Medical Association were conceived by one of the Vancouver newspapers.[16] On the whole this relationship between medicine and the newspapers is rather incongruous. The practice of medicine is thoughtful, careful and deliberate. It has to be. Newspaper work by the very sense of urgency inherent in it, is almost the opposite to this. It has to be. Knowing this, how closely can we associate our activities with the newspaper? Further we are told in the Public Relations Forum in the *Canad. M. A. J.* that "Accuracy is not absolute in the news story. It can't be. A news story, by necessity, is a distillation. It does not, it cannot contain every one of facts. The process of abstraction itself may appear to alter the content."[17] There may be some who fear that newspapers will ignore our activities. That would truly be a small loss. But no fear! Medical activity is always news. What we should fear is that the newspapers report about medical activity before it is ready to be reported. What we should fear is that our activity will be reported incorrectly. We should not expect free reporting for our benefit.

We are told in the Public Relations Forum that "doctor *must* co-operate with the press" . . . "because he has an obligation to the public as well as to his profession and himself."[17] What this means is hard to understand. To go on. There is then a quotation from a newspaper writer who says that people want knowledge about medicine and health and it must not be denied them.[17] It is even more difficult to know or understand the validity of this statement. If there is illness in a family, the doctor in attendance should be able to explain the situation to the patient or the relatives or both so that they know what is happening. If, however, some individual is truly interested in knowing more about science and medicine he can find much of value in the public library or the book store. Popular literature is not the place to get knowledge of this type.[18] I suppose some of this stems from the "do-it-yourself" trend. Surely this cannot be carried into self medical care.

Advertising people forget that doctors have much opportunity to learn how to get along with people. The earliest public relations guidance for doctors was laid down for us by Hippocrates. Through the ages doctors have learned to get along with their patients. Yet people who talk about doctor-public relations have the temerity to tell doctors how to do their work.

Does the medical profession need any special voice to speak for it? We everyone of us speak for ourselves every day in our daily work. Every day we give of ourselves in service to the public. If we go on to have too many varied means of showing ourselves to the public in a guise other than what the public expects of us, it may be said of us as did Hamlet's mother of the lady she was watching in the play, "The lady doth protest too much, methinks". There is no need for us to put ourselves in this position.

The title of this paper may be unacceptable to some who nevertheless may agree with varying amounts of the material discussed in it. They may say that there is no reason to suggest that we have to make a choice and pick one or the other. Through the ages as the doctor-patient relationship evolved, the doctor-public relationship also grew. Each plays its part today. The primary doctor-patient relationship plays the large important part. The secondary doctor-public relationship plays a relatively minor role. Because there is this intimate relationship between them, it follows that activity in one must influence the other. Present-day public relations techniques accentuate the doctor-public relationship and greatly over-emphasize its value.

The doctor-patient relationship is a healthy one. However, this attempt to raise up the very minor relationship out of all proportion to its worth must jeopardize the doctor-patient relationship because, as we said, a change in one influences the other. Discord will arise.

We must think clearly and objectively about this program of public relations we are being asked

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SHORT COMMUNICATIONS

THERAPEUTIC TRIAL OF IPRONIAZID (MARSILID) IN DEPRESSED AND APATHETIC PATIENTS*

R. L. DEVERTEUIL, M.D. and
H. E. LEHMANN, M.D., *Montreal*

THE FOLLOWING is a report on the results of a therapeutic trial made on a group of 31 psychotic patients, using iproniazid (Marsilid). This drug was originally introduced for the treatment of tuberculosis and other wasting diseases. It was found to produce, as a side effect in some cases, elevation of mood, increase in energy, heightened sensitivity to stimuli and other signs suggesting stimulation of the central nervous system.[1] It was known that the drug acted as a potent inhibitor of mono-amine oxidase[2] and caused accumulation of serotonin in brain tissue.[3] A recent hypothesis attempts to correlate this effect on enzymes with the stimulation of the central nervous system suggested by clinical observation.[4] Possible therapeutic value of the drug in states of depression or apathy has been discussed for several years, but systematic studies have been few and results inconclusive or conflicting.[5, 6] A recent paper which reports favourable results stresses that definite improvement occurred only in patients treated with iproniazid for longer than two months.[7] An average daily dose of 100-200 mg. has been recommended in most recent reports; however Scherbel, reporting on the beneficial effects of iproniazid on a group of arthritic patients, observed that the dosage could be reduced to and maintained at 10-15 mg. daily and that this dosage "has been found sufficient to maintain mental stimulation produced initially by a greater amount of the medication".[8]

*From the Verdun Protestant Hospital, Montreal. The authors wish to acknowledge with thanks the generous supply of iproniazid (Marsilid) which was provided by Hoffmann-La Roche Ltd. for the purpose of this investigation.

