wrote: ". . . all miners die. The only relevant issue is whether there are many miners in the area with pneumoconiosis who are not known to the Pneumoconiosis Medical Panel."

We accept that the Pneumoconiosis Medical Panel will be aware of the majority of miners with pneumoconiosis, but this is not the only relevant issue. The authors seem still not to appreciate that cases included in an unselected postmortem series are sampled from the general population at rates proportional to their risks of dying. If disability in life increases the risk of death, the postmortem series will include proportionally more of the disabled; if there are two independent sources of disability in life, for example, a low FEV and/or emphysema, the postmortem series will include disproportionately more of those who suffered from both sources in life. The question then is whether those miners who died are representative, or whether they died because of some aspect of their state of health which thereby makes them unrepresentative. The latter is evidently more likely.

The broad conclusions Lyons *et al.* reach are threefold and we should like to comment on two of them. The first conclusion was: "Coal workers' pneumoconiosis usually caused progressive impairment of ventilation, which was not related to radiological category in the simple form of the disease." The authors do not explain why they are justified in speaking of "causation" in this conclusion, when it is evident that the most that could be observed was association. No care has been taken to exclude other explanations for the association. The conclusion is based on their Fig. 1 in which the average ventilatory capacities of their subjects, measured within four years of their deaths, are plotted in relation to normal values given by Cotes.[1] Cotes did not produce normal values for subjects destined to die within four years; it is surely likely that, on average, the figures for such subjects would show evidence of impairment of function. Certainly it seems impossible to deduce that the observed figures represent impairment causally related to pneumoconiosis.

Moreover the average FEV of those with category 2 or 3 pneumoconiosis was 0·8 l. below expected, of those with category 0 was 1·25 l. below expected, while those with category 1 were intermediate. So far from being unrelated to category the impairment, if it can be relied on, appears inversely related to category, as was found by Carpenter *et al.*[2] in their earlier sample of Panel cases but not in the general population. The authors appear to attribute this trend to selection by respiratory symptoms, as did Carpenter *et al.* Since they then have no reliable figures for the separate categories of simple pneumoconiosis they cannot deduce that impairment of ventilation is unrelated to the radiological category.

The second conclusion was: "The presence of emphysema accompanying simple pneumoconiosis was a more important factor in determining the impairment of ventilation than the radiological category." This conclusion is based on their Fig. 2. The possible bias of a similar figure in their earlier paper due to the selective nature of the sample was pointed out (31 October 1970, p. 305), and it was also observed that the figure did not differentiate between cases of simple and complicated pneumoconiosis. This second criticism was apparently met in the latest figure since it was said to include simple pneumoconiosis cases only. However, this statement was later corrected (25 March, p. 812) and the figure pertained to all cases, and not just to those of simple pneumoconiosis. Presumably this correction also implies that the conclusion applies to all cases and not just to cases of simple pneumoconiosis, and we must repeat the earlier criticism that the association between FEV and emphysema in Fig. 2 may be exaggerated both by selection by death and by including cases of progressive massive fibrosis.

The authors wrote (5 December 1970, p. 623) that "There is always possible bias in correlating postmortem material with findings in life, but this is insufficient reason for not pursuing such studies so long as this danger is kept in mind." This does not go far enough; it must be possible to estimate and correct for bias, or at least set limits on its effects, not merely to "keep it in mind" and in practice ignore it.—We are, etc.,

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Interviews for Prospective Students

SIR,—Dr. C. M. Tonks in his "Personal View" (8 April, p. 107) has touched on a subject which interests me greatly—the interview. Having been a university medical officer for 10 years I am more than ever convinced of the value of the interview, and regret that not all prospective students have one before coming up to university, no matter what subject they choose to read.

What it is so important to remember, and what Dr. Tonks seemingly ignores, is that the interview is a two-way affair. Not only does the university find out a bit more about the prospective student, but the student finds out often considerably more about the university. As Dr. Tonks points out, the candidates are often very ignorant about the different universities. Many a student who has put the "university of X" as first choice on his list has rapidly changed his mind after the interview, sensing that for one reason or another he would not fit in or feel happy there. Others who have been accepted without an interview have later regretted it.

As for selection being dependent on the ability to pass the academic hurdles, even if one accepts that this criterion in itself is sufficient (which I don't), how can one tell which candidate will succeed? Proved ability to pass "O" and "A" level exams certainly is no criterion, as has been shown time and time again in one study after another. After all, university is not just an extension of school, in spite of the increasing prevalence to think of it as such.

