hydrate may vary within fairly wide limits, not only in different individuals, but in the same individual. The important point to consider is whether, with ordinary diet, the urine always contains a small excess of sugar. If it does so, the case is suspicious, and the ultimate prognosis very doubtful—probably bad. If the sugar is of but temporary occurrence, it can be said that in the majority of cases its presence is of no importance. This temporary increase of sugar is often observed in cases of mental disturbance. The teaching that urines containing sugar are of high specific gravity, while generally true, is not always so. In connexion with this, it is interesting to note that a sample kindly sent me by Dr. A. W. Macintosh, of the Aberdeen Royal Infirmary, contained about 1 per cent. sugar, and yet the specific gravity was, on passing, only 1005, and after cooling, 1010. On the other hand, urines of high specific gravity, such as 1030, suggest at once a suspicion as to the probable presence of sugar. This, of course, is the ordinary textbook statement, but, unfortunately, is often misleading. If, on testing such a urine with Fehling's solution, a modified reaction is obtained, this is often held as confirmatory. As a matter of fact, almost all urines of such high specific gravity as 1030 give some reaction with Fehling's test, but a little consideration would at once show that if the high density were really due to sugar, then the amount necessary to cause this would give a very decided reaction indeed. If glycuronic acid is suspected it can be separated by basic lead acetate. In doubtful cases other tests must be made use of, and in a future publication I intend to give an account of my experience of some of these tests and their results, as well as some methods by which the exact amount of sugar present can be determined. The above will serve to show the nature of Fehling's reaction, and to render intelligible certain reactions of which I have not hitherto seen an explanation. The fact that every urine contains a certain amount of sugar; that the amount normally present varies with different individuals and probably for the same individual, and that the test is at best but a relative one, indicates that the occurrence of an ambiguous reaction in a concentrated urine is generally of no clinical importance, and though largely due to carbohydrates does not usually indicate an abnormal condition. In urines of low specific gravity these ambiguous reactions do generally indicate a slight excess of sugar, but its probable bearing and importance can only be ascertained by watching the case, and by repeated examination of the urine at short intervals. In many cases it will be found to disappear, and give no further trouble; in a few it may show the starting point of a true diabetes mellitus, and in such cases early detection of the true condition is exceedingly important.

In conclusion, I would express my thanks to the various medical men who were kind enough to supply me with samples of urine from time to time during the last few years, and would particularly mention Drs. Souter, Copeland, and Chalmers, residents at the Aberdeen Royal Infirmary.

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LIGATURE OF COMMON CAROTID FOR ARTERIAL DILATATION AND EPILEPSY.*

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The following case of arterial dilatation of the left side of the head, attended by epilepsy and right hemiparesis, relieved by ligature of the left common carotid, is of interest from several points of view:

An unmarried woman, aged 32, was admitted into the Liverpool Royal Infirmary in November, 1905, suffering from a dilated and strongly pulsating condition of the arteries of the

* Read at a joint meeting of the Lancashire and Cheshire and North Wales Branches of the British Medical Association at Chester, April 10th, 1907.

left side of the head for fifteen years, epilepsy for ten years, some frontal headache, and a dull expression, with slow mental processes. It was presumed that similar vascular derangement existed inside the skull, affecting portions of the brain, and probably accounting for the epilepsy. She was put into a medical ward, under the care of Dr. Abram, for observation and report previous to operation.

It was there ascertained that the dilated vessels were first noticed on the left forehead at the age of 17, and had since spread over that side of the head, with increasing pulsation and headache. The fits began at the age of 22, and had latterly been as many as thirteen in a week. There was no aura, but complete loss of consciousness. She had bitten her tongue, but had not passed urine or faeces during a fit. There was a certain amount of right hemiparesis, but sensation was normal; Babinski's sign and ankle clonus were present in the right foot and triceps-jerk in the right arm. The pupils varied and the fundus oculi was normal. Besides the great general dilatation of blood vessels on the left side of the head, confined to the arteries, and specially affecting the main trunk, there was a thrill felt and a murmur heard. The vessels elsewhere were normal. Four days after admission she had six fits, which appeared to start in the right leg.

