ive and speech was minimally slurred. There was pronounced rigidity of the upper extremities with minimal tremor. He was started on 500 mg. of L-dopa daily and the oral dose was increased to 3 g. in two weeks. No improvement was discernible at this dosage for two months. Despite gradual increase to 5 g. daily there was no clinical improvement at the end of four months. He did not complain of nausea, light-headedness, or nervousness.

Absorption Studies.—Gastrointestinal absorption of L-dopa was studied as previously described (Rivera-Calimlim *et al.*, 1970a). After an overnight fast, 500 mg. of L-[¹⁴C]-dopa (25 μ Ci) and 1 g. of polyethylene glycol, a nonabsorbable marker, were administered orally. Timed samples of blood, urine, and gastric juice were collected and assayed for L-dopa by column chromatography and fluorometry. Calculated gastric emptying was based on the disappearance of polyethylene glycol from gastric juice (Malawer and Powell, 1967).

Basal gastric juice pH was 1.2 and gastric emptying time was seven hours. Five Parkinsonian patients previously studied had a mean gastric emptying time of three and a half hours. His serum radioactivity curve and that of these other patients is shown in Fig. 1. Fractionation of the gastric juice by the ion-exchange method of Bartholini and Pletscher (1968) modified by Peaston and Bianchine (1970b) showed significant amounts of dopa metabolites, including phenylcarboxylic acids, methoxydopa, catecholamines, and dopamine (Fig. 2).

He was given 25 μ Ci of L-[¹⁴C]-dopa, 500 mg. in 200-ml. solution, by duodenal infusion. Resultant plasma concentration compared with that after oral administration is shown in Fig. 3. Fifteen minutes after this infusion he became flushed and complained of nausea and dizziness. Blood pressure increased from 120/78 to 200/100 and pulse rate from 70 to 120 beats per minute. Gastric absorption studies were repeated after one oral dose of a 15-ml. suspension of magnesium and aluminium hydroxides (Maalox). Gastric pH was 3.5 to 4.5 during the study and gastric emptying was complete at one hour. The plasma L-dopa concentration during this study is also shown in Fig. 3.

A regimen of antacid taken 30 minutes before each dose of L-dopa in this patient has resulted in objective and subjective improvement. He has returned to full employment on a dose of 3g. per day.

DISCUSSION

Prolongation of gastric emptying time may slow the rate of absorption of L-dopa. We have recently demonstrated the capacity of animal and human stomachs to metabolize L-dopa in vitro (Rivera-Calimlim *et al.*, 1970b). Prolonged contact with gastric mucosa may lead to degradation of L-dopa by this mechanism as well as by delaying the brisk duodenal absorption indicated by the infusion study.

The clinical improvement in this patient is apparently due to alkalization of the gastric juice and correlates well with the higher serum L-dopa level attained during such treatment. Alkalization may be a simple way to enhance L-dopa effect in certain patients who are either relative or absolute treatment failures, until such time as satisfactory decarboxylase inhibitors become available to decrease extracerebral metabolism of L-dopa.

This work was supported in part by a grant from the National Institute of Mental Health (MH 07498).

L. RIVERA-CALIMLIM, M.D., M.S.
C. A. DUJOVNE, M.D.
J. P. MORGAN, M.D.
L. LASAGNA, M.D.
J. R. BIANCHINE, M.D., PH.D.

Department of Medicine (Division of Clinical Pharmacology),
Johns Hopkins University School of Medicine, Baltimore,
Maryland, U.S.A.

REFERENCES

- Bartholini, C., and Pletscher, A. (1968). *Journal of Pharmacology and Experimental Therapeutics*, **161**, 14.
- Calne, D. B., Stern, C. M., Laurence, D. R., Sharkey, J., and Armitage, P. (1969). *Lancet*, **1**, 744.
- Cotzias, G. C., Papavasiliou, P. S., and Gellene, R. (1969). *New England Journal of Medicine*, **280**, 337.
- Malawer, S. J., and Powell, D. W. (1967). *Gastroenterology*, **53**, 250.
- Mawdsley, C. (1970). *British Medical Journal*, **1**, 331.
- Peaston, M. J. T., and Bianchine, J. R. (1970a). *British Medical Journal*, **1**, 400.
- Peaston, M. J. T., and Bianchine, J. (1970b). *Clinical Pharmacology and Therapeutics*. In press.
- Rivera-Calimlim, L., Morgan, J. P., Dujovne, C. A., Bianchine, J. R., and Lasagna, L. (1970a). *Journal of Clinical Investigation*, **49**, 79a.
- Rivera-Calimlim, L., Morgan, J. P., Dujovne, C. A., Bianchine, J. R., and Lasagna, L. (1970b). *Clinical Research*, **18**, 343.

