*Papers and Originals***PSYCHIATRIC RESEARCH: A NEW "MENTAL MILLION"??***

BY

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In 1957, as a result of public and parliamentary pressure, the Government allocated a sum of £1m. a year for extra capital expenditure on mental hospitals. The sum became known as "the mental million." The purpose of this lecture is to persuade the Government that the time is now ripe for a "new mental million"—only this time the extra £1m. a year is needed for psychiatric research.

There is, of course, no magic in the round sum of £1m. a year. This is substantially less than we should be spending if we conducted our public affairs as progressive private industry conducts its business. It is also substantially less than we could be spending, with profit to our patients and to the advancement of human knowledge. But, to do any good at all, a start has to be made on a fairly substantial scale. There is, at least, a precedent for an extra expenditure of £1m. a year on mental health; and precedents are dear to governments, and even dearer to the Civil Service.

The Government's Advisory Council on Scientific Policy estimates that as a nation we spend £634m. on research. This is 2.7% of our gross national product. Of this, roughly 66% is Government spending and 34% spending by private industry. An extra £1m. for the study of the human brain and mind is therefore hardly an extravagant suggestion.

Proper Expenditure on Research

I have tried to find out what progressive private enterprise regards as a proper expenditure on research. Here we are dealing with highly intelligent business men who are concerned with the ultimate cash return on what they spend. Sound general figures are not easy to obtain. The rate of progress and potential progress varies from industry to industry. The human brain is, among other things, an extremely complicated physico-chemical computer system. It is therefore not unfair to look at the electrical components and electronics and the fine-chemicals industries. Here conservative estimates range from 5 to 10% of the turnover. If a component or product has a steady market and appears to need little research, or if a firm is going bankrupt, the figure is likely to be low. If, however, new technologies or techniques are coming along, or diversification is being undertaken, or a firm has slipped behind its competitors, expenditure is likely to be high. In either case, three-quarters or more of the expenditure may be on development research and only one-quarter on basic research. Development research is, of course, research into application, and much medical research directly concerned with treatment comes into this category. It is not unfair to say that a wise and progressive firm, working in these fields, will allocate at least 5% of turnover to research, of which at least 1% will be basic research.

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What is our national turnover in the mental health industry? I want to understate the case. Psychiatric beds make up something over 44% of the hospital beds in the country. The cost per bed is one-third of the cost of general-hospital beds. Estimates vary as to the number of patients seen by general practitioners whose illnesses are primarily psychiatric. In my experience the correct figure is about one-tenth of all patients, with lower figures in psychiatrically healthy communities and higher figures in areas of social decay. On bed costs (which of course include medical-care costs) we spend upwards of £100m. a year on the care of psychiatric patients. It follows that the total cost must be substantially higher, even in terms of direct Government expenditure.

It is impossible to compute the national loss of productivity due to psychiatric illness. Russell Fraser (1947) found that, in light engineering factories, neurotic illness was responsible for between a quarter and a third of all sick absence from work. Precise computation of the loss involved is impossible, but it must be a very large figure. Suffice it to say that even the most conservative Minister of Health is bound to pay out directly over £100m. a year for direct care of psychiatric patients. This is the absolute minimum national turnover figure. As a prudent business man, he should be investing £5m. on research, of which at least £1m. should be on basic research.

What in fact is the Government doing? The approximate expenditure of the Medical Research Council on psychiatric research over the last five years has been as follows: 1957-8, £63,000; 1958-9, £130,000; 1959-60, £170,000; 1960-1, £228,000; 1961-2, £247,000. To this must be added the comparatively small expenditures by the University Grants Committee, the National Health Service itself, the charitable foundations, and the Mental Health Research Fund. Together, they are unlikely to equal the M.R.C. expenditure. Why are we spending so little when the burden we are forced to carry is so heavy?

Before I attempt to answer these questions I must draw attention to the jump in M.R.C. spending between 1957 and 1959. This was partly due to public and parliamentary pressure; but partly also to the fact that the psychiatrist serving on the M.R.C. at that time was Professor Denis Hill. He began to show the M.R.C. how to spend money profitably on psychiatric research. He lit a candle which is going to take a great deal of putting out, which will soon I hope be converted into a powerful battery of arc lamps.

