In this area about 65% of primiparae, and 50% of all cases, are delivered in hospital, and there appears to be no reason to increase the number of beds. Indeed, as housing conditions improve the number of home confinements might well be increased without catastrophic consequences to the stillbirth rate, for this, in primiparae, appears to be related to unwanted pregnancy and prematurity rather than to the place of delivery.—I am, etc.,

Gloucester IVOR COOKSON.

Citrate Therapy Success

SIR,—A European patient holding an important position in a local commercial enterprise had been under treatment for four months for an eczema of the hands that considerably crippled him. He had begun to refer to it as a "major catastrophe."

I employed the usual gamut of local applications, antihistaminics, etc., and a careful search was made for any source of sensitizing substance—all without avail.

Your *Journal* of April 12 carried a paper by Rocha e Silva concerning the mechanism of anaphylaxis and allergy (p. 779), in which it was maintained that 4% sodium citrate is a potent treatment applied locally.

After four days' treatment, with local swabbing three times a day, the eczema disappeared almost entirely except for scarring areas where infection had supervened.

Both the patient and myself may be excused a certain gratification—and astonishment.—I am, etc.,

Leopoldville, Belgian Congo. E. W. PRICE.

Danger of "Novalgin"

SIR,—The report by Drs. F. Dudley Hart, D. G. Wraith, and E. J. B. Mansell (June 14, p. 1273) of a case of agranulocytosis in which "novalgin" was incriminated as the causative drug prompts me to record a case in which novalgin was thought to be responsible for severe granulocytopenia.

A housewife, aged 61, had suffered from recurrent pain in the back. For the relief of this pain she had been prescribed novalgin (sodium 1-phenyl-2:3-dimethyl-5-pyrazolone 4-methylamino methane sulphonate). She had taken four or six 5-gr. (0.3-g.) tablets daily regularly from June 15, 1951, until her admission to hospital on August 14. On July 20 her throat became sore and she had difficulty in swallowing, progressing to almost complete dysphagia. She developed multiple septic areas and indolent abscesses of the skin and ran a high fever with shivering attacks, becoming increasingly weak and prostrated. She was admitted to hospital on August 14, three weeks after the onset of her symptoms and eight weeks after commencing novalgin.

A blood count showed: white cells 3,500 per c.mm. (polymorphs 1% (35 per c.mm.), lymphocytes 94%, monocytes 5%); red cells 4,200,000 per c.mm. Hb=84% (12.4 g. per ml.). Swabs from the septic lesions grew *Streptococcus pyogenes* and *Staphylococcus aureus* and a blood culture was sterile.

She was treated with crystalline penicillin 250,000 units intramuscularly six-hourly, "pentnucleotide" 10 ml. intramuscularly six-hourly, and pyridoxin 100 mg. intravenously daily. There was a rapid rise in the granulocytes, and the pentnucleotide and pyridoxin were omitted after the fourth day of treatment when the polymorphs had reached 6,600 per c.mm. The penicillin was omitted after she had become afebrile on the 18th day. Sternal puncture was delayed until the sixth day and at this time a normal cellular marrow was found. There was no evidence of leukaemia or neoplasia. Her general condition showed rapid improvement and she has remained well since.

Novalgin was thought to have been responsible for the granulocytopenia in this case, for this was the only drug which had been taken during the previous two months. It is a sulphonated derivative of amidopyrine and, like it, may produce agranulocytosis. However, it is not on any dangerous drug schedule, and may be obtained by the public without a doctor's prescription. It is therefore desirable that the dangers of the drug should be generally known, and that it should be used with as much caution as amidopyrine, bearing in mind that the use of safer analgesics is to be preferred.—I am, etc.,

Orpington, Kent. K. M. CITRON.

Incidence of Drug Sensitivity

SIR,—The articles of Dr. G. Discombe and of Drs. F. D. Hart, D. G. Wraith, and E. J. B. Mansell, and your annotation on the dangers of amidopyrine (June 14, pp. 1270, 1273, and 1292) prompt me to report two cases of drug sensitivity to emphasize the importance of this problem and comment on some aspects of this form of allergy.

Case 1.—A woman aged 51, suffering from rheumatoid arthritis, had been treated between February, 1948, and September, 1951, by injection of calcium aurothiomalate (Crookes), each course of a total of 0.5 g. lasting about four months, with a three-month interval between the courses. On October 22, 1951, she was started on weekly injections at home of "irgapyrin" (Geigy) (amidopyrine in butazolidine) 5 ml., the last injection being given on December 10. At the same time she was taking two tablets daily of "allonal" (Roche) (amidopyrine and allyl*iso*propyl barbiturate). On the day after her last injection she developed malaise followed by pyrexia, diarrhoea, a dry sore throat, and severe pain in the perineum. On December 16 a white cell count done privately showed about 500 total white cells per c.mm., 80% lymphocytes; her temperature was 103° F. (39.4° C.) and she was given penicillin. Two days later she developed jaundice and was admitted to St. Helier Hospital with enlarged spleen and liver. She had a large area of induration with gangrene of the right buttock, the gangrene extending to involve the rectal mucosa. (Blood, total white cells 3,100 per c.mm., all lymphocytes; serum bilirubin 6.7 mg. per 100 ml.)

