The pharmacological tests employed failed to show any marked difference between the action of the "colloidal" preparations tested and the action of the same substances in true solution.

Note.—The expenses of this research were defrayed by a grant from the British Medical Association.

REFERENCES.

- ¹A. B. Searle: The Administration of Colloids in Disease. Report of the British Association for the Advancement of Science, 1918, 155. *The Use of Colloids in Health and Disease*, London (Constable), 1920. ²J. Laumonier: *La Colloidothérapie*, Paris (Félix Alcan), 1920. ³Dale: *Journ. of the Soc. of Chem. Industry*, 21, 39, 1920. ⁴Kütz: *Arch. f. Exp. Path. und Pharm.*, 111, 9, 1921. ⁵Schmidt: *Alkaloide, Handbuch der Biologischen Arbeitsmethoden (Abderhalden)*, I, 9. ⁶Cawston: *BRITISH MEDICAL JOURNAL*, 1920, II, 855, and 1921, I, 419. ⁷Wildish: *Ibid.*, 1922, I, 55. ⁸Voeghelin and Smith: *Journ. of Pharm. and Exp. Ther.*, 457 and 476, 15, 1920. ⁹Fargher and Gray: *Ibid.*, 541, 18, 1921. ¹⁰Heubner: *Arch. f. Exp. Path. und Pharm.*, 370, 56, 1906. ¹¹Marshall: *Proc. Roy. Soc. Edin.*, 39, 145, 1919. ¹²Marshall and Kiloh: *BRITISH MEDICAL JOURNAL*, 1915, I, 102. ¹³Simpson and Hewlett: *Lancet*, 1914, II, 1359. ¹⁴Duhamel: *C.R. Soc. de Biologie*, June 21st, 1919. ¹⁵Voight: *Biochem. Zeit.*, 409, 63, 1914. ¹⁶Petersen: *Protein Therapy and Non-specific Resistance*, New York, 1922. ¹⁷*Journ. Amer. Med. Assoc.*, 841, 69, 1917; 1634, 72, 1919; and 1218, 73, 1919. ¹⁸Rokers: *Lancet*, 1919, I, 555. ¹⁹Crookes' *Colloids*, fifth edition, p. 17. ²⁰*Colloidal Iodine*, p. 7. ²¹Crookes' *Colloids*, fifth edition, p. 41.

FIVE CASES OF DIABETES MELLITUS IN YOUNG CHILDREN.

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THE occurrence of five cases of diabetes mellitus in young children admitted within a short interval to one ward in a hospital leads me to think that at the present juncture in the history of this disease their publication may be of value. It is clear from the present literature that, for those who have few opportunities of studying a malady which is fortunately rare in childhood, it will be of importance to recognize the symptoms and, above all, the course of the disease at this early age, in order to obtain a correct perspective of the value of treatment by pancreatic extracts. It is in childhood that we see the pure type of virulent diabetes, and if very different results from those recorded in this series are obtained in the future there must be conviction that a great step forward has been made in medical knowledge. These cases were treated upon what until recently was considered to be the modern lines, and with the assistance of Dr. Spence and Dr. Donald Paterson, good medical clerks and devoted nurses, a whole-hearted attempt was made to study the effect of dietetic treatment and of such pancreatic extracts as were then available. The first case was an example of the type of problem that confronts us in hospital, and it will serve as an introduction to the main subject.

CASE I.

A boy aged 7 years was admitted on September 5th, 1920, in a state of coma. He had suffered from diabetes for eleven months, and for four months had been under "a specialist," and was sent to us when comatose. If we turn to this boy's history we find it is a characteristic one. An only child of healthy parents, he had been for the first time attending school. For two weeks, though complaining of headache and thirst, he tried to do his work and then had to stop. For six months these two symptoms remained the prominent ones, but later others were added—hunger, irritability, constipation, and polyuria (5 to 6 pints per diem). His weight at first hardly altered. The final symptoms were increasing thirst; emaciation, some vomiting, abdominal pain, and fleeting pains in the limbs. Finally drowsiness and coma.

