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Thoughts on puberty. Initiation of the gonadotropic function.

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Summary. Initiated during fetal life, the gonadotropic function suddenly damps shortly before or after birth. It resumes during the period of puberty at an exact stage of development in the young. The only hypothesis taking this process into account is that which postulates a specific hypothalamic inhibition triggered by the higher nervous structures. Infancy is the period during which this inhibition holds sway. It is characterized by a very low gonadotropin level closely resembling the young normal or castrate. This period lasts several years in man and several days or weeks in many mammals (rat, guinea-pig, cattle, sheep, etc.).

During puberty the central nervous system inhibition is gradually withdrawn ; LH secretion reaches adult levels quicker than FSH secretion. Steroids do not induce these transformations since they occur in the young normal or castrate. At all times the gonadotropic function depends on the stage of body development of the young ; delayed growth retards age of puberty no matter how long infancy lasts.

Nervous system perception of physical and chemical body constant changes, caused by growth, may gradually alter central nervous system relations with the hypothalamic gonado-neurosecretory systems.

In all mammals the sexual function is the last to be initiated during the pubertal period occurring at an exact stage of growth in the young of every species. The very specific temporal and physiological conditions in which the sexual function is activated have led to the supposition of the existence of a puberty-inducing mechanism. This process remains the object of many speculations although observation and experimentation proved long ago that puberty results from a change in the role of the central nervous system.

It seems necessary in broaching this question to study the conditions in which the gonadotropic function is set in action.

Gonadotropic function during fetal and neonatal life.

The gonadotropic function is activated at the beginning of development, but during fetal life or shortly after birth it is suddenly damped, and only very small quantities of gonadotropins, characteristic of infancy, are produced. This damping is surprising, especially as the fetal gonadotropic function is complete :

— the hypothalamus secretes GnRH :
  - observation of LH-RH neurons and fibers as in adult (man : Bugnon, Bloch and Fellmann, 1976 ; guinea-pig : Barry and Dubois, 1974) ;
  - GnRH hypothalamic activity evidenced (man : Winters, Eskay and Porter, 1974 ; Kaplan, Grumbach and Aubert, 1967 ; rat : Corbin and Daniels, 1976 ; Araki *et al.*, 1975) ;

— the pituitary secretes LH and FSH ; circulating titers reach adult values ;

— gonadotropin secretion is under effect of steroid negative feedback :
  - gonadotropin level is lower in the male than in the female fetus because the testicle secretes testosterone at an adult rate while the ovary has no concomitant steroidogenic activity ;
  - castration of the male fetus causes a rise in gonadotropin level (macaque : Winter, 1976) ;
  - in female fetuses in which the ovary does not secrete estradiol, gonadotropin level may be comparable to that of the spayed adult (man : Kaplan, Grumbach and Aubert, 1976) ;
  - artificial elevation in estradiol level (implant in the mother) lowers fetal gonadotropic level (guinea-pig : Donovan, Ter Haar and Peddie, 1974).

Since steroid negative feedback may act on fetal gonadotropic function, it may be that feto-placental estrogen holds this function in check ; as far as we know, rat fetus is the sole one protected from estrogen action by its α-feto-protein.

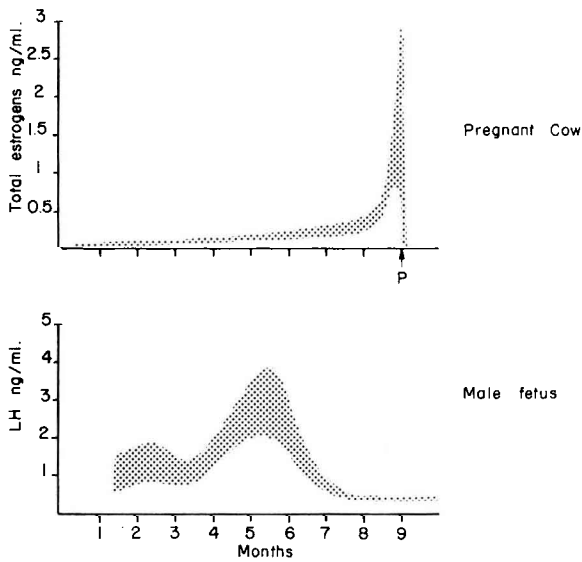

FIG. 1. — *Patterns of circulating estrogens in cow and circulating LH in calf during gestation*
— Estrogens, pregnant cow, from Henricks *et al.* (1972), Edquist *et al.*, (1973).
— LH, male calf fetus, from Challis *et al.* (1974).

Only placental steroids could be involved because in all mammals studied, although the fetal testicle secretes testosterone, the fetal ovary is inactive, and the gonadotropic function pattern is about the same in males and females. The fetal testicle secretes testosterone as long as the fetal gonadotropic function is active. A comparison of the patterns of circulating estrogen titers in the mother during gestation and of circulating gonadotropins in the fetus does not indicate that these estrogens can play a determining role in fetal gonadotropic function damping.

In cattle fetal gonadotropic secretion reaches its full development at about 5-6 months ; it is completely checked at 8 months, while maternal estrogens increase only slightly during gestation, except for a peak just before parturition at 9 months (fig. 1).

