the hair turned from dark brown to blonde in three months when the patients were taking 20 tablets (10 g.) daily. There were no general ill-effects and the colour change was much appreciated by the four women patients, who seemed inclined to keep it a secret.

The manner in which mephenesin exerts this effect on melanogenesis is not known, but experimental studies are being undertaken.

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FOETAL ERYTHROCYTES IN THE MATERNAL CIRCULATION

BY

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Since the publication by Zipursky *et al.* (1959) of a modification of the Kleihauer technique for the identification of foetal red cells, numerous workers have reported the finding of foetal erythrocytes in the maternal circulation soon after delivery. The present investigation was undertaken to find out if any factors related to pregnancy or delivery could be said to influence this occurrence.

Method

Specimens of venous blood were collected from 165 women who had experienced no complications in pregnancy or labour, and films were prepared by the Zipursky method. It was not found necessary to stain the films. Since it was intended to find out whether or not a transplacental leak had occurred, without reference to its magnitude or possible clinical consequences, even a single foetal cell observed in two longitudinal traverses of a microscope slide—that is, an average of 120,000 maternal red cells—was recorded as a positive.

The cases were studied with particular reference to parity, duration of labour, weight, and condition of the placenta and its method of expulsion. Since it was also thought that some degree of anoxia in the foetus, by reason of the possible effect on capillary permeability, might predispose to a leakage of foetal cells, the infants were assessed at birth by means of the Apgar (1953) score. Because foetal red cells which are ABO incompatible with those of the mother are rapidly eliminated, all specimens were collected within 24 hours of delivery.

Results

In the 165 cases studied foetal cells were found in 83, but in only 9 of these did the number of foetal cells observed amount to 0.02% or more of the total erythrocytes. In one case 1.5% of foetal cells was observed. No foetal cells at all were seen in the films from the remaining 82 cases. This means that in 50%

of the women there had been an escape of foetal cells into the maternal circulation. This agrees with the work of Cohen and Zuelzer (1962). That these figures are uninfluenced by parity is demonstrated in the Table.

	Foetal Cells Present	Foetal Cells Not Present
1st pregnancy	26	30
2nd "	24	22
3rd "	11	11
4th "	11	7
5th " .. or over ..	11	12

Duration of labour seemed to have no bearing on transplacental bleeding, since it was found to have occurred as commonly in women who had short labours as in those in whom labour was protracted. Further, when the first, second, and third stages were considered separately the figures remained the same.

The method of expulsion of the placenta was considered in each case and the balance between those patients who had and those who had not foetal cells remained unaffected whether the placenta was expelled spontaneously or assisted by fundal pressure. In cases where the placenta was noted as being calcified or infarcted, again there was no difference in the number of "positives" between these and the placentae which did not show these characters.

Among 105 patients with a placenta weighing less than 1½ lb. (680 g.), 43.8% had foetal cells present in the blood. The corresponding proportion among the 60 patients with placentae weighing more than 1½ lb. was 61.7% ($\chi^2=4.184$; $n=1$; $P<0.05$ but >0.025). The figures are sufficiently suggestive to point to a relationship between transplacental bleeding and the size of the placenta, and deserve further investigation. It is a result which would be expected, since in the heavier placentae a larger foeto-maternal area of contact would be available to permit transplacental bleeding.

When the ABO groups of mother and baby were noted and there was ABO compatibility, 70 cases were found with foetal cells against 62 without; but that ABO cells can be found in spite of ABO incompatibility if they are looked for carefully enough and soon enough after delivery was shown in 13 out of the 33 examined. This is a higher proportion than that reported by Fraser and Raper (1962), who found a 16% incidence, or by Cohen and Zuelzer (1962), who found 15%; but larger numbers of cases might well reduce this difference.

By the Apgar assessment the infant is given a score of from 0 to 10 for its condition of heart, respiration, tone, reflexes, and colour one minute after birth. This is repeated after five minutes, and in addition the time for the establishment of sustained respiration is noted. The results when investigated by this method showed no difference in the incidence of transplacental escape of foetal cells between the babies who were given full marks at birth and those who were given a lower assessment.

In conclusion it is suggested that transplacental bleeding of slight degree which can be demonstrated in 50% of cases within 24 hours of delivery can hardly be regarded as an abnormality, but the factors which predispose to its occurrence in otherwise normal cases remain unknown.

Summary

Specimens of venous blood were collected within 24 hours of delivery from 165 women in whom pregnancy

and delivery were normal, and examined for the presence of foetal erythrocytes.

