pital as a day centre, but financed from hospital revenue.

In a paper by us and C. M. Hyland³ the case was put that a day ward should not be provided by the hospital service to make up for the deficiencies of the welfare services, but should highlight these deficiencies so that they can be remedied. De Martino⁴ stressed that as long as the finance of the National Health Service is divided into hospital, general practitioner, and local authority services, it is essential that the hospital service should spend its money only to perform a hospital function.

We wish to draw the attention of those in the specialty of geriatric medicine to the fallacious reasoning and inherent dangers of the Department of Health's current method of financing day hospital running costs, which will penalize the smaller and busier day hospital with a high turnover at the expense of the larger day centre type of day hospital.—We are, etc.,

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- ¹ Brocklehurst, J. C., *The Geriatric Day Hospital*, London, King Edward Fund for London, 1970.
- ² Andrews, J., and Joines, D., *Report of an Investigation into the Costs of the West Middlesex and Durham Day Hospitals*, 1965, unpublished.
- ³ Andrews, J., Fairley, A., and Hyland, M., *Journal of the American Geriatrics Society*, 1970, **18**, 378.
- ⁴ De Martino, J., *Medical World*, 1968, **106**, No. 1, p. 18; No. 2, p. 16.

Immunosuppressive Drugs in Rheumatoid Arthritis

SIR,—The place of so-called immunosuppressive agents in the treatment of rheumatoid arthritis and similar diseases is now one of the most important questions in clinical immunology. Controlled trials have shown definite benefit in rheumatoid arthritis. Thus, Mason and colleagues¹ using azathioprine in steroid-treated, late rheumatoid arthritis and a committee of the American Rheumatism Association² using cyclophosphamide in rheumatoid arthritis both obtained favourable results. Arising from these results, a statistically controlled study of cyclophosphamide, azathioprine, and sodium aureothiomallate in the treatment of the earlier stages of rheumatoid arthritis is under way. It seems important to find out if these immunosuppressive drugs are able to prevent the development of the morbid anatomical changes of rheumatoid arthritis when used in good time. The criteria of improvement, except the criteria of radiological improvement, are the same as those by which anti-inflammatory drugs are measured. Since at least one of the immunosuppressive drugs, namely 6-mercaptopurine, has been shown to have aspirin-like action in experimental inflammation in animals³ it seemed essential to rule out aspirin-like action in man. This question had to be answered to interpret any possible improvement in the criteria studied in the longer term trial.

Fourteen inpatients with definite or classical rheumatoid arthritis involving the proximal interphalangeal joints took part. They had not had gold, steroid, or anti-malarial treatment. Haematological indices were followed carefully. Measurements of

grip strength, total proximal interphalangeal joint girth, and assessments of morning stiffness were made by standard methods⁴ before 9.30 a.m. on each assessment day. All patients were treated with placebo for one week. This was to establish a stable base for comparison and to allow for the non-specific improvement which often follows the admission of patients to hospital. After this, patients were allocated to one of the six possible treatment sequences of the three active drugs, aloxiprin (aluminium polyoxyaspirin), azathioprine, and cyclophosphamide. Spacing placebo periods of two to five days separated the five or seven day periods on active drug to eliminate any possible carry-over from one drug to another. Azathioprine was given at a dose of 2.5 mg/kg body weight, cyclophosphamide 1.5 mg/kg, and aloxiprin at 6 g per day. We compared the mean readings at the end of the initial period of placebo treatment with those at the end of each period of active drug treatment.

Grip strength.—There were no differences between placebo, cyclophosphamide, and azathioprine. T-tests showed a small increase ($p=0.1$) with aloxiprin.

Joint Girth.—The total period of study was associated with a reduction in joint girth. Most of this reduction occurred in the initial period of placebo treatment. Significant further reduction ($p=0.05$) occurred with aloxiprin but not with azathioprine or cyclophosphamide.

Morning Stiffness.—Assessments gave no reliable data.

Subjective Assessment.—The patient (and sometimes her nurses) noted improvement in well-being and joint symptoms on aloxiprin and deterioration on change to placebo or immunosuppressive drugs in most instances.