A wide variety of toxic side effects of iproniazid has been reported from different sources, but information is inadequate and interpretation difficult. Among the more frequently mentioned and serious of these are: muscular hypertonicity and hypermotility, hypotension with dizziness and syncope, hepatitis (of five reported cases of hepatitis, none was definitely attributable to iproniazid), œdema, constipation and mental symptoms asociated with overstimulation of the central nervous system. In one study the side effects were sufficiently severe to require termination of treatment in five patients (out of 20).[7] Several reports warn of "withdrawal symptoms" and advocate a gradual termination of treatment.

The study reported here was an attempt made to gain experience in the use of iproniazid in a large mental hospital (1650 patients) where, following the striking benefits obtained with neuroleptic drugs, attention was turning to the vast numbers of patients, particularly those in whom depression of mood and activity were marked, who would reap no benefit from the new relief available to the anxious and excited patient, and for whom no drugs of comparable value were as yet available.

SELECTION OF CASES

A total of 31 cases were selected for study. The main criterion for selection was the presence of depression, with or without anxiety, or of apathy as a well-marked clinical feature, provided the investigators were able to establish that the patient's apathy was of primary defect nature and not a secondary withdrawal reaction resulting from anxiety.* Relatively little importance was attached to age (from 32 to 83), time in hospital (from 2½ months to 17 years) or diagnostic category (13 different types).

DOSAGE AND DURATION

All but four patients received 150 mg. daily in tablet form (50 mg. t.i.d.) for most or all of their period of treatment. The remaining four patients received 100 mg. daily (50 mg. b.i.d.). In 11 cases, dosage was reduced or treatment discontinued as a result of toxic reactions and eventually all cases in this study were taken off iproniazid, pending accumulation of additional data, as a result of the high incidence of toxic reactions and of one fatality. Because of this, there is a wide variety in the duration of treatment for different patients (14-112 days).

RESULTS

Of the 31 cases studied, irrespective of diagnosis, 11 (35%) showed a significant improvement. If five patients treated less than 15 days were omitted from this study, the percentage would be 42. In seven of the improved cases, the improvement was sustained and of good quality, in four it was mild or transient; five of these 11 improved patients were discharged and one died as a result of necrosis of the liver.

Three additional patients, not improved on iproniazid, were afterwards successfully treated with electroconvulsive therapy and discharged. On the other hand, six of the improved patients had been treated with electroshock before receiving iproniazid with unsatisfactory or inferior results.

In two female patients, the depressive reaction was converted during iproniazid therapy into a state of hypomanic excitement which subsided spontaneously when the drug was discontinued.

SIDE EFFECTS AND COMPLICATIONS

This study was characterized by a high incidence (35%) of side effects. Dizziness, loss of muscular tonus, and ataxia, with or without hypotension, occurred in seven, resulting in frequent falls which in one young woman led to a fracture of the tibia, while cerebral thrombosis was suspected in one man and another man was investigated for an expanding intracranial lesion because of these symptoms, which persisted as long as the patient was continued on iproniazid. Syncope was observed in two patients and asymptomatic hypotension in one. A fatal necrosis of the liver occurred in one patient. It is noteworthy that this was one of the four patients receiving the smaller dosage schedule of 100 mg. daily, and that the dosage was reduced to 50 mg. daily (because of her improvement) 14 days before the onset of jaundice, when the drug was immediately discontinued. The patient was put on bed rest, special diet, special nursing care and cortisone, but her condition worsened rapidly and the hepatitis progressed to a fatal necrosis of the liver in a period of 12 days.

