7.4 cm/year, which is at least normal for the age group, but they did not record a pretreatment growth rate. It is probably significant that the younger sib is growing at a similar rate without HGH treatment.

The present case appears to be similar to both these reports with low and unresponsive levels of HGH, and the nitrogen retention after a short course of HGH was even more marked than that found by Zachmann *et al.* However, we have not found any evidence of growth acceleration in response to long-term HGH treatment and neither was there any effect on the anaemia. The response to oxymetholone therapy has been much more striking in growth rate, epiphyseal fusion, and improvement in haematological parameters. The transfusion requirement was not influenced by growth hormone and he needed to be transfused on 9 occasions during his year on growth hormone, although the Hb level has been satisfactory since some 6 weeks after starting oxymetholone.

The moderate anaemia of all prepubertal hypopituitary children of short stature has been shown by Jepson and McGarry (1972) to be related to a low excretion of the erythropoietin-stimulating factor and these authors suggest that both testosterone and growth hormone may play a part in the normal increase of erythrocyte values observed during growth and maturation. They showed that treatment with HGH induced bone marrow lymphocytosis with an increase in red cell mass, increased excretion of erythropoietin-stimulating factor in the urine, and expansion of the plasma volume. Testosterone was additive to HGH in some of these effects. However, none of their patients had a severe aplastic anaemia of the type recorded here. A patient with congenital hypoplastic anaemia, described by Steel, Butterworth, and Keay (1972), showed evidence of pituitary hypofunction after many transfusions and it was felt that the endocrinological defect was secondary to extensive deposition of haemosiderin within the pituitary gland. Our patient differs in that clear evidence of endocrine dysfunction existed before oral iron therapy and blood transfusion. From the endocrine point of view the classification of his short stature is uncertain. Though a brief effect was possible during the test dose, perhaps sustained nitrogen retention necessary for an increased growth rate was not possible in the face of the pre-existing basic defect of protein synthesis manifesting as pancytopenia.

Summary

A patient with idiopathic marrow hypoplasia associated with short stature and other anomalies

(Fanconi's anaemia) is described: treatment with human growth hormone for one year did not accelerate his growth rate or significantly affect his anaemia: androgen treatment considerably improved both features. Endocrine studies suggest that though he had poor and insufficient production of endogenous growth hormone to insulin-induced hypoglycaemia, the major defect in this syndrome is determined more at the end-organ than at the pituitary or gonadal level.

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REFERENCES

- Jepson, J. H., and McGarry, E. E. (1972). Hemopoiesis in pituitary dwarfs treated with human growth hormone and testosterone. *Blood*, **39**, 238.
- Perkins, J., Timson, J., and Emery, A. E. H. (1969). Clinical and chromosome studies in Fanconi's aplastic anaemia. *Journal of Medical Genetics*, **6**, 28.
- Pochedly, C., Collipp, P. J., Wolman, S. R., Suwansirikul, S., and Rezvani, I. (1971). Fanconi's anemia with growth hormone deficiency. *Journal of Pediatrics*, **79**, 93.
- Steel, C. M., Butterworth, S. T. G., and Keay, A. J. (1972). Endocrine studies in a case of congenital (erythroid) hypoplastic anaemia. *Acta Haematologica*, **47**, 109.
- Swift, M. R., and Hirschhorn, K. (1966). Fanconi's anaemia: inherited susceptibility to chromosome breakage in various tissues. *Annals of Internal Medicine*, **65**, 496.
- Tanner, J. M., Whitehouse, R. H., and Healy, M. J. R. (1962). *Standards for Skeletal Age*, Parts I and II. Centre International de l'Enfance, Paris.
- Zachmann, M., Illig, R., and Prader, A. (1972). Fanconi's anaemia with isolated growth hormone deficiency. *Journal of Pediatrics*, **80**, 159.