She was treated with antibiotics, vitamins, pentose-nucleotide, pyridoxin, liver injections, and intravenous blood, saline, and glucose. There was no change in her condition. On December 20 total white cells were 1,800 per c.mm. (lymphocytes 88%, plasma cells 11%, polymorphs 1%). She died on December 22, and a post-mortem report by Dr. D. Haler, at the request of H.M. Coroner for East Surrey (I am indebted to both for permission to quote), stated: "There were scattered petechiae and ecchymoses all over the body and a deep sloughing sore on the sacrum. There was sloughing ulceration of the pharynx. The liver was bile-stained and showed the characteristic picture of subacute yellow atrophy. The heart muscle and the adrenal glands were necrotic, and the bone marrow was reddened and apparently excessive in the sternum."

Case 2.—A 45-year-old woman was admitted on October 5, 1948, having developed a few days earlier bleeding from the mouth, bruises in the skin, and conjunctivae, pain on swallowing, tarry stools, and blood-stained urine. Her platelets were 25,000 per c.mm. One year previously, over a period of about six months, she had been given eight tablets of "sedormid" (Roche) (allyl*iso*propyl acetyl urea) without any ill effects. During the last six months, on four occasions, she had taken one to two tablets of sedormid, and each time she developed bleeding in the skin and mucosae of the nose and mouth. She had previously suffered from mild attacks of asthma, hay-fever, and eczema. There was a family history of asthma and eczema. She improved after about a week in hospital; the platelets returned to normal. The tourniquet test has remained positive, but no further purpura has occurred since.

The first patient received three drugs which cause agranulocytosis, but of these only gold is known to cause jaundice. The last course of gold injections was terminated over three months before her fatal illness started, and, although gold may be found in the urine up to about 300 days after injections and in the plasma for 100 days (Freyberg *et al.*, 1941; Hartung *et al.*, 1941), I am unaware of any case where symptoms arose at such a long interval of time after administration. It is difficult, therefore, to assess the part played by each of these drugs, but one cannot help feeling that the ones containing amidopyrine played the greatest part in causing this patient's illness. The second case does not differ substantially from other cases reported in the literature of thrombocytopenic purpura caused by the hypnotic sedormid. In both these instances the knowledge that potentially harmful drugs were being administered failed to act as a safeguard.

An interesting feature of drug sensitivity, which seems to apply generally to other allergic conditions, is its geographical distribution. In 1938 I discussed this problem in describing the first case reported in Italy of jaundice associated with exfoliative dermatitis caused by cinchophen. A review of the literature of purpura caused by sedormid reveals no case reported in the Latin countries. Discombe

discusses the curious variations of incidence of agranulocytosis caused by amidopyrine, which he considers to be related to the total consumption of this drug among the population. Palmer (1952) found that after B.C.G. vaccination Danish children showed strong positive tuberculin reaction; in Egypt, the size of the reaction was one-third of that measured in Denmark; in Greece, the size was somewhere between that of the two other countries. In a series of investigations on the effects of various factors on the allergic potency of the B.C.G. vaccine, he showed that the exposure to sunlight of the vaccine played an important part in the size of the reaction to tuberculin, independently of the number of living B.C.G. organisms present. Palmer suggested that variation of sensitivity in the children of different racial groups may play a part in their responses to B.C.G., but had not yet completed investigations on this point.

All the available evidence suggests that several factors are involved in producing allergic reactions, and much more knowledge is needed to assess this problem. Discombe's suggestion that a special committee should collect evidence on drugs causing injurious side-effects with a view to submitting representations and recommendations to the Poisons Board should be strongly supported.—I am, etc.,

Carshalton, Surrey. W. N. ROGERS.

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Anatomical Nomenclature

SIR,—It is with relief that one reads Professor T. B. Johnston's letter (July 5, p. 41) informing us that an agreed international nomenclature is to be established. While congratulating him on the active part he is playing in producing order out of chaos, I would warn him against the optimism of his last paragraph. It is true that "Poupart's ligament" has been forgotten, but "musculo-spiral nerve and dorsal vertebrae" persist in medical and surgical textbooks, radiological reports, and surgical discussions. Professor Johnston must carry his lance into the clinical field.—I am, etc.,

London, W.1. A. H. DOUTHWAITE.

