was dropped, the variance explained was 6%. Love and Miller analysed data from 1677 miners and found that, over an 11 year period, previous dust exposure (before the study) was associated with loss of FEV₁.³ Their analysis explained about 7% of the variance. Our own study explained 6.8% of the variance in FEV₁.

Thus whereas some investigators found a statistically significant association between FEV₁ and certain coal mining experience, it was very small. We found that FVC was much more closely related to years of underground coal mining than FEV₁ (though not years above ground) ($p = 0.0001$). Our data explained 16% of the variance, so most of the variation in FVC was likewise unexplained. Nevertheless, these data do not refute our suggestion that FVC has a greater association with underground coal mining than does FEV₁. We believe that the impact of mining on FEV₁ is yet to be clearly determined.

We are confused by Morgan's third point. He objects to the finding that years of underground coal mining predicts FVC without predicting FEV₁, then provides a nice rationale for this finding ("(this occurs) when the residual volume is increased without a comparable increase in total lung capacity and is a frequent finding in coal miners whether they have coal workers' pneumoconiosis (CWP) or not.")

In this connection, Morgan is wrong when he states that in pure restrictive disease the FVC and the FEV₁ are reduced to the same extent; in early restrictive disease, it is not unusual to see a raised FEV₁/FVC ratio, a result of greater reduction of FVC than FEV₁.⁴

Next, Morgan makes a common mistake when he refers to disability. "Disability" is not a medical term. It is a legal term, and is usually a decision made by an administrative judge. Our data suggest that coal mining reduces FVC, and therefore FVC is a legitimate variable to consider in the black lung disability process. Neither our data nor any other research data can define "disability."

Morgan apparently thinks that there is always a simple "inverse relation between the PaO₂ and the PaCO₂." If this were the case, we would only have to measure one and we could calculate the other.

Obviously this is not the case, Dalton's law notwithstanding. One subject may have a PaO₂ of 70 and a PaCO₂ of 40, another may have the same PaO₂ but a PaCO₂ of 38, and another may have the same PaO₂ and a PaCO₂ of 42. As we cannot agree on basic physiology, we cannot respond to his comment, except to point out that our paper did give the direction of association of the relation between PaCO₂ and exercise tolerance; it is positive, as indicated in table 3.

Morgan seems piqued that we commented on his paper, pointing out that his conclusion about the value of blood gas determinations was not based on multivariate analysis. His analysis *did not* use multivariate techniques, regardless of his reasons. Our point is that, with all the known interactions and complexities of pulmonary function and exercise tolerance, simple or non-multivariate analyses are less useful than multivariate analyses. A conclusion not based on multivariate analysis is weaker than a conclusion based on multivariate analysis. And while "surprised" is not the correct word, we do remain fascinated with the observations that some subjects with a very low PaO₂ have exercise capacities equal to normal, and that PaO₂ is not an independent predictor of exercise capacity.

Myers and Bachmann have accurately indicated that intermediate variables are inappropriate in a multivariate analysis of final effects. It is not always clear which variables are intermediate in studies such as ours. Approaches such as causal modelling help to sort this out. The epidemiological researcher's goal is to determine the model which best fits the data obtained, and causal modelling is offered as another useful tool.

We agree that "causal" is not an ideal word for this approach. We were not the first to use this technique, and we called it what it was called by others. The cautions of Myers and Bachmann are appropriate.

To conclude with a few minor comments, we did not "force" age into the regression model; the computer procedure tests all variables entered into the model. "Test failures" were excluded, but were rare; applicants for disability are generally requested to repeat the tests until acceptable results are obtained. Finally, our cases included no subjects with progressive massive fibrosis or complicated

pneumoconiosis.

We appreciate the interest in our paper, which has allowed us to review some of our findings and observations.

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Muscle biopsy as an indicator for predicting mercury concentrations in the brain

Sir,—Elemental mercury (Hg) vapour and the organic species methyl-Hg easily penetrate the blood brain barrier and accumulate in brain tissue, the brain being a critical organ for these forms of Hg.¹ The concentration of Hg in urine or blood, or both, may under certain circumstances be a good indicator of exposure. There are no means of predicting the concentrations of inorganic or organic Hg in the brain.

Methyl-Hg has previously been considered stable in brain tissue^{2,3} with a biological half life of about 70 days. Recent studies in monkeys, however, have reported a substantial demethylation of methyl-Hg following long term exposure.^{4,5} With a longer half life for part of the inorganic Hg a higher accumulation of inorganic Hg relative to organic Hg will take place.⁶

The present results from human necropsies of non-occupationally exposed subjects show a high correlation between total Hg concentrations in abdominal muscles and total Hg concentrations in occipital brain cortex (figure). There are two possibilities of exposure, Hg vapour from dental amalgams and methyl-Hg from fish. Methyl-Hg accumulates in brain tissue. During recent years several studies have shown a continuous release of Hg vapour from amalgam fillings⁷ and a significant correlation has been observed between amalgam load and Hg concentrations in the

Concentrations of total Hg ($\mu\text{gHg/kg}$ wet weight; radiochemical neutron activation analysis) in occipital cortex and abdominal muscle from 12 deceased persons.

brain at time of death⁸⁻¹⁰ and between amalgam load and urinary excretion of Hg.¹¹

Notwithstanding the origin of the Hg in muscles and brain, from metallic Hg vapour or from methyl-Hg, our data have for the first time indicated a possibility of estimating the concentrations in brain tissue based on analyses of total Hg in muscle tissue. Studies should be continued with higher concentrations of Hg in muscle and brain tissue, and speciation of inorganic and organic Hg compounds should be carried out.

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Correction

Health related selection and death rates in the United Kingdom Atomic Energy Authority workforce (1990;47:248-258).

Owing to a printing error the last lines of page 256 were omitted. They should read "the basis of health has less effect on cancer mortality than on other causes of death."¹²