

## COITUS-INDUCED OVULATION

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"We must remember that the natural sciences are as much a struggle against as for facts." (1)

Anglo-American literature concerned with human fertility seems to be devoid of substantial information on coitus-induced, paracyclic ovulation in women at any time during the menstrual cycle. Its existence is, in accordance with the strong acceptance of the "rhythm method" for contraception, stoutly denied. Typical are the following statements:

"Provoked ovulation: the suggestion that in women ovulation may result from sexual stimulation has been copied from book to book, without any scientific basis for it in the first instance. This probably arose from an extrapolation to man of the condition in the rabbit and several other species of mammals where ovulation occurs only after copulation. Likewise, there is no evidence to support the suggestion that the act of coitus hastens ovulation spontaneously." (2)

"Not a single documented case of induced ovulation in women has been published in the world literature during the past 100 years, even though literature is replete with case reports based on old wives' tales." (3)

These statements cannot stand undisputed in the face of published evidence. On two occasions the author made reference to these data (4, 5), most of them published in Germany during 1947 to 1951. The responses this triggered (3), the inquiries I received, and the questions which were raised, initiated this review of pertinent information, especially since a recent discussion of the subject by Clark & Zarrow (6) did not dwell on those details that the clinician or the clinical pharmacologist may accept as evidence of coitus-induced ovulations.

This review of coitus-induced ovulation shows its wide-spread occurrence throughout mammalian evolution [A]; it deals in some length with the neurohormonal and morphological apparatus available for mediating specific stimuli and releasing (and responding to) related hormones and biotransmitters [B and C]; points to the peculiarities of the follicular phase of the menstrual cycle [D]; discusses in detail information on paracyclic [E] and on coitus-induced ovulations (conceptions) in women [F]; takes emphasis on psychology and reproduction in women [G]; and draws conclusions [H].

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## A. Coitus-induced Ovulation in Eutherian and Mammalian Species.

As an introduction into the biological phenomenon of coitus-induced ovulation, a list of the species in which ovulation is triggered by coitus is presented in Table 1.

This compilation indicates a wide-spread occurrence of coitus-induced ovulation which synchronizes semen disposition, transport, and capacitation, as well as of ovulation, production and release of hormones responsible for creating optimal conditions for oviductal motility and secretion, and eventually for fertilization. This system is so highly effective in coordinating all necessary steps for the assurance of fertility, in so many species of different orders, families, and genera, that it makes one wonder why its principles, in toto or at least partially, have not found an even wider distribution in mammalian evolution.

An answer to this paradox may be found in those species that are "facultative-induced ovulators", or in those in which cohabitation seems to speed or hasten ovulation (Table 1). In both instances, species found involved in this ambiguous state of reproductive behavior are generally known as staunch spontaneous ovulators. Facultative-induced ovulators seem to use this mechanism as a last resort to maintain their reproductive capacity under adverse situations, when endogenous or exogenous conditions force abandonment of cyclic functions, and permanent receptiveness for the male is established in exchange. Permanent stimulation for follicle growth not only assures production and release of enough estrogens to attract males and affirm their reception, but seems to be an essential prerequisite for the priming of the hypothalamic-pituitary system to respond to the neural stimulus from vagina and cervix with an adequate ovulatory LH-discharge (39). Even in cyclic animals (rats), estrogen priming during early pro-estrus establishes a situation in which coitus triggers ovulation (32), about 12-14 hours prior to the start of the well-explored sequence of events leading to cyclic, spontaneous ovulation in this species (24-27, 39, 85). On the other hand, the well-known capacity of chlorpormazine, or other centrally inhibiting compounds, like atropine or urethane (27, 32, 86-88), to prevent the circadian LH-release during the day of estrus in the rat, is overridden if by frequent coitus via nervous stimulation, LH is discharged and ovulation takes place (39, 86, 88, 89).

The experimental situations, in which estrogens are used during pro-estrus to make animals responsive to coitus-induced ovulation, may be representative of those species in which cohabitation seems to hasten ovulation (cattle, sheep, and swine: Table 1). In these species, spontaneous ovulation can be recorded in a fixed time interval from the beginning of the heat period, if no natural service during the early part of the standing heat period (phase of acceptance of the male) is permitted. The success of artificial insemination and the selection of the best timing for semen deposition during the second half of the standing heat period are based on this observation. However, natural service early during the receptive phase hastens ovulation significantly up to 10-14 hours (cattle, sheep, swine). If artificial insemination in cattle,

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**TABLE 1:** Species which display reflex ovulation by coitus (A); spontaneous ovulating species in which, under certain conditions, coitus can induce ovulation (facultative reflex ovulators) (B); or in which coitus hastens ovulation (C).

