smokers within three months. Moderate or light smokers who reduced their daily consumption mostly managed to keep this up.

Cartwright *et al.* (1959), in their Edinburgh survey, found an unusually high proportion of men aged 55–64 who had smoked regularly in the past but had since given it up. In the present study of university staff in the same city it is shown that older members seemed less inclined to stop smoking. Fewer of the older graduates attempted to reduce their smoking, and of those who did few succeeded.

About two-thirds of the smokers who had modified their smoking habits said they had done so because of the findings of the Royal College of Physicians Report. Most of these managed to maintain their reduction. The final figure for successful modification of smoking habits as a direct effect of the report was 9.2% of all smokers among the University of Edinburgh graduate staff.

Surprisingly, although the numbers here considered were small, no higher a proportion of doctors than other academics managed to maintain a reduction. This conflicts with the evidence in the report and the stress laid in it upon the differential effect of the doctor's special knowledge of the risk of heavy smoking in reducing his own smoking habits. The conclusions to which this study seems to point are that if the report is correct in saying that medical graduates have stopped smoking more than the general population, this is more because they are graduates than because they are medical. Within professional groups doctors can claim no special merit: in their smoking habits they are no better—slightly worse—than their peers.

Summary

A survey of the smoking habits of the graduate staff of the University of Edinburgh is reported. In the first part of the study smoking habits immediately before and immediately after the publication of the R.C.P. Report *Smoking and Health* were compared. Later a second inquiry was directed to those who had reduced their smoking in order to see whether after three months the reduction was maintained.

Male medical and non-medical graduates have the same low rate of smoking; both smoke less than the general population and the same as United Kingdom male doctors.

There were twice as many heavy smokers among the graduate staff as in the general population. The percentage of heavy smokers was higher among male medical graduates than among graduates in other faculties.

Three-quarters of the smokers in the survey would welcome prohibition of smoking in certain public places.

After the report one-third of all smokers in the survey in some way modified their smoking. Older graduates did so less than younger graduates. The highest reduction in heavy smoking occurred among male doctors.

Two-thirds of all who had modified their smoking succeeded in maintaining this three months later. The most successful were those who stopped smoking altogether.

The R.C.P. Report successfully persuaded 9.2% of all smokers among the graduate staff to modify their smoking.

REFERENCES

- Cartwright, A., Martin, F. M., and Thomson, J. G. (1959). *Lancet*, **2**, 725.
 Heath, C. W. (1958). *Arch. intern. Med.*, **101**, 377.
 Lilienfeld, A. M. (1959). *J. nat. Cancer Inst.*, **22**, 259.
 McArthur, C., Waldron, E., and Dickinson, J. (1958). *J. abnorm. soc. Psychol.*, **56**, 267.
 Royal College of Physicians (1962). *Smoking and Health*. Pitman Medical Publishing Co. Ltd., London.

DECLINE IN PRIMARY INFANTILE RENAL ACIDOSIS: AETIOLOGICAL IMPLICATIONS

BY

REGINALD LIGHTWOOD, M.D., F.R.C.P.

Director of the Paediatric Unit, St. Mary's Hospital Medical School, University of London; Physician to the Hospital for Sick Children, Great Ormond Street, London

AND

NEVILLE BUTLER, M.D., M.R.C.P., D.C.H.

Consultant Paediatrician to Swindon and Salisbury Hospitals

Primary renal tubular acidosis of infants is a transient disturbance in which a lowered plasma bicarbonate level is accompanied by a relatively alkaline urine, usually with a pH of more than 6.5. The clinical picture includes anorexia, vomiting, failure to thrive, constipation, dehydration, and hypotonia (Lightwood, 1935; Lightwood *et al.*, 1936; Butler *et al.*, 1936). In Great Britain the condition first reached prominence after the second world war; at least 90 cases were reported as occurring between 1947 and 1953 (Lightwood *et al.*, 1953; Carré *et al.*, 1954; Doxiadis, 1952; Buchanan and Komrower, 1958). Shortly afterwards attention was drawn to a local fall in incidence in the Newcastle area in England (Neligan, 1955). The object of the present inquiry was to see if this reduction was general and if epidemiological methods could help in aetiology.

Data

The report is based on a questionnaire sent in 1960 to the paediatric departments of 12 provincial undergraduate teaching centres in England, Scotland, and Wales; in London the inquiry was confined to two postgraduate teaching centres attached to the Institute of Child Health—namely, the Hospital for Sick Children and the Queen Elizabeth Hospital, Hackney. For the decade 1950 to 1959 information was sought on every new case of infantile renal acidosis regarding age at diagnosis, sex, lowest recorded plasma-bicarbonate level, and highest serum-chloride level. All the centres replied to the questionnaire, although Liverpool data for 1950 were not available. Of the total of 192 cases reported, 153 were chosen for analysis as being unequivocal cases. The omissions comprised: (a) 19 reported cases in which the minimum plasma-bicarbonate level was above 16 mEq/l.; (b) 16 cases in which coexistent hypercalcaemia was reported; (c) two infants who died before biochemical investigation was complete, though both showed nephrocalcinosis at necropsy; and (d) two siblings who showed symptoms very soon after birth and are thought to be examples of the persisting (Albright) type of primary renal acidosis (in process of preparation for publication by other workers).