In the guinea-pig fetal gonadotropic function achieves full development in the last days before parturition just when placental estrogens are most abundant. Gonadotropic activity is damped only 8-10 days after birth (fig. 2), while the steroids are very low (the wide variability in circulating gonadotropin titers immediately after birth in this species may be due to parturition stress).

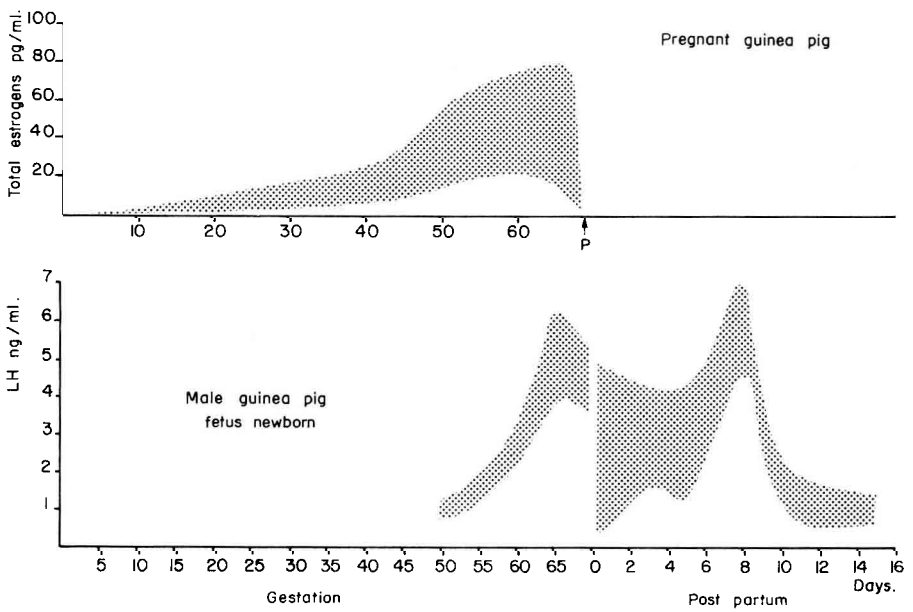

FIG. 2. — *Patterns of circulating estrogen in pregnant guinea-pig and circulating LH in the young male*
— Estrogens, pregnant guinea-pig, from Challis *et al.* (1971).
— LH, young male guinea-pig, from Donovan *et al.* (1975).

However, in man placental estrogens increase regularly during gestation to reach very high concentrations ; they are probably responsible for the damping of fetal gonadotropic function during the last third of gestation. In this hypothesis, resumption of gonadotropic activity during the first months after birth would correspond only

to the disappearance of maternal estrogens, and true damping of the fetal gonadotropic function would occur several months later (fig. 3). At the same time, testicle testosterone secretion is temporarily resumed (Forest, Cathiard and Bertrand, 1973).

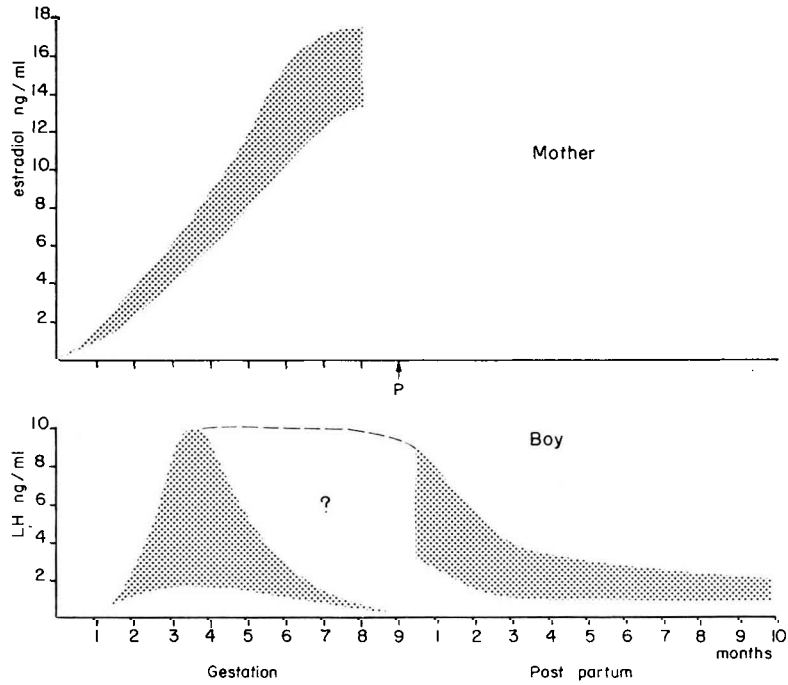

FIG. 3. — *Patterns of circulating estradiol in pregnant woman and circulating LH in male child before and after birth*

— Estradiol, mother, from De Hertogh *et al.* (1975).
— LH, boy, from Kaplan and Grumbach (1976), Winter *et al.* (1975).

In sheep and macaque the situation is comparable respectively to that in cattle and man. Patterns of fetal gonadotropic function in rat can ben compared to those in guinea-pig.

