A CASE OF
FRACTURED BASE OF SKULL WITH
LACERATION OF BRAIN, ACCOMPANIED
BY SUGAR AND ACETONE IN THE
URINE.

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THE following interesting case came under notice at the West London Hospital in July last. The patient, a police sergeant, was on night duty on Friday, July 12th. On Saturday morning, the 13th, he returned to the police station at the usual time, and there gave a written report of his night's work. From this report it was shown that he had met police constables about every hour during his rounds. Nothing strange or peculiar in his manner was noticed by any of these men, and the inspector to whom he made his night's report said he was apparently in the best of health. The patient had some food and then went to bed about 10 A.M. on Saturday morning. During the daytime he got out of bed on several occasions and went downstairs to the watercloset. Later in the day a police-constable who shared the same bedroom noticed that the patient was not quite himself, that he appeared irritable when spoken to, and later seemed "drowsy and bilious." The divisional surgeon was called in to see him at night and diagnosed the case as epilepsy. Two bruises were detected by the surgeon, one behind the left ear and the other at the inner canthus of the left eye. These bruises he supposed to have been inflicted during the epileptic fit, and his present drowsy condition to be one of post-epileptic coma. The patient was a strong, athletic man, who up to the present time had always enjoyed good health. On Sunday night, July 14th, he was admitted into hospital, when he lay on his side with closed eyes and breathing easily. He violently resented any attempt at examination, and answered incoherently when roused by shouting in his ear. The pupils were equal and normal. The pulse was 56, full and strong. He was very restless. The lungs, heart, and other organs were apparently healthy. There was no paresis. A bruise was noticed behind the left ear over the mastoid process, and another at the inner canthus of the left eye. The specific gravity of the urine was 1030. There was no albumin, but strong sugar reaction. The patient was very restless during the night, and made several attempts to get out of bed. He had incontinence of urine. On Monday, the 15th, he was quite unconscious. The restlessness had passed off. There was no paresis. The swelling and bruising behind the left ear were much more marked. Sugar was present in the urine. The coma becoming more pronounced, a consultation was held in the afternoon, when the question was raised as to whether the symptoms, in the absence of any history of injury, were not due to post-epileptic or diabetic coma. It was decided, however, to make an exploratory operation. At 6.30 on Monday evening, under an anæsthetic, Mr. Bidwell operating, an incision was commenced immediately behind the mastoid, and on turning down a large square flap an extensive fracture was discovered. This fracture was followed, and was found to extend from the centre of the lambdoidal suture behind to the posterior part of the zygoma in front, traversing the occipital (slightly) squamous portion of the temporal and parietal bones, and also part of the zygoma. The fracture was fissured and splintered. Mr. Bidwell removed the splintered portion of bone, together with some more bone around it, in the neighbourhood of the middle meningeal artery, and on opening the dura mater a large amount of lacerated brain substance mixed with fluid blood and small clots escaped. The middle meningeal artery was intact, but one of its posterior branches was ruptured. As further operative treatment was considered inadvisable the wound was closed. Although the patient appeared to improve somewhat after operation, in a few hours the coma began to deepen. Paresis set in, commencing first on the right side. Some urine was now collected and

tested. Sugar was present, and with it acetone, the tests on this occasion being carried out by Dr. Archibald Garrod. This was the first time on which the acetone test had been applied. From this time until his death the patient gradually got weaker, and died at 12.30 A.M. on July 17th, three days after admission. About six hours before death some urine was collected and tested, when it was found that the sugar and acetone had disappeared.

Necropsy.—At the post-mortem examination the following lesions were found. On removal of the scalp a fissured fracture was seen, extending from the posterior end of the zygoma to the middle of the lambdoidal suture. From a point about two inches behind the commencement of this fracture another ran across the middle fossa to the foramen ovale, and thence to the foramen lacerum medium. The trunk of the middle meningeal artery was uninjured, but a small posterior branch was torn across. A smaller fracture extended from the foramen ovale to the sphenoidal fissure. Rather below the groove for the left lateral sinus another fracture was traced from the end of the main fracture almost to the jugular foramen. A clot was lying loosely along this fracture, but the lateral sinus was apparently uninjured. The mastoid cells were full of clot, but the middle ear had escaped injury. The left hemisphere of the brain had sustained most extensive injuries, and the right hemisphere also had not escaped, the lesions here being apparently due to contre-coup, the anterior extremity of the second right temporal convolution being much lacerated, the laceration extending from the surface into the fissure of Sylvius, in which there was a large clot. The left temporal lobe had sustained an even more severe injury, the anterior extremities of the first and second left temporo-sphenoidal gyri being reduced to a pulp. The posterior extremities of the second and third temporo-sphenoidal gyri were in a similar condition, being immediately under the depressed piece of bone which was removed at the operation. In the left frontal lobe there was a large laceration with much blood clot on the orbital surface and another at the apex. In the right frontal lobe there was a similar condition on the orbital surface and another laceration at the junction of the external and orbital surfaces. The basal surfaces of both frontal lobes were practically reduced to cysts. Elsewhere, both on the right and left hemispheres there were numerous small subarachnoid effusions and a small laceration involving the third left occipital convolution. There were adhesions of the right pleura. All the other organs were healthy.