Thus, in this double-blind, short-term, crossover trial of azathioprine, cyclophosphamide, and aloxiprin in 14 inpatients with rheumatoid arthritis aloxiprin caused the expected improvement, the other drugs little or none. We conclude that any benefits shown by immunosuppressive drugs in long-term treatment of rheumatoid arthritis are unlikely to be a reflection of an anti-inflammatory "aspirin-like" action, even though such actions have been demonstrated in experimental animals.—We are, etc.,

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- ¹ Mason, M., Currey, H. L. F., Barnes, C. G., Dunne, J. F., Hazleman, B. L., and Strickland, I. D., *British Medical Journal*, 1969, **1**, 420.
- ² American Rheumatism Association, *New England Journal of Medicine*, 1970, **283**, 883.
- ³ Page, A. R., Condie, R. M., and Good, R. A., *American Journal of Pathology*, 1962, **40**, 519.
- ⁴ Boardman, P. L., and Hart, F. D., *British Medical Journal*, 1967, **4**, 264.

Solubility Test for Hb S

SIR,—A rapid and highly reliable screening test for the presence of Hb S in whole blood is available as a commercial kit.¹ Exactly comparable results can be obtained by the following method, which is based on the original observations of Itano.²

A 2.24M buffer at pH 6.7 is made as follows:

K₂HPO₄, 220.3 g; KH₂PO₄, 132.45 g; saponin 5 g; water to 1,000 ml. Put 10 mg of sodium dithionite (Na₂S₂O₄) into a small test-tube (exact measurement is not required after the appearance of 10 mg has been appreciated). Add 1 ml of buffer and mix. Introduce 0.02 ml of whole blood (from a Hb pipette) and mix. Normal blood produces a clear purplish-red solution after 3–5 min; AS, SC, and SS bloods give a cloudy precipitate. The cost of the chemicals to provide 1,000 tests is about 8s.

There are circumstances in which it might be advantageous to distinguish AS from SS blood. This can be done by the use of a 1.8M buffer, (conveniently prepared from the preceding one by adding 2 ml of water to 8 ml buffer, which gives a 1.79M buffer). When a buffer of this strength is used in the test AS blood is soluble, while SS blood gives a precipitate; the reading is not quite as easy as with the standard test but definite enough to act as a preliminary screen. If the suspected SS blood is known to have a low Hb level, it is advisable to add two 0.02 ml amounts in the test. It is also wise to include known positive and negative controls.

Fuller details will be presented later.³—I am, etc.,

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- ¹ Ballard, M. S., Radcliff, E., Sakthadeo, S., and Schorr, J. B., *Journal of Pediatrics*, 1970, **76**, 117.
- ² Itano, H. A., *Archives of Biochemistry and Biophysics*, 1953, **47**, 148.
- ³ Cook, A., and Raper, A. B., *in press*.

Obesity and Respiratory Infection in Children

SIR,—May I correct the statement made by Dr. V. V. Tracey and his colleagues (2 January, p. 16), in which they state that I used the 70th weight percentile as a criterion of obesity in infants. In the paper to which they refer calculations were made using the accepted definition of obesity as "a weight which exceeds the mean weight for height and sex by 20% or more"; in terms of percentiles this would be equivalent to the 90th percentile or greater, the figure used by Dr. Tracey and colleagues, who chose the alternative criterion of obesity.

I am also surprised that they should think that there is little published work to confirm or disprove the clinical impression of the relationship between obesity in infants and respiratory infection. May I briefly summarize the findings of studies in this area?¹

A retrospective study of 345 infants admitted to hospital with lower respiratory infection showed that infants who were obese required more antispasmodic drug therapy, but were less severely affected than those who were of average weight. Obese infants comprised 30% of the number of infants admitted with lower respiratory infection. A prospective study comprised the study of 200 infants at intervals between 1 month and 1 year old. Ninety-five per cent of infants were examined at home; data were recorded on each visit of the weight, height, subcutaneous fat thickness, respiratory infections, and feeding. The main findings were: of the 200 infants 176 (88%) had respiratory infections, 41 (20%) had lower respiratory infections. There were 459 infections in the 200 infants, of which 62 (13.5%) were lower respiratory. Male infants showed a significant increase in lower respiratory infections compared with females ($P<0.01$).