Results

The Histogram shows the trend in yearly incidence for the 153 cases. There was a progressive rise during the first four years, possibly due to increasing awareness of the condition. After 1953 a sharp reduction took place, and during the second half of the decade the number was small but fairly constant. In all, 132 new cases were diagnosed in the first five years and 21 in

Infantile renal tubular acidosis: 153 cases by year of occurrence (14 centres). Information is lacking for 1950 for Liverpool.

the second five years. In spite of this reduced incidence there was no evidence of diminishing severity as judged by minimum plasma-bicarbonate levels. The average age at diagnosis was 8.1 months, with extremes of 1 to 18 months. In 122 cases in which sex was specified 64 (52%) were females.

Geographical Distribution.—The Table shows the number of new cases diagnosed at each centre. Seven provincial centres reported only 0–6 cases per centre for the whole decade. In contrast, a relatively high incidence occurred during the first half-decade in the

Reported Cases of Infantile Renal Tubular Acidosis in Separate Centres in Consecutive Five-year Periods

University Centre	Period		University Centre	Period	
	1950–4	1955–9		1950–4	1955–9
Newcastle ..	31	0	Sheffield ..	4	1
Glasgow ..	24	5	Leeds ..	2	1
London (2 centres only) ..	25	6	Aberdeen ..	1	0
Birmingham ..	16	1	Dundee ..	1	2
Liverpool ..	13	1	Bristol ..	0	4
Cardiff ..	9	0	Edinburgh ..	0	0
Manchester ..	6	0	Total ..	132	21

other five provincial centres and in the two London hospitals, and all of them reported a marked decline thereafter, thus showing that the reduction reported by Neligan (1955) was not restricted to Newcastle.

The number of reported cases was not proportionate to the size of the centre; for example, no new cases were notified from Edinburgh, compared with 29 from Glasgow and 31 from Newcastle. However, the usefulness of such regional comparison is clearly limited by inevitable differences in nosological standards, biochemical interests, and size of the population.

Discussion

Renal tubular acidosis has many causes and can be classified broadly into primary and secondary types. The cases classified as primary are those in which no related antecedent disease has been ascertained, whereas

secondary cases have known causation—for example, glomerulonephritis; pyelonephritis; and inborn errors of metabolism such as galactosaemia, Wilson's disease, the oculo-cerebro-renal dystrophy of Lowe, Terry, and MacLachlan, and the conditions included under the term "de Toni-Fanconi-Debré syndrome." Huth *et al.* (1960) suggest a subdivision of primary renal tubular acidosis into an early "infantile" (Lightwood) type and a late or "adult" type as originally described by Albright *et al.* (1946). However, the so-called "infantile" type may sometimes manifest after the first year of life; this occurred in several of the patients in this inquiry. Therefore we suggest that the term "transient" type is better nomenclature, since the condition clears up without sequelae, except for cases in which intercurrent infection, etc., may cause death in the acute stage. Moreover, the use of the term "adult" for the Albright type is also inaccurate. The use of the term "persistent" type would be better terminology because it is a permanent disorder of renal tubular function, often genetically determined, and in a few instances it can begin during the first year of life. We have excluded from the present series (see above) two such cases of the persistent type with manifestations in early infancy. *The decline reported in this paper refers specifically and only to the transient type of primary renal tubular acidosis.*

The striking difference in incidence between the first and the second half-decades under review suggests that an environmental factor capable of damage to the renal tubules (perhaps even more than one factor) was responsible, and this calls for further investigation.

Vitamin D, administered in amounts greater than are required for nutrition, can cause a disturbance of the function of urine concentration and acidification. Thus concurrent acidosis has been observed in about 15% of cases of idiopathic infantile hypercalcaemia (Lightwood, 1955) and also in vitamin D intoxication (Galán, 1955; Ferris *et al.*, 1961). Carré *et al.* (1954) reported five instances of raised serum calcium level in 17 infants with infantile renal acidosis. Clearly there is some biochemical overlap between infantile hypercalcaemia and infantile renal tubular acidosis, and this suggests a related aetiology. In the past, similarity in clinical features between these two conditions has led to errors in diagnosis. In this communication all cases reported as having coexisting hypercalcaemia have been excluded, and returns were obtained only from teaching centres. The epidemiological data presented in this paper do not suggest that the action taken in Britain to prevent excessive intake of vitamin D was a main factor responsible for the sharp drop in incidence of infantile renal acidosis, because this drop (1953–4) preceded by at least three years the issue of advice by the Ministry of Health. This advice led to the removal of excess vitamin D from cereals, dried milks, and other food supplements in Great Britain (Joint Subcommittee on Welfare Foods, 1957).

Sulphonamides.—A sulphonamide derivative, acetazolamide, is a carbonic-anhydrase inhibitor and is known to produce an analogous state of renal tubular acidosis in animals (Berliner *et al.*, 1951) and in man (Smith and Schreiner, 1954). However, a history of sulphonamide administration is rarely a feature in reported cases of infantile renal acidosis (Lightwood *et al.*, 1953; Carré *et al.*, 1954). Moreover, with increasing employment of antibiotics the use of sulphonamides declined gradually, before and during the decade under review.