Damping of the fetal-neonatal gonadotropic function thus appears as a basic process in the evolution of the young mammal, completely independent of steroids. During its first phase of fetal activity, the hypothalamo-pituitary gonadotropic function can be compared to that in the adult in which the hypothalamus has been completely deafferentated. Limbic and cortical afferences would gradually act as extremely strong and specific inhibitors of the gonadotropic function during embryogenesis when hypothalamic control is initiated. The period during which this inhibition holds sway is called infancy.

This does not mean that fetal or placental steroids do not act on the fetal nervous system. They certainly play a role in the sexualization of that system, but have no part in the central inhibition of the gonadotropic function during infancy.

Infancy.

Fetal-neonatal inhibition of the gonadotropic function is accompanied by an apparent change in steroid sensitivity of the hypothalamo-pituitary unit ; this led to the gonadostat theory proposed by Ramirez and McCann (1963) and taken up by Grumbach *et al.* (1974). It gives a predominant role to the sex steroid sensitivity of the hypothalamus. Puberty would occur when the hypothalamic gonadostat, very sensitive to steroid negative feedback, gradually desensitizes, causing gonadotropic secretion to increase. Infancy would be a period during which very low gonadal steroid production would, however, be sufficient to maintain gonadotropic function at a very low level. Effectively, gonadal steroid production is, of course not negligeable ; the castration of impubertal macaques causes gonadal steroid titer to drop in males and females (Winter, 1976). These steroids have a negative feedback effect on gonadotropic secretion : in dysgenesic girls circulating gonadotropic titer is markedly higher than in normal girls (Conte, Grumbach and Kaplan, 1975).

However, study of patterns of circulating gonadotropin levels during infancy and puberty in young normals and castrates or dysgenesics does not favor this theory. The castration of young macaque males or females does not immediately cause a high elevation of circulating gonadotropin level as in adults (Dierschke *et al.*, 1974). Gonadotropin titer rises at a comparable age in all animals, i.e. at the onset of puberty (fig. 4).

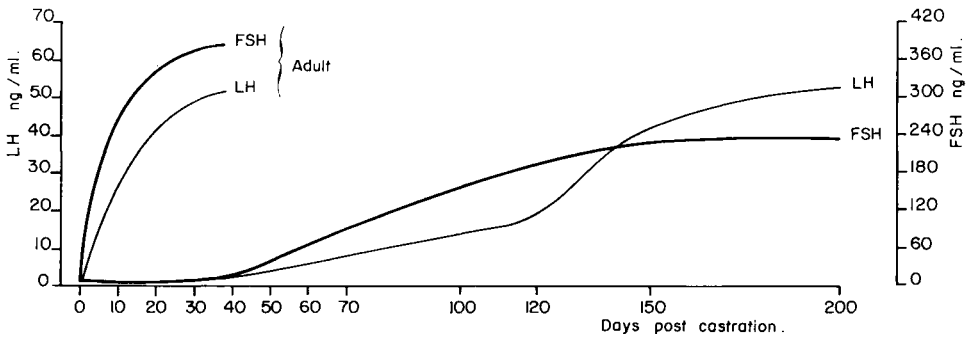

FIG. 4. — *Patterns of circulating gonadotropins in adult and immature female macaque after spaying* (from Dierschke *et al.*, 1974)

In the adult circulating LH and FSH levels rapidly increase after spaying ; the characteristic level is reached after one month.

In the immature castrate, circulating gonadotropins increase only at the beginning of puberty (in this case, 40 days after spaying). Gonadotropin rises much more slowly than in the adult.

The general pattern of circulating gonadotropin titers between birth and adolescence is the same in normal girls and dysgenesics (Conte, Grumbach and Kaplan, 1975). The level is very low between 4 and 9 years, then increases continuously from 10-12 years to reach, in dysgenesic girls, the level observed in ovariectomized or in postmenopausal women (fig. 5).

Also, when ewe-lambs are spayed at birth, there is no large increase in gonadotropic hormone secretion until 2 to 6 weeks later, at the time when secretion in nor-

mal lambs also increases (Liefer, Foster and Dziuk, 1972 ; Foster, Jaffe and Niswender, 1975). It then reaches higher titers in spayed animals.

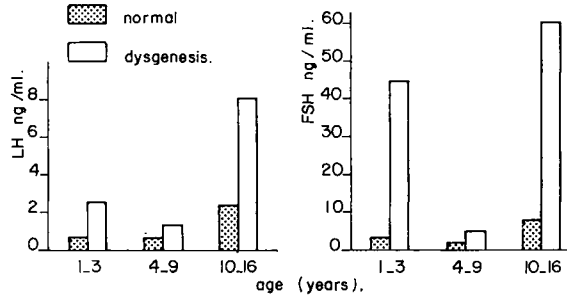

FIG. 5. — *Mean level of gonadotropin in normal and dysgenesic girls between birth and puberty* (from Conte, Grumbach and Kaplan, 1975)

Infancy may thus be defined as *the period in which the gonadotropic function is not primarily controlled by sex steroids but by a central mechanism.*

This period varies in length. Using the above definition, infancy :

— occurs in the girl between 2-3 years (when the first phase of gonadotropic function activity is over) and 9-10 years ;

