haematology to constitute a whole-time specialty, I would join issue with the writer.

Glancing through my notes of the past three months, I see that the following cases (among others) have been referred to me by practitioners: 'patients with symptoms of anaemia, generalized pruritus, enlarged glands, splenomegaly, erythrodermia. In the first group there have been examples of pernicious anaemia, idiopathic hypochromic anaemia, carcinoma of the stomach, aortic incompetence, chronic plumbism, various types of leukaemia, and other maladies. The cases of glandular enlargement have included leukaemia, Hodgkin's disease, tuberculosis, secondary syphilis, pediculosis, and secondary carcinoma, while the splenomegalies have varied from chronic myeloid leukaemia to kala-azar. That the purely laboratory aspect of these diseases would be limited and depressing is true; that the purely clinical investigation of them might be so is probable; but who can assert that a specialty which enables one to deal with the clinical, laboratory, and therapeutic aspects of so varied a collection of maladies is limited and depressing? Your writer says that "haematology is not a unified subject," and, although he was intending disrespect to the subject, I would assert that it is this very fact that makes haematology one of the widest and most interesting of specialties. Equally, his indisputably true statement that scientists investigating different aspects of haematology do not speak the same language is one of the strongest reasons for the existence of physicians whose main interest is in haematology, and who can act as liaison officers between the academically minded scientist and the patient who needs skilled attention. I would, of course, agree with the writer that the proper exponent of haematology is the clinician, though the pathologist, the geneticist, and the transfusion officer may be the best exponents of small branches of the vast subject.—I am, etc.,

London, W.1. A. Piney.

History of the Hogben Test

Sir,—In describing (*B.M.J.*, Sept. 7, p. 328) his improved method of concentrating urine for pregnancy diagnosis by recourse to *Xenopus* as a test animal, Mr. Milton's brief account of the history of the test might well convey an erroneous impression of the part played directly and indirectly by the writer in its discovery. He states: "Hogben (1930) demonstrated that if the animal was injected with anterior pituitary preparations ovulation and oviposition could be induced. This fact was subsequently made use of by Bellerby (1934) and by Shapiro and Zwarenstein who *independently suggested* that the phenomenon could be utilized as a pregnancy test" (italics inserted).

In 1929 I completed experiments which showed that *Xenopus* responds by ovulation at any time of the year to the gonadotrophic hormone of the anterior lobe of the pituitary, and that the ovary undergoes involution after hypophysectomy. As stated by Mr. Milton, a preliminary note (*Trans. roy. Soc., S. Afr.*) recorded this discovery in 1930. A later publication (Hogben, Charles, and Slome, 1931) based on more extensively planned experiments of the same sort, also including a record of others dealing with the effect of hypophysectomy on the blood calcium level and the relation of light to the pituitary control of the ovary, appeared in the *Journal of Experimental Biology*. At that time, the identity of the gonadotrophic substance in the urine of pregnant women and the anterior lobe hormone with the same action was generally accepted. I therefore made arrangements with a South African obstetrician to use *Xenopus* in order to probe its relation to the pituitary autacoids from a new angle. Dr. Zwarenstein was then taking a course of postgraduate study in my department, in which he learned my technique (Hogben, *Quart. J. exp. Physiol.*, 1923) of hypophysectomy, and with my encouragement undertook further work on the relation of pituitary and ovarian function to blood Ca and K levels, when I relinquished my chair in South Africa.

