There are, I suggest, two other cases of red-cell aplasia associated with a carcinoma and two other interesting cases in which a thymoma was found in addition; this excludes the case reported by Opsahl,¹ where the thymic carcinoma was really accompanied by a pancytopenia. Tsai and Levin² reported a case of a 64-year-old male with a haemoglobin of 3.8 g./100 ml. and a white-cell count of 6,100/c.mm. whose bone-marrow showed red-cell aplasia and who at post-mortem, three years later, was found to have a squamous-cell carcinoma of the right lower lobe of the lung; the thymus gland was reported to have atrophied. Kark³ reported a case of a 21-year-old girl with a haemoglobin of 18%, white-cell count of 4,800/c.mm., whose bone-marrow showed red-cell aplasia when she was 24 and who died later in that year with a small fungating carcinoma 2½ in. by 2 in. (6×5 cm.) arising from the anterior wall and greater curvature of the mucosa of the pyloric antrum of the stomach.

Green⁴ (Case 2) reported a case of a 78-year-old female who was found to have a haemoglobin of 2 g./100 ml. upon emergency admission to hospital. Bone-marrow aspiration disclosed a poorly cellular marrow with few erythroid elements; radiography of the chest was normal. Two months later she was again admitted to hospital, this time with a Hb of 5.2 g./100 ml., and a small mass was found in the right breast, but operation was refused. Nine months later she was re-admitted and a further chest x-ray showed nothing remarkable and that month she died. At post-mortem a benign thymoma was found in addition to the low-grade scirrhous carcinoma of the breast. (There is a printing error in the reporting of the last illness of this patient with regard to its date.) Clarkson and Prockop⁵ (Case 1) reported a case of a 57-year-old female who was shown to have red-cell aplasia and a thymoma which was removed without any improvement to her anaemia. Two years later a mass was found in her right breast measuring 3×4 cm., mobile, non-tender, situated just below the nipple. Nine months later it was removed and proved to be a carcinoma.

These last two cases might be explained away by "coincidence," but not the first two; and is this association really so rare or is it that it has merely failed to be recognized?—I am, etc.,

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- ³ Kark, R. M., *Guy's Hosp. Rep.*, 1937, 87, 343.
- ⁴ Green, P., *Canad. med. Ass. J.*, 1958, 78, 419.
- ⁵ Clarkson, B., and Prockop, D. J., *New Engl. J. Med.*, 1958, 259, 253.

Cerebrovascular Accidents and Oral Contraception

SIR,—The letter from Dr. K. J. Zilkha (31 October, p. 1132) reporting two cases of non-fatal cerebrovascular accident in patients on oral contraceptives (one on Enavid, one on Ortho-Novin), reminded me of a difficult and puzzling case seen in casualty in April 1963.

The patient was a 29-year-old white woman, para 2, fully active and apparently fit until the day of admission. After breakfast the patient had gone upstairs. Her husband, downstairs, heard a bang from above and went to see if

something was wrong. He found his wife lying in the toilet vomiting and convulsing. She then became limp, and although her eyes were open she appeared not to see him. The family doctor was called and signs of right hemiplegia with sustained ankle clonus and increased tendon jerks were noted. Neck stiffness was not present. The blood-pressure was 130/80, and she was sent into hospital. On admission she was comatose, with equal pupils which reacted to light. The eyeballs wandered from side to side, and right hemiplegia with Hoffmann and Babinski signs were confirmed. There was no papilloedema and no neck stiffness.

She was admitted under the care of Dr. J. N. Walton. Lumbar puncture revealed a clear, colourless cerebrospinal fluid with 25 mg./100 ml. protein and no pleocytosis. Hb was 13.4 g./100 ml., white blood cells 7,300/c.mm., E.S.R. 4 mm./hr., serological tests for syphilis negative. Chest and skull x-ray showed no abnormality. The electroencephalogram showed a local excess of delta activity in the left central region. Two days after admission the blood-pressure rose and respirations ceased. She was put on a respirator but did not improve, and died three days after admission.

