

not merely the estimation of reducing substances—which meet the needs of their particular laboratories.<sup>4-6</sup> Perhaps it would be helpful if details of their experiences with these methods were made available to biochemists, either through your columns or through the Association of Clinical Biochemists.

Similar problems have arisen in relation to the use of ortho-tolidine in tests for residual chlorine in water—in this case the Water Research Association has recommended an alternative test based on NN-diethylparaphenylene diamine, which is not believed to be carcinogenic—and in relation to the use of 1-naphthylamine in tests for nitrates in sewage effluents or in urine. Recently an alternative test for urinary nitrites has been proposed.<sup>7</sup> Here again it would be useful if the experience of those who have changed to alternative methods could be collated and brought to the notice of biochemists.

Since it is apparent that it will not be possible to abandon the use of all carcinogenic aromatic amines in medical biochemistry immediately, it would be wise in the meanwhile for the head of every laboratory where these substances are used to ensure that all his staff are aware of the possible dangers and of the necessary precautions, and to see that these precautions are in fact observed.—I am, etc.,

Chester Beatty Research Institute,  
Institute of Cancer Research,  
Royal Cancer Hospital,  
London S.W.3. R. A. M. CASE.

## REFERENCES

- 1 Chester Beatty Research Institute and Harlow Industrial Health Service, *Precautions for Laboratory Workers who Handle Carcinogenic Aromatic Amines*, 1966, London.
- 2 *Association of Clinical Biochemists*, 1967, News Sheet, No. 53, July, p. 2.
- 3 Henry, R. J., *Clinical Chemistry Principles and Techniques*, 1964, New York.
- 4 Kelly, D. M., *Clin. Chem.*, 1965, 11, 471.
- 5 Brown, M. E., *Diabetes* 1961, 10, 60.
- 6 Bittner, D. L., and McCleary, M. L., *Amer. J. clin. Path.*, 1963, 40, 423.
- 7 McLean, J., and Henderson, A., *J. clin. Path.*, 1966, 19, 632.

### Transplacental Transmission of Herpes Simplex

SIR,—Gregg in 1941<sup>1</sup> and Swan and his associates<sup>2</sup> in 1943 first reported clinical observations on congenital anomalies in the offspring following maternal rubella. While Swan's observations were concerned chiefly with rubella, he postulated that other virus diseases in the mother might result in foetal maldevelopment.

Herpes simplex infection of the newborn may occur by transplacental transmission of the virus as well as by the more common mode of infection from active lesions in the birth canal.<sup>3</sup> Between 65% and 98% of adults will show neutralizing antibodies to the herpes simplex virus.<sup>3</sup> The incidence of herpetic lesion in the female genital tract is greater than generally recognized. Naib *et al.*<sup>4</sup> found that of approximately 40,000 indigent patients screened for cancer by routine "Pap" smear 62 (0.16%) had initial cytological evidence of a herpetic lesion. About one-third of these were pregnant. Because of these facts and because of the fact that herpes simplex virus in tissue culture causes a high percentage of chromosome aberrations,<sup>5</sup> it is plausible to suggest that herpes simplex cervicitis during early pregnancy may cause congenital malformations.

A 22-year-old primipara was admitted to the department of obstetrics and gynaecology at the General Hospital, Malmö, Sweden, on 23 June 1966 in labour. During the third month of pregnancy she was first seen in the outpatient service. At that time the labia majora were noticed to have several small ulcerations. The routine "Pap" smear showed initial cytological evidence of a herpetic lesion. The ulcerations healed spontaneously, and the pregnancy was uneventful until the 36th week of gestation, when the patient underwent a caesarean section because of toxæmia. The child was a phocomelus and died some hours after delivery because of respiratory distress. As far as we know the patient had not taken any medication during her pregnancy. From the age of 8 years she had been treated with insulin because of diabetes mellitus, which may give malformations, but as far as is known not of this kind.

The present congenital malformations and the maternal herpes simplex infection during early pregnancy may be coincidental. As no studies of a relationship appear to have been published, we hope that others may follow up cases with cytological evidence of herpetic lesions during early pregnancy, and report cases of foetal maldevelopment if any appear.—We are, etc.,

L. CEDERQVIST.  
G. ELIASSON.  
L. LINDELL.

Departments of Obstetrics  
and Gynaecology, and Pathology  
(Cytological Department),  
General Hospital,  
Malmö, Sweden.