A Strange Attitude

When I discuss psychiatric research with my non-medical colleagues in industry I discover at once a strange attitude. It is this attitude which is the first reason why we are spending so little. They think that psychiatry is phoney science and phoney medicine—

concerned only with sex life and unconscious motivations, speculation about infantile mental trauma, anal and oral fixation, and the stuff that dreams are made of. In the long run Freud and his disciples have made the world a kinder and more tolerant and understanding place. Psycho-analysis enables us to understand much that is obscure in psychiatric symptomatology. But as a form of treatment it does not appear susceptible to statistical validation. In so far as it interprets truth, it does so as an art rather than a science. It is perhaps to be judged as an art; and I do not dare to suggest that it should be financed as a science.

In British psychiatry we have had the Maudsley to keep us scientifically straight, to train our teachers and our mental hospital doctors; one would mention Professor Mapother and Sir Aubrey Lewis, Dr. Eric Guttman, and Dr. Mayer-Gross as men who have made British psychiatry as intellectually honest a science as physics and chemistry, physiology and pathology.

Types of Psychiatric Research

At this point I usually explain to my non-psychiatric scientific and industrial friends the kind of subjects with which psychiatric research is now concerned. I talk about phenylketonuria and galactosaemia and other biochemical errors associated with mental defect. I explain how, in 0.5 to 1% of mental defectives, the condition can now sometimes be alleviated by appropriate biochemical adjustment of the diet. I talk about Gjessing and his painstaking studies of electrolyte balance in schizophrenic catatonic excitement and stupor. I mention the mental changes which poisoning by heavy metals can produce. As an example of the physical nature of mental symptoms, I describe how I once diagnosed and demonstrated typical schizophrenia in an industrial patient with insulin hypoglycaemia—and how he was given sugar just as the duly authorized officer arrived, and recovered in ten minutes. I tell how each week the medical journals recount new discoveries about chromosomes and how their abnormalities are linked with physical and mental and biochemical abnormalities; and how these discoveries sprang from another discovery, made almost by chance.

Following the work of Ford at Harwell, Lejeune (1959) in France discovered that mongolism was associated with trisomy of No. 21 chromosome. To see this it was necessary to be able to see cells dividing. Lejeune grew the cells in tissue cultures from skin, deep fascia, and bone-marrow, and an exceedingly difficult technique it was. Few people could do this type of research, so relatively few discoveries were made.

Then in 1960 Moorhead, Nowell, and their colleagues in the U.S.A., were using a commercial extract of seeds called "phytoagglutinin" to get rid of red cells in blood specimens by making them agglutinate. They happened to examine the white cells. To their surprise they found they were dividing and the chromosomes could be seen and counted and studied just as in tissue culture. Here was a method which could be applied by any pathologist in any pathological laboratory. And the result has been just such a crop of discoveries as followed the demonstration of the pathogenicity of bacteria.

Note that had Nowell been submitting a request for a research grant it is unlikely he would have mentioned normal chromosome counts in his application. Before

we start a piece of research, we cannot tell what we are going to discover. "Winners" may turn up anywhere. It follows that the proportion of really valuable discoveries made is largely dependent on the total volume of research. Attempts to skim off and back only potential "winners," whether projects or people, seriously reduce the number of discoveries of first-class importance.

