in this country were to use the vole vaccine. He gave me the impression that he believed it would eventually supersede B.C.G.

I think there is good evidence for the belief that both methods of inoculation (a) are harmless to humans, (b) increase resistance to tuberculosis, (c) are of value only in tuberculin-negative subjects. While it is true to say that B.C.G. has stood the test of time in many countries and its harmlessness has been established by its practical application on a large scale in many parts of the world, nevertheless there is good evidence that the vole bacillus has the following advantages over B.C.G.: (a) it is apparently a more potent immunizing agent; (b) its virulence is more stable (the varying virulence of B.C.G. in Norway, Denmark, and Sweden was significant and I was told on more than one occasion that some of the strains were losing their virulence); (c) there is reason to believe that tuberculin allergy following vaccination with it was greater and occurred earlier than that following B.C.G.

The time seems surely to have arrived when an authoritative body such as the Medical Research Council should institute a clinical trial, with control experiments for statistical purposes, of what they regard as the most effective method of tuberculosis vaccination. We may then be able to fill in the gaps which Continental and other workers, often through lack of opportunities, have omitted.

One final word: you say in your leader that the multiple puncture method is now considered the best method of inoculation with B.C.G. This is contrary to my own impressions, for wherever I went the intracutaneous method devised by Wallgren was, when correctly performed, regarded as the quickest, most valuable and practical, and it certainly afforded a more accurate measure of the dosage. Certainly the multiple puncture method with the Birkhaug-Rosenthal instrument seemed to meet with little favour in most of the clinics I visited.—I am, etc.,

London, W.1.

PHILIP ELLMAN.

Nicotinic Acid Tolerance Test

SIR,—In their excellent paper (May 17, p. 672) on their nicotinamide saturation test Drs. P. Ellinger and S. W. Hardwick note that, in pellagrins, there is a markedly low response on the administration of nicotinamide but that this response can be increased, in pellagrins only, by the administration of methionine.

In therapeutic tests with nicotinic acid (the precursor of nicotinamide) in hepatitis cases it was noted that the usual vasodilatory response seems to be very much delayed. To investigate this a nicotinic acid tolerance test has been devised in which the patient or control takes 200–300 mg. nicotinic acid orally. If there is no response in 15 minutes, further 100 mg. is given every 15 minutes until the flushing of the face is reported. The work has not yet reached the stage of publication. However, the preliminary results noted on over 120 cases seem to endorse and also amplify Ellinger and Hardwick's findings.

The following conclusions seem to be justified so far:

(1) In "normal" subjects—that is, in patients and controls without evidence of hepatitis—there is a response on 200–300 mg., so much so that much higher values justify further investigations of the liver functions. Two unsuspected cases of chronic amoebiasis were so detected.

(2) The tolerance seems to be within normal limits in cases of sprue, congestive heart failure (only early cases could be tested), chronic mild cholecystitis, and in one case of liver secondaries.

(3) There is a marked, increased tolerance in cases of infective hepatitis (with or without jaundice), infective mononucleosis, homologous serum jaundice, and in subacute and chronic amoebiasis. The tolerance figures range between 500 and 1,200 mg. No cases of cirrhosis or pellagra were available for the test so far.

(4) The tolerance seems to be proportionate to the inflammation of the liver parenchyma, as judged by gravity of the condition of the patient and size and tenderness of the organ, but there seems to be no connexion between the deepness of the jaundice and the tolerance figure.

(5) Tested only in generalized inflammatory conditions, the tolerance seems to be more sensitive than the usual liver functions tests. The Takata-Ara reaction will be hardly positive (+) under a tolerance figure of 1,000 mg., and signs of a deranged carbohydrate metabolism are rare under a tolerance of 700 mg. The test is useful

as a ward test, and is of some help in the diagnosis of obscure epigastric symptoms, especially in the exclusion of chronic amoebic hepatitis in soldiers returning from overseas. Like any ward test, or any test, it is probably not perfect and does not give more than a useful hint.

(6) The same tolerance values are obtained if the test is repeated eight-hourly. There is, however, a sudden decrease in the tolerance when recovery sets in, and this change can be quite dramatic—e.g., after 1–2 emetine injections.

Here a word of warning must be given. Massive doses of nicotinic acid (200 mg. t.d.s.) combined with high protein diet (shakes of household milk and dried eggs or soya flour) seem to have some therapeutic effect in cases of infective hepatitis. If higher doses are given, or the test is repeated daily, thiamine and riboflavin (6–8 mg. each) should also be given. In one case, myself, acute sprue symptoms were provoked by repeated nicotinic acid tests amounting to 1,800 mg. daily for 5 days. The symptoms quickly cleared up on massive doses of riboflavin.

