

LHRH agonist prevented the increases in testicular weight, LH-receptor numbers and steroidogenic responsiveness induced by the FSH treatment alone.

Confirmation of the extra-pituitary actions of LHRH and its agonists has been readily forthcoming. Ying and Guillemin (*Nature* **280**, 593; 1979) demonstrated a dose-dependent inhibitory effect of an LHRH agonist on gonadotrophin-induced ovarian weight gain in hypophysectomized female rats and also prevented ovulation, findings which a smaller study by Mayar *et al.* (*Proc. Soc. Exp. Biol. Med.* **161**, 216; 1979) confirmed. A preliminary report also suggests that LHRH agonists may directly influence ovum development following induction of super-ovulation (Erickson & Hsueh, *U.S.A. Soc. Gynec. Invest.* Abstract 371; 1980). In the male, Arimura and colleagues have shown that treatment with an LHRH agonist can reduce LH-receptor numbers in the testes of both immature and adult hypophysectomized rats (*Biochem. Biophys. Res. Commun.* **90**, 687; 1979). Outside of the gonads, inhibition by LHRH of progesterone production by human placental tissue *in vitro* has been reported (Wilson & Jawad *Fertil. Steril.* **33**, 91; 1980), and preliminary work in baboons by McRae, Vickery and Stevens (*Endocrinology Supp.* in the press), suggests that LHRH agonists can suppress chorionic gonadotrophin secretion by the placenta. However, such effects may not be straightforward, as LHRH agonists do not impair the placental secretion of hCG and progesterone *in vivo* in women (Casper *et al. Proc. of P.A.R.F.R. Workshop on Fertility Regulation* Harper & Row; 1980). Gonadal or placental effects of LHRH are presumably

important in explaining the local abortifacient action of LHRH on the pregnant rat uterus (Jones *Contraception* **20**, 569; 1979) and the termination by LHRH of pregnancy in rats hypophysectomized on day 12 (Bex & Corbin *61st. Endocr. Soc. Meeting, U.S.A.* Abstract 435; 1979).

The two most impressive aspects of the above findings are, firstly, that all but one of the extra-pituitary effects of LHRH and its agonists are inhibitory and, secondly, that the effects (particularly those on the gonads) are almost identical to those reported following similar treatment of intact animals. This raises the question as to whether all of the inhibitory effects of LHRH agonists in intact animals, including the contraceptive effects in women, are the result of extra-pituitary action? Although any answer must at this stage be qualified, the weight of evidence suggests this is not the case. To obtain the direct gonadal effects reported above, the investigators have used doses of LHRH agonists at least 10-times and, in most cases, over 1,000-times greater than those used in intact animals. Moreover, the direct effects reported have often been the inhibition of rather specialised changes which may not be directly relevant to the intact adult animal. Thus the acute steroidogenic responsiveness *in vitro* of Leydig cells from untreated rats is unaffected by LHRH or its agonists (Badger *et al. Endocrinology* **106**, 1149; 1980), although Clayton and colleagues (*Nature* **282**, 90; 1980) found a small decrease in the sensitivity of rat luteal cells to hCG-stimulation *in vitro* in the presence of 10^{-7} M LHRH agonist.

However, there is the very real possibility that some proportion of the inhibitory

effects of LHRH and its agonists in intact animals is the result of extra-pituitary action. Indeed, the recent demonstration of specific, high affinity ($K_A = 10^9 M^{-1}$) receptors for LHRH and its agonists on luteal cells in the ovary (see last ref. above), and on Leydig cells in the testis (Labrie *et al. Int. J. Fertil.* in the press; Sharpe & Fraser *Biochem. biophys. Res. Commun.* in the press), must mean that LHRH has some role to play at the gonadal level, particularly as these receptors have almost identical properties to LHRH receptors in the pituitary (see Clayton *et al. Endocrinology* **105**, 1369; 1979). There is also persuasive evidence that the direct effects of LHRH agonists on the gonads are mediated through such receptors, as Hsueh and Erickson (*Life Sci.* **25**, 1223; 1979) have shown that the inhibitory effects of LHRH agonists *in vitro* can be prevented in a dose-dependent manner by a structurally similar, but antagonistic, analogue of LHRH. There is also immunohistochemical evidence for LHRH receptors in mouse adrenal cells (Bernardo *et al. J. Histochem. Cytochem.* **26**, 613; 1978).

Because of the specialized portal blood system, which transports LHRH from the hypothalamus to the pituitary, and because of the rapid degradation of LHRH, it seems certain that LHRH secreted from hypothalamic neurones can never reach peripheral tissues in effective concentrations. Are there, therefore, extra-hypothalamic sites of LHRH production? Two pieces of information suggest that there are. First, there is some evidence for the placental production of LHRH (Khodr & Siler-Khodr *Science* **207**, 315; 1980), and secondly, Guillemin and colleagues



100 years ago

The *Times* Geneva correspondent writes under date June 20 that a remarkable electrical phenomenon occurred at Clarens on the afternoon of Thursday last. Heavy masses of rain-cloud hid from view the mountains which separate Fribourg from Montreux, but their summits were from time to time lit up by vivid flashes of lightning, and a heavy thunderstorm seemed to be raging in the valleys of the Avants and the Alliaz. No rain was falling near the lake, and the storm still appeared far off, when a tremendous peal of thunder shook the houses of Clarens and Tavel to their foundations. At the same instant a magnificent cherry-tree near the cemetery, measuring a metre in circumference, was struck by lightning. Some people who were working in a vineyard hard by saw the electric "fluid" play about a

little girl who had been gathering cherries and was already 30 paces from the tree. She was literally folded in a sheet of fire. The vine-dressers fled in terror from the spot. In the cemetery six persons, separated into three groups, none of them within 250 paces of the cherry-tree, were enveloped in a luminous cloud. They felt as if they were being struck in the face with hailstones of fine gravel, and when they touched each other sparks of electricity passed from their finger-ends. At the same time a column of fire was seen to descend in the direction of Chatelard, and it is averred that the electric fluid could be distinctly heard as it ran from point to point of the iron railing of a vault in the cemetery. The strangest part of the story is that neither the little girl, the people in the cemetery, nor the vine-dressers appear to have been hurt; the only inconvenience complained of being an unpleasant sensation in the joints, as if they had been violently twisted, a sensation which was felt with more or less acuteness for a few hours after. The explanation of this phenomenon is probably to be found in Prof. Colladon's theory of the way in which lightning descends, as described

in *Nature*, vol. xxii. p.65. The Professor contends that it falls in a shower, not in a perpendicular flash, and that it runs along branches of trees until it is all gathered in the trunk, which is bursts or tears open in its effort to reach the ground. In the instance in question the trunk of the cherry-tree is as completely shivered as if it had been exploded by a charge of dynamite.

Amongst the peculiar institutions of Paris are the street astronomers, who exhibit through their telescopes the moon, sun-spots, comets' tails, and other celestial objects, according to circumstances. Their charges vary from 1*d.* in the suburbs to 5*d.* on the Place de la Concorde or the Place Vendôme, where the instruments are not unworthy of a regular observatory. At the last monthly meeting of the scientific journalists M. Flammarion read an address sent to him by the corporation of these itinerant teachers of the marvels of the heavens. They state that from the beginning of the publication of the "Astronomie Populaire" the number of their customers has more than doubled.
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