— occurs in macaque between 6-8 months and 17-18 months for females ; 28-30 months for males ;

— occurs in the ewe-lamb between birth (the first phase of gonadotropic function activity ends at parturition) and 2-6 weeks ;

— lasts several days in female rat. Fetal gonadotropic function is held in check during the first 2-4 days after birth. In animals spayed at birth circulating gonadotropin titer is low and resembles that of 8-day controls, but at 15 days it is higher in spayed subjects (Slama-Scemama, 1976) ;

— is virtual in guinea-pig, supposedly beginning at 8-10 days, but spaying at all times causes a significant gonadotropin elevation 10 days later (Donovan *et al.*, 1975) ;

— probably begins at about 8 months of gestation in calf, when the first phase of gonadotropic activity finishes, and ends after birth ; at 45 days spaying causes a quick rise in circulating LH of some animals as in the adult (Odell, Hescox and Kiddy, 1970).

Puberty.

The basic process marking the onset of puberty is the resumption of the gonadotropic function of the hypothalamo-pituitary unit.

Suppression of central nervous system damping effect.

The gradual rise in the mean gonadotropin level, and especially in LH, is characterized by surge peaks of increasing frequency and amplitude (calf : Lacroix and Pelletier, personal communication ; ewe-lamb : Foster, Jaffe and Niswender, 1975 ; man : Weitzman *et al.*, 1975 ; fig. 6, 7). This release of hypothalamo-pituitary activity is related to gradual lessening of central nervous system inhibition. Pituitary hor-

mone secretion always depends closely on the waking-sleep cycle. Highest production is always observed during rest, each hormone having its own temporal schedule of increasing secretion (man : Weitzman *et al.*, 1975). These circadian rhythms of pituitary secretion depend on the higher nervous structures because after the baso-median

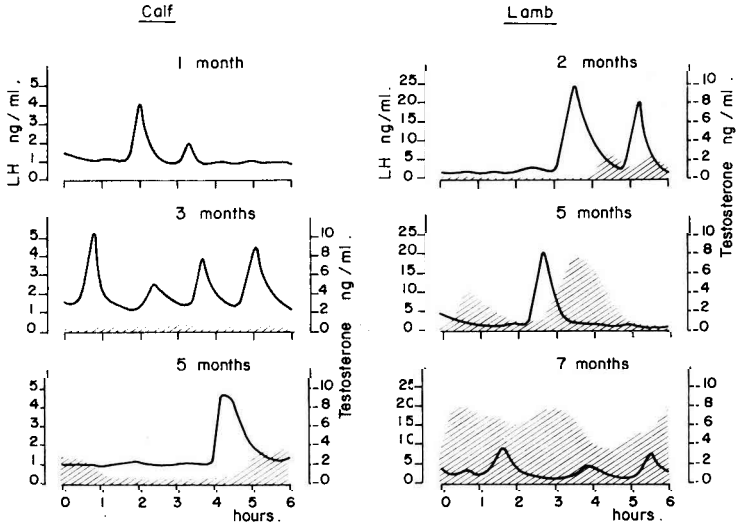

FIG. 6. — *LH and testosterone secretion patterns in calf and lamb during puberty* (Shaded area : testosterone)

— Calf (from Lacroix and Pelletier, personal communication). Between 1 and 3 months, LH surges increase in number and amplitude ; testosterone secretion remains very low. At 5 months testosterone secretion increases at each LH surge. The number of LH surges decreases.

— Lamb (from Foster, 1974). Testosterone secretion increases at each LH surge. When basal testosterone reaches a high level, LH surge amplitude decreases.

hypothalamus is deafferentated, they disappear (at least that of ACTH does), while basal pituitary secretion remains subnormal (rat : Halasz, 1969 ; macaque : Krey *et al.*, 1975). During childhood in man, gonadotropin secretion is slightly higher during sleep but is so strongly inhibited that the difference can only be shown by gross measurements in urine (Kulin, Moore and Santner, 1976). The onset of puberty is characterized by noctural suppression of the damping effect of the higher nervous structures on the hypothalamo-pituitary gonadotropic function. A characteristic elevation in serum gonadotropin is first observed during sleep (Weitzman *et al.*, 1975 ; fig. 7). Gonadotropin secretion then augments gradually during the day. Finally, at the end of puberty circadian secretion rhythm has almost disappeared (Weitzman *et al.*, 1975). Only the gonadotropic function undergoes this evolution. In the adult everything transpires as if the gonadotropic function had a greater autonomy than the other hypothalamo-pituitary functions in relation to the higher nervous structures.