In trying to interpret the mechanism of the increased nicotinic acid tolerance one is inclined to assume that the compound is either retained by the liver for the purpose of utilization in repair, or else its release by the liver is delayed by the lack (or increased utilization) of sulphur-containing amino-acids—Ellinger's and Hardwick's "methyl donors." Ellinger's and Hardwick's findings seem to support the latter assumption. They noted increased urinary output of nicotinamide methochloride on the exhibition of methionine in pellagrins, and no doubt the liver parenchyma suffers in that disease. On the other hand the fairly constant tolerance figures in the nicotinic acid test, and the constant urinary output of nicotinamide methochloride in the saturation test, do not confirm the assumption that the delay in passing the liver is caused by the lack of "donors" only; if this was the case one would expect daily increasing tolerance. Probably much more work will have to be done on the subject before the role of the liver (and that of the kidney) in the nicotinamide metabolism will be understood.—I am, etc.,

Colchester, Essex.

A. ERDEI,
Capt., R.A.M.C.

Physical Therapy of Mental Disorder

SIR,—A careful perusal of Dr. D. W. Winnicott's paper (May 17, p. 688) has led me to the conclusion that he intended it to be provocative rather than wholly serious. Dr. Winnicott's main objection to physical methods of treatment in psychiatry is that they are "unscientific," and he states, "Much of the objection to convulsion therapy would disappear if the mechanism by which results are obtained were understood." Would Dr. Winnicott, on similar grounds, say fifty years ago, have withheld digitalis in a case of cardiac oedema or quinine in a case of malaria, or would he to-day withhold malarial fever in a case of general paralysis?

The practising psychiatrist of to-day must answer the question: Shall I allow this melancholic patient to remain indefinitely in acute depression with all its mental suffering, not excluding risks of suicide or death from inanition due to refusal of food or from aspiration pneumonia due to tube-feeding, or shall I give him E.C.T. and restore him fit and well to his family in approximately six weeks? Or again, when faced by a case of acute delirium (manic or melancholic), shall the psychiatrist withhold E.C.T. and assure the relatives that death is almost inevitable, or shall he give E.C.T. with at least a three-to-one chance of success? Or again, should a psychiatrist subject an anxiety neurotic mother to months of psychological investigation, with the almost unbearable strain of her symptoms on her children and husband, not to speak of risks of suicide or infanticide, or should he not rather prefer to restore her to complete happiness and health with five or six convulsions?

A young man is suddenly stricken with an acute schizophrenic illness. The "scientific" psychiatrist must tell his father that nothing can be done and that almost inevitably the patient will rapidly drift into a condition of profound dementia. The "empirical" psychiatrist will immediately adopt treatment by insulin shock with at least a fair prospect of success. In cases selected for leucotomy (almost always mental hospital cases where both insulin shock and E.C.T. have failed, but where the residual mental capacity appears reasonably good) the choice is

again between the "scientific" method of doing nothing, thereby condemning the patient to lifelong incarceration, and the "empirical" method of leucotomy with its reasonable prospect of success.

Surely Dr. Winnicott cannot defend many of his statements as being either "accurate" or "scientific"—e.g., "convulsion therapy inevitably leads away from the psychological approach to a biochemical and a neurological one." This I submit is a highly controversial statement. My own experience is that all these physical methods require for their *correct* use accurate case histories, precise observation of their effects, and a sound psychological insight into the patient's mentality both before and after treatment. To delegate these treatments to junior medical officers in a sort of hit-or-miss fashion is of course *bad* psychiatry, which no reputable psychiatrist would defend.

Dr. Winnicott's greatest objection, however, appears to result from the implied threat such treatments have to his apparently beloved "analytical" psychology. This is too big a subject to dilate upon here, but I would ask Dr. Winnicott to consider whether he is not himself "unscientific" in assuming that the many amazing concepts of Freud (which, by the way, are outside the realm of scientific proof or disproof) are the only ones of value in the psychological approach? For example, modern child guidance, with its right insistence upon the emotional development of the early years and the importance of "security and affection," appears to derive nothing from Freudian theories but to be based upon the work of Adler (who rejected Freud's teachings) and of Cameron and others in England.

Lastly, I am of the opinion that such misconceptions as are evident in Dr. Winnicott's paper must to a great extent be placed at the door of psychiatrists themselves. When we as individuals become less "aloof" and "mysterious," and when we cordially invite all neighbouring practitioners and specialists to visit our hospitals at any time and to see their own or other patients undergoing such treatments, we shall hear very little of the "unconscious hate . . . that notoriously coloured the management of the insane up to recent times."—I am, etc.,

Armagh, N. Ireland.

ROBERT THOMPSON.

Allergic Reaction to Penicillin

SIR,—I wish to report the following case history showing a marked allergic reaction to penicillin therapy which occurred in the maternity department of Dorking County Hospital.

CASE REPORT

A primipara aged 40 was admitted as an emergency with the history of early rupture of membranes 76 hours previously, uterine inertia, and commencing foetal distress, as evidenced by passage of meconium, though heart sounds were regular and of fairly good quality. Rectal examination showed the cervix half dilated, head in brim not fixed.

Lower segment caesarean section was performed under general anaesthesia shortly after admission. Much meconium in uterus. Baby shocked but responded well.