## REFERENCES

- 1 Gregg, N. McAlister, *Trans. ophthal. Soc. Aust.*, 1941, 3, 35.
- 2 Swan, C., Tostevin, A. L., Moore, B., Mayo, H., Blach, G. H. B., *Med. J. Aust.*, 1943, 2, 201.
- 3 Mitchell, J. E., McCall, F. C., *Amer. J. Dis. Child.*, 1963, 106, 207.
- 4 Naib, Z. M., Nahmias, A. J., Josey, W. E., *Cancer (Philad.)*, 1966, 19, 1026.
- 5 Stich, H. F., Hsu, T. C., Rapp, F., *Virology*, 1964, 22, 439.

### Snakebite Poisoning

SIR,—Dr. H. A. Reid (5 August, p. 367) has drawn attention to a newspaper report of snakebite which occurred in a local man.

At the time some concern was caused by the presence of local pain and tenderness, and of dilated pupils and weakness apparently not caused by fear alone, following injury by an unusual snake. This was later identified as a European grass-snake. For the future we have learned from the incident that antivenom is kept in the zoo concerned.

Needless to say, the drama of the occasion was considerably less than was depicted in the press.—I am, etc.,

CHRISTOPHER GARDNER-THORPE.  
City General Hospital,  
Stoke-on-Trent.

### Ehlers-Danlos Syndrome

SIR,—Ehlers-Danlos syndrome may have a wide variety of manifestations. It is often difficult to be sure of the diagnosis, particularly in mildly affected individuals, since the microscopic anatomy is in "a disputed state," and the basic defect is unknown.<sup>1</sup> Thus Mr. A. P. Barabas's suggested clinical subdivision of cases (3 June, p. 612) is most helpful in elucidating the probable heterogeneity of the

syndrome, and particularly in pointing out the existence of an "arterial" type which may cause fatal haemorrhage in early adult life.

As Mr. Barabas is aware, intracranial arterial aneurysm has been reported as a complication,<sup>2</sup> and one of us recently described three cases of spontaneous carotid-cavernous fistula in Ehlers-Danlos syndrome.<sup>3</sup> Two of the patients are siblings, a sister and brother, and the sister has since died after suffering a succession of further arterial complications. A brief report of this case may therefore be of interest.

She was last seen in 1961, aged 37, with a spontaneous left carotid cavernous fistula associated with remarkable ectasia of the left internal carotid artery, and alarming haemorrhage occurred at the time of carotid arteriography. Carotid ligation was performed, and one month after operation she developed small aneurysms of the left radial artery and the left superficial temporal artery. The latter disappeared spontaneously. These episodes and further complications occurring up to 1964 have been reported.<sup>3</sup> Her previous history included life-long easy bruising and a myocardial infarction at the age of 35.

In 1965 she still had an aneurysm of the left radial artery, which was later excised at another hospital. In April 1967 the patient complained of weakness, fatigue, and fever, and then developed severe right-sided headache and blurring of vision in the right eye. On admission to hospital she showed right proptosis and third-nerve palsy, suggesting a right internal carotid aneurysm. Angiography was deferred because of the previous experience and because she also had many features of a systemic disease resembling polyarteritis nodosa. These included fever, hypertension, chest pain, weakness and extreme tenderness of limb muscles, leucocytosis, normochromic anaemia, and a very high sedimentation rate. Skin and muscle biopsy proved inconclusive, showing only slight perivascular infiltration, but a disturbance in the pattern of elastic fibres, in some parts loose and in others arranged in compact masses with a tendency to form nodules, was noted, compatible with the diagnosis of Ehlers-Danlos syndrome (Dr. Mario Montes).

She was treated with corticosteroids, and subjective improvement and disappearance of fever followed; vision improved in the right eye, and the proptosis and right third-nerve lesion both regressed. However, chest pain recurred and electrocardiographic evidence of a further anterior myocardial infarction was seen. Subsequently, a further aneurysm appeared on the right radial artery, the mirror image of that earlier excised on the left. Soon after, she suffered sudden acute swelling in the left calf with agonizing throbbing pain. This was thought to represent rupture of another aneurysm, and at operation, reluctantly undertaken, a false aneurysm was found arising from the left posterior tibial artery. Some 10 days later another aneurysm appeared on the right anterior tibial artery. Finally the patient complained of acute abdominal pain and became unconscious. Blood was aspirated from the peritoneal cavity but there was no time to attempt operation before she died. Necropsy showed that she had ruptured an aneurysm of the splenic artery; other aneurysms were found on mesenteric arteries. Polycystic disease of the kidneys and liver was also found.