There is so much change for change's sake in education that we should be very careful to do only what is likely to prove good and useful in changing our educational system. Heaven knows that there is masses to do in improving our medical education (another special interest of mine)—but for heaven's sake let's keep our interviews.—I am, etc.,

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Endocrine and Metabolic Manifestations of Cancer

SIR,—The object of my short review (18 March, p. 735) was to outline for non-specialists the various events that may occur in patients suffering from cancer and which, at first sight, might not appear to be connected with the local lesion. The cause of some of these events we think we understand as due to the secretion of polypeptide hormones by the tumour. These were listed in Table I. Others which as yet have no metabolic cause ascribed to them were listed in Table II. Readers, including Dr. J. G. Azzopardi (8 April, p. 109), who wish for more detailed documentation will find it in a more lengthy review[1] which was mentioned in the references and also in other reviews,[2-4] including one by Azzopardi.[5] The examples of tumours of various organs concerned in the production of the hormonal syndromes mentioned in the Tables were drawn partly from the literature and partly from personal experience. The histological diagnosis of the tumours has been accepted as stated by the original authors. Some may require revision. Williams, Morales, and Horn,[6] for example, have reviewed the histological sections of eight cases of carcinoma of the thyroid reported in the literature as causing "Cushing's syndrome" and rediagnosed five as being medullary rather than papillary in type. Two reported cases were accepted by them as papillary carcinomas with the comment that "this may merely represent a chance association."

The prevalence of these complications in patients with cancer cannot yet be known with accuracy since to my knowledge only two series have been reported. Why Dr. Azzopardi should deem one series (his) to be more accurate than another (mine) is difficult to understand. Azzopardi, Freeman, and Poole[7] reviewed 185 patients with carcinoma of the bronchus. I had concluded that all these patients had come to necropsy as the paper contains the statement "this illustrates the dangers of drawing conclusions (as to histological diagnosis from biopsy or sputum examination) without a thorough necropsy," but apparently I was mistaken. Azzopardi *et al.*[7] found evidence of the secretion of corticotrophin in 0·5% of patients with bronchogenic tumours; Kato, Ferguson, Bennett, and Burford[8] examined 138 cases of oat-cell carcinoma of the bronchus and found an incidence of 3%, whereas I found an incidence of 2% in bronchogenic carcinomas of all cell types. Azzopardi *et al.*[7] found that 6% of patients with bronchogenic carcinoma had hypercalcaemia. Hypercalcaemia due to osteolytic secondaries is far commoner than hypercalcaemia due to the secretion of parathyroid hormone by the tumour; the former cause should not be included within the definition of "hormonal syndromes produced by cancer." Since one-third of all patients with bronchogenic carcinoma have metastases in bone[9] it is probable that many of the cases reported by Azzopardi *et al.*[8] had hypercalcaemia due to the presence of secondary deposits in bone. In my series

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patients with bony secondaries visible on x-ray were excluded.

Mr. M. Keynes (8 April, p. 109) objects to the statement that the production of gastrin by pancreatic tumours cannot be called "ectopic." It is agreed that the non-argyrophil α_1 cells, or δ cells are identical in appearance with gastrin-producing cells of the fundus of the stomach, but have δ cells been proved to secrete gastrin under normal circumstances?

I am fully in sympathy with Mr. Keynes's difficulty with nomenclature, particularly with the use of the term "ectopic," but no really appropriate adjective has yet been suggested; "para-endocrine" seems preferable to "ectopic." The term "Cushing's syndrome" is often employed—for example, by Dr. Azzopardi—to describe the consequences of production of corticotrophin by tumours, but its use in this context is inaccurate as it manifestly is not the syndrome described by Harvey Cushing. The presence of "ectopic" production of corticotrophin by tumours is usually suspected initially by the presence of hypokalaemic alkalosis, which is very uncommon in classical Cushing's syndrome.[10] Again, the majority of cancer patients with corticotrophin production, particularly when due to oat-cell carcinoma of the bronchus, rarely live long enough to develop the physical features typical of classical Cushing's syndrome. The hormonal syndromes are best classified in terms of the hormones they secrete, rather than by eponymous diseases they resemble to a greater or lesser extent.—I am, etc.,

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Cytomegalovirus Oesophagitis

SIR,—Although the protean clinical manifestations of cytomegalovirus in the adult are now well recognized[1] we should like to draw attention to severe ulcerative oesophagitis occurring as a presenting feature.

A 35-year-old fitter was admitted in a cachectic state with a month's history of progressive difficulty and pain on swallowing. A diagnosis of Hodgkin's disease had been established 10 years earlier on cervical lymph node biopsy and subsequently he had received treatment with radiotherapy, steroids, and cytotoxic agents. On examination he was pale, jaundiced, wasted, and febrile. There was no oral moniliasis. He had bilateral pleural effusions and gross leg oedema. The liver and spleen were not palpable.