Remarks.—This case appears to us of considerable interest both from a medico-legal and from a purely medical aspect. Firstly, the absence of any history of injury does not negative the view that the patient suffered violence. In hospital practice we are well acquainted with cases of fracture, especially of the posterior fossa, in which the patient has walked up to the hospital on the following day or later, and has complained of headache without remembering any accident. Many such cases have been recorded in THE LANCET, the most remarkable being that of a man who fell on his head, but was not stunned, and had no symptoms for fourteen days, when he became comatose and died the next day. An extensive star-shaped fracture in the left mastoid was discovered at the necropsy. In another case a man aged forty fell thirty-five feet, alighting on his feet. He felt shaken, but was not stunned, and he went to work the next day. He had no symptoms until the fourth day, when he complained of pain in the ear. This, however, did not prevent him following his occupation. Three weeks after the accident he had severe headache and paralysis of the right sixth nerve. He remained in the same condition for four months, when he had very violent delirium and died within twenty-four hours. The necropsy disclosed a comminuted fracture of the petrous portion of temporal bone. Secondly, we know that glycosuria does occur in head injuries. But we are not aware that acetone has ever been found in association with the so-called "traumatic glycosuria." The urines in these cases of head injuries are not often tested, owing chiefly, no doubt, to the fact that incontinence is generally present. Thirdly, were the acetone and glycosuria in this case of any value from a medico-legal point of view—i.e., was the injury due to a fall while the man was in a state of diabetic coma, or were the glycosuria and acetone secondary to the trauma inflicted on the brain? Fourthly, if the case were one primarily of diabetic coma, would the acetone and sugar in such a case disappear several hours before death, as happened in this case? Lastly, would it

be possible for a man apparently in the best of health and without any history or symptoms whatever of diabetes to suddenly develop the coma of diabetes? These are, we think, important points to consider in giving evidence in such a case before a jury. In this case the police ridiculed the idea of foul play. The coroner's court returned an open verdict.

THE PREPARATION OF ANTIRABIC SERUM AND THE METHOD OF DETERMINING ITS STRENGTH.

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III.—MODE OF DETERMINING THE PROTECTIVE POWER OF THE ANTIRABIC SERUM.

It was evident from the results of the preceding experiments upon rabies executed in our laboratory that the importance of an exact method of determining the dose to be used against this infection was very great, it being observed that a determinate quantity of serum was alone of value in the neutralisation of a given quantity of virus. In our successive studies the difficulties which from time to time were met with in determining the power of a given serum obliged us to return to the question of dosage and to ascertain the various conditions whereby we might be able to obtain constant results. Moreover, since our researches had not simply a scientific aim, but contemplated an eminently practical one, it is clear that, until the conditions indicated had been complied with, it would have been very imprudent to pass to the application of our remedy to man. The general lines of our method follow those actually in use in serum-healing, but in their application to rabies, which is quite a special infection, they necessarily undergo some modification and additions, which we shall now proceed to specify.

