This problem has been discussed and argued frequently by psychiatrists, but I have no doubt that most would agree with your broad classification of depressions into reactive and endogenous. The evidence that these are two entirely different diseases is very strong. They differ clinically in that the endogenous depressive rarely uses the term "depressed." He complains more of apathy, lack of feeling, or loss of interest. He may be retarded in thought, speech, drive, and ability to make decisions—symptoms not found in the reactive depressive. Furthermore, the endogenous depressive is frequently deluded, the delusions being of guilt, forthcoming punishment, ruin, disease, poverty, failure, and his own misdeeds. Delusions are never found in reactive depressions. The endogenous depressive tends to blame himself for his condition, which he does not recognize as an illness. The reactive depressive, on the other hand, fully realizes that he is ill, and seeks medical advice. The endogenous depression is often worse in the mornings. The patient tends to awaken early in the morning in an agitated, restless, and particularly depressed state. The reactive depressive, on the other hand, sleeps late, but has difficulty in getting off to sleep.

Perhaps the most obvious difference is the

observations and leads to more accurate and precise clinical medicine. I think the same holds true for psychiatry.—I am, etc.,

London W.1.

S. BOCKNER.

SIR,—I would like to make the suggestion, arising from reading your leading article "Drugs for Depression" (29 August, p. 522), that since, as you correctly state, reactive factors may be present in both "endogenous" and "reactive" depression it would be better to abandon your terminology and use classical and non-classical instead.

I am studying a group of patients referred for out-patient electroplexy (E.C.T.) at St. Thomas's. I have called those classical depression who show insomnia with early waking, symptoms worse in the morning, agitation and/or retardation, loss of concentration, energy, etc., with thoughts of unworthiness or self-reproach. All patients who do not show this picture were called non-classical depression. Reactive factors and the degree of response to out-patient E.C.T. were recorded *independently* of the clinical subdivision. The following results were obtained:

Type of Depression	Totals	Response to Out-patient E.C.T.				Reactive Factors
		Excellent	Good	Slight	Nil or Worse	
Classical	109	35	40	18	16	52 (47.7%)
Non-classical .. .	117	8	33	46	30	58 (49.6%)
Totals .. .	226	43	73	64	46	

$$\chi^2 = 33.9. \quad 3 \text{ d.f.} \quad P < 0.0005.$$

entirely different affect or mood in the two conditions. The reactive depressive feels miserable and despondent, in the ordinary sense that we all feel at times, whereas the endogenous depressive has a new and entirely novel feeling. The term "depression" in endogenous depression is misleading and not descriptive of the mood as the normal person knows it. The mood has a special and abnormal quality, so that relatives note a change in the whole person, both in appearance and behaviour. The patients do not cry, as the depressed neurotic does, frequently and copiously.

Not only do these two conditions differ in symptoms, but they also have a different treatment and prognosis. Most endogenous depressions recover quickly with electroplexy (E.C.T.) and many respond to anti-depressive drugs. E.C.T. is generally valueless in reactive depressions, and drugs have only a limited value in these cases. It is quite clear that the difference between these illnesses is the difference between psychosis and neurosis. To suggest that there is a sliding scale with mild depression at one end and severe depression at the other is also to suggest that neurosis and psychosis are mild and severe forms of the same illness. Few would agree with this, and furthermore one frequently sees mild examples of both conditions.

These illnesses differ in their aetiology, symptomatology, prognosis, and treatment. What more is required to distinguish them as different diseases? In general medicine we carefully identify and separate different forms of similar diseases—e.g., the classification of nephritis. This disciplines our clinical

These results show the equivalence of reactive factors in both types, but the classical type of depression, as expected, shows a much greater response to E.C.T.

In more detailed subdivision of the material I have used the term "psychotic" depression only where there was gross loss of insight with or without depressive delusions. Manic-depressive is reserved for only those cases with definite manic swings—rare in out-patient work, about 5 in 300. The classification involutional was not used at all.

I would hesitate to start a discussion reminiscent of unimodality and bimodality in hypertension, but it seems possible in view of graded responsiveness to E.C.T. that there may be several further subdivisions of depression, distributed along different axes, and we should not cling to the simple dichotomy of endogenous and reactive.—I am, etc.,

ERIC D. WEST.

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Medicine,
St. Thomas's Hospital,
London S.E.1.