Human pathology has confirmed the prepubertal damping role of the central nervous system. Many central nervous system abnormalities, and in particular hypothalamic tumors (e. g. hamartomes), even when benign, often cause true precocious puberty (Donovan and Van Der Werff Ten Bosch, 1965). In these cases, the tumor

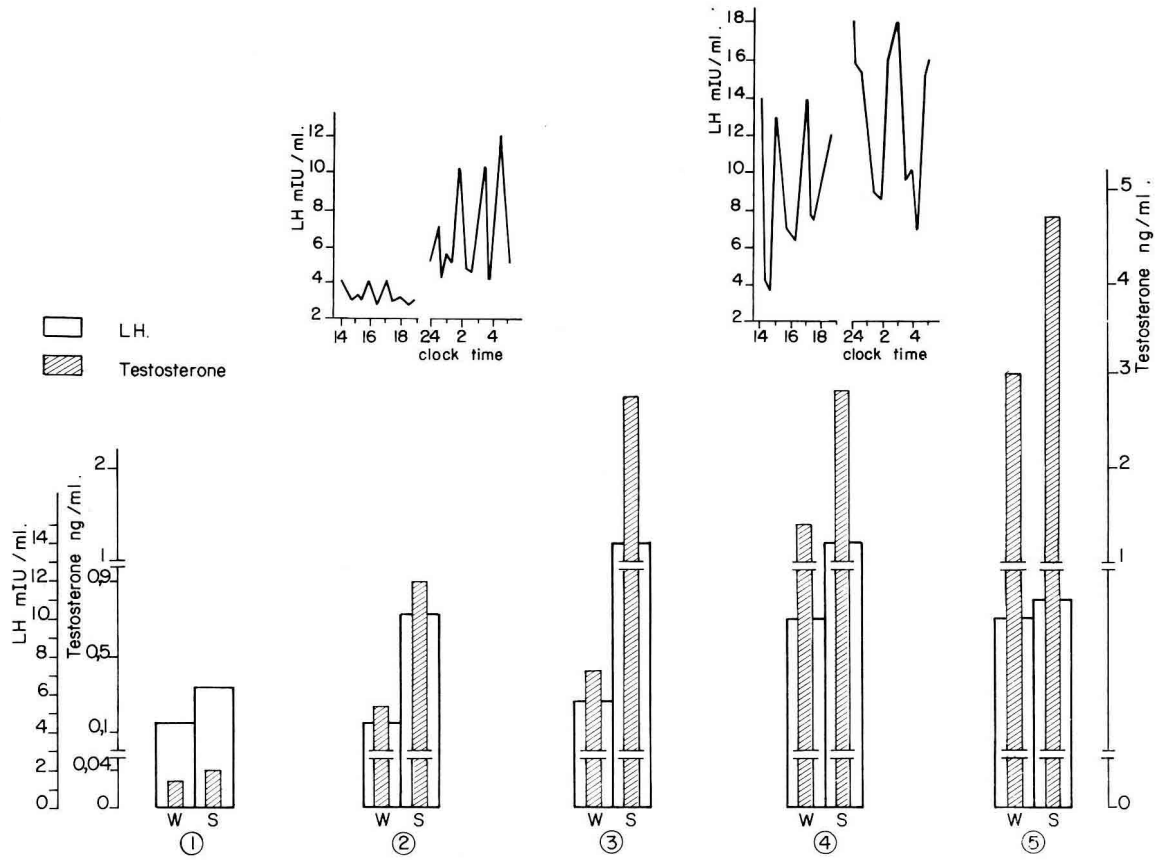

FIG. 7. — *LH and testosterone secretion patterns in man during puberty*

① : early stage 2 ; ② : late stage 2 ; ③ : stage 3 ; ④ : stage 4 ; ⑤ : stage 5 : stages of puberty as defined by Tanner (1962)

W = wake, S = sleep.

Comparison of mean LH and testosterone levels during wake and sleep in puberty (from Parker *et al.*, 1975). Mean LH elevation at night corresponds to surge amplitude increase (from Weitzman *et al.*, 1975).

probably destroys the higher afferents governing gonadotropic function damping. These true precocious puberties may occur in the first year of life. Noctural increase of the secretion of the two gonadotropins in children presenting signs of precocious puberty of nervous origin, occurs as in normal puberty (Boyar *et al.*, 1973). This puberal change in the circadian rhythm of gonadotropin secretion has only been studied in humans.

Sex steroids do not play any large part in triggering the gonadotropic activity of the hypothalamo-pituitary unit. This occurs in the same way at the normal age of puberty crisis in girls afflicted with gonadal dysgenesis and in normals (Weitzman *et al.*, 1975). Only gonadotropic blood levels differ. This activation takes place in calf and lamb before testicle testosterone secretion begins to increase (lamb : Foster, 1974 ; calf : Lacroix and Pelletier, personal communication ; fig. 6).

Finally, maturation of the nervous systems regulating LH and FSH secretion is not synchronized for the two gonadotropins.

While LH secretion in ewe-lamb spayed at 2 weeks rises between 6 and 8-9 weeks to a level very similar to that of spayed adult ewe, FSH secretion is less abundant at this time although higher than observed in normal ewe-lambs (Foster, Jaffe and Niswender, 1975) (fig. 8). In prepuberal macaque, the LH and FSH secretion titers characteristic of spaying are rarely reached after 6 months, while in the adult they are achiev-

