events are playing a prominent part in causing it. Menopausal conditions and certain cases of sexual excitability also appear to be particularly helped by bromide, as are cases in which there is much irritability.

Bromide acts by replacing the chlorides in the body, the rate of substitution depending upon the quantity of bromide given, the fluid and chloride intake, and the renal efficiency of the individual. As the salt intake varies from individual to individual, so the amount of bromide remaining in the body after a standard dose also varies. If 50 grains of bromide are given to one person who is on a low salt diet and has a small fluid intake the blood bromide at the end of twenty-four hours will be appreciably higher than when the same amount of bromide is given to a patient who is on a normal diet. Therefore prescribing bromides without knowing the chloride-fluid intake is tantamount to prescribing an indefinite quantity of bromide. This, in part, explains why certain patients, receiving 10 grains of bromide three times a day, develop toxic symptoms in four to five weeks, while others can take the same dose for twelve months and benefit from it. It is difficult, therefore, to lay down rules as to dosage for any given individual. This must be arrived at by observing the effect of varying amounts of the drug.

The treatment of bromide intoxication when established or suspected is a simple procedure. The bromide is immediately stopped, large quantities of fluid, preferably normal saline, are given by the mouth, and sodium chloride, 20 to 40 grains, is administered four-hourly. Figures given in a previous paper by one of us⁷ showed that when no salt was given relatively high amounts of bromide were still present in the blood of patients one to three months after the medicine had been discontinued.

Conclusion

As a result of our investigations we have come to realize how little is known at present of the precise indications for bromide therapy and the best methods of employing it. We do not wish to appear to overstress its dangers nor to undervalue its use. However, within the last year three doctors have been admitted to the Maudsley Hospital suffering from bromide intoxication, none of whom had appreciated the true cause of their illness through ignorance of the cumulative effect of this drug. This and other evidence suggests that throughout the country there are many similar cases being overlooked, resulting in a preventable quota of admissions to mental hospitals and much chronic ill-health.

Summary

1. Figures are quoted to illustrate the widespread use of bromides.
2. The toxicity of bromides is discussed.
3. A simple test for estimating bromide in the blood is given.
4. Symptoms and signs of fatal, severe, and mild intoxication are described and illustrated by case records.
5. Conditions predisposing to intoxication are suggested. The toxic threshold is discussed.
6. Therapeutic considerations are briefly considered.

Our thanks are due to Sir Frederick Menzies and Dr. E. Mapother for permission to publish the cases, also to Dr. Golla and the staff of the Central Pathological Laboratory of the London County Council, Mental Hospitals Department, who very kindly did the chemical tests.

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DIABETES MELLITUS IN CHILDHOOD *

BY

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The following is a summary of the cases I have seen personally during the last ten years at the Hospital for Sick Children, Great Ormond Street.

TABLE I

	Boys	Girls	Total
Number of cases	44	27	71
Deaths	4 (9 per cent.)	6 (22 per cent.)	10 (14 per cent.)
Left clinic	—	—	11*
Family history of diabetes	8 (18 per cent.)	8 (30 per cent.)	16 (23 per cent.)

* Seven of these are attending other clinics and were well when last heard of.

Diagnosis

The symptoms in children are in most cases the classical ones—thirst, polyuria, and wasting. Usually only one to four weeks elapse between apparent normal health and the appearance of clinically unmistakable disease; in some, however, the onset is more gradual, and a history of lack of well-being for several months before the onset of the typical symptoms may be obtained. The common complaints in this period have been lassitude, a stationary or decreasing weight, and occasionally enuresis; in one patient typical symptoms appeared within a week of an attempt to cure this lassitude by large doses of dextrose. Two patients who were in hospital for other reasons were found on routine examination to be passing sugar. Neither had any symptoms at the time; both have since developed into typical cases.