There was a significant increase in the proportion of infants with infection who weighed 2.5 kg or less at birth, compared with those over

2.5 kg ($P<0.01$). With increasing birth weight there was a decrease in the proportion of infants with infection. In each birth-weight group the mean gain in weight (from birth to 1 year old), and the mean thickness of the subcutaneous fat (from 1 month to 1 year old) was greater in infants with infection than in those without infection. This was most noticeable in infants of low birth weight.

Infants whose weight exceeded the mean weight for height and sex by 20% or more had a significant increase in lower respiratory infections compared with those of near normal weight ($P<0.001$). Infants whose mean thickness of subcutaneous fat was increased had a significant increase in lower respiratory infections ($P<0.05$). The coefficient of correlation between the thickness of the subcutaneous fat and length was significant ($r=-0.5$). At the same mean thickness of fat infants whose length was below the 25th percentile had more infection than those whose length exceeded the 97th percentile. Infants who were fully breast-fed had fewer lower respiratory infections than those who were not fully breast-fed ($P<0.05$). Infants whose solids were introduced under 9 weeks old had a significant increase in lower respiratory infection. ($P<0.05$).

Forty-one (20%) infants were started on solids under 4 weeks old, some infants started solids in the first week of life; one may speculate if those concerned with the health of the community have ensured that mothers are aware of the dangers of over-feeding their infants. Personally, I cannot see any advantage to the mother or the infant in starting solids early.—I am, etc.,

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Bakewell, Derbyshire

¹ Hutchinson-Smith, B., *Medical Officer*, 1970, 123, 257.

Primary Coliform Peritonitis

SIR,—By coincidence we had in the ward a patient with peritonitis without intraperitoneal cause at the time of Mr. B. T. Jackson's report (26 December, p. 786).

A 72-year-old woman was admitted with swelling of the leg thought to be due to a femoral vein thrombosis. Three days later she became confused and febrile and complained that she could not see. The lower abdomen was extremely tender and a mass could be felt in the pelvis, which seemed to be a distended bladder. Because of rapid deterioration in her general condition and what was thought to be peritonitis, laparotomy was undertaken by Mr. P. Gilroy Bevan. Generalized peritonitis with pockets of pus was indeed present, but a careful search failed to reveal a perforated viscus nor any inflammatory focus in the peritoneal cavity. The main findings of significance were enlarged, hard, and fixed kidneys, indicating severe acute pyelonephritis, and a bladder containing a litre of blood-stained pus so viscous that firm manual pressure was needed to express it. The abdomen was closed and treatment commenced with gentamycin sulphate and hydrocortisone. The patient made an uninterrupted recovery.

Proteus mirabilis was cultured from specimens of blood and urine, and the peritonitis might have been a blood-borne infection, part of the Gram-negative septicæmia consequent on a urinary tract infection. Direct spread from the genitourinary tract could not be ruled out, however; and the patient described by Mr. Jackson was treated before her death with antibiotics, which could have eradicated a focus of infection.—We are, etc.,

S. JAIN

M. J. LEE

V. MELIKIAN

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The Smoking Disease

SIR,—Your leading article on this subject (9 January, p. 61) exposes our dismal failure as a profession to influence the smoking habits of the public. A short snippet from the leader has appeared in the popular press and on television news, the shares of the leading manufacturers have lost a penny or two for a few days, a handful of the stronger minded have given up temporarily, fewer permanently, and in a few weeks all will be forgotten and "normal" smoking habits will return. A new generation of even younger addicts will be taking over.

Complacent we have been and satisfied to find that many have given up, especially doctors, and to say further that "information is not enough" while our hooked patients tell us daily "you have to die of something" or "it's the only pleasure I have."

