physicectomy should not be allowed to bias future practice. If the presence of these hormones can be abolished by newer methods then the proportion of regressions might be improved, especially if a simple reliable means can be found for identifying patients whose tumours are dependent on prolactin and growth hormone.

In conclusion, then, receptors may now be detected (at least presumptively) in human breast, prostatic, endometrial, and other cancers, and these preferentially bind oestrogen, androgen, progesterone analogue, prolactin, growth hormone, or placental lactogen. Their possible permutations and interrelationships emphasise the heterogeneity of human cancers, and breast cancer in particular—making it clear that there can be no single best treatment. Even though quadruple cytotoxics may yield the largest immediate number of remissions in breast cancer, most of these are short-lived, and after relapse there may be less chance for antihormonal treatments. The most hopeful prospect is that work may determine criteria for study of the actual breast cancer of a given patient—before it all gets into formalin—to choose the best treatment for that patient at that time.

7. Shysamala, G, Biochemical and Biophysical Research Communications, 1972, 46, 1623.

Chronic urticaria

Estimates of the incidence of urticaria differ quite widely, but all agree that it is common. In the more dramatic, acute form of urticaria there is often a clear allergic cause, and such cases may understandably lead doctors to equate urticaria in general with allergy. Yet there is no association between chronic, as distinct from acute, urticaria and a personal or family history of atopic disorders, and the competent and critical investigation of patients with chronic urticaria rarely establishes an allergic cause. In one such investigation 3 100 patients with chronic urticaria were admitted to hospital for detailed study: food allergy was considered to be responsible for the urticaria in one patient but in the remaining 99 no unequivocal aetiological factors were discovered. Possibly chronic urticaria may be caused by an abnormality (or more probably any one of several abnormalities) in the pharmacological mediators of weal formation, but the precise nature of these postulated abnormalities is still speculative.4

The management of the patient with chronic urticaria is always difficult, and one American dermatologist is reported to have said that he would prefer to have a lion in his consulting room. The observation that aspirin releases histamine in patients with urticaria pigmentosa4 was therefore a useful advance which has led to a practical and fruitful approach to this frustrating problem. Moore-Robinson and Warin5 later showed that a provocative test dose of aspirin caused a definite aggravation of the urticaria in 22% of patients. The number of substances which, like aspirin, appear to enhance the urti-
carial reaction is now considerable.6 They include tartrazine and other azo dyes, which are used to colour many foods and some drug tablets, and sodium benzoate and 4-hydroxybenzoic acid, used as preservatives in pickles, sauces, instant coffee, and other foods and beverages. Drugs such as indomethacin may have a similar action, and so may penicillin, though it usually causes urticaria by an allergic mechanism.5 The yeast candida in the gastrointestinal tract and brewer's yeast may also cause urticaria by an immunological mechanism, but they may also non-specifically enhance the urticarial weal. These observations, abundantly confirmed by much published and unpublished experience, have enabled dermatologists to devise several screening procedures for urticaria. While they do not establish the "cause" of chronic urticaria they do allow the elimination of exacerbating factors with considerable benefit to the patient.

Recently Warin and Smith6 reported an excellent example of this type of procedure. All of their 111 patients had had urticaria for at least two months. They were each given a series of identical capsules containing various doses of one of the following substances: tartrazine, sodium benzoate, 4-hydroxy-
benzoic acid, tyrosine, penicillin, aspirin, brewer's yeast, candida in pickles or lactose (as a control). One numbered capsule was taken each day, and any reactions were recorded by the patient on a chart. If the chart suggested a reaction to a particular substance all the capsules were administered again, but in a different order. If the second chart incriminated the same substance as the first, then the test was recorded as positive. After a pilot study the candida was omitted since reactions to it paralleled those to brewer's yeast, which is much easier to obtain and to handle. Exacerbations of the urticaria were induced by one or more of the test substances in 66 of the patients, with aspirin well at the top of the list.

Each patient was given an appropriate diet sheet instructing her how to reduce to a minimum her intake of the substance or substances to which she had reacted. Warin and Smith followed up 47 of the patients, and 35 of them were cured or considerably improved. They acknowledged the spontaneous cure that may occur in chronic urticaria and they therefore interpreted their findings cautiously. But their conclusion that the screening procedure and the diet were "well worthwhile" will be endorsed by other dermatologists who have made use of similar routines.

Some of these offending substances are used so extensively by the food industry that it is far from easy for a busy housewife to provide herself with the prescribed diet. It is, for example,
difficult to avoid tartrazine or sodium benzoate. One large food manufacturer does not use tartrazine in his products; perhaps others can be persuaded to find satisfactory alternatives. Nevertheless, despite the practical difficulties a few months on a diet low in a substance which has been shown to aggravate the urticaria in a particular individual is well worth the effort required. Not only is there usually immediate symptomatic relief, but after a few months of strict adherence to the diet some relaxation may be allowed, and the offending substance may then be found to be tolerated.