It is obviously incapable of proof, but I believe that some of these patients, if given a correctly balanced diet before the onset of symptoms, could be prevented from developing the disease for many years. It is therefore wise to test the urine in all cases showing debility and failure to gain weight. In a certain number sugar will be found, and it will be necessary to investigate further; the dextrose tolerance test, repeated if a doubtful or unusual type of response is obtained, will usually prove diagnostic. It is necessary to continue the test for three hours, as in some cases the only abnormality is a failure to return to normal within that time. The urine should of course be examined simultaneously to exclude a low renal threshold for sugar. It is often sufficient to give the dose of dextrose to the fasting child and to estimate the blood sugar two hours later. If it be below 0.12 gram per 100 c.cm. it is safe to exclude diabetes; if it is higher, a full investigation will be necessary.

Diet

In children the aim of treatment is twofold: first, to enable the child to be happy, active, and healthy, and, secondly, to prevent the progress of the disease. The first is relatively simple, but the second is difficult and often impossible.

Diet is still the most important factor in treatment. It must be sufficient to allow normal activity and growth, but any excess food above this is deleterious. There is no satisfactory formula whereby the caloric requirements can be calculated for any given child. The following table shows the average calorie intake which in the children in this series has allowed normal growth.

* Read in the Section of Diseases of Children at the Annual Meeting of the British Medical Association, Oxford, 1936.

TABLE II.—*Minimal Calorie Intake allowing Normal Growth in Diabetic Children*

Age	Range	Average	Holt's Average Normal
2	1,104-1,243	1,120	1,123
3	1,084-1,375	1,175	1,253
4	1,058-1,374	1,200	1,337
5	1,225-1,472	1,360	1,450
6	1,232-1,511	1,400	1,560
7	1,268-1,638	1,460	1,705
8	1,330-1,647	1,515	1,869
9	1,307-1,871	1,580	2,046
10	1,314-1,936	1,610	2,272
11	1,425-1,976	1,660	2,512
12	1,496-2,054	1,750	2,801

It has been amply shown that a low carbohydrate intake reduces the carbohydrate tolerance of a normal subject, and that some diabetics react in a similar way. All the children I have investigated have shown an improved carbohydrate tolerance on increasing the carbohydrate-fat ratio in the diet. Provided that the calorie intake is unchanged, altering this ratio from about 0.5-0.6 to 2-2.5 (which may entail increasing the carbohydrate intake by 80 to 120 grams a day) makes little, if any, difference in the demand for insulin; occasionally, indeed, less insulin is required. Table III shows the effect of increasing the carbohydrate and decreasing the fat in the diet, first with no increase in the total calories, secondly with an increase.

TABLE III
A.—*No Increase in Total Calories*

	Grams Carbohydrate	C/F Ratio	Insulin	Change in Calories
Before ...	59	0.5	40	
After ...	154	2.1	44	None
Before ...	68	0.5	60	
After ...	177	2.3	56	None
Before ...	82	0.6	42	
After ...	197	2.5	42	None
Before ...	79	0.7	24	
After ...	185	2.5	25	None
Before ...	101	0.85	29	
After ...	182	2.4	22	None
Before ...	71	0.7	8	
After ...	152	2.3	8	None
Before ...	61	0.7	16	
After ...	122	2.0	16	None

Summary.—4, no change in insulin; 1, increase 4 units; 2, decrease 4 and 7 units.

B.—*Increase in Total Calories*

Before ...	70	0.6	22	
After ...	180	2.6	28	80
Before ...	18	0.5	30	
After ...	164	2.3	34	25
Before ...	66	1.0	24	
After ...	146	2.6	28	340
Before ...	85	0.8	20	
After ...	142	1.6	19	90
Before ...	65	0.55	36	
After ...	179	2.6	40	40
Before ...	54	0.5	48	
After ...	159	2.2	50	150
Before ...	70	0.55	23	
After ...	185	2.5	26	55
Average increase ...			3	110

Summary.—All but one showed increase in insulin with increase of calories.

The diet now prescribed is almost the same as that of a normal child, except that it is necessary to know the composition of the food to be eaten. The use of sugar has also to be restricted. The usual household foodstuffs are utilized. The older diabetic foods, with their low carbohydrate, high fat, and protein contents, find no place in the modern diet. There is a place for attractive foods of standard composition, such as certain brands of ice-cream and chocolate the analysis of which is revealed and guaranteed by the manufacturers. If they are used they must of course displace articles of corresponding food value in the diet.