In the matter of treatment by operation, as the vascular changes outside the skull involved branches of the external carotid, and as those inside might possibly have concerned the middle meningeal—itsself also a branch of the external carotid—it was suggested by Dr. Abram that ligature of this division of the main trunk might wisely be attempted.

With that view on November 27th, 1905, seventeen days after admission, the left common carotid was exposed and its bifurcation sought in the usual place, but no sign of it found there. The wound had been freely made in the line of the vessel, and was now extended at right angles. It was eventually found that there was an unusually high division of the carotid at the level of the jaw. The external carotid was barely within reach of the finger and could hardly, if at all, have been accessible for ligature. Moreover, pressure on it did not control the strong pulsations outside the head. They were only allayed by compression of the common carotid, which was then tied with prepared catgut. The vessel was much widened, as surmised before operation.

The wound healed simply and quickly by first intention; the patient was immediately relieved of her headache and all other inconvenience, and remained without fits for a time. On April 5th, 1907, she came to hospital, and was then examined by Dr. Abram and Mr. Parker. Her sister said that the fits returned about three months after operation, but much more mildly and seldom. Although during the period after their return she had sometimes been free for as much as three weeks at a time, they had latterly become more frequent, and now numbered about one a week. Her memory, also, and power of speech were failing; but in other respects she was healthy and cheerful, in great contrast with her condition before operation. Examination of the fundus oculi showed again no abnormality, and Babinski's sign was no longer present in the right great toe.

The total disappearance of outside arterial dilatation, the cessation of wild pulsation, mitigation of the right-sided hemiparesis, together with the improvement in her appearance and comfort, are quite conspicuous; but the ten years' epilepsy before operation has permanently affected her mental powers, the further deterioration of which was notably arrested during the three months' total freedom from fits. The vascular changes are not likely to have been confined to those perceived outside the left side of the head; the accompaniment of right hemiparesis, epilepsy and headache having been probably due to some such internal derangement.

ON THE CULTIVATION OF THE MENINGOCOCCUS IN THE PRESENT EPIDEMIC OF CEREBRO-SPINAL MENINGITIS IN BELFAST.

BY

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DURING the present epidemic of cerebro-spinal meningitis in Belfast we have made bacteriological examinations of the fluid obtained by lumbar puncture during life (that is, during the first week of illness) from 31 cases, from 27 of which we obtained the *Diplococcus meningitidis* of Weichselbaum by culture on appropriate media. (See below.) One of the negative cases showed intracellular, Gram-negative cocci in the pus cells; and another negative

case was clinically acutely maniacal and probably not a case of the prevalent disease.

Moreover, we have culturally examined the fluid obtained by lumbar puncture after death (necropsy being refused) from 37 cases, with positive result in 22; the remaining 15 cases did not furnish us with the meningococcus, but occasionally with Gram-positive cocci. And thirdly, from the spinal fluid or pus, taken at *post-mortem* examination, we recovered the meningococcus in five out of six cases examined. Thus out of a total of 75 cases examined we were able to cultivate the specific coccus in 52 instances from the cerebro-spinal fluid.

As regards the identification of the coccus, we rely upon the following characteristics:

1. The colonies on suitable agar (see below) are smooth circular discs, with smooth regular contour; they have a peculiar translucent grey colour, closely suggesting the appearance of colonies of *Coli communis*, are only slightly raised above the surface of the medium, and according to the propinquity of the colonies to each other they vary in size from a mere pin-point to discs measuring 5 mm. in diameter after forty-eight hours' growth, but even after eighteen to twenty-four hours' growth the more isolated colonies are 1 to 2 mm. in diameter. These colonies, when first recovered from the cerebro-spinal fluid, are always discrete, never confluent.

2. The colonies, microscopically, are composed of cocci which are indistinguishable in shape and size from the gonococcus—that is, diplococci whose apposed surfaces are flattened or slightly concave. Moreover, there are numerous isolated cocci, smaller than the gonococoid forms, that are spherical in shape, like staphylococci. The older the culture the more numerous are these isolated cocci, the younger the culture the more abundant are the gonococoid forms; but even after four or five days' growth there are always present the typical diplococcal forms with their flattened apposed surfaces.