On my return to England in 1930 I made contact with Prof. Crew, who had started a pregnancy diagnosis unit, pointed out the advantages of a test animal which ovulates visibly and can be used repeatedly, intimated that it might be long before I should have a laboratory fully equipped to resume such work, expressed the hope that he would follow it up, and sent him toads from the small stock I had brought back. By 1932, when Dr. Bellerby and Dr. Landgrebe had joined my staff in London, Zwarenstein reported to me the virtual impossibility of maintaining ovarian activity of *Xenopus* under laboratory conditions; and subsequently published in the *Journal of Experimental Biology* (Shapiro and Zwarenstein, 1933) an account of what he called the captivity effect, implicitly controverting my expressed view that *Xenopus* is peculiarly fitted for gonadotrophic assay. At first Crew's colleagues themselves experienced similar difficulties; and, since a test based on the use of freshly caught animals whose natural habitat is highly localized could have no international value for medicine, I recognized that extensive use of *Xenopus* for gonadotrophic assay must await fuller elucidation of conditions for maintaining its reproductive activity in the laboratory.

Working with me in London, Bellerby and Landgrebe therefore undertook at my suggestion a series of investigations (Bellerby, 1933; Alexander and Bellerby, 1935; Bellerby and Hogben, 1938; Bellerby, 1938; Landgrebe, 1939), severally published in the *Biochemical Journal* and *Journal of Experimental Biology*, to vindicate the use of an amphibian test animal by studying: (*a*) the effect of diet, overcrowding, light, etc., on the fertility of *Xenopus*; (*b*) the possibility of breeding *Xenopus* in the laboratory without recourse to importing new stocks; (*c*) the action of pituitary extracts on the British common frog. *Pari passu* Bellerby (1932–3) carried out a series of tests showing that *Xenopus* responds to the gonadotrophic substance in the urine of pregnant women. For the reason stated above I discouraged early publication of our results as of merely academic interest until we could also announce a fool-proof regimen of animal husbandry. Meanwhile I had privately communicated to Zwarenstein and to his junior colleague Shapiro, both about to visit Britain, the fact that my regimen did in fact ensure persistent ovarian activity of imported stocks, and that their so-called *captivity effect* was due to defective care of their animals. I also invited them to see my new set-up. Accordingly, Zwarenstein and Shapiro enjoyed the hospitality of my laboratory during their visit to London in 1933. We then demonstrated to them both the results of our pregnancy tests and the success of our own method of maintaining ovarian function of *Xenopus* over an indefinite period of time in an artificial habitat.

On returning to South Africa, Zwarenstein and Shapiro made similar tests on *Xenopus freshly caught* from local ponds, and issued a note (*Trans. roy. Soc., S. Afr.*) recording their successful outcome shortly before a preliminary announcement of work in my laboratory (Bellerby, 1934) appeared in *Nature*. For a sufficient reason I made no unfavourable comment on this. At that time Zwarenstein and Shapiro had not yet withdrawn their previous assertions about the so-called *captivity effect*, in conflict with my original claims with reference to the peculiar suitability of *Xenopus* for assay of gonadotrophic substances. Indeed, the practicability of the test was not finally vindicated until Landgrebe (1939) completed a long series of experiments under my direction setting forth the conditions which ensure that *Xenopus* will continue to respond to gonadotrophic preparations in a laboratory environment. In fairness to two of my colleagues I must add this. By luck or good management I had equipped my Cape Town laboratory with what proved to be a satisfactory lay-out for prolonged survival experiments for earlier work (Hogben and Slome) on the pituitary *vis à vis* the chromatic function. Though publication of the *captivity effect* of Zwarenstein and Shapiro materially delayed preliminary announcement of pregnancy tests, it had a salutary result. Certainly other workers would have experienced difficulties which eluded my own system of laboratory care; and the test itself could vindicate its credentials only after explicit clarification of the essential conditions of artificial culture in the hands of others who did not start with the advantage of my own intensive experience of work on *Xenopus*.

Presumably it was for reasons here given that Crew, himself acquainted from the start with the inside history of difficulties besetting the final accomplishment of a project I nursed from the date of the parent discovery in 1929, suggested the association of my own name with the *Xenopus* method of pregnancy diagnosis as those of Zondek and Aschheim and of Friedmann were already associated respectively with methods relying on the mouse and the rabbit as test animals.—I am, etc.,

Lancelot Hogben.