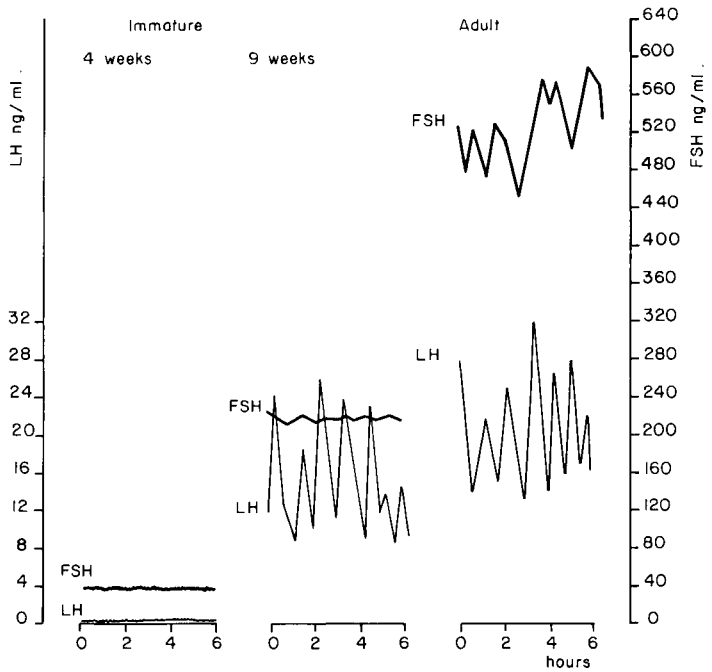

FIG. 8. — *Gonadotropin level in pubertal and adult spayed* ewe (from Foster *et al.*, 1975)

Impubertal ewes were spayed when 2 weeks old. At 4 weeks LH and FSH levels are very similar to those in normal lambs. At 9 weeks LH secretion closely resembles that found in adult ewe spayed 6 months previously ; however, FSH secretion is lower.

ed after 1 month (Dierschke *et al.*, 1974). Moreover, it appears that the mean LH level characteristic of the spayed adult is reached quicker than the FSH level (fig. 4).

Role of gonadal steroids.

Sex steroids at all times have negative feedback effect on pituitary hormone secretion levels and the variations in steroid sensitivity observed during initiation of the sex function are the *result* and not the *cause* of gonadotropic function pattern.

During puberty there is gradual adjustment between gonadotropin secretion titers and the gonadal steroid secretion which they induce. This adjustment is always characterized by a transition period in which mean gonadotropin level is higher than in the pubertal subject because gonad response is triggered slowly and can only be induced by gonadotropic effect. The rise in testicular testosterone secretion, characteristic of prepuberty, is noctural at first and closely related to gonadotropin secretion rhythm in man (Boyar *et al.*, 1974) ; it occurs only at LH surge peaks (lamb : Foster, 1974 ; calf : Lacroix and Pelletier, personal communication) (fig. 6-7).

Transitory rise in mean level of circulating LH is due essentially to more numerous surge peaks and wider amplitude than in the adult (calf : Lacroix, Garnier and Pelletier, 1977 ; ewe-lamb : Foster, Jaffe and Niswender, 1975 ; Foster *et al.*, 1975).

	Number of LH surges per hr.
Ewe-lamb 9 weeks.....	0.53
Ewe-lamb 9 weeks, spayed.....	1.03
Adult ewe.....	0.03
Adult ewe, spayed.....	1.05

In female rat transitory elevation of gonadotropin secretion is especially sharp and much higher than in male rat (Döhler and Wuttke, 1974, 1975). This is explained by the presence of α-feto-protein until 20 days ; this protein binds estradiol strongly but not testosterone (Nunez *et al.*, 1971), preventing feedback control of gonadotropin secretion more efficiently in the female than in the male.

When steroid production increases, the mean rate of circulating gonadotropin decreases by a smaller number of surges and diminution of amplitude (LH : calf, Lacroix and Pelletier, personal communication ; lamb, Foster, 1974). During the final phase of puberty transformation of the gonadotropic hypothalamo-pituitary unit, the mean gonadotropin level rises slowly as the circulating steroid level continues to increase, especially in the male (fig. 6, 7).

If variation in hypothalamo-pituitary unit steroid sensitivity was basically important in gonadotropic maturation, experimental or pathological change in steroid level should alter the conditions of that maturation. However, this is not the case. Androgen-secreting tumors of the testicle, estrogen-secreting tumors of the ovary may at all ages in the human child cause manifestations of precocious puberty ; these are only steroid-dependent morphological changes : increased growth rate, advancement of bone age with phallic development and voice change in boys, and breast enlargement

and menarche in girls (Donovan and Van Der Werff Ten Bosch, 1965). Removal of the tumor causes signs of puberty to disappear, proving that the gonadotropic function was not activated. Accidental ingestion of estrogen may cause temporary breast enlargement and menarche in girls (Cook *et al.*, 1953) without triggering puberty.

The rise in gonadal steroid titer does not remove the damping effect of the nervous system on gonadotropin secretion.

Initiation of estradiol positive feedback in the female.

Even estradiol positive feedback control of gonadotropin secretion, the last mechanism characteristic of the puberal female to be triggered, does not seem to depend on the presence of estradiol, although it is logical to suppose its differentiation due to increasing estradiol titers in the young female.