3. The organism is Gram-negative. The larger gonococoid forms retain the dye somewhat more resistantly than do the smaller isolated cocci, so that thorough washing with absolute alcohol must be practised in order to remove the stain from the former, but even with repeated washing in alcohol it is found that the larger forms cling, in certain cases, to the dye, but if a contrast stain is used, for example, weak aqueous solution of fuchsin, even the resistant cocci part with the last vestige of the original stain, and are coloured an intense pink. We use Czapelewsky's modification of Gram's method, namely, two minutes in carbol gentian violet, one minute in Lugol's solution, wash thoroughly in absolute alcohol. After which the film is thoroughly dried, and aqueous fuchsin is applied for a second or two to one-half the area of the dried film, wash quickly in water, dry and mount. Thus one half the preparation is pink, the other half colourless; if the organism is really Gram-negative the microscopic examination is much facilitated by the stained half of the film.

4. The organism does not grow at 20° to 22° C.

5. Dextrose and maltose containing media are fermented to the extent of acid formation, whereas galactose and saccharose remain unchanged.

This failure of Weichselbaum's coccus to form acid in media containing galactose has been insisted upon by v. Lingelsheim,¹ who finds that acid is produced in maltose and in dextrose containing media, but that no other sugar used by him undergoes this change—for example, laevulose, galactose, mannite, dulcitol, cane sugar, lactose, and inulin. Kutscher² confirms this statement, stating that he has repeatedly been able to verify its exactness.

We repeat that in Belfast we have not found that any one of our strains ferments galactose; acid was never formed in any instance in media containing this sugar, although abundant growth occurs in both solid and fluid media provided a little raw ascitic fluid is added thereto. The galactose used by us was obtained from Messrs. Baird and Tatlock, who write that the sample was prepared by Merck of Darmstadt; we have also used galactose made by Kahlbaum. In common with other observers, we have found that gas is not produced from sugars by the meningococcus.

The above five criteria, when taken in conjunction, are, we think, sufficient to identify a coccus obtained from the cerebro-spinal fluid (or blood) of patients suffering from meningitis—in other words, to stamp the organism as

being Weichselbaum's *Diplococcus intracellularis meningitidis*.

Media used to Cultivate the Meningococcus.

We find that the most satisfactory solid culture medium is the following:

Raw ascitic fluid	...	...	1 part.
3 per cent. agar	...	...	2 parts.

The agar is made in the usual way, but we find that Chapoteaut's peptone is the best to use.³ Witte's peptone is good, but not so much so as the French preparation. A convenient laboratory name for these media is "chapasgar" (or "wittasgar," as the case may be)—obviously a mnemonic word comparable to "nasgar." In making the medium, allow the agar to cool to 55° C., and then add the ascitic fluid, which has been warmed to about the same degree; place in tubes, allow to solidify in the slanting position, and rest for several hours; then incubate for twenty-four hours, so as to insure sterility.

On such slopes the meningococcus lives for a week (sometimes two weeks), and subcultures can easily be propagated, provided the *ose* is well laden with the growth from the lowermost part of the tube—that is, by taking the moist growth near the condensation water. We have abundant growths on this medium, some in the fiftieth to sixtieth generation and above. It is well in the earliest generations to transplant every day, but after three or four transplantations every fourth or fifth day will be found to be amply sufficient.

The organism lives much longer in certain fluid media—for example, from bouillon to which three parts of raw ascitic fluid have been added the coccus is in many instances easily recoverable after thirty days' incubation. Our experiments on this point are still in progress, as the tubes are not yet devoid of living cocci; an agar slope streaked with a single loopful from a three weeks old culture in ascitic bouillon will be covered by an abundant growth within twenty-four hours at 37° C. The same vitality is shown in bouillon to which glucose or maltose with a little raw ascitic fluid are added, although the meningococcus *more suo* is apt to give unpleasant surprises in this particular; still we have, in two instances, recovered the organism after sixty-three days (fifty days at room temperature) and in one instance after seventy-five days.

