Urine contained much glucose, acetone, and aceto-acetic acid. Condition improved slightly, but pyrexia continued; signs at bases of both lungs. Ten days later patient became comatose and died. *Post mortem* examination showed purulent prostatitis, septic bronchopneumonia, and slight macroscopic changes in pancreas, sections of which are being cut.

Case 3.—Male, aged 25. Admitted under Dr. R. A. Young, September, 1921, for thirst and loss of weight. Much sugar, acetone, and aceto-acetic acid in urine. Patient refused strict diet and was eventually discharged unimproved.

FIG. 8.—Curves of alveolar CO_2 tension from a series of cases of severe diabetes mellitus: an average normal curve is shown for comparison. In this figure the readings recorded at the moment of the meal are, in Case 2 and Case 3, assumed: several readings were taken in each case before the meal, but not actually at the last moment before giving it. The normal curve is the average of a series of observations.

Case 4.—Female, aged 25. Severe diabetes for four years. Has been sugar-free on diet of less than 1,000 calories per diem for over a year; during last three months tolerance has fallen lower, and she now passes small amounts of sugar on lowest diet compatible with N-equilibrium. No acetone or diacetic acid in urine. Blood sugar curve typical of diabetes mellitus.

A few milder diabetics rendered sugar-free by dieting and having now a fair sugar tolerance, whom we have been able to investigate, have shown curves of alveolar CO_2 not differing from the normal picture seen in health.

If the interpretation which we have given above of the normal curve of alveolar CO_2 tension following a meal be correct, the extreme and protracted drop in tension seen in severe cases of diabetes indicates that in this disease there is hypersecretion of the pancreas. Now, it has been pointed out by Allen and others that the internal secretion of the pancreas is inversely proportional to its external secretion, and, on that hypothesis, the success which has attended the treatment of the disease by the principle of "alimentary rest" is explained. We would suggest that, in severe cases of diabetes, the external secretion of the pancreas is of an extreme degree, analogous to the hypersecretion of the stomach seen in patients suffering from Reichmann's disease. Alimentary hypersecretion is a phenomenon which is exceedingly difficult to demonstrate by any direct method; in the case of the stomach it can be done by accurate measurement both of the amount of juice aspirated at varying periods, and the degree of concentration of this juice; there being no convenient sphincter below the pylorus, it is impossible to collect more than small samples of the pancreatic juice in man, but we are at present devising means of confirming our findings by some such direct method. We wish in the meantime to draw attention to our observations, and to note that our belief that they indicate a condition of pancreatic hypersecretion is not in discordance with existing clinical and laboratory data, even though the conception itself be a novel one.

The parallelism between these curves of CO_2 tension and the curve of blood sugar commonly seen in a diabetic is a fact which must strike anyone familiar with the latter, and we hope in a later paper to bring forward further evidence as to this. The comparative rarity of macroscopic or microscopic evidence of gross pancreatic disease in cases of diabetes seen *post mortem* has long troubled students of this disorder,

and has made it almost impossible to harmonize theory with Minkowski's experimental production of the disease by pancreatectomy; we feel that the present observations supply valuable evidence towards the elucidation of this problem.

As to treatment our experiments with atropine suggest that a considerable degree of control over pancreatic activity may be acquired by the direct application of the drug to the duodenal mucosa; we are not yet in a position to produce clinical evidence in support of this suggestion, but hope to do so at a later date.

We would, in conclusion, express our thanks to our colleagues and co-workers at the Middlesex Hospital for their valuable help and permission to investigate cases under their care. The respiratory observations here recorded form part of a report to the Medical Research Council; the expenses of one of us incurred in this research have been partly defrayed by a Government grant made through the Royal Society.

SUMMARY.

1. The variations in alveolar CO_2 tension after a meal depend, in a subject at rest, on the secretions of acid and alkali into the stomach and duodenum.
2. Confirmation of this is given by the curves of alveolar CO_2 pressure from subjects with varying degrees of gastric secretion, or with pancreatic insufficiency.
3. Further confirmation is supplied by the results of experimental introduction of food direct into the duodenum.
4. The application of atropine to the mucosa of the stomach or duodenum appears to arrest the secretion of acid or alkali into the organ to which the drug is applied.
5. The writers believe that, like salivary and gastric secretion, pancreatic secretion must be a slow, continuous process interrupted by a more vigorous flow whenever food traverses the pylorus.
6. The fasting level of alveolar CO_2 tension in any subject represents a balance between the continuous loss from the blood stream of acid via the stomach, and alkali via the pancreas and duodenum.
7. Cases of severe diabetes frequently show a low fasting level of alveolar CO_2 tension even when no ketosis is present.
8. Cases of severe diabetes investigated by the writers have, after a test meal, shown a fall of alveolar CO_2 tension greater than that seen in any other condition so far examined.
9. It is suggested that this is due to a condition of hypersecretion of the pancreas, analogous to the gastric hypersecretion seen in cases of Reichmann's disease.

