later, whereas in 20 with a history of severe cerebral accident before operation 9 developed them later. Similarly in 784 patients without severe myocardial disease there was no subsequent coronary thrombosis, whereas in 18 patients with severe myocardial damage there was one post-operative coronary thrombosis. Spinal cord damage occurred in two others, and this was a serious matter. In expert hands, however, this complication should reach a low irreducible minimum.

Contraindications to inducing hypotension were (1) myocardial disease; (2) arteriosclerosis, whether local or generalized; (3) a history of previous cerebral vascular accident; (4) anaemia, chronic pulmonary disease, congestive heart failure, and other conditions affecting oxygen transport; and (5) malignant hypertension. The *only indication* for hypotension was when its advantages to the patient and the surgeon were definite and were likely to outweigh the accepted risks.

Discussion

MR. GEOFFREY PARKER (London) said he had been prejudiced against the use of methonium compounds at first, but was now happier about them. The bloodless field made it wonderfully easy to demonstrate all the steps in an operation such as prostatectomy. Dr. C. T. BARRY (Edinburgh) said that with methonium compounds he had had 8 deaths in 212 cases. He thought a high spinal was more reliable. Four of his eight fatalities had been due to severe paralytic ileus. Dr. R. F. WOOLMER (Bristol) said that vasoconstriction was Nature's way of combating shock, and yet the opening speaker had advocated methonium in the treatment of established shock. He thought that the exponents of this method were confusing "shock-shielding" with "shock-hiding." Dr. M. H. A. DAVISON (Newcastle), after considerable experience, had abandoned the methonium drugs. He pointed out that the opening speakers had recorded three deaths on the table in less than 2,000 cases, whereas there had been only one such death in the last 60,000 cases at his hospital. He emphasized, too, the very real risk of cerebral damage in many cases. Dr. A. R. HUNTER (Manchester) described the limited use of hexamethonium in neurosurgery, chiefly to make the impossible possible. The method was mainly of value with angiomas, aneurysms, and vascular meningiomas. Some patients had prolonged hypotension, and a few had shown intolerance by developing venous congestion in the operative field. There was also a significant increase in post-operative vomiting. Dr. P. R. BROMAGE (Chichester) said that in the presence of complete afferent blockade from the operation site eosinophil counts suggested that the adrenocortical response was delayed until the effects of the block had worn off. In the arteriosclerotic subject the electroencephalogram showed delayed return of normal alpha rhythm after profound hypotension.

Dr. GILLIES, in reply to a question by Mr. N. E. Tanner on whether the induction of hypotension was indicated in the surgery of portal hypertension, said that he did not consider the method suitable. The hazards of bleeding in such patients were great. With reference to Dr. Barry's remarks on paralytic ileus he quoted a personal communication from Dr. F. Holmes, at Edinburgh, reporting 19 non-fatal cases of paralytic ileus in 155 orthopaedic operations (mostly on the hip) in which hexamethonium had been used. Dr. Davison's emphasis on possible cerebral damage was important, although Nilsson's observations were on few cases and all effects were transient. With spinal block anything above 10 degrees head-up must be considered dangerous. The head-down position should never be much below horizontal, otherwise a dangerous congestion might ensue.

Dr. WYMAN congratulated Dr. Davison on his long series of cases without a death on the table. He felt, however, that such events were largely unpredictable and that such a satisfactory experience could be purely due to chance. Contrary to Dr. Bromage, he thought that there was a normal eosinophil response to operation.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Smoking and Lung Cancer

SIR,—It would seem, according to some of the critics of our conclusion that "tobacco-smoking is a factor in the production of carcinoma of the lung" (for example, Professor R. D. Passey, February 14, p. 399), that we ourselves based that conclusion in part—and even largely—upon the observation that over the last 50 years cigarette smoking and the recorded mortality from lung cancer have risen together. In fact our conclusion is based upon evidence that is *entirely* independent of that time correlation. The time correlation was, of course, our starting point—it suggested that smoking was a factor worth investigating. But having applied that stimulus it ceased to have any interest whatever for us until our epidemiological inquiry was over and had *alone* led us to the conclusion we have quoted above.

