phrenia had the following blood picture: Hb 150% (cyanmethaemoglobin method); P.C.V. 70%; W.B.C. 16,800/mm³ (neutrophils 90%); platelets 450,000/mm³. There was a good response to venesection and ³²P. In March 1972, when severely paranoid, he became unsteady on his feet. Examination of the central nervous system was normal: the Hb was 121%; P.V.C. 68%; platelets 267,000/mm³; leucocyte alkaline phosphatase score 115 per 100 neutrophils (normal 30-100). Soon after venesection numbness developed down the left side: it improved in a few days. Exaggerated left lower limb reflexes and an equivocal left plantar response were later apparent. By June the left lower limb was spastic with ankle clonus and an extensor plantar response, the left arm was weak, and there was urinary incontinence. A cerebral tumour was thought possibly to be causing a progressive hemiplegia. Chest and skull radiographs and a brain scan were normal. After increasing loss of consciousness he died in July.

Postmortem examination showed no evidence of neoplastic disease nor any endocrine, respiratory, cardiovascular, or renal abnormality associated with a secondary polycythaemia. The spleen weighed 270 g and histological examination showed only venous congestion. The bone marrow was hyperplastic and all elements were increased in relatively normal proportions. The brain was generally oedematous with recent thrombotic occlusion of the superior cerebral veins on both sides and a patent superior sagittal sinus. Cut sections showed petechial haemorrhages within the white matter of the right and left frontal and parietal lobes. Histologically the appearances were of early venous occlusion. At the right frontal and left occipital poles were old infarcts with cyst formation typical of lesions from arterial occlusion. There was less cerebral arteriosclerosis than might have been expected in a man of his age.

We emphasize again that the clinical picture as it progressed over several months resembled a slowly-growing cerebral tumour. We wish to thank Dr. J. E. Ffoulkes-Edwards for permission to report this case.—We are, etc.,

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Malignant Lymphoma and Acute S.L.E.

SIR,—The interesting report by Drs. A. G. Cudworth and A. Ellis (29 July, p. 291) of a case of malignant lymphoma and acute systemic lupus erythematosus prompts me to record that I have seen two cases of Hodgkin's disease with clearly defined lupus erythematosus syndromes—one in a man aged 24 and the other in a man aged 41. We have also seen a number of other malignant reticuloses which were preceded by various conditions of an allergic or auto-immune nature, including arteritis.¹ In most cases the connective tissue disorder of essentially non-malignant character has preceded the irreversible, or malignant, lymphoma, but nearly all our cases of reticuloses, including chronic lymphocytic leukaemia, lymphosarcoma, and reticulosarcoma, and the paraproteinaemias, have had histories of recurrent or chronic inflammatory conditions of various origin² acting as a stimulus to the reticuloendothelial system. In addition, high antibody titres against toxoplasma were found in approximately 90% of these patients (compared with an incidence of 56% at the most in controls matched for age³).

Such a stimulus, be it chemical, viral, bacterial, protozoal, or allergic, will lead to

a reactive proliferation of the target tissue, with or without the production of antibodies. The number of mitoses in a proliferating tissue is increased and with it the number of spontaneous mutations will rise. Mutations may also be promoted by some of the drugs given or even by the stimulating agent itself. Though the majority of mutants have no chance of survival, with an increased total number the number of survivors will also increase. Some of these mutants will multiply and grow to become an abnormal cell clone.—I am, etc.,

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Lumbar Disc Problems

SIR,—I am surprised that one of the calibre of Mr. A. H. G. Murley should expect us to accept his beliefs (26 August, p. 529) in this scientific age when nothing is acceptable unless it can be reasonably proved by adequate demonstration or experiment. In the case of disc lesions this has long since and very adequately been done by James Cyriax¹ and also by many others who have contributed adequate evidence to show that disc lesions are indeed commonplace rather than rarities.

Whether damage to the posterior joints predisposes to disc prolapse is another question. Cyriax has proved that these joints are rarely capable of being the cause of the pain. It is a great misfortune that people I have come across who have had their back-ache cured after more than 20 years either by manipulation or traction should have had to suffer so long without effective treatment simply because they had been told that they were suffering from chronic muscle or joint sprains. Finally, I am astonished to see Mr. Murley confess that he manipulates sprains. I will certainly avoid him when I sprain my ankle, but when my knee locks owing to my torn cartilage I should be delighted to visit him for manipulation, which is the appropriate treatment for an internal derangement of a joint, be it meniscus or disc.—I am, etc.,

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Sheerness, Kent

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Undergraduate Curriculum

SIR,—The symposium on the undergraduate curriculum as a preparation for general practice at the B.M.A.'s Annual Meeting (5 August, p. 339) was disappointing, its title unfortunate. I hope medical schools, old and new, will not alter their curricula to be preparations for a particular discipline but continue to concentrate on the undergraduate's education, especially as he has

spent his years in the sixth form specializing in two or three relatively narrow subjects.¹ If we take education to be the means by which new knowledge is discovered and new interpretations put on established ideas, and it must produce the urge to question pre-suppositions, then I fully support the introduction of the undergraduate to the discipline of general practice. The student will have the opportunity of gaining a further understanding of human behaviour and to observe the many variations by the patient in the presentation of his fears at the time of first contact (from the request for a tonic to the self-diagnosis). Such experience must surely benefit the student whatever his future. It is neither appropriate nor advisable to consider this as a preparation for future general practitioners, any more than his study of pathology as a preparation for future pathologists.