It seems worth emphasizing that this patient had thin and unusually smooth skin, but it was not redundant or hyperelastic, and her joints were not unusually lax. As noted previously,<sup>3</sup> her brother had a similar left-sided carotid-cavernous fistula at the age of 30, but we are not aware that he has ever had other arterial complications, although we have not yet had an opportunity to examine him. A full study of the family is in progress; there is no other positive evidence of Ehlers-Danlos syndrome, although there are

instances of subarachnoid haemorrhage and of unexplained deaths.

This case, which will be presented in detail, supports Mr. Barabas's contention that there may exist an "arterial" type of syndrome. It provides a particularly florid example, with a similar illness occurring in milder form in a brother. Although usually regarded as an autosomal dominant trait,<sup>1</sup> the possibility of different modes of inheritance in a heterogeneous syndrome has always to be considered, and one might speculate that some cases of the "arterial" form might be transmitted as autosomal recessives. If this were so parents would not be expected to show the trait, and absence of family history could be compatible with this mode of inheritance, as in the case of Rubinstein and Cohen,<sup>2</sup> another of our own,<sup>3</sup> and number 27 of Barabas.

The features of systemic illness (fever, etc.) in our patient are not well explained and it may be noteworthy that they had occurred in milder form earlier in this patient's history. We wonder whether others have had similar experiences and whether more acute episodes of arterial damage may occur in the course of Ehlers-Danlos syndrome.—We are, etc.,

ROBIN M. BANNERMAN.  
CARL J. GRAF.  
JAMES F. UPSON.

Buffalo General Hospital,  
Buffalo, New York, U.S.A.

#### REFERENCES

- 1 McKusick, V. A., *Heritable Disorders of Connective Tissue*, 1966, 3rd ed., p. 179. C. V. Mosby, Saint Louis.
- 2 Rubinstein, M. K., and Cohen, N. H., *Neurology (Minneapolis)*, 1964, 14, 125.
- 3 Graf, C. J., *Arch. Neurol. (Chic.)*, 1965, 13, 662.

### Warning of Massive Pulmonary Embolism

SIR,—Dr. W. G. Smith (5 August, p. 370) rightly stresses the importance of early recognition and treatment of "warning" pulmonary embolus. This may not, however, be quite as usual as he suggests.

Coon and Coller<sup>1</sup> reported warning emboli in 25% of their cases of fatal pulmonary embolism, and Little, Lowenthal, and Mills<sup>2</sup> found that 7 of their 37 cases of fatal pulmonary embolism had evidence of warning embolus, an incidence of 19%.

A review of St. Thomas's Hospital records for the years 1959-64 shows a total of 76 cases of fatal pulmonary embolism. A definite warning embolus was recorded in 13 (17%) of these cases. In a further 16 cases symptoms of dyspnoea or chest pain were not considered sufficient for a definite diagnosis to be made, and in the remaining 47 cases sudden and profound collapse of the patient was apparently unheralded.

These figures suggest that massive fatal pulmonary embolism usually occurs without any warning. It is therefore all the more important to regard any symptom or sign of pulmonary embolus, however slight, as a potential "warning," and to treat it with the seriousness it deserves.—I am, etc.,

Middlesex Hospital,  
London W.1.

DAVID NEGUS.

#### REFERENCES

- 1 Coon, W. W., and Coller, F. A., *Surg. Gynec. Obstet.*, 1959, 109, 259.
- 2 Little, J. M., Loewenthal, J., and Mills, F. H., *Brit. J. Surg.*, 1966, 53, 657.

### Chemical Treatment of Skin Cancer

SIR,—Your leading article (15 July, p. 125) on this subject made good sense. On several occasions I have witnessed Dr. Frederick Mohs at work in his clinic, and have been deeply impressed by both the logic of his chemosurgical method of therapy and the care with which he carries it out. The success he achieves in cases of advanced skin cancer and cases of cancer which have recurred after previous radiotherapy or surgery is unequalled by that attainable by any other method.

Dr. G. M. King (19 August, p. 495) states that his results from treatment with 5% 5-fluorouracil (5-FU) ointment, though it is much too early to assess the long-term success rate, have been "quite impressive." This statement can carry little weight, firstly because it is unsupported by figures which can be interpreted by others, and secondly because it is easy to obtain "quite impressive" results in the treatment of skin cancer by a wide variety of methods. The results would certainly have to be far more impressive than those obtained by E. Klein and his colleagues<sup>1</sup> with 20% 5-FU to justify the widespread adoption of this method of treatment. The possible value of 5-FU in the treatment of solar or arsenical keratoses is in my view a matter for separate evaluation.—I am, etc.,

Chester Beatty Research Institute,  
London S.W.3. FRANCIS J. C. ROE.