Buccal Oxytocin

SIR,—Your leading article on "Buccal Oxytocin" (19 September, p. 705) prudently draws attention to the necessity in using buccal oxytocin for the same close and continuous observation of the patient in a fully equipped hospital maternity unit as is required when oxytocin is given by the intravenous route. When giving intravenous oxytocin the

dose may be controlled with precision (as with the Palmer infusion pump) and altered according to the nature of uterine response. The effect is immediate and control is complete. With buccal oxytocin, on the other hand, when the mouth may contain up to 800 units oxytocin, absorption is beyond control. In spite of the closest observation of the patient there can be no control of the effect once absorption from the mouth has taken place. The knowledge that uterine activity falls by 50% within 15 minutes of withdrawal of oxytocin tablets,¹ far from being a comfort, must be regarded as a positive indictment of the method. Uterine hyper-tonus of a very few minutes' duration can produce devastating results. Apart from killing the foetus or causing permanent damage it may cost the mother her life. The close observation of the patient taking buccal oxytocin can only be aimed at the recognition of the dangerous complications of the method and will do little in the way of preventing them. The introduction of buccal oxytocin must surely be regarded as a retrograde step in obstetrics.—I am, etc.,

Department of Obstetrics
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Jessop Hospital for Women,
Sheffield 3.

F. A. BEST.

REFERENCE

- ¹ Elstein, M., and Wright, H. P., *J. Obstet. Gynaec. Brit. Cwlth*, 1963, **70**, 1005.

Propranolol for Angina

SIR,—One must feel some doubt about the validity of the conclusions reached by Dr. J. Hamer and his colleagues (19 September, p. 720) when they allude to the efficacy of intravenous propranolol in improving the effort tolerance of patients with angina pectoris. They show that of thirteen patients who were limited in their exertions by angina before the administration of this drug five remained free from angina and eight required greater effort to cause angina immediately after the drug was given. They do not advert at any stage to the well-known effect of exertion in temporarily increasing the effort tolerance of patients with effort angina. In my experience the case of classical "second wind" angina is not uncommon, but I would suggest that some degree of "second wind" is to be found in nearly all patients with this coronary syndrome. What results might be expected under the same circumstances in these patients if sterile water were administered instead of propranolol?—I am, etc.,

Dublin 4.

RISTEARD MULCAHY.

Excessive Consumption of Drugs

SIR,—At a time when the overall drug consumption rate is rising, awareness of interaction between various medicaments is increasing, and attention is rightly focused on illicit and excessive drug taking, the following cases and observations seem noteworthy.

A man aged 54, being treated for a chronic anxiety state, became ataxic and clouded mentally. Investigation and inquiry led to the detection of a serum-bromide level of 235 mg. per 100 ml. (the normal serum content being

negligible), which fell subsequently with corresponding clinical improvement. He had simply bought a bottle of 100 5-grain (324-mg.) tablets of potassium bromide (costing a few shillings) over the counter and helped himself. It appears hazardous for such a toxic substance, as yet not on Schedule 4, to be temptingly available to those all too likely to seek relief from stress, often using them in possibly synergic addition to prescribed medication.

In a further case bromism resulted from the repeated dispensing of a bromide-sedative mixture, there surprisingly being no limit at present on the number of times this is permitted. A female patient aged 56 years became grossly deluded and hallucinated, her disorientation indicating a toxic confusional state rather than a paranoid schizophrenic psychosis, although no physical lesion was detectable. Her husband, with familiarity breeding unawareness, at first denied that she had been taking drugs, but finally recollected the occasional use of medicine originally prescribed 20 years previously. A fall of serum bromide from over 160 mg. per 100 ml. resulted in her psychosis remitting. Looking at the tattered, yellowed, but regularly used prescription, now two decades old, one wonders how often this situation might occur elsewhere, and with what consequences.

Other cases have been seen where addiction to chlorodyne has developed, this mixture also being freely available for general purchase. It is hoped that further publicity of this fact will hasten measures already being considered to control this abuse.

Considering further the question of self-medication it is likely that vying for popularity with much advertised laxative, analgesic, and vitamin preparations are the non-medical "booster" and "tranquillizer" products. These may be purchased without restriction, though they contain significant amounts of phenacetin and are likely to be taken in excess. Phenacetin may in excess cause chronic interstitial nephritis and papillary necrosis. "Phenacetin nephropathy," being sought by pathologists, is now being reported more frequently, and not without reason did the United States Federal Food and Drug Administration issue an Order (8 August 1964) requiring preparations containing phenacetin to carry a warning that prolonged use or large doses could cause damage to the kidneys.

It is gratifying that the Pharmaceutical Society has recommended to the Ministry of Health a comprehensive scheme for the quality control of drugs and medicated products. However, this sampling and testing does not apparently deal with the abuse of over-consumption as described above.

These experiences and findings are seemingly not unique, and, if so, strongly indicate the need for urgent investigation and remedial action.—I am, etc.,

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Cheadle, Cheshire.

The overall results of serological response to vaccination are shown in the Table, and the response to one strain (A2/Eng/1/61) illustrated in the Figure. A high proportion have responded to vaccination with a significantly raised antibody level against all the virus strains. Titres against the new A/Ned/1/64 strain not included in the vaccine are as high as those against A2/Sing/1/57. The antibody induction against B/Tai/4/62 was as effective as against the antigenically distinct strain B/Eng/939/59, although the former strain has not been isolated in this country and the resting (prevaccination) antibody in the community is low or absent. It seems likely that the present group of patients were, in fact, undergoing a primary response to this strain.