That epidemiological approach and the results it gave are also, perhaps, being underestimated by Professor Passey and others. In drawing our conclusions we were not dealing with a handful of uncontrolled patients, nor making light-hearted suggestions, such as those he quotes about breast cancer and Edwardian corsets, based upon a few clinical impressions and a vivid imagination. We set about a most carefully designed survey, a survey that took in, all told, nearly 5,000 patients, was carried out in Greater London and four provincial cities, and occupied nearly five years. Evidence based on 1,465 lung cancer patients and 1,465 carefully matched controls does, we submit, carry some weight. In view, however, of the emphasis that has been placed, quite wrongly in our view, upon the correlation in time we might perhaps remind the reader briefly of the salient features of that survey. We have endeavoured to bring all its important results together in one single table, given below (for details of the absolute numbers, which vary according to the items, and for technical tests of significance, etc., the reader must see Doll and Hill (*British Medical Journal*, December 13, 1952, p. 1271).

The Proportion of Patients Interviewed who were Noted to have Given Characteristics

Section A. Equalities

	Characteristic	Carcinoma of the Lung Patients	Control Patients
1	Sex	Equalized in design of observations. No significant difference in 74 out of 76 categories.*	
2	Age		
3	Places of interview (5 areas)		
4	Occupations		
5	Social class (males) number falling in classes I and II	15%	17%
6	Social class (males) number falling in class V	17%	16%
7	Number with previous residence near a gas works	23%	22%
8	Number with different forms of heating in living room for 30+ years:		
	Coal fire	86%	85%
	Gas fire	1.6%	2.2%
9	Number with previous history of asthma, chronic nasal catarrh, pleural effusion, or pulmonary tuberculosis	17%	15%
10	Regular users of petrol lighters	43%	41%
11	Number of smokers who said they inhaled	65%	67%
12	Smokers of mainly hand-rolled cigarettes	21%	19%
	Users of one of 4 main named brands of cigarettes	57%	57%
	Users of mixed brands	34%	32%
	Regular users at some period of Turkish cigarettes	4%	5%
13	Number of male snuff-takers, occasionally or regularly	3%	4%
14	Number of non-smokers amongst women in the provinces	57%	57%

* In two occupational groups—miners and policemen—there was a relative deficiency of cancer cases.

Observed Proportions of Patients with Given Characteristics
Section B. Inequalities

	Characteristic	Carcinoma of the Lung Patients	Control Patients
1	Number of men who were non-smokers: Greater London, 1948-9 Greater London, 1950-1 Bristol, Cambridge, Leeds Newcastle	0.3% 1.0% 1.3% 0.0%	4.2% 4.2% 4.4% 5.3%
2	Number of women who were non-smokers: Greater London	30%	54%
3	Number of men smoking 25 cigarettes or more daily (or the equivalent in pipe tobacco): Greater London, 1948-9 Greater London, 1950-1 Bristol, Cambridge, Leeds Newcastle	26% 26% 24% 21%	13% 16% 11% 12%
4	Number of women smoking 25 cigarettes or more daily: All areas	11%	1%
5	Number who started smoking before the age of 20: Men Women	80% 29%	77% 24%
6	Number who had given up smoking for more than 10 years: Men Women	1% 1%	4% 4%
7	Number of male smokers who, as a rule, smoked cigarettes only Number of male smokers who, as a rule, smoked pipes only	74% 4%	69% 7%
8	Number of male cigarette smokers who had used cigarette holders occasionally or regularly	5%	12%
9	Number of males who had chewed tobacco occasionally or regularly	3%	5%
10	Number of men aged 45-74 smoking 25 ciga- rettes or more daily (standardized rate): Patients with carcinoma of the lung Patients wrongly diagnosed as lung cancer Patients with other respiratory diseases Patients with other forms of cancer Patients with other diseases	24% 	
11	Number with previous history of: Chronic bronchitis Pneumonia	17% 17%	11% 10%

In the upper part of the table, Section A, we set out the principal characteristics in which our carcinoma of the lung group did *not* differ appreciably from the control patients—that is, those patients whom we took into the inquiry as a standard of comparison. To limit the possible variables, the design of our survey deliberately made them equal in sex, age, place of interview, and, largely, in hospital of admission. It will be seen that they have also revealed themselves to be remarkably alike in other characteristics—their social class and their occupations, their residence near a gas works, their heating in the home, their previous history of certain respiratory diseases. In relation to smoking they do not differ in their use of petrol lighters, of hand-rolled cigarettes, of different brands of cigarettes; they do not differ in the habit of inhaling. With these striking equalities—particularly in some aspects of smoking—it would seem to us to be unreasonable to argue that either our controls or our cases are biased, and therefore not comparable, or that the information given by the two groups is not equally reliable.