Necropsy was performed by Dr. G. W. Pearce, to whom I am indebted for the following report: "Brain 1,440 g. There was a slight symmetrical enlargement and congestion of the brain which was considered to be due to the patient having been on a respirator for over 24 hours prior to death. Thrombosis of the left middle cerebral artery 18 mm. from its point of origin from the internal carotid artery was found. There was softening and infarction within the distribution of this artery. A segment of the right anterior cerebral artery 2 cm. in length lying immediately above and behind the genu of the corpus callosum was also thrombosed, giving rise to a corresponding degree of brain infarction. There was no abnormality of the brain-stem, and mild atheromatous changes only were found in the circle of Willis and vertebral system.

"A patent foramen ovale (heart 240 g.) was found, but was occluded when the atria were not tensioned, and there was no sign of raised right-sided pressure. There was no source of emboli within the heart and there was no thrombosis within the nervous system. Other organs showed no abnormality apart from congestion. The absence of embolic disease suggests that the thrombosis in the two cerebral arteries was primary."

This patient had started on Conovid (norethynodrel and mestranol) two weeks prior to her collapse, as she was anxious to avoid further pregnancies.

Investigations by Egeborg and Owren (cited by Dr. Zilkha) have shown an increase in Factors VII and VIII in patients taking norethynodrel, and this has been thought to play a part in the increased clotting tendency. Recently a case of Factor X (Stuart Prower) deficiency¹ has been described who had remissions while pregnant, and who has responded well to treatment with norethynodrel. Whether or not Factor X is increased in normal patients on oral contraceptives is not yet defined.

In the case described arterial thrombosis was demonstrated at necropsy at two distinct sites on opposite sides of the brain. The cases recorded by Schatz *et al.*² of thromboembolic disease associated with norethynodrel included one woman aged 39 who developed left popliteal artery thrombosis requiring amputation. A case of non-fatal anterior cardiac infarction has also been recorded in a 34-year-old woman taking Conovid.³

The rarity of cardiac infarction in young women not of familial hypercholesterolaemic stock is well known, but Watson *et al.*⁴ reported two cases of cardiac infarction in young pregnant women, and collected another

24 cases from the literature. This underlines the observations by Haber in his Factor-X-deficient patient, where pregnancy and norethynodrel produced remissions.

It appears that, in addition to the hazard of venous thrombosis and thromboembolic phenomena, arterial thrombosis is perhaps a hazard of oral contraceptive treatment.—I am, etc.,

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- ² Schatz, I. J., Smith, R. F., Breneman, G. M., and Bower, G. C., *J. Amer. med. Ass.*, 1964, 188, 493.
- ³ Boyce, J., Fawcett, J. W., and Noall, E. W. P., *Lancet*, 1963, 1, 111.
- ⁴ Watson, H., Emslie-Smith, D., Herring, J., and Hill, I. G. W., *ibid.*, 1960, 2, 523.

Need for Gastric Lavage

SIR,—The article on the treatment of acute poisoning (10 October, p. 927) was a valuable summary of current thought, but we do not think the statement that gastric lavage must be performed on all cases known to have taken drugs less than eight hours prior to arrival in hospital can go unchallenged.

As long ago as 1929 doubts about the value of gastric lavage were raised by Starkenstein *et al.*,¹ and in 1933 Marriott pointed out that in the absence of the cough reflex gastric lavage could be lethal.² In 1942 Harstad *et al.*³ carried out an extensive investigation into the value of gastric lavage. They used 10 litres of fluid and in 38 of their cases no drug whatsoever was recovered from the washings.

0-10 mg.	was recovered in	7 cases
10-100 "	" "	17 "
100-260 "	" "	8 "
over 500 "	" "	2 "

By adding radio-opaque material to their lavage fluid they were able to demonstrate that a considerable amount entered the small gut, and by adding charcoal they demonstrated at post-mortem how much of the lavage fluid had entered the lungs. They were of the opinion that the poison passed rapidly into the small gut and that after four hours it was rare to find significant amounts in the washings. They felt, too, that lavage hastened absorption of the drug and they noted that coma sometimes deepened after it. They found that death was often due to aspiration pneumonia and they felt this was a more important cause of death than paralysis of the respiratory centre. Their conclusions were that lavage was never beneficial in the unconscious patient, but that aspiration of the gastric contents might be so if performed less than four hours after ingestion of the drug in the conscious patient.