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Raised IgA in idiopathic pulmonary haemosiderosis

The aetiology of idiopathic pulmonary haemosiderosis (IPH) is still unknown. Various hypotheses such as congenital weakness or fragility of the capillaries, milk allergy, abnormal growth and function of the alveolar epithelial cells (Soergel and Sommers, 1962) have been suggested, but not confirmed. Steiner's (1954) theory of an autoimmune antigen-antibody reaction mechanism with the lung as the shock organ is supported by findings such

as eosinophilia and the response to treatment with steroids, and seems plausible. Since several other conditions with lung involvement such as cystic fibrosis, bronchiectasis, and chronic sinopulmonary disease are known to be associated with immunological abnormalities (South, *et al.*, 1965, 1967; Biegel and Krumholz, 1968), the possibility of an immunological disorder in IPH was investigated.

Material and methods

From 1 May 1971 to 30 April 1973, 31 children with IPH aged 14 months to 14 years were studied in our clinic. Diagnosis was based on typical history, anaemia, characteristic lung x-ray, and was confirmed by showing siderophages in sputum or gastric washings. Sera of 35 relatives (parents and sibs) were also studied.

Immunoglobulins were estimated by radial immunodiffusion technique (Mancini, Carbonara, and Heremans, 1965). Commercial IgM, IgG, and IgA antisera (Hyland) were used in homemade plates. Dilutions of pooled adult sera titrated by the National Institutes of Health (Cancer Research Laboratory, Maryland) were used as standards. Values were compared to those of age- and sex-matched healthy controls.

IgA salivary levels were estimated in 25 of the patients, 22 of their relatives, and 150 age matched healthy individuals.

Whole saliva was collected in test tubes during continuous stimulation of salivary flow by application of citric acid crystals on the tongue. After centrifugation at 2000 r.p.m. for 15 min, the supernatant was kept at -20°C until the tests were performed. Salivary IgA concentrations were measured by electroimmunodiffusion (Merrill, Hartley, and Claman, 1967). Serum dilutions were used as standards.

Rabbits were immunized with 3 weekly injections of 2 ml pooled IPH sera + 2 ml Freund's adjuvant and bled via cardiac catheterization 7 days after the 3rd injection. The serum was adsorbed with a pool of normal sera, and was used for immunoelectrophoresis of the patient's sera.

Statistical evaluation of results was done by the paired 't' test on logged data.

Results

Serum levels of IgM and IgG did not differ

FIG.—IgA levels of children with IPH and of age- and sex-matched controls.

significantly between patients with IPH and controls (Table). There was a highly significant increase ($P < 0.001$) in IgA levels in patients compared with controls (Fig.).

No significant difference was noted between relatives (geometric mean of IgA 110 mg/100 ml) and controls (IgA 124 mg/100 ml). Salivary IgA levels ranged from 1.7 to 17.1 mg/100 ml in the patients (mean 5.5 mg/100 ml) and from 1.3 to 19 mg/100 ml in controls (mean 5.9 mg/100 ml in controls). Salivary IgA levels in relatives ranged from 1.5 to 23 mg/100 ml (mean 14 mg) and in the controls from 1.3 to 21 mg/100 ml (mean 12.8 mg).

IPH sera did not show any unusual precipitin line in immunoelectrophoresis and did not give IgA precipitate when tested with exhausted IPH specific antiserum.

TABLE

Immunoglobulin levels (mg/100 ml) in sera of children with IPH and of age- and sex-matched controls

	IgG		IgM		IgA	
	IPH	Controls	IPH	Controls	IPH	Controls
Geometric mean	1286	1.067	134	131	178	92.3
Range	650–2000	600–2000	80–280	64–270	45–550	22–220
P	NS		NS		<0.001	

Discussion

Immunoglobulin studies in idiopathic pulmonary haemosiderosis have been done to our knowledge in only one case so far in which IgA was decreased (Krieger and Brough, 1967).

Children with IPH studied in this series had a significant ($P < 0.001$) selective increase of serum IgA. High serum IgA levels have been observed in several conditions with pulmonary involvement such as cystic fibrosis of the pancreas (Schwartz, 1966; South *et al.*, 1967), chronic bronchitis, and pulmonary emphysema (Biegel and Krumholz, 1968; Falk, Siskind, and Smith, 1970). In most of these conditions there is an increase in serum IgM and IgG as well. This general rise in immunoglobulin levels has been attributed to stimulation by recurrent infections. This was not the case in the series of cases of IPH.

Assuming that the raised levels of IgA in children with IPH might be due to the presence of a fraction of IgA with specific antigenic determinants, in addition to the common ones, IPH sera were tested with specific IPH rabbit antiserum; no evidence of the presence of a pathological component could be shown by this technique.