Placental Transfer of an IgG Paraprotein Associated with Prolonged Immunosuppression

British Medical Journal, 1970, **4**, 94-95

During a screening survey of newly-born infants for urinary tract infection 8 out of 600 infants investigated were found to have a significant bacteriuria (Littlewood, Kite, and Kite, 1969). Plasma protein electrophoresis was carried out as part of the survey on all the infected infants, and in one of them, a boy aged 6 days, a deficiency of normal IgG associated with the presence of an IgG type κ paraprotein was found. The plasma of the mother was therefore investigated and a previously unsuspected asymptomatic paraproteinaemia was discovered.

CASE REPORT

The mother, aged 35 years, had been in good health and had no symptoms. She had had normal deliveries 16 and 11 years before the present delivery, a stillbirth after antepartum haemorrhage due to placenta praevia 13 years earlier, and a normal infant delivered by caesarean section after an antepartum haemorrhage six years earlier. The present pregnancy was uncomplicated and delivery at 39 weeks was spontaneous and by the vertex.

The infant was a male weighing 3,630 g. Moderate asphyxia responded rapidly to simple resuscitation. On the sixth day a urine specimen taken as part of the screening survey showed evidence of a urinary tract infection.

Infant.—The midstream urine specimen was cloudy and contained a trace of protein, 2,600 white cells/cu.mm., and more than one million *Escherichia coli* per ml. Two further urine specimens on the sixth and seventh days before treatment was started contained 8,000 and 4,000 white cells/cu.mm. respectively, with more than one million *E. coli* per ml. in each of them. Haemoglobin 18.1 g./100 ml. White blood cells 13,200/cu.mm. Blood urea 70 mg./100 ml. Blood culture negative. An intravenous pyelogram on the 12th day of life was normal. Serum protein electrophoresis on cellulose acetate membrane showed a narrow intensely staining band of intermediate γ mobility, with pronounced deficiency of normal γ -globulin (see Fig.). Immunoelectrophoresis showed that the paraprotein was an IgG of type κ .

Mother.—Serum protein electrophoresis showed a paraprotein of mobility identical with that in the infant and a similar deficiency of normal globulin. A faint band of β_2 mobility was thought to be IgM and IgA which had become visible because of the reduced background of IgG (see Fig.). This paraprotein was also an IgG of type κ . Immunoglobulin concentrations are shown in the Table. Urine contained no Bence Jones protein by the method of Putnam, Easley, Lynn, Ritchie, and Phelps (1959), and no paraprotein was seen on electrophoresis of the urine after concentration.

Immunoglobulin Concentration (mg./100 ml.)

		IgG	IgA	IgM
Mother	17 days postpartum ..	3,100 (710-1,540)	100 (60-490)	100 (42-261)
	2 years ..	3,500 (710-1,540)	80 (60-490)	30 (42-261)
Infant	17 days ..	900 (600-1,080)	<10 (<10)	25 (20-65)
	39 ..	300 (280-880)	<10 (<25)	25 (20-60)
	95 ..	300 (120-850)	<10 (<50)	25 (20-110)
	2 years ..	310 (490-1,390)	35 (24-164)	25 (36-200)

Normal range (mean $\pm$ 2 standard deviations) for age for each immunoglobulin is given in parentheses and is derived from the data of Allansmith, McClellan, Butterworth, and Maloney (1968).

Haemoglobin 14.6 g./100 ml. White blood cells 6,900/cu.mm., with a slight neutrophilia. Platelets 220,000/cu.mm. Sternal bone marrow was of normal cellularity and showed mild granulocytic hyperplasia and normoblastic erythropoiesis. Megakaryocytes and lymphocytes were present in normal proportions. Plasma cells formed approximately 3% of all nucleated cells and, though occasional binucleate forms were encountered, nucleolated plasma cells were not found. Iron stores were low, but the erythroblasts contained a normal distribution of siderotic granules. Blood urea 25 mg., plasma uric acid 6.5 mg., and calcium 10.0 mg./100 ml. X-ray films of the chest, lumbar spine, and skull showed nothing abnormal.

Cellulose acetate membrane electrophoresis of serum proteins of mother and infant showing gradual disappearance of paraprotein band in the infant.

Progress.—The infant's urinary tract infection responded satisfactorily to a two-week course of ampicillin 125 mg. six-hourly. Subsequent clinical progress to the age of 2 years was uneventful. The paraprotein gradually disappeared from the plasma and was barely visible on electrophoresis of the specimen taken at 95 days. The total IgG concentration at this time was normal for his age, but at 2 years the concentration was below the lower limit of the normal range, and the IgA and IgM concentrations were also low (see Table). The mother has had no complaints and was in good health two years after the birth of the child. Initial treatment with a short course of cyclophosphamide 50 mg. t.d.s. for 11 days and later b.d. for 14 weeks did not affect the clinical and biochemical findings. The IgG paraprotein was unchanged in appearance on electrophoresis.