Myschetzky, from the Poisons Centre at the Bispebjerg Hospital, Copenhagen, speaking at a meeting at the Royal Society of Medicine on 24 March 1964, suggested that gastric lavage should be discontinued as it was of no value in recovering a significant quantity of drug and was often dangerous. He said their practice was to recommend lavage only on conscious patients who had swallowed tablets less than an hour prior to admission. A small pilot series carried out by us confirms the very small amounts of drug usually obtained by lavage. We used a large-bore gastric tube aspirated with a stomach pump

and then washed out with 1,080 ml. of fluid only.

The Table summarizes the amounts recovered in patients with barbiturate overdosage.

0-10 mg.	...	...	7 patients
11-100 "	...	...	5 "
101-250 "	...	...	4 "
251-500 "	...	...	3 "
over 500 "	...	...	3 "
		22	"

It will be seen that in no case did we fail to obtain some evidence of the drug, whereas Harstad *et al.* failed to do so in over half their cases. This may be because they used large volumes of fluid.

Dr. J. J. Alpert (19 December, p. 1593) advocates emesis. This can, of course, only be of value with a fully conscious patient, and in our experience few who have ingested significant amounts arrive in hospital early enough for this to be practical. It may have its place as a home remedy, but does not seem to us to have a place in hospital practice. We feel that at the moment the position regarding lavage should be summarized as follows—lavage with a small volume of fluid may be useful if strict precautions are taken to protect the lungs and the time since ingestion is short.—We are, etc.,

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DAVID CARO.
E. KAWERAU.

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Nephritis and Skin Diseases

SIR,—An association between nephritis and some common skin diseases is recorded by Dr. R. Summerly and Dr. P. W. M. Copeman (28 November, p. 1369). I here give brief details of a similar case.

The patient, a female of 61, consulted me with general malaise, dysphagia, fever of 102° F. (38.9° C.), and a generalized blotchy erythematous rash, urticarial in places. She blamed the illness on a horse-fly bite several days previously, as she had always before reacted severely to insect bites, though never in such a manner as this. Other factors considered as a possible cause were two Anadin tablets taken a week previously and Thermogen plaster applied to a strained back at the same time.

After two days of treatment with antihistamines her condition had deteriorated generally. Urinalysis disclosed considerable albuminuria. She was admitted to Freedom Fields Hospital, Plymouth, under the care of Dr. H. A. W. Forbes, for further investigation. Blood urea was found to be 260 mg./100 ml., with a severe acidosis. E.S.R. 65 mm./hr. Mid-stream urine, numerous pus cells, scanty red blood cells, and *Streptococcus faecalis* grown on culture. Hb 68%, blood-pressure 140/60 mm. Hg. Investigations for L.E. cells negative. Chest x-ray—heart enlarged; lung fields normal. Over the course of several months her condition slowly improved, and at the last count her blood urea was 105 mg./100 ml.

This patient had a history of scarlet fever in childhood and two general practitioners had recorded on her card in the past a high pulse pressure and aortic diastolic murmur. These signs were not elicited during the present illness, or on subsequent investigations, but do suggest the possibility of rheumatic heart disease and the streptococcal hypersensitivity discussed by Summerly and Copeman. It is also possible to

implicate the horse-fly bite as an antigenic stimulus, or, indeed, one of the components of Anadin tablets (aspirin, phenacetin, caffeine, and quinine).

—I am, etc.,

East Loos, Cornwall.

J. C. GATES.

Unusual Object

SIR,—I can recall that a house-physician had an experience similar to that described by Dr. P. N. Stanbury (26 December, p. 1660). After a residents' party, when he had consumed a quantity of alcohol, the house-physician went to the ward and drank straight down about a pint of milk. Next morning he was feeling extremely ill, and after vomiting several times brought up an object larger but similar to that described, undoubtedly solidified milk. It was thought by its shape that this object had been obstructing the pylorus, and the instant relief of all symptoms on disimpaction confirmed this view.—I am, etc.,

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SIR,—Dr. P. N. Stanbury (26 December, p. 1660) may be interested to know that I too have had a case of a child who vomited a solid mass of caseinated milk, which appeared to have been causing an obstruction in the pylorus. In my case the child had an acute tonsillitis with a pyrexia and persistent vomiting for three days. The vomiting ceased dramatically immediately after the mass of solidified milk had been vomited.—I am, etc.,

Great Yarmouth,
Norfolk.

