of drink to such an extent that his ability to drive properly is for the time being impaired, which is all the present law requires. The British Medical Association Special Committee (1960) suggested that clinical examination only revealed positive clinical signs when the subject was "half-seas over," and this is certainly my experience.

I strongly disagree with Dr. Freeman's views on the importance of the pupils. I can only look back on 65 cases, compared with his 400, but I have not seen widely dilated and fixed pupils once, and I have certified about the same percentage as he. The last case I was asked to see was quite drunk (he could not stand up), but his pupils were normal, and so, incidentally, was his pulse and pulse pressure. However, I would agree about the importance of nystagmus. It has been present in nearly all the cases that I have certified.

The police surgeon, I would like to suggest, is no better qualified to judge drunkenness than the station sergeant; he should stick to what he is qualified to judge—the presence or absence of disease—and this, I understand, is what he was originally asked to do. If he must certify, then I suggest that he must do it more on clinical impression, not necessarily backed by positive physical signs.

Why is it that the courts are so sacrosanct? The law says that they must take into account the results of urine analysis, or the refusal to provide a specimen of urine for analysis, but, as Dr. Freeman points out, they have been reluctant to attach any importance to these things. I was involved in one case where the police evidence was very strong, and the urine showed 270 mg./100 ml. of alcohol; the man was found not guilty, and awarded damages against the police. One can understand the jury finding him not guilty, because they do not know any better, but it is difficult to explain why the learned recorder awarded the damages. I have never heard or seen this sort of thing openly criticized. Why is it, too, that the policeman's evidence is so often discounted when the doctor fails to certify, having seen the subject when he has sobered up? It is my impression that this invariably is the case, and it is so patently ridiculous.

The sooner legislation is enacted that lays down a blood-or-urine-alcohol content above which conviction is mandatory the better.—I am, etc.,

Southampton, Hants.

M. G. BRIDGER.

Correlations of Alcohol Levels

SIR,—In an experiment performed in 1962¹ a comparison was made between blood, breath, and urine alcohol levels, where the breath level was measured using the Breathalyzer, with the subject breathing directly into the instrument. The correlations reported were: blood and breath 0.956; blood and urine 0.944; breath and urine 0.882.

It might be concluded from these figures that the relationship between breath and urine alcohol measurements leaves much to be desired, but it has been suggested by Dr. B. M. Wright that, since the urine reflects blood levels attained at an earlier stage in the observations, a more legitimate comparison would be derived by pairing each urine figure with the breath or blood figure obtained half

an hour previously, rather than with the figure obtained at virtually the same time as the urine.

Using the results from the same experiment, this procedure gives correlations of: blood and urine 0.952; breath and urine 0.975. Still higher correlations are obtained if the figure used for blood or breath is the average of the figure obtained at the same time as the urine and the figure half an hour previously. The correlations are then: blood and urine 0.984; breath and urine 0.977.

Whichever method of correlating is used, an estimate of the blood or breath level may be attained by dividing the urine level by 1.3.—I am, etc.,

Medical Research Council,
Statistical Research Unit,
University College Hospital
Medical School,
London W.C.1.

I. D. HILL.

REFERENCE

- ¹ Begg, T. B., Hill, I. D., and Nickolls, L. C., in *Alcohol and Road Traffic*, p. 277, 1963. B.M.A., London.

The Discharged Schizophrenic

SIR,—I feel that Dr. D. H. W. Kelly and Dr. W. Sargent (16 January, p. 147) are a little euphoric when they refer to the large percentage of discharged psychotic patients who "now live and work happily back in the community again." They make no reference to the need to support these patients, especially those of the "residual symptom group" with regular follow-ups in the home.

In this district, presumably owing to the shortage of mental welfare officers and/or psychiatric social workers, it is the family doctor who has to cope with these patients as they teeter along precariously balanced on the brink of insanity. It is we who have to cope with the disturbed children and harassed husbands of the "odd," "peculiar," often hostile mother; we who have to support the frightened wife whose husband is symptom-free—but for how long she never knows—and we also who get the urgent call from factory or home to cope with the disturbance resulting from a psychotic relapse (42% of Dr. Sargent's patients relapsed and needed readmission).

By all means let Drs. Kelly and Sargent claim the credit for emptying their mental hospitals, but not that the average discharged schizophrenic lives "happily," nor that he is other than a strain, often a severe one, on the community to which he has been returned.—I am, etc.,

London S.W.14.

J. H. S. HOPKINS.

Treatment with Phenothiazines

SIR,—Dr. William Sargent and Dr. D. H. W. Kelly (16 January, p. 147) once again point out the benefits associated with weight gain during the treatment of schizophrenia. I have noticed in some cases that the gain in weight during treatment with phenothiazine derivatives is more marked when these are given 15–30 minutes before food. This may be because their local anaesthetic effect on the gastric mucosa reduces feelings of nausea, distension, or satiety, enabling the patients to take larger meals. It could be due to higher blood

levels inducing a greater hypothalamic effect or it could be a placebo response. "Tonics" and "appetite stimulants" are commonly given before meals, and patients told to take tablets or syrups then are likely to expect that an increase in their food intake will follow. It would seem more logical to make trial of or utilize these effects rather than unthinkingly to continue the traditional postprandial administration of these drugs.—I am, etc.,

S. CLIFFORD ROGERS.

Rugby, Warwickshire.