Of the 48 patients in the group one had a local and three a general reaction. The local reaction consisted of a sore arm lasting one week and the general reaction a mild 'flu-like illness. All continued their normal activities and all have asked for revaccination this year. Most consider that they have had less acute respiratory exacerbations than in previous years and less than their families and friends this year.

Continued study of this and a control group is in progress to determine the degree of clinical protection induced and to relate this to serological response. Further blood samples will be taken to assess the duration of raised antibody levels. These results will be published more fully later.

I am grateful to Messrs. Evans Medical Limited for providing facilities for the serological investigations reported above.

—I am, etc.,

London N.13.

R. J. BLOW.

Polyvalent Influenza Vaccine in General Practice

SIR,—The recent report to the Medical Research Council (1 August, p. 271) shows a marked serological response to oil-adjuvant influenza vaccine containing a single virus strain (A2/Sing/1/57). In general practice it would seem desirable to use a polyvalent influenza vaccine giving protection against a number of antigenically different, common epidemic strains especially for elderly patients suffering from chronic chest or heart disease. For practical purposes this needs to be a single injection with minimal side-effects.

Accordingly vaccination was offered to selected patients in the autumn of 1963 and 239 accepted; 48 of these had blood samples taken before and three months after vaccination.

The vaccine used was a commercially available polyvalent oil-adjuvant vaccine (Admune, Evans Medical Limited) containing: A2/Sing/1/57 1,500 haemagglutinating units, A2/Eng/1/61 500 haemagglutinating units, B/Eng/939/59 1,000 haemagglutinating units, and B/Tai/4/62 500 haemagglutinating units per dose. This is approximately one-fifth of the amount of antigen customarily employed in conventional saline vaccines. A single dose of 0.25 ml. was given by deep intramuscular injection into the deltoid. Haemagglutination-inhibition titrations on the 48 paired sera were performed by the

W.H.O. plastic-plate method using test strains identical with those in the vaccine, except in the case of A2/Sing/1/57, where a homologous but more antibody-avid test strain was used.

After the tests were completed a new variant Asian strain (A/Ned/1/64) was reported, and it seemed of interest to determine whether a satisfactory antibody level against this new strain had been induced by the vaccine used. This was done with 15 pairs of the paired sera, randomly selected.

Haemagglutination-inhibiting antibody levels to A2/Eng/1/61 strains of 48 adults before and after vaccine.

Haemagglutination-inhibiting Antibody Response of 48 Adult Patients to a Single Dose of Polyvalent Oil-adjuvant Influenza Vaccine

		Virus Test Strains (8 haemagglutinating units)				
		A2/Sing/1/57	A2/Eng/1/61	B/Eng/939/59	B/Tai/4/62	A2/Ned/1/64*
Geometric mean titres	Prevaccine	40.7	63.7	6.9	7.6	42.6
	Post-vaccine	507.0	1,455.0	229.1	266.5	609.5
Percentage of patients with antibody titre > 1/48	Prevaccine	39.6	58.3	12.5	12.5	33.3
	Post-vaccine	97.8	100	87.5	83.3	100

* The A/Ned strain was not included in the vaccine. H.I. tests were done on 15 pairs of sera.

Aphthous Ulcers and Vaccination

SIR,—Whilst the relationship of recurrent aphthous ulcers of the mouth to recurrent labial or genital herpes is still under dispute¹ cases are seen in which outbreaks of typical aphthous ulcers coincide with recurrences of such herpetic lesions. A wide variety of treatments are recommended for these conditions,²⁻⁵ but all disappoint at times in practice. Smallpox vaccinations have been advised since the days of Dr. Edward Jenner (quoted by R. D. Andrews⁶), but I have yet to find a reference to any series, however small, treated in this way.

Following a stimulating letter from Dr. F. J. Stokes I have repeatedly vaccinated six patients who had all been suffering from recurrent aphthous stomatitis for more than 18 months. Two were revaccinated six times at 14-day intervals, three five times, and one twice. These patients remained free of ulcers for between 19 and 52 weeks after the first vaccination, the first five relapsing and the last being free at follow-up.

These figures give limited support to the view that revaccinations are of value, and if any practitioners care to let me know of their own results I shall be happy to collate the figures.—I am, etc.,

Rugby.

S. CLIFFORD ROGERS.

REFERENCES

- White, H. H., *Lancet*, 1964, 1, 329.
- Ibid., 1963, 2, 1320.
- Natarajan, R., *ibid.*, 1964, 1, 830.
- Crichton, W. H., *Brit. med. J.*, 1964, 1, 231.
- Ibid., 1963, 2, 1644.
- Andrews, R. D., *Lancet*, 1962, 1, 322.