Artificial elevation of circulating estradiol titers, brought on by implants, does not cause estradiol positive feedback on gonadotropins to appear earlier (macaque : Dierschke, Weiss and Knobil, 1974). Conversely, estradiol positive feedback is triggered normally in absence of circulating estradiol : in the 14-year old dysgenesic girl estradiol treatment causes LH surge as in the normal girl at first menstruations (Reiter, Kulin and Hamwood, 1974). In female rats spayed at birth, ovary transplantation at about 30 days is followed by the appearance of normal cyclicity (Pfeiffer, 1936), proving that gonadotropic function cyclicity is triggered.

Estradiol positive feedback effect on gonadotropin release appears gradually (fig. 9) : LH surge is obtained in ewe-lambs at 4 weeks by estradiol treatment (Land, Thimonier, and Pelletier, 1970). The response obtained increases progressively with age : 40 ng at 7 weeks, 75 ng at 12 weeks, 100 ng at 20 weeks (Foster and Karsch, 1975). At 27 weeks, the same amount of LH is released as in the adult. Similarly, the first LH surges induced in the young macaque female or girl are lower than adult surges (Dierschke, Weiss and Knobil, 1974 ; Presl *et al.*, 1976). Moreover, estradiol positive feedback effect appears successively on LH then on FSH : in macaque and girl after the first menstruations an estradiol treatment causes LH but not FSH surge (macaque : Dierschke, Weiss and Knobil, 1974 ; girl : Presl *et al.*, 1976 ; Reiter, Kulin and Hamwood, 1974) ; the simultaneous surge of these gonadotropins occurs several months later. In female rat, positive estradiol feedback action on FSH is also acquired later than for LH (Caligaris, Astrada and Taleisnik, 1973 ; Wuttke and Gelato, 1976).

Nervous FSH regulation occurs last. It is probably the final process marking the acquisition of puberty, as Critchlow and Bar-Sela (1967) believed.

Role of adrenal steroids.

The nature and quantity of steroids secreted by the adrenals change at puberty. In man adrenal steroid secretion increases slightly beginning at 6-7 years of age (Sizonenko and Paunier, 1975 ; Collu and Ducharme, 1975). The role of adrenal steroids in triggering puberty processes has thus been programmed. They certainly play a role in the appearance of secondary sex characteristics (especially in hairiness and bone maturation) (Tanner, 1962).

Congenital hyperplasia of the adrenals, characterized by abnormally high androgen secretion, regularly causes precocious pseudo-puberty (accelerated bone matura-

tion, development of secondary sex characters). The cases of true precocious puberty following this syndrome are doubtful. Adrenal hyperplasia may be accompanied by noctural elevation in LH, and even FSH, secretion (Boyar *et al.*, 1973). However, as GnRH tests on children are not conclusive of precocious gonadotropic function maturation (Lee and Gareis, 1976), and as adrenal deficiency in Addison's disease does not prevent normal increase of gonadotropin secretion at normal puberty age (Sizonenko and Paunier, 1975), adrenal steroids are not likely to play a major role in triggering gonadotropic function.

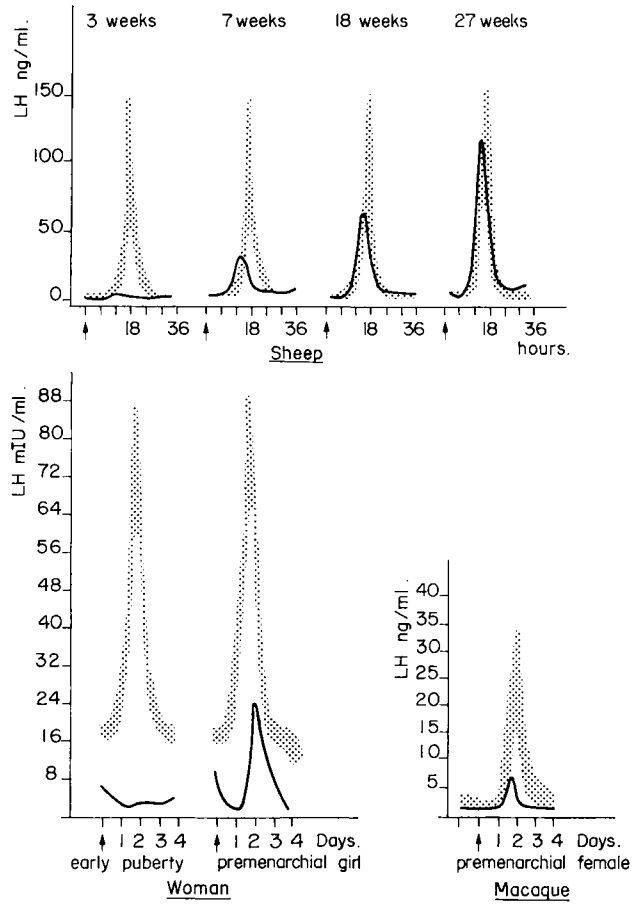

FIG. 9. — *Gradual appearance of positive estradiol feedback on LH secretion during puberty*

↑ Estradiol treatment may cause positive feedback in adult. Shaded area : comparative LH surge in adult.

— Sheep (from Foster and Karsch, 1975). Gradual increase of LH response to E_2 with age. Comparison with surge induced in adult ewe in anestrus.