A Real Science

One more example of modern psychiatric research will serve to drive home the point that this is now real science. "Scoline" is widely used in surgery and electric convulsion therapy to produce muscle relaxation. Among the muscles paralysed are those of respiration. One in 2,000 individuals develops a prolonged apnoea lasting up to an hour or more. This has been found to be due to a reduction of serum cholinesterase activity to about a quarter of its normal level. Now come the odd discoveries. A number of the perfectly normal relatives of those who show scoline apnoea also show a reduction in serum cholinesterase activity. Kalow, a Canadian pharmacologist, showed that in the scoline-sensitive people and their relatives the phenomenon was not just a quantitative reduction in serum cholinesterase but was due to the presence of a different enzyme (Kalow and Genest, 1957). Harris and Whittaker (1962), of King's College, London, have shown that, whereas the cholinesterase activity appears to peter off gradually, like the tail-end of a curve of normal distribution, if the qualitatively different enzyme is studied, there are three distinct groups of people—those with normal serum cholinesterase activity, those with a minor qualitative difference in activity, and those with a major qualitative difference. Those with the major qualitative difference are the scoline-sensitive people, and those with the minor difference are the recessive carriers. The whole thing is a neat genetic picture of an inborn error of metabolism, which had normally no external manifestation until doctors started using scoline as a muscle relaxant.

Three Lessons

This story has two lessons—and perhaps a third. First, other drug sensitivities may be due to other inborn errors of metabolism. Here is a huge field which is starting to be investigated. Already we have the odd story of sensitivity to the antimalarial primaquine. This shows itself as an acute haemolytic anaemia in 10% of negro males. It is in fact a genetically determined sex-linked sensitivity, due to lack of glucose-6-phosphate-dehydrogenase in the red cells. It appears that the condition is the same as the middle Eastern disease favism, resulting from a diet of fava beans. The gene and the bean are the hereditary and environmental factors which interact to produce the disease. In psychiatry we shall be finding many more real genes and metaphorical beans as a background to mental illness in the years ahead.

The second lesson of scoline apnoea is that something which looks like the tail-end of a curve of normal distribution may on careful study turn out to be a specific biochemical and genetic entity. At once one thinks of schizophrenia, and the other mental illnesses with an ill-defined genetic basis. It may well be that schizophrenia, like mental defect, is a clinical syndrome with a number of different biochemical and environmental causes.

The third lesson is this. Professor Harris is a genetic biochemist, with an M.R.C. unit. I have noticed that the M.R.C. looks with a very kindly eye on genetic studies. Is this perhaps linked with the necessity to answer Parliamentary Questions about the volume of research into the effects of atomic radiation? If this be so, it merely proves that the M.R.C. are human after all, and that they do not always have the right reason for doing the right things. But that, after all, is often the way that science gets forward.

One further word about psychiatric research. It is not all biochemical or genetic. Social factors in causation and in treatment can be examined by scientific methods. Epidemiological studies seldom give ultimate answers, but they often give provisional ones, of both practical and theoretical value. Prediction studies of criminals are a case in point. Of course, in such work one must be just as ruthless with oneself in testing one's findings as in any other scientific work. Recently Dr. Sidney Chave and I were making a psychiatric survey of a new town. Our full findings will be published in the autumn under the title of "Mental Health and Environment." But one incidental finding illustrates the need for scientific ruthlessness. We had constructed a ten-point scale designed to measure general satisfaction or dissatisfaction with the environment. We applied this to our new town community, and to our delight we found 89% of the adult population were satisfied with their new environment. But, of course, we had only half the picture. We applied the same test to a sample of the general population of Britain and to a North London borough exporting population to the new town. In both the figure was 91% satisfied with their environment! A further analysis of the figures revealed that satisfaction with one's home environment is directly dependent on the length of time one has lived in a place. Like so much social research, the answer is obvious—when one has found it. Inevitably, social measuring instruments are less exact than biochemical ones. But in both the techniques of sampling and of control series have to be rigidly and honestly applied.

I hope I have now said enough to show that psychiatric research is real research and real science. If more evidence is needed it can be found in the Mental Health Research Fund publication—*Aspects of Psychiatric Research* (O.U.P.). Here is a picture of as vigorous a growing-point in medicine as is to be found over the whole field.

The second reason why we are starving psychiatric research is more sophisticated. It involves a short study of the social biology and social psychiatry of the M.R.C. itself. As a small grant-holder I must at once declare an interest—and a potential source of bias.