Other Causes.—Heavy metals can cause renal tubular damage. In spite of a time relation between the decline in new cases of infantile renal acidosis and the withdrawal, in 1953, of mercury from teething powders (B.M.J., 1954), which quickly resulted in a virtual disappearance of pink disease, mercury intoxication has not been incriminated as a cause of infantile renal acidosis. Moreover, the carefully controlled metabolic studies of Williams *et al.* (1951) showed a normal range of plasma bicarbonate in 22 cases of pink disease. However, we are not aware of any published data on urinary excretion of mercury (or other heavy metals) in cases of primary renal tubular acidosis.

The decline reported from one Scottish, one Welsh, and five English university centres was matched by experience in Belfast and in Lyons. In Belfast 12 cases of infantile renal acidosis were diagnosed at Queen's University Paediatric Clinic between 1953 and 1955 inclusive, and none between 1956 and 1960 (F. M. Allen, personal communication, 1961); in Lyons no new cases were admitted to the paediatric clinic between 1956 and 1960, although 14 had been diagnosed during the preceding four years (M. Jeune, personal communication, 1961).

Summary

A ten-year survey (1950 to 1959 inclusive) of new cases of primary renal tubular acidosis of transient type (infantile renal acidosis) showed a sudden decline after 1954 in seven university teaching centres in England, Scotland, and Wales. Confirmatory evidence is presented from Belfast and Lyons. This decline and the transient nature of the disturbance point to an environmental causation not yet determined. The operation of certain exogenous factors which are known to damage the renal tubule—for example, vitamin D, sulphonamide, and mercury—is considered, but no one of these seems to explain the sudden change in the frequency of infantile renal tubular acidosis.

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REFERENCES

- Albright, F., Burnett, C. H., Parson, W., Reifstein, E. C., jun., and Roos, A. (1946). *Medicine (Baltimore)*, **25**, 399.
 Berlner, R. W., Kennedy, T. J., and Orloff, J. (1951). *Amer. J. Med.*, **11**, 274.
Brit. med. J., 1954, **1**, 265.
 Buchanan, E. U., and Komrower, G. M. (1958). *Arch. Dis. Childh.*, **33**, 532.
 Butler, A. M., Wilson, J. L., and Farber, S. (1936). *Pediatrics*, **8**, 489.
 Carré, I. J., Wood, B. S. B., and Smallwood, W. C. (1954). *Arch. Dis. Childh.*, **29**, 326.
 Doxiadis, S. A. (1952). *Ibid.*, **27**, 409.
 Ferris, T., Kashgarian, M., Leviten, H., Brandt, I., and Epstein, F. H. (1961). *New Engl. J. Med.*, **265**, 924.
 Galán, E. (1955). *Rev. cuba. Pediat.*, **27**, 199.
 Huth, E. J., Webster, G. D., jun., and Elkinton, J. R. (1960). *Amer. J. Med.*, **29**, 586.
 Joint Subcommittee on Welfare Foods (1957). Report. H.M.S.O., London.
 Lightwood, R. (1935). *Arch. Dis. Childh.*, **10**, 205.
 — (1955). *Rev. port. Pediat.*, **18**, 335.
 — MacLagan, N. F., and Williams, J. G. (1936). *Proc. roy. Soc. Med.*, **29**, 1431.
 — Payne, W. W., and Black, J. A. (1953). *Pediatrics*, **12**, 628.
 Neligan, G. A. (1955). *Arch. Dis. Childh.*, **30**, 301.
 Smith, L. H., and Schreiner, G. E. (1954). *J. Lab. clin. Med.*, **43**, 347.
 Williams, H., Macdonald, W. B., and Callow, V. (1951). *Med. J. Aust.*, **1**, 363.

POLYCYTHAEMIA AND ANAEMIA IN NEWBORN MONOZYGOTIC TWIN GIRLS

BY

J. M. LITTLEWOOD, M.B., M.R.C.P.Ed., D.C.H.

Department of Paediatrics and Child Health, University of Leeds

The occurrence of anaemia and polycythaemia at birth in monozygotic twins was first recorded by Herlitz (1941), who described two cases. Further instances were reported by Klingberg *et al.* (1955) and Bergstedt (1957). The first cases to be described in this country were the four reported by Kerr (1959). Differences in the haemoglobin levels of monozygotic twins have been noted by Seip (1956), and significant variations in the haemoglobin levels at birth in such pregnancies are probably commoner than previously reported cases would suggest.

History of Cases

The present example of monozygotic female twins (Fig. 1) is of interest because of the great difference in haemoglobin levels and the fact that the anaemic twin (II) was the larger. Complicating hyperbilirubinaemia was encountered in the

FIG. 1.—Twins 10 hours after delivery. The smaller twin (I) severely cyanosed; the larger twin (II) notably pale and limp.

FIG. 2.—Placenta showing sharp demarcation between the larger pale portion on the left and the smaller deeply congested portion on the right.