

ocytes which have not entered the prophase of the first maturative division are sexually bipotent. Through the stimulating action of medullarin, these cells leave the cortical region of the gonad and are attracted into the newly formed medullary tissue, where they become spermatogonia. The oocytes which had already entered the prophase of the first maturative division at the time of the sexual inversion do not leave the cortical region, and the inhibitory action of medullarin causes their complete degeneration. Before degenerating, however, those oocytes which have not passed the pachytene stage may, under the combined influence of cortexin and medullarin, show cytological aberrations comparable with changes which normally occur in spermatocytes⁵. Similar inter-sexual germ cells have been described in *Rana esculenta* by Galgano and in *Rana catesbiana* by Swingle⁶.

I later examined the effects on amphibian tadpoles of the principal sex and suprarenal cortical hormones of the adult. Previous research had shown that testosterone will masculinize the gonads of all individuals (Gallien, Witschi), whereas oestradiol in small doses has a feminizing and in large doses a masculinizing effect (Padoa). More recent work of Padoa has also demonstrated the masculinizing action of progesterone, and the feminizing action of one of the suprarenal cortical hormones (desoxycorticosterone)⁷.

My experiments to date on tadpoles of *Rana agilis* have shown that in influencing the sexual differentiation of the gonad each of the above hormones acts through a different mechanism. The follicular hormone (oestradiol) in small doses feminizes the rudimentary gonad by stimulating growth of the cortex. On the other hand, the suprarenal cortical hormone produces the same effect by inhibition of medullary proliferation. If the treatment is started early enough ovaries are formed which are permanently and completely devoid of medullary tissue⁸. The testicular hormone (testosterone) masculinizes the gonad by direct stimulation of the medullary tissue, whereas the hormone of the corpus luteum (progesterone) exerts the same effect indirectly by inhibiting the differentiation of oocytes in the cortex. Thus with progesterone the ovaries develop normally to the stage at which the cortex contains primary and secondary oogonia. The subsequent gradual masculinization of the gonads is associated with partial or complete absence of oocytes and with failure to regress on the part of the medulla, which therefore takes control (Fig. 2). I am not yet able to explain the mechanism of masculinization by large doses of oestradiol, which was discovered by Padoa.

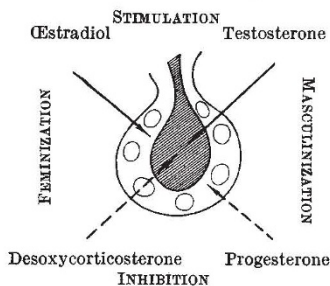


Fig. 2. SCHEME TO REPRESENT THE EXPERIMENTAL ACTION OF HORMONES ON THE SEXUAL DIFFERENTIATION OF THE GONAD. THE SHADED PORTION REPRESENTS THE MEDULLA, THE EXTERNAL WHITE LAYER THE CORTIX; THE CIRCLES CONTAINED IN THE CORTIX INDICATE GERM CELLS. THE CONTINUOUS ARROWS INDICATE STIMULATION THE INTERRUPTED ARROWS INHIBITION

The main point of interest is that the actions of the above substances are remarkably similar to those normally attributed to the sex 'realizers' and inducers. Thus oestradiol in small doses and testosterone act like the primary female and male realizers respectively, whereas desoxycorticosterone and progesterone imitate the inhibitory action of cortexin and medullarin. This leads me to suspect that the sex realizers and inducers are sterols like the sex and suprarenal cortical hormones of the adult.

I intend continuing this work and extending it to the Amniota, which resemble the Amphibia in the mode of development of the gonad. Preliminary observations have shown that in the chick embryo, as in the Amphibia, the medullary tissue of the gonad is derived from the inter-renal blastema⁹.

¹ Witschi, E., "Handb. der Vererb.", 2 (1929). Witschi, E. (in Allen's "Sex and Internal Secretions") (Baltimore, 1934). Witschi, E., *Scientia*, 63, 146 (1940).