#### REFERENCE

- 1 Klein, E., Stoll, H. L., Milgrom, H., Traenkle, H. L., Graham, S., and Helm, F., *J. invest. Derm.*, 1966, 47, 22.

### Hazard from Nylon

SIR,—I was interested to read of the case of ischaemia of the finger-tip of a small infant reported by Dr. G. G. Noott (5 August, p. 370). A similar case came under my care not long ago in which a loop of fibre inside the baby's glove had strangulated the finger-tip, resulting in gangrene of the part.

This is a hazard I had not come across before, and it seems obvious that mitts made of material would be much safer than knitted gloves or mittens on tiny babies.—I am, etc.,

Epsom District Hospital,  
Epsom, Surrey. E. N. CALLUM.

### Treatment of Mendelson's Syndrome

SIR,—Dr. G. Taylor's letter (5 August, p. 368) outlines a very comprehensive regimen of treatment when aspiration of gastric contents has occurred, and states that "vomiting and regurgitation of stomach contents . . . should be regarded as preventable." However, apart from the excellent recognition that all women in labour must be suspected of having a full stomach, irrespective of their last oral intake of food or drink, and the advice on giving oral antacids before anaesthesia, he omits emphasis of the use of various techniques available at induction of anaesthesia for prevention of inhalation of gastric contents. Presumably these are taken for granted, but in such an important subject, where prevention is considerably superior to cure, any mention of prevention (points (1) and (2)) should stress the importance of a well-organized technique of induction, maintenance, and termination of anaesthesia.

Several methods are available for induction of anaesthesia: varying the position of the patient, general anaesthetic agents used,<sup>1-3</sup> use of cricoid pressure,<sup>4</sup> or use of regional analgesia.<sup>5-8</sup>

No method can guarantee 100% safety, and, although we are grateful for any new methods of treating Mendelson's syndrome when it has occurred, we should strive our utmost to reduce the incidence of this complication by taking all possible steps to avoid its occurrence.—I am, etc.,

General Hospital,  
Southend-on-Sea.

M. J. WATT.

#### REFERENCES

- 1 Inkster, J. S., *Brit. J. Anaesth.*, 1963, 35, 160.
- 2 Bourne, J. G., *Proc. roy. Soc. Med.*, 1954, 47, 416.
- 3 Wylie, D., *ibid.*, 1955, 48, 1089.
- 4 Sellick, B. A., *Lancet*, 1961, 2, 404.
- 5 Lee, J. A., and Atkinson, R. S., *Synopsis of Anaesthesia*, 1964, 5th ed., p. 681. Bristol.
- 6 Steel, G. C., *Proc. roy. Soc. Med.*, 1962, 55, 933.
- 7 Sadove, M. S., Levin, M. J., Rant-Sejdinal, I., *Canad. Anaesth. Soc. J.*, 1961, 8, 405.
- 8 Thorne, T. C., *Proc. roy. Soc. Med.*, 1954, 47, 301.

### Stewart-Morel Syndrome

SIR,—A woman, 77 years old, was admitted to our unit complaining of headache, vertigo, exertional dyspnoea, and some joint pains. It was noted that she exhibited hirsutism, and she told us that it has been necessary for her to shave each day for about 20 years. She did not remember when she started menstruation, but her periods were regular and she had had the menopause at about the age of 45 years.

On examination there was pallor, slight pitting oedema of both ankles, and lipomatosis of both arms and thighs. Her blood pressure was 220/

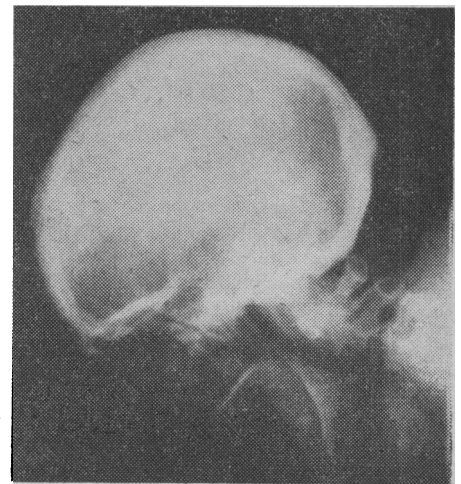


FIG. 1



FIG. 2