On admission he smelt strongly of acetone and was comatose. The action of his heart was feeble and his face grey. The abdomen was scaphoid, and the urine contained 2.2 per cent. of sugar. Death was sudden.

Among these symptoms I should dwell upon irritability as one which repeatedly appears in the young when the disease is making headway, and upon abdominal and other pains as occurring just before the onset of the coma.

There was no necropsy, and a more unsatisfactory case than this for all concerned can hardly be imagined. The second case was much more instructive.

CASE II.

C. N., a boy aged 5½ years, was admitted on December 11th, 1919, with a history of symptoms of two months' duration. These symptoms were thirst, nocturnal enuresis, and occasional pain in the upper part of the abdomen. The sugar had been detected three weeks before admission, when the boy was attended by a doctor for colic due to eating green apples. Unless an attack of measles

in June, 1919, could be claimed as a factor in causation, there was not a single event in the boy's history to suggest a cause for the diabetes.

I dwell for a moment on the symptom of nocturnal enuresis. We see many cases of this disability, but very few are due to diabetes. It is, then, very unfortunate if one should overlook testing the urine thoroughly in a case of nocturnal enuresis and happen upon a diabetic child. This boy was well nourished and walked into hospital. His skin was dry and his tongue beefy. The knee-jerks were present but difficult to obtain; the fundi were normal. The urine had a specific gravity of 1042, was acid, contained 6 per cent. of glucose, and also acetone and diacetic acid.

Treatment.

His appetite was poor. He was placed on a low diet of tea, bovril, two eggs, and some minced meat. The calorie value of this diet was about 250, and in four days the urine was free from sugar, acetone, and diacetic acid.

We then started to test his carbohydrate tolerance, and by December 30th we had reached a diet of calorie value 914, which contained 78 grams of carbohydrate. The weight of the boy was 18 kilos, and accordingly the calorie value per kilo was $\frac{914}{18} =$ practically 50 calories per kilo. Authority has stated that 40 are sufficient to maintain weight, but this boy barely held his own when in bed on 50 per kilo.

On January 1st we let him get up on the same diet for three days, and his weight increased, but a slight trace of sugar appeared in the urine. He returned to bed, whereupon the sugar disappeared, but his weight began to fall again.

By January 18th we had increased his carbohydrate tolerance to 86 grams, but after four days there was a slight trace (under 0.5 per cent.) of glucose. We accordingly decided that his carbohydrate tolerance was about 80 grams.

We then turned our attention more particularly to the fat tolerance, which we raised to the limit of 110 grams. During the next month we made tentative experiments in dieting, with these obvious points in view:

1. To obtain a diet which his parents could give him when he left hospital—one, that is to say, not too expensive for their resources, and fairly satisfactory for the boy.
2. A diet which, while keeping him sugar-free, maintained his weight.

This, whatever may be the opinion of others, is, I am convinced, very essential. We must try and maintain the weight in children. "Keep them thin" may be a motto for adults, but not for children. His diet finally had a calorie value of 836, but this would only admit two small slices of bread and two tablespoonfuls of milk pudding.

We failed—though the value of 46 calories per kilo body weight was attained—to maintain his weight in hospital, and after a long stay we sent him out with a fair diet. On admission he had weighed 2 st. 11 lb.; on February 15th, 1920, he weighed 2 st. 9 lb.

The diet for guiding his parents when he was at home was:

- Breakfast.*—One egg, one buttered rusk, and an ounce of bacon.
Lunch.—Clear broth, one buttered rusk.
Dinner.—Mince 2 oz., cabbage 6 oz., potatoes 2 oz.
Tea.—One orange, one cup of milk, one buttered rusk.
Supper.—One buttered rusk, one cup of cocoa.

This was the skeleton outline—fish and other vegetables could be substituted—and it was useful as a working basis.

Three weeks later he was readmitted, with urine specific gravity 1039, glucose 3.9 per cent., and a faint trace of acetone. We ascribed this to eating too many vegetables. He had gained weight.

Once again in hospital we had difficulty in getting him to maintain weight, but on a diet of 926 calories he just held his own. In a month, however, he was able to take 122 grams of carbohydrate and a diet of 1,124 calories, on which he had gained a pound. The urine (specific gravity 1014) was free from sugar and ketone bodies.