1. DOSE OF THE VIRUS.

a. Importance and difficulty of the determination of the dose of the virus in rabies.—In our preceding research we unfortunately had not taken the dose into account. We limited ourselves to the production of the infection as is commonly done in antirabic institutes—with a highly variable material, regulating the dose by the concentration of the emulsion and by the quantity injected. To graduate the power of the infection we make use only of virus—the fixed virus and the canine virus. It is certain, however, that in rabies the question of the quantity of the virus which is used in the test infection ought to have no less importance than the differing strength of the virus itself, as has already been reliably demonstrated in the two typical infections upon which serum-healing has been founded. We know, in fact, that in tetanus the smallest fraction of the established dose of the poison suffices to kill, because the animals die without being affected at all by the injections of the serum, which would otherwise have surely saved them against the exact dose of the poison. If these difficulties are found, then, in experimenting with soluble and therefore exactly measurable toxic substances, how much greater ought they to be when in the material employed for experimental infection one has to deal with living germs—that is, instead of with an intoxication, with an infection properly so-called, and with an infection of which we do not know the active agent or the manner of artificially cultivating it. In the intoxications, the quantity of antitoxin introduced into the body remaining constant, if there is any excess of injected poison the least quantities of toxine not neutralised by the serum are manifested by morbid phenomena proportional to their dose. In the infections, on the other hand, including rabies, as will be demonstrated later, a small quantity of germs not rendered inactive by serum, proceeding to develop, ultimately kill the animal (after some considerable time perhaps)—in general, as much later as the residual quantity of the virus is less. Although the toxic infection can be utilised for the determination of the serum, in the case of rabies the inquiry must be restricted to the quantity of serum capable of completely neutralising in the body a given quantity of virus, without, that is, the

animal presenting any morbid phenomena, its sole effect, therefore, being to postpone a fatal result.

b. Directions for the preparation of the infecting material.—In rabies we must make use of a natural cultivation of the virus which contains a large quantity of foreign materials, all constituents of the nervous system. As yet there is no artificial way of making a cultivation of the virus of rabies; this constitutes an inconvenience, especially with the canine virus, which is extremely variable in intensity, according to its derivation. The fixed virus we may consider is certainly relatively, if not absolutely, more constant. With this last virus the activity can also be varied by several factors—the individual condition of the animal; the rapidity with which it dies; the part of the central nervous system which is chosen for the infection; and, lastly, the period of preservation in glycerine. We have tried to reduce to a minimum all these inconveniences. For the fixed virus we have always allowed the animals to die spontaneously, because, having killed one of them, actually *in extremis* and for a long time paralytic, the dilutions, usually active, were unsuccessful. To obviate all mistakes which could arise from the diverse quantity of germs contained in the various regions of the nervous system we have always taken the material from the same part—that is, from the bulb. From the great frequency with which we made our experiments, not always having the opportunity of practising infections from head to head, we have often been obliged to have recourse to infections with virus preserved in glycerine. But, since the duration of this preservation is not indifferent in the determination of the degree of virulence, we have always tried to make use of a virus which had been collected for not more than three or four days. In the case of the virus “*da strada*” we have not been able to put into practice all these precautions—unassociated as we are with any anti-rabic institution. We have usually chosen a virus which killed in from sixteen to twenty days, obtaining results which would represent a mean between those obtained with a virus of varying derivation. However, the canine viruses have been rejected as being either too weak or too energetic, and we have had among the last of these one which gave the first signs of disease at the eighth day and death at the eleventh. The material was preserved like the fixed virus, but rather longer, we having observed that the differences which can come from its gradual attenuation, by its preservation for three or four months in glycerine, are less marked than those which we come across when having frequent recourse to the virus of another animal. For the rest, along with every series of experiments numerous controls are always made as a guarantee that the material employed had preserved its virulence to the desired degree. The virus of rabies which is found in the nervous system presents another disadvantage compared with bacterial culture, and much more as compared with soluble toxin—it exists in a solid and insoluble form. It is necessary, therefore, to reduce it to the state of greatest sub-division, whereby the injection is made to represent a condition of mean stability. To this end we take a piece of virus always in a quantity of 10 grammes, exactly weighed, and break it down for a long while in some combination of fluid, in the common conical graduated glasses, by means of a rod of glass polished with emery; it is then slowly mixed with the desired quantity of sterilised distilled water.

c. Choice of the most suitable dilution of the canine virus.—It is known how in the rabid nervous system the virus may be highly concentrated, so that it is necessary to make certain dilutions before being able to follow the varying duration and intensity of the morbid phenomena. And, further, we meet with extended series of dilutions from which we obtain a progressive lengthening in the period of incubation before any effect whatever appears. These facts have been demonstrated specially upon the fixed virus by the experiments of Pasteur and of Babes. It is worth noting that in the emulsion of virus which is commonly used to infect rabbits one finds a multiple of the minimum fatal dose of the same virus, a multiple for several reasons variable, and which would render useless any precise measure it might be desirable to use in testing the anti-rabic serum. We have chosen for the infection of our rabbits a dilution always definitely determined, and however stronger the emulsion it always produced death without delay after the ordinary period of incubation. Wishing to have a means of measurement which should demonstrate not merely the higher degrees of the power of the serum we were obliged to keep the virus at a dilution not too concentrated. In the