G. HURST.

New Dermatitis

SIR,—I am prompted by your leading article (19 December, p. 1547) entitled "A New Dermatitis" to report that we have recently seen a patient with a clinical syndrome apparently identical with that described by Sweet.¹

A 66-year-old female gave a past history of erythema nodosum in 1937 and severe osteoarthritis of hips and knees. She presented in May 1964 with a two-week history of malaise and aching in her limbs, neck, and back. A rash had appeared on her hands on the day of admission to hospital. It consisted of raised discrete patches of erythema on the dorsum of the hands and forearms, a plaque on the back of the neck and one on the right knee. General examination revealed a few small discrete cervical lymph nodes, marked hypertension, and a firm liver edge just palpable below the costal margin. She ran a remittent fever up to 102 to 103° F. (38.9-39.5° C.). Within the next few days the skin lesions, which were painful and irritating, became confluent and some areas began to develop small vesicles. Her E.S.R. was 62 mm. at one hour; total white cell count 14,300/c.mm. of which 82% were neutrophils. There was 0.3 part per 1,000 of albumin in the urine with occasional pus cells. Electrophoresis of the plasma proteins showed a moderate increase in α_1 and α_2 globulins. Blood cultures were sterile. Tests for L.E. cells and antinuclear factor were negative. Biopsy of the skin lesion showed a normal epidermis but marked dermal inflammatory reaction consisting of histiocytes and polymorphs. Culture of material from the biopsy was sterile.

Possible diagnoses considered included erysiploid of Rosenbach (although there was no his-

tory suggestive of contact with infected material), septicaemia, or a "collagenosis." A course of tetracycline followed by penicillin and streptomycin were without effect on the rash or pyrexia.

At this point Dr. P. J. Hare suggested the condition described by Dr. Sweet. Treatment was started with prednisolone, 10 mg. three times a day. The pyrexia fell to normal within 24 hours and the skin lesions faded over the next week with desquamation. After two weeks the blood leucocytosis had subsided. During the succeeding months she was gradually weaned off steroids and they were stopped in October without recurrence of symptoms.

This would seem to be a further example of acute febrile neutrophilic dermatosis.—I am, etc.,

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REFERENCE

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Buccal Oxytocin

SIR,—Since my return from Sweden my attention has been drawn to the correspondence in your columns on buccal oxytocin and in particular to the letter by Professor J. H. M. Pinkerton (28 November, p. 1393). A woman does not go into labour because of uterine contractions (which occur during all her reproductive life) unless they are preceded by changes in her vagina and cervix, in the composition of her blood, and probably by altered response to stimuli in her hypothalamus. These changes are associated with an increased sensitivity of her myometrium to oxytocin. It is nearly 30 years since I postulated that the hypothalamus controlled menstruation, ovulation, pregnancy, and parturition; that the onset of labour resulted from the removal of an "inhibition," not from an increase of oxytocin in the blood; and that the effective concentration of oxytocin in the blood matched the effective concentration of antidiuretic hormone (A.D.H.). The very first drip used for inducing labour was calculated on this assumption, and the amount then used (5 mU/min.) is the amount I advocate to-day.¹ Dr. Caldeyro-Barcia² agrees that the maximum amount of oxytocin given should not exceed 8 mU/min., and Dr. Hendricks³ affirms that 80% of his induction cases did not need more than 5 mU/min. of Syntocinon. The truly physiological oxytocin drip can be given to any patient deemed worthy of a trial of labour, whatever her past obstetric history. Most of those who use the oxytocin drip for inducing labour use higher concentrations of oxytocin, but it has never been shown that the pharmacological drip is more effective than the physiological one, and it is certainly less safe. Nevertheless oxytocin given into a vein can be stopped immediately, and I know of no centre in this country using this method efficiently where rupture of the uterus has occurred.

It is thus surprising that Professor Pinkerton writes: "Just how safe . . . [the buccal route] . . . is compared with the intravenous method is not yet established" notwithstanding the fact that he knows of six cases of rupture of the uterus occurring in a relatively small series of cases in which this route has been used. One wonders how many foetal or maternal deaths must occur before this point is settled.

The supposed advantages of the buccal route are: (1) that it is easy to use; and (2)