From March 31st to August, 1920, he lived at home and kept well but did not gain weight. Then he broke down with hunger, thirst, irritability, and polyuria. There was sugar but no acetone in the urine. He was admitted on August 28th, when only a trace of sugar was demonstrated. This time the specific gravity of the urine was never above 1026, and only traces of sugar and acetone appeared when we were building up his diet. The result on this occasion was encouraging, and he left the hospital in October, 1920.

About Christmas he became thirsty, lost strength, and suffered from polyuria. Alarm was aroused three days before he came to the hospital by a "bilious" attack and drowsiness.

On admission he looked ill and drawn, and his urine was loaded with ketone bodies and sugar. There was general abdominal tenderness. In spite of intravenous alkaline injections he died that night in severe convulsions.

The *post-mortem* examination naturally interested me greatly, for I had never had an opportunity of seeing one in a child after so protracted an attack of diabetes. His illness had extended over almost three years. As usual there was very little to see and no long description is needed. The liver was large, pale, and flabby; the kidneys appeared natural. The pancreas was small and soft, and microscopy showed no increase of fibrous tissue but atrophy of cells. The gland looked exhausted, and the cells of the islands of

Langerhans were atrophied and separated by connective tissue.

We know that much caution is required in interpreting *post-mortem* changes in the pancreas owing to the autolysis that occurs after death, but this was a clear case of atrophy of the pancreas.

The third case was of especial interest because there had been a history of only one week's illness.

CASE III.

A girl aged 9 years was admitted on February 23rd, 1921, for sudden thirst, rapid wasting, and a nasty taste in her mouth. She had always had good health, and this was her first illness of any kind. Both her parents were healthy, her father aged 34, her mother 36.

The patient was thin and languid, passing 20 oz. of urine of a specific gravity 1042, containing 8.6 per cent. of sugar and ketone bodies. We put her on equal parts of milk and water, with a calorie value of 381. The sugar and ketone bodies disappeared, the urine falling in specific gravity to 1020; weight 3 st. 4 lb. Then we rebuilt the diet up to one of over 1,000 calories, and she gained steadily—leaving, sugar-free, in April. In June she was still sugar-free.

In September, 1921, she "caught a cold," and a fortnight later, being weak and generally ill, her urine was examined and found to contain sugar, and she was brought to hospital on September 24th. The child seemed quite ill and looked pale. Urine: specific gravity 1040, 2.9 per cent. sugar, ketone bodies present.

After admission she was very quiet and refused her food, and on September 28th fell into coma with profound collapse, dying early on the morning of September 29th. Efforts were made with an intravenous injection of a 2 per cent. solution of sodium bicarbonate—large doses by rectum—and drachm doses of glucose to restore her balance, but she never rallied.

Post-mortem examination was refused.

Here was a very remarkable and treacherous case. The first attack came like "a bolt from the blue," swift and threatening. The crisis passed and no case seemed to be doing better, for there was steady gain in health and weight and disappearance of the sugar. For months the child seemed well—and then came an infection in the shape of a "cold," and once more the swift onslaught. It was possible that the few days in hospital before death were not managed to the best advantage, but I do not think that this made any essential difference to the final issue. We must be wise indeed if, with scant opportunities for seeing diabetes in childhood, we can always anticipate an attack of coma.

Watching a series of these cases would convince one that there is something more than diet involved in these sudden relapses. Not for one moment do I suppose that, good though these children were and devoted their parents, it is probable that a strict diet can be maintained. One of the children was a member of a working man's large family—can one believe that the children did not have pity upon the sister whose diet was so dull, and provide her with occasional treats? Granting this, children who left hospital losing ground in every way actually improved in some instances at home. The breakdowns were more mysterious than a matter of diet—for example, when the weather became cold and treacherous and there were sore throats and coughs, my various cases would come back within a week or ten days with sugar in the urine. Three came back into the ward within a week, although from different families and different localities.

CASE IV.

My next case, a boy aged 8 years, had been suffering from lassitude, weakness, thirst, and polyuria for eleven months. His condition first attracted attention by his general weakness after he returned from school.