In view of the history and expected stormy convalescence penicillin therapy was instituted immediately after delivery. The preparation used was penicillin in oil, given intramuscularly with a preliminary dosage of 400,000 units followed by 200,000 units 12-hourly. On the second day after delivery paralytic ileus developed. Treatment consisted of morphine, half-hourly duodenal aspiration through a Ryle's tube, acetylcholine, intravenous drip, radiant heat to abdomen, and turpentine enemata. Response to treatment occurred within 48 hours. On account of a sustained low-grade pyrexia during the puerperium due to a mild genital-tract infection, penicillin in oil in the above dosage was continued for 16 days, the total dosage being 6,400,000 units.

On the day following cessation of penicillin therapy a severe urticarial reaction occurred. It affected the face and limbs and later involved the trunk also. It was unaccompanied by fever or tachycardia, but caused such severe pruritus as to keep the patient in the next bed awake by the vigour of the scratching. Adrenaline, calcium gluconate, and local sedatives gave some relief, but fresh patches kept appearing for a total duration of 6 days, and then cleared up completely. Mother and baby were sent to the hospital convalescent home and discharged well and thriving 5 weeks following delivery.

I would add that this patient had not previously had any penicillin therapy.—I am, etc.,

Dorking, Surrey.

J. C. CUTHBERT.

"Benadryl" Treatment of Penicillin Allergy

SIR,—Accounts of the allergic response to penicillin have appeared recently in the journals. These reactions have been both to intramuscular and local applications of the drug. The commonest reaction is urticaria alone, but occasionally a full anaphylactoid response is seen, with fever, hydrarthrosis, enlargement of the lymph glands, and bronchial spasm. This often occurs 10 to 14 days after the commencement of penicillin treatment and resembles serum sickness. The intense pruritus which accompanies the urticaria is usually the most troublesome feature, causing scratching and inevitable insomnia.

A patient of mine (G. A.), a girl aged 19 years, developed a paronychia, and I first saw her with pus under the left thumb-nail and slight lymphangitis. The nail was removed, penicillin in oil, 125,000 units in 1 ml., was given daily for three days, and the thumb healed uneventfully.

Ten days after the commencement of penicillin she developed an urticarial rash on the back and shoulders; this was associated with intense itching. She had no family or personal history of allergy, and as far as could be ascertained she had not been exposed to any other allergen. The following day, after a sleepless night, she had a temperature of 100° F. (37.8° C.), there was generalized urticaria, which was most marked about the face, and she was also dyspnoeic. On examination the axillary and inguinal glands were enlarged; on auscultation of the chest there was a marked expiratory wheeze; there was no evidence of hydrarthrosis. Calcium lactate 30 gr. (2 g.) and phenobarbitone 1 gr. (65 mg.) were given six-hourly, but the following day the symptoms had increased.

Having used "benadryl" (dimethyl aminoethyl benzhydrol ether hydrochloride) successfully in angioneurotic oedema, I commenced treatment with 100 mg. (two capsules) at once and a further 50 mg. six-hourly. The response was most dramatic; within an hour all urticaria had disappeared, the itching and dyspnoea ceased, and the patient was symptom-free. There has been no relapse.

While further cases will have to be described, "benadryl" appears to be the drug of choice in the long-term treatment of anaphylactoid phenomena; "benadryl" being perhaps to adrenaline what trinitrin is to amyl nitrite.—I am, etc.,

Liverpool.

GEOFFREY DEAN.

Pruritus Ani as an Allergic Condition

SIR,—The association of pruritus ani with allergy is hardly investigated. The unsatisfactory results of treatment in many cases, however, make it desirable to get better information on aetiological factors in these conditions. A case of a man who came into my observation first on July 8, 1946, illustrates this well.

The patient was 66 years old. There was a family history of allergy; the son suffered from asthma, a daughter had attacks of urticaria. The patient has had sinus and antrum operations for "sinus infections" from 1898 on, the last time in 1929. In 1943 piles were operated and "proctocaine" injected. The skin proved to be allergic to skin disinfectants. All these years the patient suffered from severe irritation of the anal region which "made life miserable" to him. Three weeks before he saw me first he again had piles removed by operation. A slight attack of pruritus had occurred 40 years earlier. He has also suffered from urticaria and eczema on his head; otherwise he has been a healthy man all his life.

On examination I found a scar on his right forehead due to the operation on his right frontal sinus. The anal region was in an irritated state, excoriation, thickening, and oedema of the skin were marked, and there were cracks and slight fissures in the perianal region. The middle lobe of the prostate gland was moderately enlarged. A differential blood count showed a hyper-eosinophilia of 6%; basophils, 4%; polymorphs, 67%; lymphocytes, 23%. Skin tests gave positive results to moulds, cheese, and other food proteins. His condition was worse when constipated.

From his faeces *Bact. coli* and *Staph. aureus* were cultured and used for an autogenous vaccine together with a desensitizing mixture of the positive allergens. Apart from that the patient was given vitamin E and testosterone tablets. Local treatment was discontinued. His condition started to improve after three weeks, and the anal findings showed a normal picture and normal skin conditions with no irritation from about six weeks after the treatment. The patient was last re-examined on May 8 and was found absolutely well and the anal region normal. As repetition