² Vannini, E., *Mem. R. Accad. d'Italia*, 13, 731 (1942). Vannini, E., and Busetto, I., *Atti R. Ist. Veneto Sci. Lett.*, 104 (1945).

³ Vannini, E., *Atti R. Ist. Veneto Sci. Lett.*, 104, 55 (1945).

⁴ Vannini, E., *Atti R. Ist. Veneto Sci. Lett.*, 102, 7 (1943).

⁵ Vannini, E., *Arch. Zool. Ital.*, 30, 363 (1942).

⁶ Galgano, M., *Arch. Ital. Anat. Embry.*, 37, 1 (1936).

⁷ Padoa, E., *Pub. Staz. Zool. Napoli*, 19, 185 (1943).

⁸ Vannini, E., *Atti R. Ist. Veneto Sci. Lett.*, 103, 535 (1944).

⁹ Vannini, E., *Mem. R. Accad. d'Italia*, 14, 493 (1943).

PUBLIC HEALTH AND EXPERIMENTAL MEDICAL RESEARCH

A PRINCIPAL feature of the 1945 issue of *The Fight against Disease*, the organ of the Research Defence Society, is the fourteenth Stephen Paget Lecture, given by Sir William Savage, entitled "Public Health and its Debt to Experimental Medical Research". Public health, said Sir William, is concerned with all measures which operate to promote or to maintain the health of the community, the direct treatment of disease being usually outside its scope. It is, therefore, not a science, but includes the application of many sciences to all its purposes. Because the development of many sciences has depended upon research which involved the use of experiments upon animals, developments in public health during the last fifty years have also depended upon this use of experimental animals. We now have, speaking generally, sufficient knowledge to control most of the infectious diseases, but we cannot always apply that knowledge, because its application would be prevented by interference with the liberty of the subject, the reluctance of many people to respond to preventive measures or to endure the inconveniences involved.

Sir William discusses, as examples of public health practice, the control of the enteric fevers, diphtheria and whooping cough. During the years 1871-75, the deaths due to enteric fevers were 371 per million; in 1939-40 they were 3 per million. This striking evidence of the application of the results of scientific research may be contrasted with the fact that, until recently, there has been a marked, but not a conspicuous, decline in the mortality due to diphtheria. During 1856-65 the deaths due to diphtheria were 247 per million; during 1936-40 they were 62 per million. The control of this disease falls into three stages. The first stage was the recognition of the disease as a clinical entity; the second stage began with the introduction in 1894 of specific treatment of

the disease with diphtheric antitoxin, which dramatically reduced the mortality, but did not reduce the prevalence of the disease; the third stage began with the introduction of specific immunization, which was introduced in 1926 in Canada and the United States and was only gradually adopted elsewhere. In Britain it has been widely practised only during the Second World War. The figures given by Sir William clearly show the value of this immunization and reinforce the campaign of the British Ministry of Health to popularize it. Another striking example of its value is the statement made by Dr. Stowman, chief of the Epidemiological Service of the United Nations Relief and Rehabilitation Administration (*Brit. Med. J.*, 742, May 26; 1945), a statement which Sir William was no doubt not in a position to mention, that diphtheria was the most prevalent epidemic disease in Europe during the recent War. Some 15,000 people died of it in Germany alone, and in Norway and the Netherlands its incidence was, in 1943, fourteen times or more greater than it normally is. The number of carriers of the disease also increased enormously. Diphtheria began, indeed, to rival tuberculosis as the principal cause of death. In England, however, and Hungary, immunization has actually reduced the incidence.

Whooping cough, the third example taken by Sir William, is a disease which has only been notifiable during the last few years. There is little evidence of its decline. Ninety per cent of the deaths due to it occur in the age-group less than five, and the deaths per million at all ages are still considerable (475 per million in 1941). Whooping cough is, however, difficult to diagnose in its early stages when infection may be spread, and general immunization is, in the present state of our knowledge, probably not worth while. Sir William thinks, however, that immunization of all children less than five, and especially of those less than two, would eliminate nearly all the deaths at these ages and also the after-effects.