The M.R.C. Theory

The M.R.C. is a very good organization. But it has a theory behind much of its activity. Briefly the theory is this: find good men and then back them—or, to be more precise, wait until good men come along, and then back them. In two ways the results have been excellent. They back very few failures—probably fewer than any comparable organization in the world. Their output of quality work for money spent is very high indeed. And those whom they back are, on the whole, given a high degree of freedom to follow wherever the scent leads, without having to stop to report progress at frequent intervals, as so often happens with other grant sources.

Now for the bad sides of the picture. If one waits for good men to come along and is then highly selective, a great many good men will never come at all. Good men are usually practical. They look at career opportunities, and make their decisions accordingly. Time and again, on the Research Committee of the Mental Health Research Fund, we have seen good men start off in psychiatric research. Indeed, we have helped them to do so. At the end of three years they have opted for clinical psychiatry simply because there were no jobs available in psychiatric research. I have seen M.R.C. units closed down—not, I hasten to add, psychiatric ones—because the director had retired without the vacancy ever being advertised, because the M.R.C. was convinced there was no one available to fill the post. If industry ran its research in this way it would soon grind to a standstill. Of course, if one never fills a post unless one is certain, some failures are avoided. But these are the price of progress. One has only to think of the unexpected successes of the men who grow to the job. If our universities were run on the same basis as M.R.C. units, some mistakes would be avoided, but half the chairs would be vacant and many a potentially first-class professor would be lost to teaching and research.

In this sphere I criticize the M.R.C. on two counts. First, there is no shortage of good men wanting to make a career in psychiatric research; this is the considered experience of the psychiatric research workers I have questioned. The M.R.C. has simply failed to find them. Secondly, if there were such a shortage the remedy would be to create the posts and careers to attract them.

Too Big a Job

Why has the M.R.C. failed to find the good men? The reason is simple. The job is too big for the existing organization. The members of the M.R.C. itself are first-class medical scientists. But only one is a psychiatrist. The subject is already so complicated and difficult that he cannot know more than a small part. On our Mental Health Research Fund Research Committee we have usually had ten psychiatric research workers. Yet only one or two of us have usually been able to give a valid opinion on a proposed line of research; and quite often none of us have known individual applicants for grants. How much worse must it be on the M.R.C.? It is the same with regard to M.R.C. staff. I have a very high opinion of the secretary—and his medical colleagues. But medical research, even without psychiatry, is so huge a subject that no one man can channel good advice to his committee on all of it. And, of course, as he delegates, so the advice gets less good. The simple truth is that there is an optimum size for all human institutions, beyond which they should divide into two or more fully autonomous new bodies.

I must confess to a sense of disappointment about the Clinical Research Board. One had hoped that here, alongside the M.R.C., would be a new source of funds and stimulant of research—in friendly, or not so friendly, rivalry like Independent Television and the B.B.C. Instead, we appeared to have gained little more than a subcommittee of the M.R.C.

I am driven to the conclusion that sooner or later, and indeed the sooner the better, we must have a psychiatric research council alongside the M.R.C., with its own staff and budget and similar spending powers.

To say this is not a criticism of either the intelligence or the integrity of the M.R.C. Nor is it a criticism of the very real contributions it has already made to psychiatric research. It is simply to say that natural healthy growth has now made the job too big and complicated for an otherwise excellent machine.

The one valid objection I see to this proposal is that psychiatric and general medical research have a substantial area of overlap—a muzziness at the edges as it were. It is in this area of overlap that many of the most exciting advances are taking place and that generous financial support is particularly necessary. But the same applies to the whole of biological science. Physics and chemistry continually spill over into biology, with dramatic and valuable results. But this does not stop our supporting them, independent of medicine. A neat parcelling-out of subjects without overlap appeals to civil servants. But the real world of science is not like this, and practical scientists know the value of having more than one possible source of support, especially where government is concerned. Official negativism in one department may be quite irrational, and a little healthy rivalry between councils in the support of projects and possibilities is in my view to be encouraged. Again, one must reiterate that a certain amount of waste is the price of progress.

No Need to Wait

A psychiatric research council may take a little time to achieve. But there is no need to wait before getting ahead and spending our new mental million a year now.