Underground education completed, his continuing education will be modified to include an element of training. At some stage he will opt for the discipline of general practice. His training now will need the same guidance and intensity as for other disciplines.

New departments of general practice are springing up in our medical schools and pressures are exerted in those schools, at present without a chair, to keep abreast of the times and up with the Joneses. I agree with Professor P. B. Beeson that their concern with undergraduate education, though important, will be small. Postgraduate training will be a formidable challenge in the coming years. No mention has been made of the need for research in general practice, what we are trying to do, how best to achieve it, and the better use of present and future facilities.

I have no doubt of the need for such departments in our medical schools. The understanding of their function is obviously urgent.—I am, etc.,

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- 1 James of Rusholme, Lord, *Proceedings of Royal Society of Medicine*, 1971, 64, 441.

Dysphagia and Sarcoid Granulomas

SIR,—In the unusual patient described by Dr. R. J. Davies (2 September, p. 564), who had had sarcoidosis for 14 years, the Tensilon test was negative but the muscle atrophy around the lesions in the oesophagus was reminiscent of that seen in myasthenia gravis.

Four reported cases of myasthenia had sarcoidosis,¹ and at least 30 more had giant-cell myocarditis, which possibly may arise from subclinical sarcoidosis.² Myocardial sarcoidosis is more common than was realized,³ particularly as the infiltration in the late stages cannot be identified with any certainty. Possibly idiopathic cases of cardiomyopathy may begin as sarcoidosis. Probably autoimmunity is a factor in this type of heart disease⁴ as well as in generalized sarcoidosis.⁵ Eosinophilia is sometimes seen in the later condition⁶ and random eosinophile counts of 7%, 8%, and 10% were found in three of my five patients with unexplained cardiomyopathies. Even when no initial symptoms or signs occur the long-term effects of sarcoidosis can be severe. Much time has been spent defining the

disease, but the late changes are rarely described.

Giant-cell granulomas were seen in the retro-orbital tissues of several of the seven reported cases of sarcoidosis with exophthalmos⁷ and muscle atrophy, fatty deposits, lymphorrhages, and fibrosis were found around the orbit of patients with ophthalmic Graves's disease.⁸ Professor E. J. Field and Mr. E. A. Caspary,⁹ using their macrophage electrophoretic migration (M.E.M.) test, found the immunopathology of sarcoidosis in a patient referred to me with exophthalmos, hyperthyroidism, and myasthenia.¹⁰ Their M.E.M. test was negative, however, in another patient of mine who had had myasthenia without thyroid disease for 27 years.¹⁰ In this case the T-lymphocytes may originally have been sensitized but, if so, these cells are now dead. The patient possibly now has acquired immune deficiency, because she developed a spontaneous rectovaginal fistula last year. The results of the M.E.M. tests were more selective in Professor Field's cancer cases,¹¹ but an association may perhaps exist between neoplasms and sarcoidosis.¹² Both sarcoid and cancer cases may show either raised or deficient immune responses. The connexion between neoplasms and immunity therefore is likely to be indirect. Cancer and, for instance, the hyperthyroidism found in sarcoid thyroiditis appear to be by-products of raised immunity. The primary cause of both may be an infectious agent. Cell division normally is strictly controlled, but high levels of immunity sometimes appear to overcome this form of inhibition and spontaneous tumours develop. Release of the control apparently allows the cells to proliferate wantonly. Whether or not natural defensive immunity plays a primary part in limiting the spread of cancer remains an open question.—I am, etc.,

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Chilworth, Surrey

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- 10 Field, E. J., and Caspary, E. A. Personal communication.
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- 12 MacGregor, G. A., *British Medical Journal*, 1972, 1, 375.

Aflatoxins and Reye's Disease

SIR,—The syndrome of encephalopathy and fatty degeneration of the viscera (Reye's syndrome¹) has been reported from many countries as a cause of death or serious illness in young children. The aetiology remains unknown.² One of us³ has suggested that contamination of foods by aflatoxins, the toxic products of strains of *Aspergillus flavus*, was a possible cause. This suggestion was based on the strong suspicion from pathological appearances that the liver lesions were toxic in origin, the similarity of the

lesions to those of experimental aflatoxin poisoning, the special sensitivity of young animals to aflatoxins, and the limited possibilities of exposure of some affected children to toxins except through foods. Recently circumstantial evidence has been presented that a similar syndrome occurring frequently in northern Thailand might be caused by aflatoxins from fungal-contaminated rice.^{4,5} This evidence includes the identification of aflatoxins in the organs of affected children.⁶ Aflatoxins have been sought in the tissues of two children dying in Auckland recently.