At autopsy, no other lesion was found, the liver necrosis being of the type sometimes seen in response to toxic agents. A study of this case, and of two others showing a hypotensive reaction to iproniazid which occurred only several weeks after the drug was started and persisted and progressed for two to three weeks after decrease or withdrawal of the drug, suggests that some side effects of the drug may be delayed and cumulative, a possibility which has not yet been sufficiently stressed. Unfortunately, not enough time was available to study the value of a much smaller maintenance dose of iproniazid, as advocated by Scherbel.[8]

DISCUSSION

Our results in 35% of patients showing significant improvement with iproniazid could be questioned because they were not obtained under double-blind conditions. In previous publications from this hospital, some inherent difficulties in any clinical double-blind experiment have been

*It has been our experience that a number of patients whose behaviour is characterized by apathy respond well to chlorpromazine or other neuroleptic drugs, and in these cases we assume that the patient's withdrawing and apathetic behaviour served as an active defence against intolerable anxiety produced by life stresses.

pointed out.[9, 10] Our conviction that the improvement we saw was in most of the patients the therapeutic result of iproniazid treatment is based on the fact that most of the improved patients had served as their own controls, not having shown any favourable response to other therapies before iproniazid administration. All of these patients were well known to the investigators, and coincidental improvement or recovery as an outcome of the natural history of the condition could in most cases be ruled out.

At the risk of emphasizing well-known facts, it should be noted that this is not the first drug which has proved successful in the treatment of depressive conditions. The amphetamines, nicotinic acid, the barbiturates, testosterone, and other steroids, to name a few, have all been reported and used as effective therapeutic agents in depressions. At this time, there still exists no specific pharmacological therapy for depressive states or any other treatment that can be compared in prompt and general effectiveness to electroconvulsive therapy.

There would appear to be good reasons why the term "energizing drugs", which has recently been proposed for iproniazid and drugs with similar action, should not be permitted to become a stock phrase in the physician's vocabulary. Such a term would imply that all that is wrong with a patient in whom such drugs would be effective is a loss of vital or "psychic energy". The scientific authenticity of such a concept is, however, still questioned and psychiatrists who are accepting it have not yet come to an agreement with regard to an unambiguous definition of the term. The term "energizer" carries a deceptive notion that in depressed conditions energy is reduced, while in reality the situation is more complex and the maintenance of the inhibitory state which we observe clinically as a psychic depression involves a considerable expenditure of biological defence reactions to stress. In the new field of psychopharmacology, special caution is indicated to avoid seductively simple "explanations" which may be suggested by plausible terminology. The terms "tranquillizing", "ataractic", and "energizing" all ascribe to these drugs the value of producing a simple and predictable change in the organism. In fact their action is far more complex and less dependable than is implied in the use of such terms, and in the interest of a sober, professional attitude and of objective scientific thinking, it would appear advisable to avoid all terms which carry subjective value connotations and insist on less persuasive but more precise and neutral terminology.

The theory that mental stimulation is closely related to an increase in cerebral serotonin is attractive but has not yet been confirmed, nor is there any evidence that the fluctuations of serotonin contained in the brain are causally related to corresponding changes in mental function. Iproniazid is a powerful inhibitor of the enzyme mono-amine oxidase which is responsible for destroying serotonin in the brain. The amphetamines and drugs related to iproniazid, e.g. isoniazid, have also an inhibitory effect on mono-amine acids, but it has been claimed that they are less effective in this respect than iproniazid and hence less effective therapeutically in depressive conditions. In this connection, it should be noted, however, that Salzer and Lurie[11] observed with isoniazid a considerably higher percentage (68.3%) of good therapeutic results in depressed patients than we did.

Whatever its mode of action, iproniazid in our experience has proven effective in counteracting depressive symptoms. In certain cases, it was even effective after electroconvulsive therapy had failed. It seemed to hold particular promise in chronic and otherwise refractory cases which often presented a particularly difficult therapeutic challenge. The frequency of undesirable and serious side effects in our small sample at the recommended dosage, however, was high enough to deter us from continuing its use, at least until a sufficient amount of data has accumulated to determine the true incidence of serious side effects in a large sample.

SUMMARY

Iproniazid (Marsilid) was used in the treatment of 31 patients in a mental hospital.

The dosage used was 50 mg. three times a day (27 patients) or 50 mg. twice a day (four patients) over periods from 14 to 112 days.

The drug proved effective in counteracting depressive symptoms even in some cases where electroconvulsive therapy had failed. Thirty-five per cent significant improvement was obtained.

Side effects and complications consisted in dizziness, ataxia, loss of muscular tonus, hypotension and syncope. One patient sustained a fracture of the tibia in a fall due to ataxia. One patient died from acute toxic necrosis of the liver.

A theory concerning the mode of action of iproniazid is discussed, and attention is drawn to other pharmacological agents reported successful in the treatment of depressive conditions.

Iproniazid appears to be a drug with an interesting therapeutic potential in depressive conditions. At the present time the authors have discontinued its use because of the high incidence of serious complications in their small sample group.

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