How, then, can we explain the picture given by Section B of our table? Here we have brought together the various ways in which the carcinoma of the lung patients *do*, as a group, differ from the control patients. They include significantly fewer non-smokers and a marked excess of relatively heavy smokers in both sexes, with, in men, a consistency in time and space that is striking; they include more persons who started smoking earlier in life and fewer who have given up; they include relatively more cigarette smokers and fewer pipe smokers; they include fewer users of cigarette-holders and fewer chewers of tobacco. In short, broadly speaking, they differ radically in the *amount* of tobacco they have smoked, and they differ, it seems probable, in the *way* they have smoked. Other groups of patients do not reveal this difference in the amount smoked—including, be it noted, a group originally, but wrongly, diagnosed as carcinoma of the lung. It is the privilege of the lung cancer group to be so marked. The only exception lies in the equality of non-smokers amongst the few

women we observed in the provinces (as shown in Section A).

The two groups are also different, Section B shows, in their previous history of chronic bronchitis and pneumonia. We give reasons in our paper for supposing that this comparison may be fallacious, though we do not wholly dismiss it. Chronic bronchitis is held by many to be related to smoking. There is also some evidence (not included in the Table) that the carcinoma patients had passed more of their lives in urban areas, which is consistent with Stocks's work on the urban/rural incidence rates. Basically, then, it is the contrast between Section A and Section B of our Table that leads us to the belief that tobacco smoking is of aetiological importance in lung cancer.

This evidence, we repeat, is quite independent of the time correlation. No critic has offered any alternative explanation of it that carries conviction—and indeed the only one that has been put forward at all is that subjects with a particular constitution may be prone both to smoking heavily and to carcinoma of the lung. We have put forward our own interpretation and belief—that the figures simply mean what they show.

Professor Passey and Dr. Gallop ask, If the reported increase in lung cancer is due to tobacco smoke, how does it come about that there is no increase in the incidence of cancer in other parts of the respiratory tract, such as mouth, tongue, and pharynx, which suffer a greater exposure to the smoke and for a longer time? There are, however, analogies for such events, however curious they may appear to be. For instance, in nickel refining in South Wales it is well known that some undetermined carcinogenic agent, acting in the first quarter of the present century, produced a gross excess of cancer in two sites, and two sites only—the ethmoid and the lung. Why not the mouth, the tongue, and the pharynx? Similarly, no excess in any site but the lung has followed the exposure of the Schneeberg miners. A declining cancer rate in the buccal cavity is, in fact, consistent with the hypothesis put forward by some that cancer in these sites is related to the prevalence of pipe-smoking.

We made perfectly clear in our paper that we did not believe that *all* cases of lung cancer were due to smoking—indeed, we called that a most unlikely event and pointed out that we had observed certain cases who had never smoked. One of us (R. D.) has, indeed, elsewhere attempted to calculate from our data the death rates of men and women non-smokers, and on the assumptions made those death rates did not differ materially (Milroy lectures, in the press). We need hardly point out that with *far* more women than men non-smokers in the population a relatively greater proportion of deaths in women must be of non-smokers—though their death rate among them might still be negligible. The difference in past tobacco consumption between the sexes is, it appears to us, quite capable of providing the main explanation of the present sex ratio of mortality. Trade statistics show that of the total tobacco consumption of the country 25 years ago only 2.5% was smoked by women. We do not believe that Dr. Shera need invoke sex hormones as a factor.

Professor Passey suggests that the only "satisfactory solution of the problem would be the study of a large group of smokers in comparison with an equally large group of non-smokers." This we are endeavouring to make in our observations of the mortality amongst those doctors who told us their smoking habits some 15 months ago—but we hardly like to appear impatient.

Finally, he asserts that "when doctors disagree it is bad for the patient." We might remind him that in the past they often have disagreed. They disagreed when Lord Lister endeavoured to introduce antiseptic measures. It was bad for the patient. Quite often he died.—We are, etc.,

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