Foetal cells were found in 50% of cases.

Parity, duration of labour, condition of the placenta and its method of expulsion, and the state of the infant at birth, as judged by the Apgar method of assessment, were found to have no influence on transplacental leakage.

Large placentae appear to be positively correlated with escape of foetal cells into the maternal circulation.

Foetal cells were found when there was ABO incompatibility between mother and foetus, but less frequently than when there was ABO compatibility.

The cause of transplacental leakage of foetal cells remains unknown.

My thanks for the statistical analysis are due to Dr. Donald Mackay, medical statistician, Northern Regional Hospital Board, Inverness.

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Medical Memoranda

Parkinsonism Occurring with Methyldopa Treatment

Methyldopa ("aldomet") is a drug recently introduced for the treatment of hypertension (Gillespie, 1960; Oates *et al.*, 1960). It has received considerable publicity, mostly complimentary, in the medical press. Side-effects have not been troublesome, although lassitude, tiredness, and fatigue (Irvine *et al.*, 1962; Daley and Evans, 1962), and depression (Dollery and Harington, 1962) have been reported.

The case is reported of a patient who developed definite extrapyramidal signs while receiving the drug and who had developed similar signs previously on reserpine.

CASE HISTORY

A man aged 57 was admitted to Glasgow Royal Infirmary for assessment and treatment of hypertension. Clinical examination revealed a patient with typical signs of Parkinsonism. His gait was shuffling, the limbs showed cogwheel rigidity, and his face was expressionless. There was evidence of cardiomegaly, the second aortic sound was accentuated, and the blood-pressure was 230/130 mm. Hg. Fundi showed grade III hypertensive retinopathy.

Investigations.—Blood picture normal; E.S.R., 1 mm.: blood urea, 37 mg./100 ml.; serum electrolytes normal; W.R. and Kahn negative; urine microscopically and chemically normal; chest radiograph—evidence of left ventricular enlargement; I.V.P. normal; E.C.G., left ventricular hypertrophy; catechol amines, 193.5 µg./day.

It transpired that he had been taking compound tablets containing reserpine for some months, during which time he had noticed increasing stiffness and difficulty in locomotion. The drug was withdrawn and gradually the extrapyramidal signs and symptoms disappeared completely.

However, he remained hypertensive (diastolic B.P. around 130 mm. Hg), and it was considered that further hypotensive treatment was necessary. He was stabilized on methyldopa 250 mg. q.i.d. (diastolic B.P. 100–110 mm. Hg), and was discharged from hospital without evidence of Parkinsonism.

When seen as an out-patient four weeks later there was slight evidence of a return of Parkinsonism, and two weeks later this was more marked, his condition being similar to that when he was first seen. No change was reported or seen in his condition until methyldopa was withdrawn, when both subjective and objective improvement was noted with disappearance of limb stiffness, return of facial expression, and improvement in mobility.

COMMENT

There seems little doubt that the return of Parkinsonism in this patient was directly related to hypotensive therapy with methyldopa.

No previous cases of drug-induced Parkinsonism with methyldopa have been reported, but it may be that other cases will come to light after attention has been drawn to this complication of therapy and when more patients have received the drug.

Extrapyramidal signs are well known to physicians who use phenothiazines (Rees, 1960; Ayd, 1961; Weatherall, 1962) or reserpine (Harington, 1960), and they are generally reversible by withdrawal of the drug.

Both chlorpromazine and reserpine are intimately involved in the metabolism of adrenaline and serotonin (Courvoisier *et al.*, 1953; Pletscher *et al.*, 1956; Paasonen and Vogt, 1956; Costa and Rinaldi, 1958). Since methyldopa interferes with the decarboxylation of 3,4-dihydroxyphenylalanine and 5-hydroxytryptophan (Sourkes, 1954) and the subsequent formation of serotonin and noradrenaline, a similarity of effect might be anticipated.

I would like to thank Dr. Alexander Brown for allowing me to report this case and for helpful advice.

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Rehabilitation after Hindquarter Amputation

A woman of 38 was admitted to Garston Manor for rehabilitation after a right hindquarter amputation for malignant melanoma three years previously.

A year after the operation she had been fitted with a prosthesis but had never been able to wear it for longer than two hours. She could not sit in comfort wearing it and was unable to travel on public transport. Being a dressmaker, she tried to work at home, as she had to help support an aged mother. She worked propped up on cushions, but after half an hour the pain in her back was so severe that she would have to rest lying flat to ease the pain. She was able to earn very little.