There are also some specific points about the properties of the drug which may be relevant. Phenoxybenzamine is not easily soluble, and the concentrate we produce is an acidified mixture of ethanol and propylene glycol containing 100 mg phenoxybenzamine in 2 ml for intravenous use after dilution. This solution (pH 2.7-2.8) is a local irritant even when diluted according to the directions in the package insert if, for instance, it leaks from a vein. With regard to repeated long term use, it may be relevant that phenoxybenzamine is mutagenic in some *in vitro* tests (Anon, 1983). Phenoxybenzamine by intraperitonal injection in the rat has been reported (like many other substances when given by this unphysiological route) to give rise to sarcoma (National Cancer Institute, 1978), and formal oral carcinogenicity studies in the rat are in progress. Conversely, phenoxybenzamine orally has been in use for 24 years without evidence of human carcinogenicity emerging.

The relevance of these facts to the use Professor Brindley has described is entirely unknown, but they should be borne in mind when considering the risks and benefits of treating individual patients. Smith Kline & French Laboratories do not endorse this use of 'dibenyline injection'.

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MANIA AS A SEQUEL TO A ROAD TRAFFIC ACCIDENT

DEAR SIR,

A 23 year old, single female was in a car crash in March 1981. She was a front seat passenger, wearing a seat belt, in her fiance's car which was involved in a head-on-collison with a bus. She received multiple lacerations to her face and neck, fractures of the transverse processes of 3rd and 4th lumbar vertebrae and compression of the body of L3. Abdominal pain was followed by shock. A diagnosis of an intra-abdominal bleed, confirmed by peritoneal tap, was treated conservatively.

She was unable to remember details for a period of time preceeding her accident and was described as quite confused and amnesic for a major part of her 12 day stay in the general hospital. When told that her boyfriend was in another hospital, she enquired if he too had been in an accident. On discharge home her family found her to be talking continuously. She was normally a quiet, easy going girl, who had to be encouraged to get out of bed in the morning. Now she started getting up at 6.00 a.m. and told her mother that she wanted to pull her weight in the house and that she was going to do the housework. She was unable to sit down, and continually tried to do all the cleaning in the house. Six weeks following discharge from hospital she returned to work and her employers contacted the family, with concern, as she was described as overactive in her work. Two weeks later her mother noticed her behaviour becoming stranger. She was restless at home and talked more than usual. She became religous and claimed that she was 'Mary' and then later that she was the 'Virgin Mary'. She started spending money in what was described as a 'sillier manner'. She claimed to have special powers.

At this stage she was admitted to a psychiatric hospital on a Temporary Certificate. On admission she maintained that she felt great and wanted to be with her husband, Brendan, who had died 'on The Cross' the previous week, that she had two children and that she had special powers that would cure other patients. She admitted to auditory hallucinations coming from a dustbin, saying the voice was that of her husband, Brendan, telling her that she was terrific and great. On testing, her concentration and memory were poor. She was unable to give the months of year or an accurate history of events. She was distractable and exhibited flight of ideas. She was disinhibited on the ward.

She was treated with a mixture of Lithium, Haloperidol intravenously and Chlorpromazine orally. Psychological testing revealed no brain damage and an IQ on the Borderline Mental Handicap Level. An EEG showed mild abnormalities (a repeat 4 months later was normal).

Family history revealed that both parents were alive, healthy and in their 50's. Father was described as a heavy drinker. Her birth weight had been 8 lb and her milestones were normal. School, where she was described as middle of her class, ended at 13 years. She had a good work record and was in her present job in a factory for 6 years. She made friends easily and had an active social life, described as normal. She had had no previous psychiatric illness or psychiatric contact. Her maternal aunt in Australia was thought to have suffered from a post-natal depression.

Her mania required approximately 4 months inpatient treatment with a return of elation early on when her medication was reduced. Final resolution of the elation was followed by mild depressive mood swings. She has been maintained on a small dose of Perphenazine, usually 4 mg. at night, and in the last year requires sleeping medication for some days prior

to her menses. She had two mild episodes of depression lasting some months and requiring chemotherapy. Her work record has not been as good as it was pre-accident. She terminated her engagement and has had some contact with new boyfriends, but no lasting relationship.

Her legal advisors requested some indication of the prognosis for mania following head injury or road traffic accidents. A search of the literature failed to reveal hard facts upon which to base the medico-legal report. This was surprising in view of the amount of literature available on depression and head injury. I would be grateful, therefore, if your readers could either through your columns or by direct correspondence acquaint me with a prognosis of the cases of mania following road traffic accidents of which they have had knowledge and experience.

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INFORMED CONSENT—OR THE UNWITTING PARTICIPANT

DEAR SIR,

In his paper on informed consent (*Journal,* October 1983, **143,** 416–8) Max Hamilton states that it is a product of the anti-medicine movement, comprising material that patients mostly don't understand, so here "the nonsense enters". And "if it is meaningless in the clinical situation, it is equally so in a clinical trial". In summary, he is no advocate of it. However, there is another side of the medal that he did not discuss.

First, evidence before a court, followed by a lengthy discussion in the *Lancet* in 1982, showed the necessity of obtaining informed consent. Professor Hamilton must have overlooked this discussion. It concerned the death of a 84-year old widow following bone marrow suppression induced by 5-FU after an operation for carcinoma of the rectum. The efficacy of 5-FU was tested by means of an infusion via the portal vein. This patient had not been asked informed consent; she was an unwitting participant in this potentially dangerous randomised controlled trial, as were other participants (Brahams, 1982).

Second, experimenting doctors can have conflicting interests. There are personal interests, of financial or scientific origin (status, promotion, funds), and there are patient-directed goals. These interests may clash, and personal reasons for conducting research may override the obtaining of informed consent, as I have found.

Third, the World Medical Association adopted the Declaration of Helsinki (1964, revised in 1975 in Tokyo) and approaches this problem also from the standpoint of patient protection. The main effect of the Helsinki Declaration is the setting up of an independent committee to consider, comment on and guide research proposals (para. 1.2) and the insistence on (preferably written) informed consent. The UNO covenant concerning Civil and Political Rights also prohibits medical experiments without consent (art. 7), but is not applicable to the USA, which has not yet ratified it.

Fourth, contrary to Hamilton's suggestions most patients do seem to want to know as much as they are able to understand about their treatment and the alternatives; surveys showed that "people have a universal desire for information, choice and respectful communication about decisions" (Caplan, 1982). They expected to have as much information about their treatment options as physicians could reasonably be expected to provide.

Fifth, it is my opinion that any investigation or treatment that is not an accepted norm in medical practice may fall outside the "consented area". Then, obtaining informed consent becomes necessary. Ethical committees should not be able to substitute their permission for that of the patient, as is the case now according to the Helsinki Declaration (Kemperman, 1982). If the patient is not capable of understanding the basic plan of management, he or she should be excluded from the trial. The patient should have the initial responsibility, even if he or she may show later on the wish to delegate it.

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PSYCHOSIS AND ANTIDIURETIC HORMONE

DEAR SIR,

There are certain features of Lever and Stansfield's report of a patient with Addison's disease, psychosis and the syndrome of inappropriate secretion of antidiuretic hormone (IADH) (*Journal,* October 1983, 406–10) that we feel merit further comment.

First, in attempting to explain the development of