Insulin Treatment

Insulin must be given in sufficient amount to remove all symptoms of the disease. It may be argued that it is not necessary to do more than this; but my experience has been that if the blood sugar is consistently high, even with no symptoms, the disease increases in severity at a greater rate than in those cases in which a more or less successful attempt has been made to keep the blood sugar within the normal range. In some cases in which the blood sugar has been maintained at a satisfactory level the disease appears to have remained stationary, even permitting the annual increase in diet to be made without increasing the insulin; no permanent improvement has, however, been observed.

In children there may be an extraordinary degree of instability of the blood sugar, as is shown in Table IV.

TABLE IV.—*Variation in the Blood Sugar during the Day*

	Blood Sugar (Grams per 100 c.cm.)			
Time	Case 1	Case 2	Case 3	Case 4
12 noon	0.174	0.049	0.132	0.218
2.30 p.m.	0.182	0.122	0.045	0.167
5 p.m.	0.039	0.370	0.140	0.097
8 p.m.	0.240	0.314	0.356	0.360
11 p.m.	0.366	0.205	0.400	0.316

Insulin given at 7.30 a.m. and between 3.30 p.m. and 4.30 p.m. Breakfast at 8 a.m., dinner at 12 noon, tea at 3.45 p.m. or 5 p.m., supper at 6.30 p.m.

Unless very large doses have to be administered it is kinder to avoid three injections a day. Therefore, to enable the needful dose of insulin to be given and at the same time to prevent hypoglycaemic symptoms some four or five hours later on, it is necessary to order small intermediate meals. These take the form of a mid-morning lunch, usually the school milk (1/3 pint), with a biscuit or an apple, and a rather late supper. This requires a much greater rigidity in the composition of the individual meals than is needed in the adult. For this reason I have been afraid to try the modern "free" or unrestricted diet that is being advocated, except in two older children who have passed the unstable age. In these it is working satisfactorily.

The recent introduction of protamine insulinate by Professor Hagedorn may help to solve this problem, since the rate of absorption of the insulin has been considerably retarded. It is now being tried out in some of my cases. In one it has been a remarkable success; in the remainder the improvement has not been very marked.

Home Care

Almost any type of diet and treatment is successful in the steady routine of a hospital ward. The acid test is the return to home life. I do not regard as successfully treated any child who is not able to live a normal life at home and at school. He should work, play

games, swim, and run with the best. I have, however, to admit of one or two exceptions. Owing to the very general tendency to low blood sugar just before the mid-day dinner, strenuous exercise at that time must be forbidden, as also is cycling in traffic at all times when hypoglycaemia is possible, since loss of balance is often an early symptom. It is important to minimize the psychological effect on children of knowing that they have diabetes. By showing them that when they take the diet and insulin they have made themselves normal, and, just as important, by persuading the rest of the family to treat them as if they were normal, much good can be done, and in most cases a sense of inferiority does not develop.

Hypoglycaemia

Hypoglycaemic symptoms vary to an even greater degree in children than in adults. As is well known, the blood sugar level can fall much lower in children without producing symptoms than in adults, the usual level at which symptoms are shown being about 0.05 gram per 100 c.cm., though this is subject to much variation from case to case and from time to time in the same patient. Occasionally symptoms are shown at levels higher than normal—in one child at as high a level as 0.16 gram per 100 c.cm.

In addition to the usual hunger, shakiness, and hot or cold sweats, with subsequent drowsiness and coma, children often show fretfulness, tearfulness, or bad temper as early signs. Abdominal symptoms—colicky pain, nausea, vomiting, or diarrhoea—are not infrequently noted. Sometimes there are no warning symptoms and the child abruptly becomes unconscious; an observer, however, can usually see a change in the child's expression, together with pallor of the face several minutes before. The treatment is, of course, to give sugar by mouth; it is rare for more to have to be done. However, it is not wise to leave the child too long in the hypoglycaemic state. In one case in which the duration of hypoglycaemia was about twelve hours a further forty-eight hours elapsed before consciousness was regained, and normal mentality did not return until nearly six months had passed. A dose of 0.5 c.cm. of 1 in 1,000 adrenaline, or 10 units of pituitrin (pitressin) may have to be given, and occasionally intravenous glucose.