When a culture has been once established on chapasgar, it will grow well on ordinary agar if transplanted every day or every other day. For opsonic work, where a growth of well-nourished cocci is needed, it can be procured by growing the organism on chapasgar, making daily transplantations, and for the actual emulsion transplant from a chapasgar culture to ordinary agar and incubate for six hours at 37° C. Here the cocci are mostly the gonococcal forms, staining beautifully and intensely, besides forming a perfect emulsion.⁴

The coccus grows abundantly in gelatine to which raw ascitic fluid is added if kept at 37° C. Such tubes, when cooled, resolidify, no gelatine peptonizing ferment having been at work. From certain of these cultures the organism was recovered after thirty days' incubation.

Indol is produced in ascitic bouillon; eight strains were tested for this point, the cultures being examined after thirteen days at 37° C, pure H₂SO₄ being run in, and on addition of a drop of 0.1 per cent. sodium nitrite, the characteristic pink colour appearing.

RECOVERY OF THE MENINGOCOCCUS.

In examining the cerebro-spinal fluid culturally we proceed as follows: If pus is present, a little of it is lifted up on a platinum loop and streaked over the surface of chapasgar in a Petri dish; at the same time an *ose* full of the supernatant fluid, clear or turbid, is spread over a slant tube of chapasgar. When the fluid obtained by lumbar puncture is limpid, 1 c.cm. is poured over the Petri dish, and also a single loopful is spread over a chapasgar slope.

The plates and tubes are incubated for eighteen to twenty-four hours at 37° C., and the colonies, if any, are then subcultured. The following examples may be of interest:

About 10 c.cm. of a perfectly limpid puncture fluid were obtained. The single loopful on the agar slope furnished about 300 colonies, whereas 1 c.cm. on the Petri dish furnished 90 only.

Again, a turbid fluid was examined microscopically, and it was only after long searching that a few cocci were found within certain of the cells, and yet a loopful of this fluid furnished by culture 137 colonies.

Again, a thick puriform exudate on the lumbar cord showed

many cocci in a great number of the pus cells, and yet the cultures obtained showed a marked paucity of colonies—under twenty on a Petri dish.

The meningococcus was also recovered from the blood in 3 out of 15 cases.

The blood was taken from the bend of the elbow; the skin having been washed with mercuric iodide, being prepared as for operation, then a sterile needle was introduced into the vein and about 10 c.cm. of blood allowed to run directly into 300 c.cm. of peptone water. This was incubated for twenty-four to forty-eight hours at 37°, and loopfuls were then smeared over chapsagar. The first successful case was that of a boy whose blood was taken on the eleventh day of his illness. He died sixty-three days afterwards. The second case was a girl of 15 years, whose blood was examined on the second day of illness; she died twenty-four hours afterwards. The meningococcus was still living in the flask of peptone water nineteen days after the blood was added.

In the third case the blood was taken on the fourth day of disease; this patient died ten days later.

SUMMARY.

The meningococcus in the present Belfast epidemic has so far been isolated from cerebro-spinal fluid in 52 cases out of 75 examined, and from the blood of living patients in 3 out of 15 cases.

The organism is Gram-negative, does not peptonize gelatine, produces indol, forms acid from glucose and maltose, but not from galactose, gas is never produced, grows well in media containing raw ascitic fluid, lives for at least a week on "chapsagar," lives from two weeks to a month on ascitic bouillon, lives for two weeks to two months in fluid sugar media.

We are very greatly indebted to Drs. Ernest H. M. Milligan, W. J. Leighton, and Wm. Patton, house-physicians at the fever hospitals of Belfast, for supplying us with most of the lumbar-puncture fluids, and especially for the promptitude with which the samples were sent to the laboratory. To Dr. Gardner Robb, chief physician of the fever hospitals, we wish to extend our sincere thanks for many favours.

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THE RÔLE OF THE VARIOUS ELEMENTS IN THE DEVELOPMENT AND REGENERATION OF BONE.

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[Abstract of a Paper communicated to the Royal Society.]

THE present inquiry has been undertaken with the view of obtaining data, chiefly by direct experiment, as to the rôle which the various elements play in the development and reproduction of bone. This communication deals with a part of the subject under two heads: A, the potentiality of the periosteum as a factor in the production of bone; and B, the regeneration of bone from proliferation of osseous tissue. The following is a brief summary of the paper:

A.—POTENTIALITY OF PERIOSTEUM AS A FACTOR IN REPRODUCTION OF BONE.