Case 1.—A 22-month-old Polynesian boy whose illness was typical of the syndrome as previously defined.³ There was a prodromal illness, drowsiness progressing to coma and to death in a decerebrate state, raised serum transaminase levels, and typically diffuse and uniformly severe fatty changes in the liver at necropsy.

Case 2.—An 8-month-old Caucasian girl was investigated because, as in Case 1 of a previous report,³ the association of severe bile duct proliferation with diffuse fatty change in her liver was considered consistent with the chronic effects of such a toxin. This child had thrived until 5 months' old when she began vomiting and there was progressive weight loss and lethargy. Hepatomegaly, an elevated serum transaminase, and episodic hypocalcaemia were noted before her death in liver failure. A wide range of negative investigations included studies for inborn errors of metabolism and heavy metal poisoning.

Assay Methods.—Liver tissue in approximately 10-g samples was extracted by the method of Eppley.⁷ Extracts were chromatographed on silica gel (Merck No. 5562/0001) and developed in chloroform-ethanol 98:2. Visual comparisons were made under ultraviolet light with an aflatoxin B₁ standard (Markov Chemicals Ltd., Israel) and two mixed aflatoxin standards (M.R.C. "Porton 41," and U.S. Dept. of Agriculture "SA 14/4"). The derivatives-formation method⁸ was used for the further identification of fluorescing materials.

Results.—Four separate extractions were made of liver tissue from Case 1 and three extractions of the liver of Case 2. Tissue had been stored at -4°C for from 3 weeks to 4 months before study. All seven extracts contained a blue fluorescing material with the same R_f as aflatoxin B₁ and, variably, a green fluorescing material with R_f corresponding to aflatoxin G₁. Estimates of the former material as aflatoxin B₁ in each extract ranged from 5 to 50 µg/kg wet weight, but the pooled extracts contained insufficient material for further identification by derivatives formation. All fluorescing materials extracted from 10 control livers differed in R_f from aflatoxin standards and non-identity was confirmed by derivatives formation.

Though inconclusive, these results encourage a further search for aflatoxin-like materials in the syndrome of encephalopathy and fatty degeneration of the viscera. All reported cases of Reye's syndrome may not have had a single aetiology, particularly those in which the liver pathology has not conformed to the criteria laid down in earlier reports.^{1,3} A search for aflatoxins is indicated where, as in the cases of Reye's disease recorded in Sydney between 1950 and 1963¹ and in Auckland between 1959 and 1966,³ epidemiological features favour a new and presumably single environmental factor.⁹

The findings in Case 2 support the original hypothesis of an aetiological link between a chronic liver disease and the acute syndrome, but if the material in the liver was aflatoxin then this has persisted longer than has been reported experimentally.¹⁰ It is of interest but probably coincidental that Case 1 was from an immigrant family with, for

New Zealand, a large daily consumption of rice, and that the symptoms of Case 2 began after the introduction of solid foods of which "baby-rice" was the first given. Rice in New Zealand is mostly imported from Australia and the United States with about 10% coming from Thailand in 1971.

This work was supported by a grant from the Medical Research Council of New Zealand.—We are, etc.,

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Future of the B.M.A.

SIR,—The following comments on the Council's supplementary report on Sir Paul Chambers's report (*Supplement*, 16 September, p. 168) may be of interest.

Autonomy by its psychological impact promotes selfish, sectional interests and creates a feeling of "separateness" which is neither realistic nor in accord with the "brotherhood" concept of the Declaration of Geneva. This contrasts with the terms delegated authority and subcommittee, which impart a feeling of "belonging" or "cohesion." Autonomy is infectious and begets autonomy, dividing the profession into more and more splinter groups, thereby dissipating the strength and influence of the profession as a whole. There is no doubt that autonomy weakens the influence and authority of the B.M.A., promotes fixed attitudes in craft committees before there is time for consultation between them, delays vital decisions, causes duplication of work, and incurs additional unnecessary expense.

It is unrealistic and unsound in a health service which will be administratively and functionally integrated to attempt to promote "craft autonomy." General practitioners and hospital doctors cannot achieve functional integration unless they trust one another and learn to work together. Therefore while the need for B.M.A. craft subcommittees will remain the need for autonomy will diminish and finally cease. Sir Paul Chambers's unbiased criticism of the B.M.A. organization is fully justified, and while his report contains minor inaccuracies and the proposed solutions are not entirely acceptable to all B.M.A. members criticism has been exaggerated. His recommendations merit much more consideration in depth than they have received and more thought requires to be given by his critics to other ways of achieving his objective, with which no loyal member of the B.M.A. can be in disagreement. In doing