At present most of our eggs are in one basket—the Institute of Psychiatry at the Maudsley. We have a few at Edinburgh, Aberdeen, and Newcastle, at the Middlesex and St. George's, at St. Thomas's, Guy's, and elsewhere. But there are many more eggs than baskets—and, with all due respect, some which are in are in danger of going addled.

At present a professor of psychiatry, who is almost always a first-class research brain, devotes his time to the following activities:

1. *Clinical work.*—In order to qualify for a merit award under the N.H.S. I understand he must do seven clinical sessions a week. He is frequently asked to see colleagues and their relatives. It must be remembered that one psychiatric examination often takes an hour and a half.

2. *Teaching*—didactic and clinical.

3. *Examining*—at his own and other universities.

4. *Fund raising.*—He must write letters to support his staff's applications for research grants. Often the fund administrators demand amendments and interviews; and often applications are rejected, when the whole process starts again. He must then report regularly to the fund-givers on progress achieved—unless he is fortunate enough to have his own M.R.C. unit. He must assess, for the fund-givers, the applications of his colleagues elsewhere.

5. *Administration.*—He must run his own department, and play his part on committees of his own medical school, hospital, and university—and often on a regional board as well. In the U.S.A. they order things differently. Happy the American professor with four committees a year—and one of those optional. In America the price of autonomy is insecurity and liability to be sacked if one runs a bad department. I am not at the moment advocating this, but personally I think it a price worth paying.

6. *Support of medical societies*—local, national, and international—and the entertainment of visitors.

7. *Book-reviewing*, and writing commissioned general reviews of his subject.

8. *Research.*

It must now be apparent why our eggs are in danger of going addled. Without staff a professor in this modern world cannot do research at all. Yet this is the very part on which he should be concentrating—because it is the most difficult part of all.

The answers to this situation dispose of a fair section of our new mental million. Note that I propose that almost all of it should be allocated for research within the universities. It is here that the best milieu for immediate research is available; and it is here that the greatest long-term impact, in terms of undergraduate and postgraduate students stimulated and trained, is likely to be achieved. To train our future doctors and researchers there must be a psychiatric professorial unit in every medical school. Each unit should have two professors—one primarily clinical, one primarily for research, but both teaching. Each unit should have at least two readers (many now have none), six lecturers and assistant lecturers, the necessary technicians and secretaries, a departmental business manager, and a minimum of 40 to 60 beds, with a high proportion of single rooms.

Next we need a second institute of psychiatry, preferably in North London to balance Maudsley, which should take over and staff a large mental hospital—I venture to suggest the Friern.

Third, we need an institute for mental deficiency, again with a substantial hospital unit of its own. Here there are difficulties in effective university linkage, since large mental-deficiency institutions are almost always far out in the country. But this is not an insoluble problem.

I fear my mental million is gone—and more than gone. The men and women are waiting to do the work. As to buildings, it is worth remembering that the best research is often done in makeshift premises. Nobel Prizes are won in huts.

What can we offer in return for the new mental million?

Mental illness is an awful and tragic affliction. We are just starting to see what it is about, and how we may hope to beat it. Psychiatric research is very difficult work indeed—in my view the most difficult of all human activities. Within 48 ounces of grey and white matter the plays of Shakespeare, the speeches of Demosthenes, and Newton's *Principia* had their origin and found their form. What wonder the thing sometimes goes wrong. What wonder that silver-tongued psychopaths sometimes lead men to wars and prophets of half-truth offer easy solutions to problems which have perplexed men since they first formulated ideas. There is only one way to find out how the brain and mind work—that is, the way of science. By applying science we can defeat mental illness—and in the process I shall be surprised if we do not gather another fine flower on the road. In studying disease we learn about health. And on the mental health of humanity the future of our children and their children depends.