Surely it is time for the profession and the B.M.A. as leaders of it to take the initiative in this important matter of health education and to press for action at Westminster in view of this latest report. Or must this carnage continue uninhibited for a further 20 years, producing a further million deaths, until the publication of *Smoking and Health* (No. 3)—I am, etc.,

G. H. WILLIAMSON

Cheltenham, Glos

Relative Hazards in Smoking

SIR,—By its publication of *Smoking and Health Now*¹ the Royal College of Physicians has rendered valuable service. Once again the College has drawn the community's attention to the increasing toll of suffering and premature death (not to speak of economic loss) from lung cancer, diseases of the heart and circulatory system, bronchitis, and emphysema attributable to smoking. Most of the College's recommendations will be found to be acceptable by the man in the street. Many of them have been advocated for years past by the National Society of Non-Smokers.

With due deference to its distinguished authors, I have two main criticisms to make of the report. Firstly, from comments in the national press resulting from variations in the report in figures, estimates, and forecasts, there has been a tendency to minimize the mortality attributable to smoking. To cite an example: an article in a leading Sunday newspaper reads: "There is something faintly indecent about wondering whether the country can afford to get rid of a drug which kills 27,500 people a year."² There are grounds for believing that the annual toll of deaths in England and Wales, mostly attributable to smoking, from lung cancer, heart and circulatory diseases, bronchitis, and emphysema may soon pass the 100,000 mark.

Secondly, in many personal contacts, it is obvious that the average reader has been left with the impression that health hazards from pipe and cigar smoking are negligible. This impression, sad to say, was reinforced by a reply to a question put on 2 February by Sir Brandon Rhys Williams to Sir Keith Joseph who said: "The Royal College of Physicians' report came down categorically on the side of the view that cigar and pipe smoking is less dangerous than cigarette

smoking." The Secretary of State corrected this a few moments later in a reply to Sir Gerald Nabarro by saying, in part: "I must record that Swiss and German research shows cigar and pipe smoking is as dangerous as cigarette smoking."³ The report actually said: "But in Swiss and German retrospective surveys, the risk of lung cancer appeared to be greater among pipe and cigar smokers than among cigarette smokers." The italics are mine.

Much more research is needed on this particular aspect of the smoking problem before an opinion can be reached as regards relative dangers. What is certain, and this is mentioned in the report, is that condensates from cigar and pipe smoke contain more polycyclic hydrocarbons and produce cancer more readily on animal skin than condensates from an equal amount of smoke from cigarette tobacco. Furthermore, not only do some pipe and cigar smokers inhale smoke, but all absorb nicotine with consequential harmful effects on circulatory and nervous systems. A heartening statement in the report is that approximately 80% of doctors no longer smoke.

Parents, school teachers, and religious leaders share with doctors a heavy burden of responsibility (by example rather than by precept) in cooperating to the full with Government, local authorities, and voluntary agencies in the antismoking campaign, particularly where children and teenagers are concerned.—I am, etc.,

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¹ Royal College of Physicians of London, *Smoking and Health Now*. London, Pitman, 1971.

² *The Observer*, 10 January, 1971, p. 11.

³ *Hansard*, 2 February 1971, p. 1435.

Y-Fluorescence of Interphase Nuclei

SIR,—In our paper (16 January, p. 138), because of the complexity of the tables, we purposely omitted reference to numbers of cells counted in the normal controls and the individual cases, though, in our conclusions, we made recommendations as to the numbers that should be studied for discrimination. As the omission might be irksome to some, and detailed specification a burden to both editor and reader, may we state that in no instance did we analyse fewer than 50 cells, and generally scored at least 100 cells per slide.

We also take the opportunity of advising a change in the staining technique described in the paper. In order to increase the bench life of quinacrine mustard solution, it is now dissolved in absolute methanol (or ethanol) at 0.5 mg/ml. The stain solution is mixed immediately before use with an equal volume of double strength SSC solution (35 g/litre sodium chloride, 17.6 g/litre sodium citrate). This solution is also used as the initial wash, rinse, and mountant as described previously. This increases the contrast of the brightly fluorescing areas of the interphase nuclei and enhances the bands of metaphase chromosomes.—We are, etc.,

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