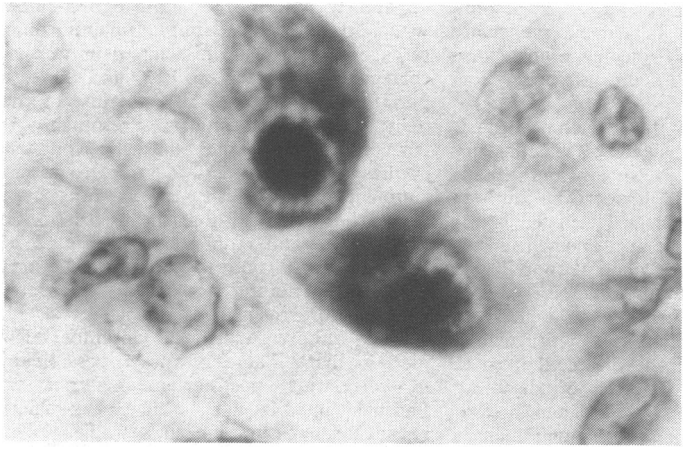

FIG.— Cytomegalic cells in the floor of the oesophageal ulcer (x 1,500).

There were crops of petechiae and subcutaneous nodules over the whole of the trunk. A barium swallow showed gross irregularity of the oesophageal mucosa with three prominent ulcer craters and numerous other tiny ulcerations. The appearances were considered to be highly suspicious of monilial oesophagitis, but there was no improvement with nystatin. His condition continued to deteriorate and he died three weeks later.

The main findings at necropsy included those due to invasive Hodgkin's disease and those attributable to disseminated cytomegalovirus infection. The distal third of the oesophagus and the fundus of the stomach showed confluent elevated white plaques up to 3 cm diameter. Microscopically, the epithelium was denuded and there was a non-specific mononuclear infiltrate in the lamina propria. Large numbers of degenerative cytomegalic cells were present (Fig).

In seriously debilitated patients such as those with advanced malignant disease or those on immunosuppressive therapy opportunistic infection with cytomegalovirus is not uncommon and organs such as lungs, adrenals, spleen, pancreas, and kidneys are frequently involved.[2] Lesions of the gastrointestinal tract, excluding the liver, are rare, and it is often difficult to define the specific role of the cytomegalovirus in their production.

Levine, Warner, and Johnson[3] have described patients with cytomegalic inclusions in ulcers of jejunum, ileum, and colon, and a similar lesion in the anus and rectum has been reported in a woman dying from primary cytomegalovirus infection.[4] Previous comment has been made of oesophagitis in cytomegalovirus infection[2] and it seems likely that the gross ulcerative change in the oesophagus of our patient was due primarily to cytomegalovirus infection. It is possible that other forms of apparently non-specific ulceration of the gastrointestinal tract in debilitated patients might be related to cytomegalovirus infection.—We are, etc.,

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Tropical Splenomegaly, Sickle-cell Trait, and P. falciparum Infection

SIR,—The diagnosis of tropical splenomegaly (T.S.S.) is not as straightforward as Dr. Marianne Janosi (4 March, p. 628) implies. She points out a number of features, but there are recent series with a number of anomalies by her criteria. For instance, the size of the spleen may be very variable, and macroglobulinaemia has not been a constant finding. In the series of Stuiver *et al.*[1] there are 7 out of 29 cases with spleens palpable less than 10 cm below the left costal margin including some with only 2 or 3 cm splenomegaly. Although Lowenthal *et al.*[2] found only two cases of 19 in Zambia with normal IgM, a normal IgM was reported in four of eight cases from Uganda by Ziegler *et al.*[3]

Our patient was small. He weighed 45 lb (20·5 kg) and was 46 in (117 cm) tall. Consequently, his spleen, palpable 7·5 cm below the left costal margin, was proportionally large for his age. We excluded HbS-β thalassaemia, as HbA was the major component, and HbA2 and HbF in the propositus and his two siblings were normal.

Dr. Janosi draws attention to some of the difficulties in diagnosing T.S.S. It is usually stated that T.S.S. is a diagnosis by exclusion.[4,5] Sagoe[5] suggested more rigid criteria for diagnosis. If Dr. Janosi and her colleagues also recognize a series of positive diagnostic features, may be invite her to report them.—We are, etc.,

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Duodenal Ulcer and Gastric Cancer

SIR,—Eight male cases of gastric cancer in men have been found in this average size practice since 1961. Four of these had a long-standing history of duodenal ulceration. All smoked heavily and developed chronic bronchitis and emphysema. Three were seamen. In none of them was gastric cancer

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