Combining the Antidepressant Drugs

SIR,—The report of Dr. L. W. Bowen (5 December, p. 1465) of a death associated with combined antidepressant drugs is disputed by Dr. W. W. Sargent (23 January, p. 251). As the pathologist concerned in this case, I now have the coroner's permission to enter into the discussion. Dr. Bowen's report was, in fact, published without my prior knowledge and there are several omissions in the pathological presentation which have a bearing on the interpretation of the death. Firstly, in the post-mortem findings there were, in addition to evidence of myocardial degeneration, small bilateral clear pleural effusions and pulmonary oedema. These findings taken together formed the basis on which the immediate cause of death was attributed to heart failure due to myocardial degeneration. This could hardly have been the whole explanation, as the history clearly pointed to an acute cerebral disturbance and there was certainly nothing macroscopically wrong with the brain or its vessels. Furthermore, there was no evidence of pneumonia or other infection to account for the hyperpyrexia. Analysis of fluids and tissues was therefore undertaken and it was from the interpretation of these results, coupled with the clinical aspect, that a secondary cause of "Combined action of antidepressant drugs" was arrived at. Here the wording of Dr. Bowen's report is liable to misinterpretation, as I made no suggestion that myocardial degeneration was brought about in any way by drug action.

Dr. Sargent does not accept that there is any evidence that the combined action of desipramine and phenelzine played a part in this death unless there was overdosage, but he does seem to agree that the signs and symptoms resembled those of desipramine overdosage either alone or in combination with phenelzine. It is not true that the only evidence that she had not taken an overdose of desipramine was the amount of tablets left in the bottle. Poisoning (in the ordinary sense, meaning substantial overdosage) was excluded by analysis. These analyses were undertaken by Dr. A. S. Curry, of the Home Office Forensic Science Laboratory in Nottingham, and I do not think that anyone knowing Dr. Curry's reputation as a toxicologist would doubt his results. Also Dr. Sargent gives little credit to the knowledge and experience of "the Coroner and his medical advisers" in suggesting that we have forgotten about psychiatric patients hoarding drugs for suicidal purposes. Such an explanation is not required until evidence of overdosage has been established.

In summary, this was the case of a woman who had been taking phenelzine (and chlorpromazine) regularly, and during the few weeks before her death took desipramine

intermittently. The immediate cause of death was heart failure, although the clinical symptoms suggested overdosage of one or other of the antidepressant drugs. Analysis showed no evidence of overdosage, and the conclusion that the combined drugs taken in substantially normal dosages had produced these symptoms and contributed to her death seems a more reasonable explanation than that put forward by Dr. Sargent. Surely such a patient can be hypersensitive to the newly introduced drug (desipramine) in combination with the drug (phenelzine) which she has tolerated for so long. With all due respect to Dr. Sargent, the fact that previously she had shown no adverse reaction to a different drug (amitriptyline) in combination with phenelzine seems irrelevant to me.

It may well be that cases like this are extremely infrequent, but need one therefore deny that a small risk exists? If the probable benefit to the patient is greatly in excess of the small risk, then experienced psychiatrists like Dr. Sargent are presumably justified in using this line of treatment without fear of litigation. Those with less specialized experience in using antidepressant drugs will probably prefer to heed the warnings of the Witts Committee and other authorities. One such authority, Dr. Hollister, writing on "The Toxicity of Psychotherapeutic Drugs" in the current *Practitioner*,¹ states that "Any such combination is far too dangerous for general clinical use."—I am, etc.,

G. F. M. HALL.

Department of Pathology,
General Hospital,
Nottingham.

REFERENCE

- ¹ Hollister, L. E., *Practitioner*, 1965, **194**, 72.

SIR,—A high proportion of patients with a depressive illness will respond to an antidepressant drug or, if refractory, electroconvulsive therapy. But a small number will either not respond at all or quickly relapse. It is in these patients that combined antidepressant therapy is sometimes remarkably effective.

Eight of my patients are at present receiving a combination of amitriptyline (150 mg. a day) and either iproniazid (Marsilid) (50–100 mg. a day) or isocarboxazide (Marplan) (20–30 mg. a day). All have been seriously disabled by their symptoms continuously for between two to seven years and have failed to respond to antidepressant drugs given alone or combined with tranquillizers and/or E.C.T. The severity of their symptoms is reflected in the fact that one has had a modified prefrontal leucotomy and three others have been considered for this operation. All have at some time during their illness contemplated the possibility of suicide. All these patients are now sufficiently well to be able to work and again lead useful lives. Their symptoms are suppressed rather than cured, as with all antidepressant drugs, and attempts to stop or reduce the dosage of one or both of these drugs result in symptoms returning.

