has been questioned by Von Gierke (Miller *et al.*, 1947) whether there is any pituitary abnormality at all. But our two cases showed clinical abnormality suggesting pituitary dysfunction—namely, the progeria-like features in Case 1 and a Brissaud type of picture in Case 2 (see Fig. 1). Case 2 showed signs of cirrhosis of the liver manifested by engorged abdominal veins and slight ascites, but no evidence of defective liver function was detected biochemically.

That the disease is a congenital disturbance occurring in the same family has been noted by Ellis and Payne (1940) and by Sarmiento and Gortes Mendoza (1947). When the disease occurs in one member of the family there is a possibility that other members of the same family may have the disorder in a mild form. The cases described by us are brothers, and six members of the family, including the father and mother, showed an abnormal adrenaline response. Other abnormalities, such as transient ketonuria, septal defect in the heart, a flat glucose-tolerance curve, and naevus, were also noted in other members of the family (Table VI). The father and mother were, however, not consanguineous.

It is tempting to postulate that the factors contributing to an abnormal adrenaline response may be regarded as recessive characters, the presence of which in the parents has produced full-fledged cases of glycogen disease in two sons and minor disabilities manifested by an abnormal adrenaline response and transient ketonuria in two other siblings. The presence of such congenital abnormalities as a ventricular septal defect in one son and a capillary naevus in another is of interest.

Summary

Von Gierke in 1929 gave a clear account of the disease, now named after him, under the heading of "hepatonephromegalia-glycogenica." Fewer than 50 cases had been described in the literature up to 1946. A few more have since been reported. No case, to our knowledge, has been reported from the Orient.

Two brothers suffering from the disease came under our observation. The clinical features and results of investigation are described.

The other members of the family—five siblings (all boys), the father, and the mother—were also investigated. Three of these other brothers showed presumptive evidence of the disease and the parents showed some anomalies of carbohydrate metabolism. Two other brothers showed some congenital defects.

The significance of various tests and some theories of causation are discussed.

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PINK DISEASE AND MERCURY IN SHEFFIELD, 1947-55

BY

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The early reports on mercury as a possible factor in the aetiology of pink disease appeared some years ago (Fanconi *et al.*, 1947; Warkany and Hubbard, 1948). There is still some disagreement on the subject (Naish, 1955), but repeated warnings that mercury may be dangerous to infants (Gaisford, 1949; James, 1951; Holzel and James, 1952; Farquhar, 1953; Dathan, 1954) have deterred doctors from prescribing the metal and caused manufacturers of teething powders to remove it from their products. The consequent reduction in the number of infants receiving mercury must be considerable, and it becomes important in any appraisal of the hypothesis to know if there has been a corresponding fall in frequency of the disease. Since the incidence of pink disease (Logan, 1949) and the extent of the teething-powder habit (Holzel and James, 1952) vary in different parts of the country, the requisite inquiries can with advantage be made on a local scale, and it is the object of this report to give the findings in Sheffield.

Sheffield has been a suitable centre for such an inquiry, for the disease is relatively common in the area and its study has been encouraged by the establishment of a special clinic for pink disease at the Children's Hospital (Colver, 1955).

Mercury Ingestion Among Infants in Sheffield, 1946-8 and 1953-5

Warkany and Hubbard's (1948) report led clinicians to inquire into teething-powder customs in this country (Leys, 1949; Holzel and James, 1952), and one such inquiry was made retrospectively in 1948 among the parents of patients undergoing treatment at the Children's Hospital. Two hundred mothers were selected who had other children, aged 12 months to 2 years, not attending the hospital. They were asked if they had given these latter infants teething powders between the ages of 4 and 12 months: 64 recalled that they had, and 60 were able to name the brands used. It emerged that 52 had administered brands known to contain mercury. Six mercury-containing brands, which may be termed A, B, C, D, E, and F, were involved, and they had been used as follows: 19 mothers used brand A, 17 B, 7 both A and B, 5 C, 1 both B and C, 1 D, 1 E, and 1 F. These powders had been purchased without prescription from chemist or general dealer almost equally. It was estimated from the foregoing figures that roughly a quarter of Sheffield infants were receiving mercury in the form of teething powders at the age when pink disease usually occurs.

A similar retrospective inquiry, differing in that 45 of the mothers questioned attended the Jessop Hospital for Women, was conducted in 1955. Of the 200 mothers, 39 had this time administered one or more of the brands A, B, C, and F, but not brands D and E. They had been used as follows: 22 mothers A, 8 B, 4 both A and B, 4 C, and 1 F. There had been no marked reduction, therefore, in frequency of purchase since 1946-8. There is to-day, however, the important difference that mercury is no longer present in a large proportion of the powders which formerly contained the metal. For instance, among 183 of the aforementioned powders recently bought by myself from 80 chemists and 80 general dealers mercury was not present in 131 (47 of

93 brand A, all of 77 brand B, 6 of 10 brand C, and 1 of 3 brand F powders), and, while no precise conclusion can be drawn, these findings do suggest that the proportion of Sheffield infants to-day receiving mercury powders is nearer to one-tenth than the one-quarter surmised for the 1946-8 period.