3 Tas, J, Dermatologia, 1967, 135, 90.
4 Thompson, J S, Annals of Internal Medicine, 1968, 69, 361.
5 Calnan, C D, Lancet, 1957, i, 996.

New look at monoamine oxidase inhibitors

Despite nearly 20 years’ clinical use, the place of the monoamine oxidase inhibitor drugs (MAOIs) in psychiatry remains uncertain. They are inconsistently prescribed—a panacea to some practitioners, poison to others. Recently interest in them has been revived.1

Though they are used much less than the tricyclic antidepressives, the MAOIs have been claimed to have special value in some psychiatric syndromes. These include reactive, neurotic, or atypical depressive conditions; depressive-anxiety states; phobic anxiety; and phobic anxiety-depersonalization syndromes. The few controlled studies made have indicated that patients in hospital with typical depressive illnesses of moderate or severe intensity fare badly with MAOI treatment.2 3 Depressed outpatients do better: in one trial1 phenelzine was effective in outpatients over the age of 35 with atypical features such as anxiety, fatigue, phobias, and somatic complaints.

In reported trials, depressed patients who improved with MAOI therapy had unequal changes in their symptoms. Subjective disturbances (both depression and anxiety) did not improve with phenelzine as compared with placebo; on the other hand, retardation, agitation, and somatic symptoms of anxiety were usefully controlled.1 Patients with longstanding phobic anxiety also respond to MAOIs. In one study2 those receiving an average daily dose of 45 mg of phenelzine improved significantly more than those treated with placebo, both on overall assessment and in their work record. General anxiety and panic also decreased. Patients with phobia and depression tended to improve less than those not depressed. Tyrer et al suggested that phenelzine acts in phobic patients as an anxiolytic rather than an antidepressive. Similarly, iproniazid has anxiolytic effects in severely agoraphobic patients.4 Relapse is likely to occur if the MAOI is withdrawn.

The time before clinical response occurs ranges from a few days to several weeks, tranylcypromine usually acting more rapidly than phenelzine or isocarboxazid. There is a delay before REM sleep is suppressed by MAOIs, and the time of this suppression apparently coincides with clinical improve-

ment.7 Among the MAOIs, phenelzine and tranylcypromine are generally thought most effective, the former having the lower reported incidence of hypertensive crises. Though this group of drugs has a reputation as being dangerously toxic, from his extensive experience Tyrer1 has concluded that “they are generally safe provided that proper caution is exercised with dietary and drug intake.”

Despite their clear biochemical properties there have been surprisingly few attempts to relate the actions of these drugs to the clinical response produced. Amine concentrations in brain tissue taken post mortem from patients maintained on MAOIs in their terminal illnesses have generally been found to be raised. Nevertheless, about a quarter of these specimens showed no evidence of MAO inhibition at all.8 Therapeutically, estimating the MAO activity in the blood platelets or urinary tryptamine excretion may provide information on peripheral MAO inhibition. Though the relation between peripheral and central MAO inhibition is not clear, the success of the MAOIs in one trial1 may have been due to careful monitoring of platelet MAO and the adjustment of drug dosage to maintain an inhibition of at least 80%. Phenelzine is metabolised by acetylation, and people in whom this process is slow (“slow acetylators”) are quicker to attain high degrees of MAO inhibition and show a more prompt clinical response than fast acetylators.9 Hence some of the variations in clinical response and contradictions in the results of clinical trials may be due to pharmacokinetic differences among individuals.

Finally, there is the vexed question of whether MAOIs should be combined with tricyclic antidepressive agents. Some have hailed such combinations as most effective; others have stated that they are hazardous; uncontrolled studies of the combination have failed to show convincing evidence of their value. Nevertheless, at present two controlled trials of combined treatment are underway in London teaching hospitals which should help to settle the matter.

The resurgence of interest in the MAOIs is timely. Other types of treatments for depression and phobias are far from satisfactory, especially in those patients who seem to respond to MAOIs. More comparative evaluations with proper biochemical control are still needed.

2 Medical Research Council Clinical Psychiatry Committee, British Medical Journal, 1965, i, 881.
7 Dunkley, D L F, and Oswald, I, Archives of General Psychiatry, 1973, 28, 353.

Curry kidney

The frequency of renal calculi, and indeed of renal disease, varies in different countries. Climate, the composition of the water, personal habits of eating and drinking, and the genetic background of the population have been invoked to explain these differences. In Fiji the Indians, who came originally from all parts of the Indian subcontinent and are therefore of varied ethnic origin, make up some half of the population; yet they are virtually the only sufferers from stones.1 2 All 16 operations for kidney stones at Lautoka Hospital in 1969, for instance,