— Woman (from Presl *et al.*, 1976). In premenarchial girl, but not in early puberty, estradiol treatment causes LH surge. This is very low if compared to the natural surge in cyclic woman (from Ross *et al.*, 1970).

— Macaque (from Dierschke, Weiss and Knobil, 1974).

Except for man, the role of the adrenals has only been studied in prepubertal female rat. Adrenalectomy causes puberty to appear later. However, this delay may be avoided if females are treated with prolactin, and prolactin injections may advance puberty in female control rats (Gelato *et al.*, 1976). Thus, the adrenals may act indirectly by modifying prolactin secretion. This observation, rather than confirming the active role of the adrenals, puts more emphasis on the possible role of prolactin in triggering puberty.

In this regard, a large, brief prolactin peak has been noted in the 70-day old lamb (Courot, 1974) ; its significance is not known. No comparable observations have been noted in calf (Lacroix and Pelletier, personal communication).

Conclusion.

The gonadotropic function develops during fetal and/or neonatal life before differentiation of the central nervous system leads to control of hypothalamic gonadotropic regulation. Strongly damped by the higher nervous structures during infancy, it is gradually initiated during puberty.

Steroids, responsible for all visible manifestations of puberty (secondary sex characters, sexual behavior, menstruation, etc.), appear to play no role in pubertal transformation of the central nervous system.

When the gonadotropic function resumes, damping is not suppressed definitively thus leading inevitably to adult gonadotropic function. Initiation of this function always depends closely on the state of body development of the young. A delay in growth retards puberty in mammals which have practically no infancy, as well as in man. High weight loss after puberty may even result in gonadotropic function regression : nervous anorexia in young girls causes a return to noctural elevation of circulating gonadotropins if weight loss reaches 25 to 40 p. 100 (Weitzman *et al.*, 1975). Only gonadotropic function is affected, the secretion of other pituitary hormones depending on the hypothalamus remains normal (Beumont *et al.*, 1976).

The close inter-dependence between gonadotropic function initiation and growth seems to be a safety measure preventing reproduction before a certain stage of body development.

Growth causes changes in physical and chemical body constants which should alter the central nervous system relations with the neuro-gonadotropic secretory units of the hypothalamus. In man the approach of puberty is best estimated by changes in metabolism (Frisch, 1974). The onset of pubertal processes occurs when critical basal metabolism is the same in girls and boys, although the latter are 2 years older and weigh 6-8 kg more (Frisch, 1974). Bedridden girls habe more precocious puberty than others because this state lowers metabolism and critical metabolism for onset of puberty processes is thus reached more rapidly (Osler and Crawford, 1973).

To understand the initiation of the gonadotropic function, we must study central nervous system patterns of perception of the state of body development, which must be orientated to avoid constantly confusing the causes of puberty with its consequences.

The relations between the central nervous system and the neuro-gonadotropic secretory units of the hypothalamus must be well understood even after puberty.

Directly related to this observation is the photoperiod, causing changes in gonadotropic function activity in seasonally reproductive animals ; castrated subjects evidence wide seasonal variation in circulating gonadotropins. Modifications in steroid sensitivity have also been named as the causes of this process.

The experiment of Critchlow and Bar-Sela (1967), although too limited for generalization, still shows the direction which research should take in studying the causes of puberty. Very focalized lesions of the cortico-medial amygdala nucleus or of the stria terminalis induce precocious puberty in female rat. Hypothalamic lesions may also cause precocious puberty, but efficient lesions are situated in diverse regions. Critchlow and Bar-Sela thus thought that precocious puberty in all cases resulted from suppression of the damping effect of the amygdala on gonadotopin secretion ; efficient hypothalamic lesions were those severing connections between the amygdala and the hypothalamus. This clearly illustrates the importance of relations between the central nervous system and the hypothalamus in triggering the gonadotropic function.

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Résumé. Mise en place pendant la vie fœtale, la fonction gonadotrope régresse brutalement peu avant ou après la naissance. Elle reprendra au cours de la période pubertaire, à un stade précis du développement du jeune. La mise en place d'une inhibition spécifique de l'hypothalamus par les structures nerveuses supérieures reste la seule hypothèse rendant compte de ce phénomène. Le temps pendant lequel cette inhibition ne se relâche pas correspond à l'enfance, caractérisée par un niveau de gonadotropines très bas et peu différent, que le jeune soit normal ou castré. Elle dure plusieurs années chez l'Homme, quelques jours ou semaines chez beaucoup de mammifères (rat, cobaye, bovin, mouton, ...).

Au cours de la période pubertaire, l'inhibition exercée par le système nerveux central est progressivement levée. La sécrétion de LH est plus rapidement de type adulte que la sécrétion de FSH. Les stéroïdes n'interviennent pas comme cause de ces transformations qui se produisent chez le jeune normal ou castré. A tout moment la mise en place de la fonction gonadotrope dépend de l'état de développement corporel du jeune : un retard de croissance retarde l'âge de la puberté, quelle que soit la durée de l'enfance.

La perception des changements des constantes physiques et chimiques corporelles provoqués par la croissance, au niveau du système nerveux, pourrait entraîner une modification progressive de ses relations avec les systèmes neurosécréteurs gonadotropes de l'hypothalamus.

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