Osler Memorial Tablet

SIR,—After attending the summer meeting in Oxford last month of the Paediatric Section of the Royal Society of Medicine, with cases and demonstrations in the Osler Lecture Theatre and tea in Osler House garden, one naturally visited the Oslers' old home, "The Open Arms," 13, Norham Gardens, to pay tribute to the memory of one of the greatest clinicians of all time. Sir, imagine one's surprise to find, pinned to the front door, a notice: "The Bureau of Statistics has moved to other premises." The spacious and once beautiful house was empty and in disrepair, and the huge garden a wilderness, overrun with weeds.

It makes one sad to think that this once famous house bears no tablet commemorating the fact that Osler once lived there and, in his will, bequeathed it to his own beloved college, Christ Church, as a suggested home for future regius professors of medicine at Oxford. May I, Sir, suggest that a fund be opened at once to erect such a tablet, the balance of the proceeds from which to go towards some worthy cause such as the committee in charge of its distribution might think fit? The council of the Osler Club of London, jointly with the council of the Osler Society of Oxford, would seem to me to be the appropriate body to put this suggestion into effect; and I appeal to the profession in Great Britain, the United States of America, and Canada to give it their whole-hearted support.—I am, etc.,

London, W.5. L. CARLYLE LYON,
Assistant Honorary Secretary,
Osler Club of London.

College of General Practice

SIR,—As a new apostle of a century-old idea, Dr. John Hunt (June 28, p. 1410) proves himself convinced of his mission, yet graciously devoid of dogmatism. He shows the utmost deference to the comity of existing medical institutions. Already, too, he has the Rt. Hon. Henry Willink sponsoring the revival, as chairman of the steering committee. Are we in for squalls?

Dr. Hunt addresses himself at some length to the mooted title. "What's in a name?" we may rejoin, adding, "It's what it does that counts." But, at the outset, this wary advocate wants his venture to escape the odium of a wrong label alienating the support that he solicits. He passes on to the possible activities of the College.

Yes, an H.Q. by all means, for it is as vital as the nucleus to the cell. Specially commendable is the early consideration he gives to improving the students' clinical education.

But surely it is the up-grading of practice in the public regard that is the mainspring underlying this revival movement. Are we losing caste in society? During the last decade or two an uneasy feeling on this admittedly rather intangible aspect of practice has grown into a professional concern—this, and its corollary, the influence of status on the efficacy of doctoring. Nothing less than the soul of medicine is at the stake. Does the fire brook delay?

A youngster, taken with acute osteomyelitis, will scarcely appreciate a daily visitor feeling his pulse and, with sympathetic mien, speaking tender words and advice. But give him a shot of penicillin to his bottom and he will soon be greeting your return with a smile. So with a young man, possibly a father, smitten with a dolorous carbuncle of kidney. This is trenchant truth, yet for every one of such there will be scores seeking succour for maladies lacking spectacular cures. What valuable help do we dispense to them? There comes in the art of medicine, which is being ousted by the prodigies of science, and, losing this, we lose caste.

The master of the art is the G.P., daily surrounded by the grim realities, who earned in our profession the coveted title of guide, philosopher, and friend. His armamentarium includes a word of comfort and cheer, an understanding of the unvoiced dreads that may be sapping the morale of a patient—loss of livelihood, anxiety for the children, the collapse of a precious scheme, the prospect of incurable pain. Indeed, the young man with his kidney trouble may be much in need of a reassuring word about getting back to work.

This factor in doctoring counts for very much with humanity, and is not acquired by study but caught by seeing it in action and day after day, which brings home to young folk how greatly patients appreciate the uplift that the doctor's visit may mean. A few months with the ace of exponents—an experienced G.P. gifted with a little innate pedagogy, perhaps—is the training medium *par excellence*. I hope the steering committee may include in its deliberations the possible creation of a cadre of G.P. pedagogy.—I am, etc.,

Bristol. A. WILFRID ADAMS.

Improving General Practice

SIR,—In the *Journal* of May 10 (p. 1030) I read with great pleasure the letter of my respected colleague, Dr. Desmond MacManus (who is a little senior to me, for I am a general practitioner with 30 years' experience), which comments on the address of Sir Cecil Wakeley on "Clinical Research in the National Health Service" (April 26, p. 917). I would like to declare my agreement, naturally enough, with Sir Cecil's address and also with Dr. MacManus's addition. It is very true that "clinical research is a painstaking investigation of individuals in the course of treating and caring for patients" and "that the essence of clinical research is that it is carried out by a clinician, be he general practitioner or specialist." It is also true that the general practitioner, who