He was admitted to hospital in September, 1919, in what as the sequel showed was to be a feature of his case—an acute condition of acetonæmia. I did not see him then, and can only record that he went out improved. He appeared to have kept well, and certainly gained weight for nine months, when, fourteen days before he came under my supervision, he became irritable, weak, sleepless, and suffered from polyuria.

His second admission to the hospital was August 9th, 1920. The only history we could get was an injury to his right calf before the first symptoms of the disease commenced. The parents were healthy, as also was his only sister.

This boy was a very home-sick one, and on his readmission he had an acetonæmic attack, with vomiting. The specific gravity of the urine was 1010; it contained no sugar, but great excess of ketone bodies.

In this case it was urgent to control particularly the fats, and as the ketone bodies diminished a little sugar appeared and the child lost weight. The strict diet soon got rid of sugar and ketone bodies, but the loss of weight called for an advance upon this.

The blood was examined on August 24th by Dr. Spence, who found the blood sugar normal, but the curve a true diabetic one, as the chart exemplifies.

By August 27th he was so much better that we had him on a practically normal diet, except that bread and potatoes were cut

down by half because of an occasional slight leakage of sugar. From the 19th to the 26th he was in fact on a good diet, free from all sugar and ketone bodies; but his blood sugar estimation, though giving a normal blood sugar content, showed after carbohydrate a true diabetic curve.

We eventually sent him out on October 12th sugar-free, though, in spite of every care, sugar would sometimes appear mysteriously in small quantities. I thought, in spite of the blood test, that we were going to have a successful result if we could only keep reasonable control of him when out of hospital. His diet was the following:

Breakfast.—Milk one glass, one egg, one rusk and butter.

Lunch.—One glass of milk.

Dinner.—Clear broth, mince, cabbage, potato.

Tea.—One orange, one glass of milk, one egg, one rusk and butter.

Supper.—One rusk and butter, one cup of cocoa, cheese, lettuce.

The boy kept well from October until the beginning of February, 1921, attending the hospital every fortnight.

In February, within a week he became irritable, drowsy, languid, and thirsty. He was admitted to hospital threatening coma, with sugar 4.8 per cent. and ketones in the urine, which had a specific gravity of 1040.

An interesting feature now was some bronzing of the face and a yellow discoloration of the palms of the hands. He was treated with skimmed milk, given glucose 2 drachms four-hourly, and large doses of sodium bicarbonate by the mouth.

He rallied well, and we raised him eventually to a diet of 1,616 calories, on which he just held his own. After two months in hospital he left with a sugarless and ketone-free urine in April. This time we had difficulty in ridding the urine of the ketone bodies, which made me uneasy as to the future.

Until August, 1921, he kept on the whole well, though leaking sugar at intervals, but at the beginning of this month he developed headache, polyuria, thirst, pains in the limbs, drowsiness, and deep breathing. The urine had a specific gravity of 1026, and was loaded with sugar and ketone bodies. The knee-jerks were absent. Treatment with stimulants, intravenous sodium bicarbonate, calomel, and sodium bicarbonate by the mouth saved him, but for several days his life hung in the balance. This time with all our efforts, and with occasional starvation days, we could never get him free from some sugar or acetone. He left the hospital in October, 1921.

He left the hospital losing ground and in an apparently hopeless condition, but it would have been sheer cruelty to keep him longer away from his home, particularly as we were doing him no good. To my astonishment he then commenced to improve, and though not free from sugar kept well through the winter, until February, 1922—that is, for four months. Then all his symptoms reappeared synchronously with the formation of a small abscess on his scalp. He came to hospital on February 14th, smelling strongly of acetone, breathing deeply, and very drowsy. The urine had a specific gravity of 1032, and contained sugar and great excess of ketone bodies. In spite of every effort he died in coma on the 6th.

The *post-mortem* examination showed, as in Case II, a fatty liver, but the pancreas was shrunken and even more wasted than in the former case. Microscopy showed no active reaction, no trace of inflammatory change, but similar shrinking of the cells of the islets and relative increase of connective tissue.

CASE V.

