant for. The whole of the upper temporal convolution and part of the supramarginal lobule were in a state of yellow softening due to thrombosis of some of the terminal branches of the middle cerebral artery. It is worthy of note, therefore, that the auditory word centre may not have been entirely destroyed, since the second temporal convolution seems not to have been at all involved. In the previous case, reported by Claus, it should also be observed that the second temporal convolution was only very slightly involved. It is merely said that its upper border was affected ("had a brown colour").

The third case, curiously enough, has often been quoted as though it were a typical example of word deafness rather than one of an unusual character. It was recorded by Giraudeau,[9] and some of the principal details are these.

The patient, a woman, aged 40 years, had previously enjoyed good health, though she had never menstruated. She had suffered for three months from headache. She had the greatest difficulty in understanding questions, only replying after they had been three or four times repeated. Even then, whatever subsequent questions were put to her, she followed her first idea, and her subsequent replies had no relation whatever to the questions put to her. Tactile sensibility was preserved, as well as the senses of taste and smell, and her motor power was unaffected; there was no word blindness. The psychical affection rapidly increased, and on the ninth day after her admission the word deafness was complete, and whenever she was addressed she invariably said, "I do not understand," and then began to weep. The next day she fell into a state of coma and died. At the necropsy a sarcomatous tumour of the size of a walnut was found occupying the posterior part of the first and second temporo-sphenoidal convolutions of the left hemisphere, the rest of the brain being healthy.

Here the details are fortunately more ample. Although this patient's speech was limited, there was clearly neither aphasia nor paraphasia, and this may, I think, be explained either by supposing that the lesion on the early days did not destroy the whole of the auditory word centre—which is more than possible, seeing that the lesion was a tumour and also that the word deafness was not absolute; or else that the patient was a strong "visual"—a person, therefore, in whom the excitation of Broca's centre might have been brought about directly from the visual word centre, both in spontaneous speech and in reply to written questions. And to the latter she is expressly said to have replied "verbally