The clinical evidence supports this suggestion, penicillin-stomatitis starting in the areas receiving the most trauma, namely the tip and sides of the tongue, even in the later stages the more protected areas tending to escape. Though the pastilles and the trochisci both contain sucrose, the trochisci contain the greater quantity. It may be that continuous sucking of such a base alone would produce stomatitis, the importance of the penicillin being merely that more intensive treatment is prescribed when penicillin is an ingredient than when it is not. While Dr. Kerfoot's observations suggest that this is improbable with the lozenges that he prepares it is conceivable that the continuous abrasive action of sucrose crystals on the buccal mucosa, supplemented perhaps by the osmotic effect of a hypertonic solution, may be sufficient to cause stomatitis in the absence of penicillin. Observations on the point are desirable.

Quite apart from the relationship between the trochiscus and stomatitis there are other grounds for criticism. Dr. MacGregor stressed the importance of a viscous base if the maximum effect is to be obtained on the tonsils, quoting the references for his opinion. This being so I will merely state that I am in complete agreement with him. The trochiscus is unsuitable for use in plastic surgery of the mouth because it is so hard that the patient will not tolerate it, and even if he can be persuaded to maintain it in a less sensitive part of his mouth the base accumulates in intra-oral wounds and has to be removed manually.

In conclusion I would stress that I consider the trochiscus penicillini highly unsatisfactory for the reasons stated, and hope that the manufacturing companies will soon devise a more suitable base. Until then, I believe the original pastille devised by Dr. MacGregor and myself to be the most satisfactory, in spite of its limited keeping properties.—I am, etc.,

London. W.C.1.

DAVID A. LONG.

Delayed Reaction to Penicillin

SIR,—The recent article by Dr. A. I. Suchecki (Dec. 21, 1946, p. 938) on allergic reactions to penicillin prompts me to record a case where the reaction was unusually delayed.

CASE REPORT

At Forest Isolation Hospital, Mansfield, a girl of five years, suffering from bronchopneumonia following whooping-cough, received 400,000 units of penicillin in four-hourly doses from Dec. 15-19. The penicillin used was an ordinary commercial brand in aqueous solution, injected intramuscularly. Rapid improvement was followed by a slight relapse ten days later, and sulphathiazole 8 g. was given orally from Dec. 30 to Jan. 4.

On Jan. 27—i.e., 39 days after cessation of penicillin and 23 days after cessation of sulphathiazole—she developed a raised, pink, blotchy rash, generalized in distribution but most marked over the sites of penicillin injections; oedema, especially of the hands, lips and eyelids; pruritus of moderate degree; pyrexia of 101°-103° F. (38.3°-39.4° C.); and considerable bronchospasm, which was temporarily relieved by adrenaline. There was no arthralgia, no hydrarthrosis, no lymphadenopathy, and no jaundice, and the urine was normal in all respects. The features which persisted longest were the oedema (which subsided on Feb. 1) and the rash (which disappeared on Jan. 31). On the neck the fading of the urticarial eruption coincided with the appearance of a number of petechiae.

The most delayed penicillin reaction previously known to me was Dr. J. N. Turnbull's case (Jan. 18, p. 111), where the reaction occurred 35 days after cessation of parenteral treatment. A delay of 39 days before the appearance of an allergic reaction is certainly most unusual, yet the features were unlike those of a sulphonamide drug rash and were completely in line with those of penicillin reactions as described by Suchecki and others.—I am, etc.,

Mansfield.

I. A. G. MACQUEEN.

Endocrines in Gynaecology

SIR,—The fact that the action of hormones depends not only on the hormones themselves but also on the mode of reaction to them of the target cells is well known in endocrine biology, and is bound up with the general conception of "biological field"—a conception which we owe to the brilliant work of J. Needham and C. Waddington. Albright coined the

characteristic expression "Seabright bantam syndrome." The male Seabright has female feathering, which is attributed not to any predominance of female hormone in the bird but to the special reaction of its feathers to male hormone. This conception enables us to understand much of the physiopathology of endocrine diseases.

Mr. Aleck Bourne (Jan. 18, p. 79) has rightly stressed the importance of this biological principle in practice. Endocrine diseases are not diseases of one of the six classical glands of internal secretion but disturbances in the balance of a whole system of constitutional or metabolic regulation composed of the genes, endocrines, neurovegetative system, psycho-associational cortex, certain environmental factors, and the reactivity of the cells—the "competence" of the biologists. Thus endocrinotherapy is not the sole method of treatment of "endocrine diseases." On the contrary, its one-sided application may do harm by upsetting the balance of the system of constitutional regulation, as shown by the bad effects of an exclusively endocrine treatment in certain eunuchoidisms in the young and by the disasters of attempts at rejuvenation with testicular organotherapy.

At the Annual Meeting of the B.M.A. at Oxford in 1936 I opened a discussion on physical methods in endocrinotherapy, in which I stressed the importance of physical medicine in modifying the balance of the system of constitutional regulation and thus its superiority, in certain endocrine diseases, over organotherapy. In endocrine as in all other diseases we deal with the complete psycho-physical personality. It is curious that psychiatry and endocrinology, the two branches of medicine which have contributed to our modern concept of total personality in disease, seem to revert to the comfortable one-sidedness which they have been fighting; psychiatrists stress unduly the psychological factors at the expense of the organic factors, while endocrinologists seem to dwell exclusively on the hormones with which we have been flooded.—I am, etc.,

London. W.1.

A. P. CAWADIAS.

Endocrine Receptors in Relation to Cancer

SIR,—No doubt the idea that an endocrine stimulus or impulse must be received as well as transmitted has occurred to many, though I agree with Mr. Aleck Bourne (Jan. 18, p. 79) that it has not been given the prominence which Mr. Bourne rightly, I think, considers it should receive. The idea, however, was the main point of a paper, entitled "A Theory of Cancer" published in the *Lancet*, 1920, 2, 1,298. It did not attract any particular attention as far as I know, and I only remember it because I wrote it and because I have never ceased to think of endocrine glands in general as structures which not only transmit a particular kind of energy but whose effectiveness depends on the proper reception of the message transmitted. I suggested, in fact, that sensitivity to hormone messages was a necessary function of every normal cell of every tissue, and I endeavoured to trace the sequence of events that must occur in a group of cells in which this function was being imperfectly carried out as the result of a failure to cope with an excessive demand on the regenerative capacity of those cells. I was not thinking of special hormones but of what I called the "co-ordinating hormone," a hypothetical hormone whose existence it seemed to me to be a logical necessity to assume, as in no other way could the harmony of growth and function of all normal tissues be explained.

I venture to recall these points now as a comment on Mr. Bourne's paper because I thought that the idea of receptors (or, as I called it, cell sensitivity) could be applied to Dr. A. Paine's then recently published paper (*Lancet*, 1920, 2, 692) on the origin of cancer. Dr. Paine's views may be epitomized in the following quotation from his paper: "We have thus traced cancer to its source; it springs from a degenerate cell, a cell that has in some manner been damaged or injured, and from such a cell all cancer cells are descended." In my paper I attempted to show that cells so degenerated gradually failed in all their functions, both special and general; I tried to make the point that this failure must include the failure to respond to the message of the co-ordinating hormone and that failure in this function must inevitably result in cancer.—I am, etc.,

Leicester.

T. C. CLARE.