The last case, a girl aged 7½ years, was admitted on May 28th, 1920. This case we got early, for there had only been three weeks' history. The symptoms were: inordinate eating and drinking, rapid wasting, and polyuria, the urine being noticeably pale in colour. There was not the slightest hint in the family or personal history, or in the surroundings, as to the cause of this sudden breakdown.

The child looked ill and was wasted, and suggested the diagnosis of diabetes. The specific gravity of the urine was 1045, and there was much sugar with ketone bodies.

By June 12th, on skimmed milk, with calorie value reduced to 513, and carbohydrate 52 grams, the sugar in the urine was reduced to a trace and the ketone bodies eliminated.

In July she was keeping free from sugar.

This child left hospital in October, 1920, free of sugar and ketones, apparently well, but with a blood curve of the diabetic type as shown by Dr. Spence. She kept well, but unfortunately ceased to come up to hospital for two months

previous to her next admission in February, 1921. It would be wearisome to detail the subsequent history, but, in a few words, the child broke down again in February, 1921, and once more we sent her out, in April, 1921, sugar-free and looking well, but in the notes I had expressed the opinion that there was increasing difficulty in attaining this result and that the outlook was bad. In July it was interesting to read the note of an enthusiast below this to the effect that she was looking splendid and was sugar-free.

Shortly after this note, in the same month, she broke down again. In her case we had difficulty in raising the calorie value as there was some sugar appearing; and particular difficulty was experienced in trying to raise the carbohydrate tolerance. However, in September we had got the calorie value up to 1,546, carbohydrates 50 grams, and the patient had gained a little weight.

On September 30th half a slice of bread brought back sugar, and later some mince produced the same result.

In October we managed to give one ounce of potato and a quarter of an ounce of bread, and a diet of calorie value 1,600. Now and again a trace of sugar would appear, but we then discharged her under supervision with the following diet:

Milk.—8 oz. every four hours.

Breakfast.—One egg, cheese 1 oz., two tomatoes, weak coffee, bread 1/4 oz.

Dinner.—Broth, cabbage, 8 oz., potatoes 1 oz., fish 2 oz., cheese 1 oz., one egg.

Tea.—Broth, one orange, lettuce 6 oz., cheese 1 oz., one egg.

Supper.—One egg, weak tea, an onion, bread 1/2 oz.

In 1921 a yellow discoloration was noticed on the palms of the hands and soles of the feet.

Once more she kept well through the winter—her mother taking infinite trouble—but broke down again in February, 1922. From that date onward she always appeared thin and drawn, but was out of hospital until the autumn, when again all the symptoms returned: diet proved ineffectual, and the child became very unhappy. It was apparent that the last stage was reached, and at urgent request she went home, dying in coma in November, 1922. There was no necropsy.

The experience gained from these cases was not unexpected, but was very disappointing, for we had all, according to our lights, worked most diligently at them; yet all five died within three years. In all the cases of any duration we invariably went through three stages of thought: first the belief that we were succeeding—a belief which was never confident; then the uneasy feeling that we were losing ground; and finally, the realization that our efforts were fruitless. We protracted the illnesses, but nothing more, and this very partial success was so unsatisfactory from the children's point of view that had not there been always a hope that some new advance might appear, or some unexpected improvement arise, it seemed hardly worth while.

The course of the illnesses and condition of the pancreas suggested to me an abiotrophy comparable to a myopathy.

That diet only touched the fringe of the problem seemed also beyond dispute. No doubt our methods were open to criticism—no dietetic therapy could escape this fate—but no criticism would alter, in my opinion, the essential fact that the disease was materially untouched.

The remarkable periods of comparative quiescence, the unexpected outbursts, and the sudden improvements under apparently less favourable surroundings, all pointed to a mysterious hidden hand working against us.

Finally, with new methods in sight, I would venture to repeat that this series of cases may be of some value to those with fewer opportunities to form a clear idea of new results. If, as we all hope, these are much more favourable in the diabetes of the young, they will be seen more clearly against this black background—painted, as it were, at the eleventh hour.

This fact, if nothing more, is to be learned from these cases—that even in the young, with careful dieting (and presumably some care will always have to be taken with the diet), sugar and ketone bodies may disappear for weeks and months. When I write "disappear" I mean this in a practical sense—namely, ordinary careful examinations at reasonable intervals compatible with workaday medical practice.