Some Complications

Some diabetic children suffer from periodic attacks of nausea and vomiting, with or without abdominal pain. These attacks are sometimes the outcome of hypoglycaemia. Hypoglycaemia has been shown to cause an outpouring of adrenaline, and I visualize these children as being unduly responsive to the effects of adrenaline on the alimentary tract. In some, the effect passes off with no untoward symptoms; in others, a ketosis occurs, due both to the adrenaline itself and to the fasting entailed by the symptoms. This may bring about a typical attack of diabetic coma within as short a time as eighteen hours. Sometimes the attacks are due to excitement, or to a long journey, or to a focus of infection, thereby showing a close kinship to the periodic vomiting or bilious attacks of other children.

The condition is controlled easily in a few hours if treated at once, preferably at home. The treatment consists in giving sugar by mouth (lemonade is the easiest form) and sufficient insulin to keep the urine nearly sugar-free. The first solid meal should be easily digestible, and need not conform to the diet. As soon as the appetite returns, the normal diet is resumed. Sodium bicarbonate alone or with infusion of gentian is helpful in controlling the nausea, and will sometimes ward off an attack.

A similar set of symptoms may be associated with the onset of any acute infection, although more commonly they are absent. In either case, if a febrile condition is present extra insulin is required, and, since the diet is usually not tolerated, glucose or cane-sugar drinks must be given, together with a suitable invalid diet, until the child's condition improves. The dose of insulin is controlled by the urine tests. In general, the safest way to deal with a diabetic emergency is to administer plenty of sugar and fluids. This can do no harm so long as sufficient insulin is given to prevent the urine from showing a positive ferric chloride test. In the absence of laboratory control it is wisest to allow the urine to contain some sugar until a definite diet can be resumed. Less severe infections, such as the common cold, while not interfering with the diet, usually cause a disturbance of the carbohydrate metabolism. Extra insulin should be prescribed to correct this. Usually an increase of from 2 to 4 units will be enough to bring the urine sugar to the accustomed level. Shocks and accidents also often have a bad effect on the sugar metabolism. I have known a sudden shock in a child to precipitate a coma within twenty-four hours. If it is remembered that this may happen, it is relatively easy to control the disturbance with extra insulin and with appropriate sedative measures.

The author wishes to thank the members of the staff of the Hospital for Sick Children for permission to treat the children admitted under their care.

GLIOMA RETINAE TREATED BY RADON SEEDS

BY

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(With Special Plate)

Foster Moore's work at St. Bartholomew's Hospital on radiotherapy for malignant intraocular neoplasms has proved that glioma retinae is radiosensitive, and that in a number of cases this neoplasm has been completely destroyed by the application of radon seeds. An opportunity arose for studying the effects of a 3.5 millicurie seed inserted through the sclera into an eye which contained an extensive mass of glioma, and leaving this *in situ* for ten days before removal of the eye.

Histological investigations showed that the effective range of the radon in this case was 3 to 4 mm. in all directions around the site of the seed. Within this zone necrobiosis, chromatolysis, granulation and vacuolation, and typical changes in irradiated cells were obvious. Outside the 4 mm. radius the cells of the neoplasm appeared to be damaged in some places, but the histological changes were not so well marked or so uniform as within the 3 to 4 mm. radius from the radon seed.

Other observers have given the area of destruction from radon seeds as follows.

Dose	Area destroyed
0.7 mc.	1.5 mm. in radius
2 mc.	3.5 mm. in radius

Whatever the strength, 8 mm. is the maximum area of necrosis.

In Foster Moore's clinic at St. Bartholomew's Hospital it is at present the practice to use radon seeds of 1 or 2 millicuries in strength, screened by platinum 0.5 mm. thick, with a thin groove filed around the centre of the platinum envelope for the purpose of retaining a 000 black silk suture. This silk thread is tied securely in the groove,