In preparing this lecture I sought the help of twenty colleagues. The views are mine, but the backing of fact is theirs. I should like to thank Dr. J. A. V. Bates, Professor G. M. Carstairs, Dr. J. L. Crammer, Dr. Alick Elithorn, Dr. Trevor Gibbens, Dr. E. H. Hare, Dr. J. A. Harrington, Professor Harry Harris, Professor H. McIlwain, Professor P. Polani, Dr. Linford Rees, Dr. Derek Richter, Professor

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TEN YEARS AFTER PNEUMONECTOMY FOR CARCINOMA

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There have been many accounts of the physiological consequences of pneumonectomy (Cournand *et al.*, 1950; Gaensler and Strieder, 1951; Friend, 1954; Björk, 1956; McIlroy and Bates, 1956; Jones *et al.*, 1960), but few attempts have been made to distinguish the early and direct effects of this procedure from such adaptive or degenerative processes as may develop over the succeeding years. The object of the present study is to compare the clinical and physiological findings in a group of patients one year after pneumonectomy for carcinoma with those occurring in another group 10 years after.

Material and Methods

Ten-year Group.—Of 15 patients known to have survived pneumonectomy for carcinoma for more than 10 years, two lived too far away to attend and a third was found to have developed a carcinoma in the other lung. The 12 remaining patients were studied; these had all undergone pneumonectomy for carcinoma between 10 and 13 years prior to the time of the investigation.

One-year Group.—For comparison, the first 10 patients who had been subjected to pneumonectomy after January 1, 1958, and had survived for a period of at least nine months were studied. These 10 patients had all undergone pneumonectomy for carcinoma, by the same technique as the 10-year Group, between 9 and 15 months prior to the investigation.

In both groups the following investigations were carried out: (1) A clinical history and examination. (2) A chest radiograph. (3) A 12-lead electrocardiogram. (4) Measurement of lung volumes, including the residual volume by a closed-circuit helium technique. (5) Tests of ventilatory capacity included maximum voluntary ventilation at 80 respirations a minute (maximum breathing capacity; M.B.C.), maximum inspiratory and expiratory flow rates, and forced expiratory volume in 1 second (F.E.V.₁). (6) Arterial puncture was performed and the arterial oxygen saturation measured by spectrophotometry in the 10-year group of patients. (7) The arterial CO₂ tension was measured by a rebreathing method (Campbell and Howell, 1960) in the one-year group. This method was not available when the 10-year group were examined, the plasma bicarbonate level being measured instead. (8) The pulmonary diffusing capacity (DL) was measured in both

groups by the single-breath carbon monoxide method (Ogilvie *et al.*, 1957).

Information regarding the pre-operative state and immediate post-operative progress of the patient (including history, examination, chest radiograph, physiological tests, and histology) was obtained from the hospital case-records.

Results

Age, Sex, and Size (Table I).—The 10 patients in the one-year group and 10 of the 12 in the 10-year group were men. In the one-year group the average age was 55 years at the time of operation and 56 at the time of study. The corresponding ages in the 10-year group were 51 and 61. The averages of height, weight, and body surface area were approximately the same in the two groups.

TABLE I.—Age, Sex, and Size

	One Year	Ten Years
No. of patients	10	12
Sex { Male	10	10
Female	0	2
Age { At operation	55	51
At time of study	56	61
Height	67 in. (170 cm.)	67 in. (170 cm.)
Weight	146 lb. (66.2 kg.)	143 lb. (64.8 kg.)
Body surface area (sq. m.)	1.76	1.74

Findings Before and at Operation

A history of chronic bronchitis preceding the symptoms of carcinoma had been recorded in the case-notes of two patients in the one-year group and one patient in the 10-year group (Table II).

TABLE II.—Pre-operative Findings

	One Year	Ten Years
Side { Right	3	8
Left	7	4
Radiograph { Collapse	6	9
Peripheral round lesion	3	1
Hilar mass	1	2
Histology { Squamous	4	7
Oat-cell	3	3
Simplex	3	2
Symptoms or signs of bronchitis	2	1
Pre-operative vital capacity (ml.)	2,989	2,905

The routine pre-operative examination had revealed no significant abnormalities apart from those attributable to the carcinoma and the signs of bronchitis