Any remedy may, then, produce this effect, or rather be coincident with it; but if this remedy in addition wards off acetonæmic attacks, or tides children over the sudden relapses, we shall be in a better position.

THE second international congress of military medicine and pharmacy will be held in Rome from May 28th to June 2nd, with General della Valle, Director-General of the Italian Army Medical Service, as president. The subjects for discussion include the relation of the transport service to the medical service; the collaboration between the civil and military authorities in matters of health, physical education, tuberculosis, venereal disease, alcoholism, etc.; disinfection and disinfection in peace and in war; the treatment of chest wounds; and the scope and methods of chemical laboratories in relation to the army. Further information may be obtained from the Secretary of the Congress, at the Ministry of War (Direzione Centrale del Servizio Sanitario Militare), Rome.

REMARKS ON BOTULISM AS SEEN IN SCOTLAND IN 1922.

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THE general circumstances attending the food poisoning tragedy at Loch Maree Hotel in August, 1922, became sufficiently familiar to the public through the agency of the press and the proceedings at the public inquiry; but as this outbreak was the first of its kind known to have occurred in Britain it has been thought advisable to describe its principal features, so far as they came under the notice of the medical observers. It will be borne in mind that the scene of the calamity was a remote spot some twenty miles distant from the nearest railway station, and ten miles from the residence of the nearest medical practitioner. Some of the victims and other guests had frequented the hotel in the fishing season for many years, and it was admitted by those who were in a position to know that the management and catering at the establishment were of a particularly high order.

All was well at bedtime on Monday, August 14th. On the morning of Tuesday, August 15th, six guests were suffering from nervous symptoms. On Tuesday afternoon one, and on Wednesday morning another, of the gillies became indisposed, and thus the number of sufferers was increased to eight.

Before giving notes of the individual cases we may summarize the more general features of the illness as follows: The onset was with diplopia and unsteadiness on standing (less or none of the unsteadiness while lying in bed); palsy of ocular muscles (internal or external, or both); palsy of elevators of upper eyelids with contraction of frontales; inability to protrude the tongue; nasal or thick speech, or loss of speech; dysphagia; palsy of diaphragm; paresis of costal respiratory muscles; paresis of upper limbs and dorsal muscles of neck; complaint was made with regard to the throat (the patient pointing to the region of the larynx or of the pharynx); vomiting was severe in some cases, slight or absent in others; diarrhoea in some; in some cases complaint was made of abdominal discomfort or pain. There was no fever, no cough, and no disturbance of sphincters. The heart was normal; intelligence was preserved; there was little or no headache.

In most of the cases the illness began on the Tuesday morning with diplopia and unsteadiness on standing. The nervous symptoms were more obtrusive than the digestive; and, so far as was made out, the damage was confined to motor neurones, and mainly, if not solely, to lower motor neurones. The cranial nerves involved were apparently the third, fourth, sixth, ninth, tenth, eleventh, and twelfth. In certain cases there was involvement also of motor elements in the spinal cord, and particularly in the cervical region. It was surprising to note how completely the facial muscles appeared to escape, while their neighbours supplied from the brain stem above and below the facial nuclei suffered so severely. The condition of the face below the level of the eyes was therefore in striking contrast to that which is often seen in the victims of the Parkinsonian type of lethargic encephalitis.

One patient called attention to his lips, but it was not clear whether he referred to a motor or a sensory disturbance. No other sensory defect was recognized in his case, and, so far as could be ascertained by objective examination, the power of the orbicularis oris, if impaired at all, was not lost.

All the patients succumbed. The most fortunate were those who died on the first day, since they were out off by rapid failure of the heart, with very little suffering. Those who survived for a day or two had the greatest physical suffering, and it was painful to witness how for hours, and while in full possession of consciousness, they had to maintain the struggle for breath which resulted from the paresis of the ordinary muscles of respiration; and to this cause of distress there was added the inability to see, to speak, or to swallow. Those who survived longest formed an intermediate group with respect to the amount of physical suffering.