(1) To test this, a complete cylinder, constituting a portion of the shaft of a long bone, was removed while the periosteum was preserved intact. This showed, ten weeks afterwards, an osseous defect, constituting a gap in the continuity of the shaft.

(2) Periosteum free from osseous plaques was removed and transplanted. This was not followed by reproduction of bone, but by absorption of the periosteum.

(3) Duhamel's silver ring experiments are discussed, and the correctness of the deductions drawn therefrom are questioned.

In order to test whether the bone cells or the periosteum produces the bone which covers the silver rings, three experiments, each differing from the other, were performed, in which silver rings were placed on bone deprived of its periosteum, with the result that in each case the rings became covered with bone.

B.—THE REGENERATION OF BONE, FROM PROLIFERATION OF OSSEOUS TISSUE.

The periosteum is shown to be a limiting membrane controlling the osteoblasts, as illustrated in fractures, when the periosteum is intact and when it is torn. The production of callus is not inherently greater in the lower animals than in man—the amount of callus in both depends on the limitation of the periosteum and the amount of movement. (4) Direct experiment, showing that a long bone deprived of its periosteum continues to grow; (5) so also do the flat bones of the skull. (6) Bone may be made to grow in the midst of lacerated muscles by the mechanical distribution of osteoblasts. Observation. Rider's Bone. Suggestion as to the production of myositis ossificans.

(7) Can shavings of nude bone grow on being placed between muscles in a gap in the continuity of the shaft? Experiment and result seven weeks after show that not only do they grow but that they also proliferate to a very marked extent.

Is there any direct evidence to show that transplanted living bone actually grows and proliferates instead of forming, like blood clot, a passive framework for the granulation tissue to penetrate, which framework will then become absorbed? There is, as may be illustrated (8) in an instance of bone grown in sponge filled with granulation tissue.

(9) To test the osteogenic power of bone cells constituting the shaft of a long bone, they were grown inside of a glass tube. Result.

(10) Intrahuman transplantation of bone. Result 28 years after. Data are obtained from this experiment as to the growth of the humerus from the proximal and distal epiphyseal cartilages respectively. Also as to interstitial osseous increase—evidence of the increase in length of the diaphysis from the epiphyseal cartilage toward which the nutrient vessel runs.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL.

DYSTOCIA FROM ENCEPHALOCELE.

BEING summoned to Mrs. X., 38, 8-para, I found her in the second stage of labour, with inefficient pains. The child was in the fourth face position, and the waters that had come away were meconium stained; no sign of fetal life was made out. Rotation by hand and subsequently by forceps—under chloroform—failing, podalic version was done with much difficulty, being obstructed by a curious fluctuating tumour near the head. While preparations were being made to exercise traction on the after-coming head, a sudden sharp uterine pain shot it out, accompanied by a gush of sanious fluid and the disappearance of the "tumour" from the uterus. The swelling was then seen to be due to a large encephalocele. The child was dead. The mother subsequently did well.

Necropsy.—Full-time female child, normal size; very thick neck and small chin. Fronto-parietal part of skull normal in size; occiput smaller than usual. From occiput there sprang mesially a large encephalocele, which when empty and pendent reached to the sacrum, and without undue expanding held some 30 oz. of water. The sac walls were formed of skin, brain membranes, and thinned-out and expanded brain-cortex. The sac cavity was in free communication with the cerebral ventricles, by an opening roughly circular in shape and 1½ in. in diameter. The cerebral tissue entering into the sac formation appeared to consist of occipital lobes only; the remainder of the cerebral hemispheres was of normal size. The tentorium was absent. The cerebellum was represented by a peculiar tongue-shaped prolongation (perhaps the vermis only) extending 2 in. downwards on the dorsal aspect of the cord. Sections taken from this process, when cut and stained, showed a modified cerebellar tissue. All the organs of the body were examined, but no other abnormality was found.

REMARKS.—The mother informs me that three and a half years ago she had, what must have been from her description, a similar pregnancy, being a male child with a frontal meningocele, the size of a large orange. Her description of the child indicated also a spina bifida in the dorso-lumbar region, a small apple in size. This child lived seven weeks. Between these two abnormal pregnancies a healthy (girl) child was born, and is now 2 years old. No