

or rabbits⁷⁴ the formation of new corpora lutea may be evoked, in some cases certainly preceded by ovulation, without disturbing normal parturition. This is not a constant finding⁹² and in other hands extracts of anterior hypophysis¹⁰² or placenta⁴⁴ have impaired the birth mechanism or³⁵ produced abortion or reabsorption of the fetuses. Immature male rodents react less strikingly to treatment of this kind than do females; there is accelerated development of the seminal vesicles and accessory glands, to a lesser degree of the penis and testes;^{96, 107, 121, 18} the endocrine activity of the testes is said to be increased,¹⁹¹ but spermatogenesis may actually be inhibited.^{16, 36} In doves, however, the testes may be very greatly enlarged after implantation or injection of glycerol extracts of anterior hypophysis.⁸⁷ The ovaries of senile female mice may be reactivated so that œstrus cycles may reappear,¹¹⁸ but when implants were made into mature mice, which for unknown reasons showed no œstrous cycles, the first induced œstrus was not followed by renewed cyclic activity.⁶⁷

In rabbits, ovulation following the injection of extracts of anterior hypophysis has been observed,¹⁴ but the formation of lutein cysts in the ovary⁵⁴ appears to follow; this latter change has also been seen in dogs.^{17, 86} Implants made into apes may stimulate follicular growth,² or may produce enlargement of the uterus without visibly affecting the ovaries;²⁹ several workers, however, have insisted on the independence of the endocrine activities of the ovary.^{78, 116, 110} In human subjects, implants failed to induce menstruation in a case of delayed puberty, or after the menopause, but good results were obtained in the treatment of various menstrual disorders²⁸ and soluble preparations have also been used with some success;^{17, 120, 60, 76, 91} hyperæmia and hyperthermia in the pelvic region may be noted, but not invariably.²² Since in the case of hydatid mole and malignant chorionepithelioma the pathological tissues^{74, 5, 51, 90} and the urine^{5, 122, 77} contain large quantities of the hormone, an explanation of the frequent appearance of lutein cysts of the ovary in these conditions, or in the presence of hypophyseal tumour,¹⁰⁸ seems not far to seek.

The most widely known of the chemical char-

acteristics of the hormone is its instability; it is destroyed by boiling and injured at 60°C., or by exposure to strong acids or alkalis,^{118, 17} or to digestive enzymes,⁵⁶ and in consequence is ineffective when given by mouth, except in very large doses and under the most favourable circumstances.^{119, 56, 98} It is diffusible and dialyses rapidly, a fact which may be taken advantage of in its preparation.^{118, 17} It is said to be soluble in water or dilute acids, but insoluble in fat solvents, and is purified¹¹⁹ by precipitating it from aqueous solution by the addition of alcohol. We have not been able to find specific claims of the maximum potency and concentration obtainable by such means; commercial preparations may contain 50 rat units per c.c., but are decidedly toxic.⁴⁷ Dickens²⁷ has described a new preparation from the urine of pregnancy by precipitation with saturated ammonium sulphate and subsequently with tannic acid. His preparation is active in doses of 0.01 mgm. by injection, is not destroyed by pepsin or trypsin, but is unstable in acids or alkalis, and is insoluble in alcohol. Where œstrin is present in the original material (placenta or pregnancy urine) it is usually removed by extraction with ether or some other fat-solvent; we do not feel confident, however, that a quantitative separation has always been obtained in the preparation of either fraction.

Alkaline extracts of the anterior hypophysis promote growth^{45, 82} and acromegalic and splanchnomegalic distortion,⁸⁴ with enlargement of the gonads,¹⁰⁵ and temporarily lower the non-protein nitrogen of the blood,¹⁰⁴ while they produce extensive luteinization in the ovary and lead to a suppression of œstrus;^{41, 78, 54, 62} extracts made with dilute acid, however, are not growth-promoting,⁶⁴ but promote premature puberty,^{41, 83, 12, 13, 58, 17, 110} yet they are not free from the tendency to cause luteinization, and to impair the birth mechanism; this is also true of the extracts from placenta or urine, which are devoid of growth-promoting power.^{41, 44, 112, 73} Evans believes that the alkaline extracts actually antagonize the puberty-accelerating effect of acid extracts or of implants.⁴¹ That the ovarian response to implants, to acid hypophyseal extracts, or preparations from placenta or urine, may take the form either of follicular or of luteal development has been regarded by many workers¹⁷ as a question