As regards medical prescribing of mercury no data are available by which to compare the position in 1946-8 with that to-day, but there can be little doubt that it also is much reduced. Thus the chairman and secretary of the Sheffield Pharmaceutical Committees recall that seven years ago they would expect to see three or four prescriptions for calomel or grey powder each week, whereas it is now many months since either of them saw the last. Their colleagues speak in similar terms, and almost all the family doctors with whom the matter has been discussed say that they have stopped prescribing mercury for infants.

Incidence of Pink Disease in Sheffield, 1947-55

It is not possible to learn accurately the incidence of pink disease in a community, as the condition is not always recognized and is not notifiable. The study of incidence trends must therefore be based on indirect evidence. In this respect mortality rates have in Sheffield been too small to permit conclusions, and the best index of incidence trend has been the number of cases treated at hospital each year. All these patients are not referred to hospital, but discussions with family doctors suggest that the majority at any rate of definite examples of the disease are in fact sent to hospital, and column 2 of the Table shows the numbers attending the various paediatric units in the city each year for nine consecutive years.

Patients with Pink Disease Treated at the Sheffield Children's and City General Hospitals during 1947-55. Figures in Parentheses Represent Fatalities

Year	Total No.	No. Living Outside City Boundary	No. with Untraced Addresses	No. Living Within City Boundary
1947	65 (4)	30 (1)	3 (1)	32 (2)
1948	69 (3)	25 (1)	15 (1)	29 (1)
1949	57 (0)	26 (0)	0 (0)	31 (0)
1950	64 (2)	27 (1)	0 (0)	37 (1)
1951	55 (4)	19 (2)	1 (0)	36 (2)
1952	45 (2)	19 (0)	0 (0)	26 (2)
1953	36 (1)	15 (1)	1 (0)	21 (0)
1954	20 (1)	3 (1)	0 (0)	17 (0)
1955	15 (1)	9 (1)	0 (0)	6 (0)

The down trend in incidence during the last three or four years will at once be noted, but is to be regarded with reserve as five new paediatric clinics were established in 1948 in near-by towns, and by 1952 or so these may have begun to deal with many patients who might formerly have been referred to Sheffield hospitals. To eliminate this factor it is necessary to exclude from present consideration all patients except those living within the city boundary; the numbers of the latter are shown in column 5 of the Table. The numbers of patients shown each year in column 5 are much smaller than those in column 2, but again a down trend in incidence during the last three or four years is shown. The 1955 figure of six patients a year is the lowest encountered in nine consecutive years and amounts to less than a quarter of the average incidence for these nine years. The recent down trend is believed to indicate a true decline in the incidence of the disease in the city.

Discussion

There is evidence, therefore, of less pink disease and less mercury ingestion among infants to-day than in 1948. There is also evidence that the decline in the incidence of the disease has taken place mainly during the last two or three years of the intervening period, and if it could be shown that the decline in mercury ingestion also took place mainly during the last two or three years then the case for the mercury hypothesis would be so much the stronger. There is no direct evidence on this point, but the circumstantial evidence is suggestive enough to be worth recording. Thus,

so far as teething powders are concerned, three of the most effective measures securing a reduction in mercury ingestion have been: (a) the action of the manufacturers of the two most popular brands (A and B) of powder in Sheffield in removing the metal from their products; (b) the recall by one of these firms of practically all old mercury-containing stocks from the retailers and a similar though less complete recall by the other; and (c) the action of the medical officer of health in arranging for members of his staff to visit retailers and to draw their attention to the possible dangers of selling mercury medicaments for babies. It cannot be ignored that these three measures were initiated at approximately the same time that the down trend in the incidence of the disease was first observed.

Conclusions

Mercury ingestion among infants and the incidence of pink disease have declined in Sheffield during the past nine years.

Yearly figures show that the down trend in the incidence of the disease has occurred only during the last three or four years, and there is circumstantial evidence that this was the period when the decline in the ingestion of mercury was mainly taking place.

These associations support the contention that the ingestion of mercury may be an important factor in the aetiology of the disease.

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POTASSIUM-LOSING PYELONEPHRITIS

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Two definite cases of potassium-losing pyelonephritis have been recorded (Brown *et al.*, 1944; Davidsen *et al.*, 1951), and one possible case (Sayers *et al.*, 1955). Milne *et al.* (1952) describe hypokalaemia developing in a case of hyperchloraemic renal acidosis with osteomalacia. Conn (1955), who describes renal potassium loss in a case of primary aldosteronism, is of the opinion that the cases described by Earle *et al.* (1951), Evans and Milne (1954), and Wyngaarden *et al.* (1954) suffered from primary aldosteronism. A further case report of another patient suffering from potassium-losing pyelonephritis is presented.

Case Report

A 51-year-old woman was admitted urgently on April 10, 1955, with a history of eight days' bilateral renal pain, polydipsia, polyuria, pyrexia, and frequent vomiting. Forty-eight hours before admission a marked generalized weakness developed without drowsiness, and for twenty-four hours she