Considering environmental improvements, Sir William discusses the great progress that has been made. Taking the control of human tuberculosis as an example, he states that the decline of the mortality due to the measures taken against it "is perhaps the most striking statistical fact in relation to public health".

Among the measures taken against this disease is the practice of mass miniature radiography of civilians, which is the subject of the Medical Research Council's Special Report upon it (Special Report Series, No. 251; 1945. H.M. Stationery Office. 3s. net). This report is a guide to administration and to the technique of a mobile apparatus which uses 35 mm. films, and it gives the valuable results obtained. Messrs. Watson and Sons (Electro-Medical) Ltd. also issue a brochure on the use of mass miniature radiographical apparatus. Dr. W. Pointon Dick (*Brit. Med. J.*, 568, Oct. 27; 1945) concludes, as a result of mass miniature radiography of factory groups in Middlesex, that there are probably 3,000 undiagnosed people in that county who need treatment, half of them being without symptoms. Dr. J. F. Brailsford (*Lancet*, 808, Dec. 22; 1945), in a valuable discussion of mass radiography, testifies to its value.

The work that has been done on the welfare of the mother and child is also dealt with by Sir William Savage. His discussion of the importance of food supplies is marked by the reminder that, although the control of human tuberculosis is advancing, 40 per

cent of the milk cattle of Britain are tuberculous, which means that, although only about 1 per cent of these cattle are at any one time excreting tubercle bacilli into the milk, even this rate of contamination involves an infection of the milk supply of 5-7 per cent. Sir William has calculated that in 1929 about 2,000 deaths in England and Wales, mostly deaths of children, were due to the bovine type of tubercle bacillus, and he thinks that the figure is nowadays about 1,500-1,600.

Sir William concludes with a section on the importance of adequate nutrition and defines three phases of the development of preventive medicine. The first phase was the great drive, pioneered by Chadwick and Simon, towards environmental improvements. The second phase was the attack upon special diseases, such as tuberculosis and venereal diseases. Our widened knowledge permits us to go forward with the third phase, which aims at the prevention of deviations from health, whatever their cause may be.

G. LAPAGE

CHEMICAL IMPREGNATION OF TREES AND POLES FOR WOOD PRESERVATION

UNDER this title, in Circular No. 717, B. H. Wilford, entomologist of the United States Department of Agriculture, Research Investigations (Supt. of Documents, U.S. Gov. Printing Office, Washington 25, D.C.), discusses methods of preserving the life of trees and poles used for fencing and other agricultural purposes.

The United States are not alone among the countries which, through the centuries, have experimented with the object of finding some cheap process to be used with the object of preserving or protecting wood from decay or attacks by insects and fungal pests. As the author says, there is a general and constant need in the United States for cheap, durable woods for fence posts, rural utility poles and rustic construction "presumably including wooden buildings". Suitable woods of natural durability are relatively scarce, whereas perfectly useful timbers are plentiful but not durable". Considerable investigation work with the object of pointing out this disability has been carried out in the United States, Canada, India and elsewhere. Simple methods and inexpensive materials were the main objects of the research. The investigations were carried out to find treating methods and chemicals that would be: (1) destructive or repellent to injurious insects and fungi over a reasonably long time; (2) harmless to man and other warm-blooded animals; (3) easily applied for ready absorption and even distribution of the chemicals within the tree or pole; (4) inexpensive with respect to the chemicals and materials used, and the labour required; (5) non-injurious to the treated wood, that is, containing nothing that will stain the wood or weaken it structurally; and (6) non-corrosive to hard wear.

Chemical impregnation of green trees and poles by sap-stream methods is an old idea that has been used to advantage for centuries. It had, however, fallen into abeyance, as it is not applicable to commercial use. Investigations made between 1930 and 1940 in North Carolina and South Carolina with a number of methods, 58 chemicals and chemical combinations