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HEMIPLEGIA IN A YOUNG CHILD, FOLLOWED LATER BY LOCOMOTOR ATAXIA.

BY

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THE explanation of the rather complicated signs in the following case is probably as follows. The patient inherited syphilis, and developed a vascular lesion at the base of the brain when 3 years old, probably a syphilitic thrombosis in an artery at the left internal capsule. This gave rise to the right hemiplegia and aphasia at the time, and to the slight diminution of size and strength of the right side, which is the more marked where there is the greater differentiation of function—that is to say, most in the hand, least in the trunk—and to the right Babinski, and to the increased jerks in the right arm. A couple of years ago locomotor ataxia set in, and she developed the droop and the diplopia; we have no proof that the Argyll Robertson pupil, the inequality of the pupils, and the loss of knee-jerks developed at the same time, but we surmise it.

A girl, aged 17 years, was admitted to the Royal Victoria Hospital, Belfast, on August 19th, 1921, under Dr. Calwell. Her father had died, aged 48, from angina pectoris. She is the only child alive; four sisters and one brother died before two years of age; two were premature, one died aged 7 weeks and the other aged 8 months. Her personal history, as given by the mother, is that she had a sudden attack of right-sided paralysis with aphasia when 3 years old; she recovered her speech in two weeks and the use of the arm and leg was regained in a year. Ever since she has had a "halt" in her gait, and no spring in the right foot; she says the right side is weaker than the left.

On admission, the various systems were found normal, except as follows: The right upper and lower extremities are smaller than the left, and this holds both as regards length and circumference; the difference varies from one 1/4 inch to 1 1/2 inch. It is more marked in the arm than in the leg, and most marked in the hands; the left metacarpus measures 1 1/2 inches round, the right only 6 inches. No difference is seen in abdomen, buttock, or back; the left knee-joint is slightly swollen, but the x rays show no bony change.

The right foot is pes cavus with some equino-varus; there are some slight athetoid movements of the right foot which interfere somewhat in taking the reflex. The gait is not characteristic; she lifts the right foot as in high stepping, gives it a slight indefinite shake, and brings it down awkwardly more on the toes; the left foot comes down a little on the heel.

With reference to her reflexes, there is no plantar reflex on the left; there is a true Babinski type on the right, but obtained satisfactorily only once every three or four times; no knee nor ankle jerks are present in either. Co-ordination and topognosis with feet is poor, slow, uncertain, and clumsy. In the upper extremities, supinator, triceps, and biceps jerks clearly more marked in right, indeed exaggerated; co-ordination and topognosis is good with both. Romberg is doubtful, although the patient was uncertain in standing and bending with her eyes closed. The sensory system is normal, the speech normal.

In the eyes there is ptosis of left lid, sometimes marked, sometimes slight; there is paralysis of the left external rectus; fine lateral nystagmus is present in the right eye when looking upwards and outwards. The discs are normal and sight good; there is diplopia when looking to the left, and in the left eye the field of vision is slightly contracted. Argyll Robertson pupil is present in both eyes; the left pupil is larger than the right. A Wassermann test of the blood was returned from the laboratory as double positive, by both Harrison's and Fleming's methods.

It is interesting to notice the presence of the Babinski reflex and the loss of knee-jerk in the same limb; this latter reaction depends on the condition of the tone of the muscle. If the tone is marked we have a brisk reaction; if excessive we have a clonus; but in this case where we would expect an excessive tone as we have in the arm, the tone is lost owing to the syphilitic affection of the posterior roots, containing the sensory fibres of tendon and muscles, and so we get loss of both knee-jerks. A weak point here is the absence of any history of lightning pains.

A plantar reflex has the following explanation: a family group of congeries of cells in one or two adjacent segments of the spinal cord has in time past been so often subjected to the same stimulus, and called upon to react in exactly the same manner that the total forms an organic whole, and the reaction is automatic or "a reflex." The cells in the lumbar enlargement are influenced by not only the cortical fibres through the crossed and uncrossed pyramidal fibres, but also by the descending tecto-, rubro-, cerebello-, and Deiters'-spinal fibres. When the influence of the cortical fibres is removed by a lesion, say in the internal capsule, the other descending fibres have full sway and the type of reflex goes still further back, say from that of our arboreal ancestors to that of our still more remote ancestors of the plains, and so we get a dorsi-flexor or Babinski instead of a plantar flexor reflex. This reflex does not depend on a tone condition, and so in this case it is retained.