COMMENT

IgG is not synthesized in significant amounts by the normal fetus or newborn (Good and Papermaster, 1964) but is acquired by transport across the placental membrane with a selectivity which depends on some property of the part of the IgG γ (heavy) polypeptide chain which is in the Fc fragment (Brambell, Hemmings, Oakley, and Porter, 1960). Thus the discovery of a circulating IgG paraprotein in the infant reported here indicated the presence of a monoclonal proliferation of cells of the lymphocyte-plasma-cell series, not in the infant but in the mother. The IgA paraprotein in a mother described by Kosova and Schwartz (1966) was not detected in her infant's serum, an observation which is consistent with the failure of normal maternal IgA (and IgM) to cross the placenta. Though the relevance of the infant's plasma protein abnormalities to his urinary infection must remain a matter for speculation, it seems probable that his defence mechanisms were impaired, because almost all the IgG he received from his mother was a paraprotein lacking the diverse antibody activity of normal IgG.

As in the baby described by Rádl, Masopust, Jodl, and Kithier (1968) there was a delayed maturation of the infant's IgG, IgA, and IgM. While a raised IgG of one subclass, such as the mother's paraprotein, can enhance the catabolism of other immunoglobulins of that subclass (Fahey and Robinson, 1963), it seems unlikely that the mother's paraprotein alone had thus caused the delayed maturation seen in all immunoglobulin classes in this infant. It is possible that some other humoral factor had crossed the placenta from the mother, for there is some evidence that a humoral mechanism can suppress synthesis of normal immunoglobulins in patients with paraproteins (Hobbs, 1966). It may also be that such a humoral mechanism could have had an even greater effect on the newly developing system of the baby, for the mother at that time appeared normal, though two years later she herself was showing suppression of normal IgM with borderline IgA.

Requests for reprints should be made to Dr. J. M. Littlewood, Seacroft Hospital, York Road, Leeds.

J. M. LITTLEWOOD, M.D., M.R.C.P.ED., D.C.H.

I. HUNTER, B.SC.

R. B. PAYNE, M.D., M.R.C.PATH.

D. W. MILES, M.B., B.SC., M.R.C.P.

Department of Paediatrics, Seacroft Hospital, Leeds, and
Department of Chemical Pathology and Medicine,
University of Leeds.

REFERENCES

- Allansmith, M., McClellan, B. H., Butterworth, M., and Maloney, J. R. (1968) *Journal of Pediatrics*, **72**, 276.
Brambell, F. W. R., Hemmings, W. A., Oakley, C. L., and Porter, R. R. (1960). *Proceedings of the Royal Society. Series B*, **151**, 478.
Fahey, J. L., and Robinson, A. G. (1963). *Journal of Experimental Medicine*, **118**, 845.
Good, R. A., and Papermaster, B. W. (1964). *Advances in Immunology*, **4**, 1.
Hobbs J. R. (1966). *Scientific Basis of Medicine. Annual Reviews*, p. 106.
Kosova, L. A., and Schwartz, S. O. (1966). *Blood*, **28**, 102.
Littlewood, J. M., Kite, P., and Kite, B. E. (1969). *Archives of Disease in Childhood*, **44**, 617.
Putnam, F. W., Easley, C. W., Lynn, L. T., Ritchie, A. E., and Phelps, R. A. (1959). *Archives of Biochemistry and Biophysics*, **83**, 115.
Rádl, J., Masopust, J., Jodl, J., and Kithier, K. (1968). *Helvetica Paediatrica Acta* **23**, 555.

Isotopic and Radiological Investigation of Renal Function for Hypertension

British Medical Journal, 1970, **4**, 95-96

CASE REPORT

A 46-year-old man with hypertension was seen in February 1969 complaining of mild anginal pain, mainly while driving a car.

On examination he was seen to be a healthy well-built man. His standing blood pressure varied between 200/130 and 180/120. The fundi showed arteriovenous nipping but no haemorrhages or exudates. A random urine test showed no protein and no casts. The uncorrected long axes of the kidneys on an intravenous pyelogram (I.V.P.) on 5 March 1969 were: right 11 cm., left 13 cm. Contrast excretion was symmetrical, but the middle and lower calices on the right side were not well filled. This appearance led to the suspicion of a renal artery stenosis, but the failure to fill some of the calices in the right kidney also raised the suspicion of a neoplasm.

Because of the possibility of a neoplasm it was felt that a scintigraphic investigation of the kidneys would be the quickest and simplest method of obtaining further information. A mark III Nuclear Enterprises Gamma Camera was used and eight scintiphotos were taken over a period of 40 minutes after the injection of 1.5 mCi of ^{99m}Tc Fe ascorbic acid complex (Harper *et al.*, 1966). A further scintiphoto was taken three hours after the injection. These scintiphotos showed a striking difference in renal size,