Martinez-Tello, Braun, and Blanc (1968) observed an increase in the number of IgA producing cells in the bronchial tree in chronic pulmonary disease, and Falk *et al.* (1970) suggested that increased levels of serum IgA might reflect increase of secretory IgA in the respiratory system. In order to investigate this possibility, saliva IgA levels were estimated in IPH children, relatives, and controls. IgA concentration in saliva has such wide variations in the present series as well as in others (Haworth and Dilling, 1966; South *et al.*, 1967) that it is difficult to draw conclusions. Nevertheless, in the samples that were studied IgA salivary levels did not differ from those of normal controls, either in the children or their relatives.

Summary

Levels of immunoglobulin G, A, and M were studied in 31 children with idiopathic pulmonary haemosiderosis and in 35 relatives. A selective increase in serum IgA was observed in the patients. IgA levels in saliva did not show any difference compared with those of normal children.

REFERENCES

- Biegel, A. A., and Krumholz, R. A. (1968). An immunoglobulin abnormality in pulmonary emphysema. *American Review of Respiratory Diseases*, **87**, 217.
- Falk, G. A., Siskind, G. W., and Smith, J. D. Jr. (1970). Immunoglobulin elevations in the serum of patients with chronic bronchitis and emphysema. *Journal of Immunology*, 105.

- Haworth, J. C., and Dilling, L. (1966). Concentration of gamma A-globulin in serum, saliva, and nasopharyngeal secretions of infants and children. *Journal of Laboratory and Clinical Medicine*, **67**, 922.
- Krieger, I., and Brough, J. A. (1967). A deficiency and hypochromic anemia due to defective iron mobilization. *New England Journal of Medicine*, **276**, 886.
- Mancini, G., Carbonara, A. O., and Heremans, J. F. (1965). Immunochemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry*, **2**, 235.
- Martinez-Tello, F. J., Braun, D. G., and Blanc, W. A. (1968). Immunoglobulin production in bronchial mucosa and bronchial lymph nodes, particularly in cystic fibrosis of the pancreas. *Journal of Immunology*, **101**, 989.
- Merrill, D., Hartley, T. F., and Claman, H. N. (1967). Electroimmunodiffusion (EID): a simple, rapid method for quantitation of immunoglobulins in dilute biological fluids. *Journal of Laboratory and Clinical Medicine*, **69**, 151.
- Schwartz, R. H. (1966). Serum immunoglobulin levels in cystic fibrosis. *American Journal of Diseases of Children*, **111**, 408.
- Soergel, K. H., and Sommers, S. C. (1962). The alveolar epithelial lesion of idiopathic pulmonary hemosiderosis. *American Review of Respiratory Diseases*, **85**, 540.
- South, M. A., Wollheim, F. A., Warwick, W. J., Cooper, M. D., and Good, R. A. (1965). Local deficiency of immunoglobulin A in the saliva of patients with chronic sinopulmonary disease. *Journal of Pediatrics*, **67**, 940.
- South, M. A., Warwick, W. J., Wollheim, F. A., and Good, R. A. (1967). The IgA system. IgA levels in the serum and saliva of pediatric patients. Evidence for a local immunological system. *Journal of Pediatrics*, **71**, 645.
- Steiner, B. (1954). Essential pulmonary haemosiderosis as an immunohaematological problem. *Archives of Disease in Childhood*, **29**, 391.

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Gestational age assessment in infants of very low birthweight

Although birthweight has in the past been used to provide statistics in the newborn period, duration of gestation is a better guide to morbidity and mortality. This is particularly so towards term when weight is influenced by factors such as parity, altitude, maternal height, ethnic grouping, and maternal diseases. But accurate age assessment is just as important and necessary for infants born prematurely. The Dubowitz scoring system (Dubowitz, Dubowitz, and Goldberg, 1970) using both the external criteria of Farr *et al.* (1966) and the neurological evaluation of Amiel-Tison (1968), is accepted by many as the method of choice. The accuracy of this method, originally established in Britain, has recently been confirmed for populations in Nigeria (Brueton, Palit, and Prosser, 1973),