The patient has greatly improved in general health and weight since admission to hospital; she feels stronger and says she has more control of the ptosis and locomotion. She has received one injection of 0.3 gram and twelve of 0.45 gram of novarsenobillon; but the Wassermann is still positive.

ASTHMA AND THE RADIUM MENOPAUSE.

BY

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With a Note by

SIR HUMPHRY D. ROLLESTON, K.C.B., M.A., M.D., F.R.C.P.

WHILST it is frequently found that women with an asthmatic personal or family history are peculiarly liable to develop the disease in a more severe form during the period of the menopause, there appears to be no case on record of exceedingly intractable asthma due, at any rate in part, to the artificial completion of the menopause by the introduction of radium into the uterine cavity.

So many instructive conclusions and interesting surmises can be drawn from the following case that it appears worthwhile to publish the details.

The patient, Mrs. X., had lived in the same house for three years, and during that time had not suffered from asthma. She is now aged 47 years. There is no asthmatic, unstable,

or neurotic family history. In 1906 she had the radical operation performed on both maxillary antra for acute supuration in those cavities. In 1909 she had an attack of asthma, which was the only one prior to her present illness.

In October, 1920, she developed a peculiar mental condition, which Sir Maurice Craig diagnosed as being due to cerebral anaemia caused by excessive monthly loss of blood. On his advice the menopause was artificially induced by the introduction of radium into the uterine cavity. This radium was lent by Dr. N. S. Finzi and the dosage worked out by him. In ten days she was mentally quite normal and menstruation has permanently ceased.

As soon as she commenced to resume partially her ordinary life a purulent secretion appeared from both antra, accompanied by exceedingly troublesome asthmatic attacks. At that time I considered the asthma to be purely an anaphylactic symptom caused by organisms from the nasal discharge, to which organisms or their products the patient was hypersensitive. On this assumption I asked Mr. Philip Franklin to put her nose thoroughly in order. He straightened the septum, removed a large spur of bone, scraped away some carious bone from the ethmoidal region on the right side, and enlarged the openings into both antra to allow of more adequate drainage of the cavities. At the time of operation Sir Kenneth Goadby made a bacteriological examination of the sputum and swabs from the right and left antra and high up in the nasal fossa. He reported that the sputum contained large numbers of pus cells and long chain streptococci, whilst both nasal and antral swabs showed large numbers of streptococci and also Gram-negative bacilli (probably Friedländer's).

An autogenous vaccine was made, and she was given twelve progressively increasing doses. No improvement was noticed. Asthma was practically continuous; bronchitis was marked at both bases; the patient was losing weight, could get no rest by day or night, and was rapidly going downhill.

During this time I made exhaustive trials of practically every known medicine, inhalation, nasal spray, hypodermic injection, and powder which had any reputation whatsoever in controlling asthmatic attacks, but none had the slightest beneficial effect. At that stage I was still hopeful that, the nose being now in excellent order, the vaccine treatment would ultimately be curative. This belief was bolstered up by the fact that the eleventh and twelfth injections were followed by a generalized urticaria, especially round the site of injection, and these two injections definitely excited two particularly severe asthmatic attacks. This was taken to imply that the patient was undoubtedly sensitive to the products of the nasal discharge, and consequently it was logical to continue the vaccine, though, of course, in smaller doses until tolerance was obtained.

In August, 1921, Sir Humphry Rolleston saw the patient in consultation with me. His opinion, now proved to be entirely accurate, was that, whereas the nasal discharges were certainly the main factor in the production of the asthma, some other factor must also be present, in view of the fact that the vaccine was not curative. Feather pillows, dogs, cats, eggs, etc., were all in turn excluded, and the patient was going from bad to worse.

On October 2nd her condition was extremely critical. The asthma was perpetually present both day and night, and was most distressing both to herself and to her relations. The pulse was weak, irregular, and almost imperceptible at times; the temperature ran up to 102° F., and a fatal issue appeared imminent. Dr. Canti saw her in consultation with me, and made an exhaustive pathological examination, including even a spectroscopic examination of the blood, but no light could be thrown on the subject. Oxygen inhalations and hypodermic injections of strychnine were urgently necessary.

On October 10th, thinking that the menopause might be the additional factor I had been looking for the patient was given by the mouth ova-mammoid compound (British Organotherapy Company, Ltd.), consisting of ovarian extract 1 grain and mammary gland extract 1 grain, four times daily. The result was as unexpected as it was striking. On the following day the asthma and bronchitis, which for a year had never been absent, were markedly improved, and by the third day the asthma had entirely disappeared with the exception of a very minor attack in the early morning. The treatment was persevered with and she improved progressively. She is now to all intents and purposes cured.

During the whole course of treatment neither peptone nor serum was given.