No one will deny that combinations of antidepressant drugs are liable to show side-effects and sometimes to bring about signs of marked over-stimulation. But I suspect that amitriptyline is much safer in this respect than imipramine (Tofranil), just as the hydrazine monoamine-oxidase inhibitors

are probably safer than tranlylcypromine (Parnate). This may be related to the fact that amitriptyline has, on the whole, more of a sedative and less of a stimulant action than imipramine. Like Dr. Sargent (23 January, p. 251) I have seen no serious side-effects from combining iproniazid or isocarboxazide with amitriptyline, although excessive weight gain, incoordination, and hypotensive effects may require dosages to be reduced. To the best of my knowledge no deaths, apart from those due to suicidal overdosage, have been reported, in contrast to when imipramine is combined with an M.A.O.I.

As Dr. Rees and Dr. Pare¹ emphasized recently, it is often misleading to consider drugs of the same class as exhibiting similar toxic effects and potentiating activities, since each drug has its individual characteristics. This surely needs to be applied here. The combination of amitriptyline with an M.A.O.I. can be extremely effective, and it would, in my view, be wrong to condemn this treatment on what appears to be emotional rather than scientific grounds.—I am, etc.,

Department of Psychological Medicine,
Westminster Hospital,
London S.W.1. P. J. DALLY.

REFERENCE

- ¹ Rees, L., and Pare, C. M. B., *Lancet*, 1963, **2**, 1279.

SIR,—The indications and risks of combining the antidepressant drugs were discussed and put into perspective at a symposium held at St. Bartholomew's Hospital recently.¹

Combining the two groups of antidepressants clearly increases the risk of side-effects. On the other hand, this risk is minimized if they are given by physicians experienced in the use of antidepressants and thoroughly acquainted with their pharmacology. In such hands the increased incidence of side-effects is often justified in severely depressed and otherwise resistant patients because of the clearly increased antidepressant effect of the drugs in combination.—I am, etc.,

C. M. B. PARE.

Department of Psychological Medicine,
Saint Bartholomew's Hospital,
London E.C.1.

REFERENCE

- ¹ *Scientific Basis of Drug Treatment in Psychiatry*, 1965, in press.

SIR,—For the last 13 years I have been treating a lady, now aged 51, for a depressive illness. During this time she has had two hospital admissions, five courses of E.C.T., as well as a trial of almost every new antidepressant drug as these became available. Her psychiatrist stopped her last course of E.C.T. in February 1964. She was no better. In desperation, and encouraged by the writings of Dr. William Sargent, I began to treat her cautiously with a combination of Parstelin (tranlylcypromine and trifluoperazine) and Tofranil (imipramine) in February 1964. Although she has not fully recovered she is, almost a year after this treatment was started, in her own words "tons better." Whereas previously I had been sent for frequently because she felt so

awful she now comes to see me about once a month for a check-up and an adjustment of dosage.

I wonder, Sir, whether those who condemn these very useful drugs and the very occasional need to combine them really have to bear the everyday, year-after-year burden of looking after these patients?—I am, etc.,

Sheffield 2.

H. M. HALLE.

Diagnosis of Amphetamine Addiction

SIR,—I read this letter (2 January, p. 57) with special interest, as in this area of Lanarkshire we find the problem of drug dependence a chronic and continuing one. While numerically the numbers of patients involved is small they do cause a quite disproportionate degree of irritation to both the police and the hospitals by their activities. While we do not seem to have any organized traffic in these drugs a small number of "problem" families undoubtedly overindulge to the extent of producing psychotic and antisocial behaviour.

Could I make the point that it must be rare indeed to encounter an amphetamine user in pure culture? In my experience the picture is almost always blurred by a concurrent barbiturate dependence—usually one of the short-acting variety. Doubtless this is taken to modify the unwanted and unpleasant somatic symptoms of tremor, sweating, etc., produced by excessive doses of sympathomimetic substances. In view of this would it not be better to refer to the condition as amphetamine/barbiturate addiction—the more so when one remembers the quite clear-cut type of dependence that the two drugs produce.¹

I am afraid I have not seen the changes in the buccal mucosa as described, nor am I happy about the allegedly diagnostic chewing movement. In any tense and anxious person habits of chewing, teeth grinding, and licking of the lips are so common as to make the presence or absence of these signs of no value whatever in diagnosis of a toxic psychosis of such a subtle type as these drugs produce. And are the signs in rabbits of any real value?

To make a tentative diagnosis of a drug intoxication in the surgery or out-patients department is very much a clinical problem and is like the recognition of early schizophrenia a matter of a *general impression* coupled with a largely subconscious awareness of the differential diagnoses. While this may sound rather crude by the standards of pure science I am sure that it is the only approach to the problem, and that to search for physical signs of very doubtful validity will only at this point confuse the clinician further.

Amphetamine/barbiturate addicts are as unreliable as any when it comes to admitting their activities, and I would be very suspicious of the confident statement that "When confronted with this evidence they usually 'come clean.'" A positive diagnosis is really impractical unless biochemical facilities of above average are available for examination of urine specimens. Connell² has summed up the position well, but even the simplest and shortest methods he describes are pretty exacting in time, equipment, and most of all experience in the laboratory technician. From