GENUS	SPECIES	A	B	C	REFERENCES
<u>Monotrema</u>					
<u>Marsupialia</u>	<i>Potorous tridactylus</i>	+			7
	<i>Didelphis azarae</i>	+			8
<u>Insectivora</u>	<i>Erinaceus europaeus</i> (Hedgehog)	+			9
	<i>Neomys sodicus bicolor</i>	+			7
	<i>Blarina brevicaudata</i> (Shorttailed shrew)	+			7, 10
	<i>Scatopus</i>	+			7, 11
	<i>Sorex palustris navigator</i>	+			7
	<i>Suncus marinus</i> (Asian musk shrew)	+?			7, 12
<u>Dermaptera</u>					
<u>Chiroptera</u>	<i>Pteropus</i>	+			7
<u>Edentata</u>					
<u>Rodentia I</u>	<i>Citellus tridecemlineatus</i>	+			13
	All Sciuridae	+			7
	<i>Microtus californicus</i>	+			7
	<i>Microtus guentheri</i>	+			7
	<i>Microtus agrestis</i>	+			14-16
	<i>Microtus ochrogaster</i>	+			17, 18
	<i>Microtus pennsylvanicus</i>	+			19-21
	<i>Microtus pinetorum</i> (Pine vole)	+			21
	<i>Clethrionomys glareolus</i> (Bank vole)	+			22
<u>Rodentia II</u>	<i>Myocastor</i> (Beaver)	+			7
<u>Rodentia III</u>	<i>Mus musculus</i> (Mouse)			+a	
	<i>Rattus norvegicus</i> (Rat)			+ab	
	<i>Phenacomys</i>	+			7
<u>Lagomorpha</u>	<i>Oryctolagus cuniculus</i> (Rabbit)	+			33-39
	<i>Lepus europaeus</i> (Hare)	+			40
<u>Cetacea</u>	<i>Tursiops truncatus</i> (Bottleneck dolphin)	+			41
	Most Odontocetes	+			42
<u>Proboscidae</u>					
<u>Carnivora and Pinnipedia</u>	<i>Lutra lutra</i> (Lynx)	+			7
	<i>Felis domesticus</i> (Cat)	+			43, 44
	<i>Mustela nivalis</i> (Weasel)	+			45
	<i>Herpestes auropunctato</i> (Mungo)	+			7
	<i>Ursus arctos horribilis</i> (Grizzly bear)	+?			46
	<i>Ursus americanus</i>	+?			47
	<i>Procyon lotor</i> R. (Raccoon)	+			48
	<i>Mustela furo</i> (Ferrett)	+			49, 50
	<i>Mustela vison</i>	+			51, 52
	<i>Mirounga leonina</i> (Sea elephant)	+			53
	<i>Canis familiaris</i> (Dog)			+c	54

(continued)

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TABLE 1: (continued)

GENUS	SPECIES	A	B	C	REFERENCES
<u>Perissodactyla</u>					
<u>Artiodactyla</u>	<i>Bos taurus</i> (Cattle)			+	56-59
	<i>Ovis aries</i> (Sheep)			+	60-63
	<i>Sus scrofa</i> (Domestic pig)			+	64-67
	<i>Camelus bactrianus</i> (Camel)	+			68,71
	<i>Camelus dromedarius</i> (Dromedary)	+			68,71
	<i>Lama glama</i> L. (Lama)	+			69,71
	<i>Lama vicugna</i> L. (Vicuna)	+			69,71
	<i>Lama pacos</i> (Alpaca)	+			70,71
<u>Primates</u>	<i>Macaca mulata</i> (Rhesus monkey)			+?	72-74
	<i>Homo sapiens</i> (Man)		+	+	75-84

- (a) in strains with spontaneous permanent estrus (23-29);
- (b) in animals with light (30) or post-natum androgen treatment induced permanent estrus (31), or in animals conditioned during proestrus with estrogens (32).
- (c) in the bitch, not coitus but daily exposure to males hastens significantly preovulatory LH-release (54); as a result, ovulations coincide with the first and second day of standing heat (55).

applied vaginal (90) or intracervical (91), is accompanied by rectal manipulations of the uterus, conception rates are significantly increased (90, 91). These manipulations, known to cause (via nervous pathways) immediate oxytocin release (92), seem to imitate "orgasm" (during which milk ejection in a number of species has been well recorded: 92, 93) and may well hasten ovulation, as clitoral stimulation does in cows (59); while cervical stimulation tends to hasten the ovulatory LH discharge in this species (59).

The standing heat period in those species where nervous stimulation of the genital tract causes advancement of ovulation, may be defined as a phase in which one or more ripe follicle(s) are waiting for a nervous, coitus-induced LH-discharge. Enough estrogens have been provided to stimulate the central and the peripheral organs involved to attract the male, probably by pheromones, and accept his sexual advances; consummation, during which the penis seems to initiate neural impulses which, in turn, trigger the ovulatory LH-discharge. Species known for their spontaneous ovulation(s) seem to become temporarily, for the good of optimal reproductive effectiveness, induced ovulators. If coitus is missed during the responsive part of the heat period, nothing is lost, since inherent mechanisms for spontaneous ovulation ensure release of the egg cell(s); a step which is obviously essential for maintaining cyclic functions in those species. However, recent observations indicate at least in one poly-ovulatory species, the rat, not all mature follicles capable of releasing ova do so when ovulating spontaneously (94). Coital activity, the maximum of which is known to occur in the rat in close timely proximity to the critical period for (spontaneous) ovulatory release of LH (95), seems to trigger an additional release of LH, resulting in an increased number of ova released from all mature follicles (94). Other species, like the horse, seem to show less or no duality in this respect and may be exclusively spontaneous ovulators.

In a number of spontaneously ovulating species, abbreviation of the standing heat period after vagino-cervical stimulation has been noted (rat: 96; cattle: 97; sheep: 98), as in induced ovulators (cat: 99; ferret: 100), indicating in the former, as it has been shown in the latter, advancement of ovulation. However, recent studies have shown that even in ovariectomized females with estrogen (and progesterone)-induced heat, copulation or mechanical vagino-cervical stimulation by a purely neural mechanism effectively terminate heat behavior (sheep: 101; guinea-pig: 102). For this heat-shortening effect in ewes, coitus does not seem to be essential, since similar effects can be achieved by activities with masculinized ewes (103) or contact with males, without allowing coitus (97). Hastening of ovulation and shortening of the standing heat period might be achieved through the same nervous pathways when copulation takes place, but the latter can be achieved independently through yet unknown mechanisms. Thus, in the proestrous bitch, daily exposure to males for acceptance testing advances the ovulatory LH-peak to coincide with or even to precede the beginning of the acceptance period, while prevention of exposure to males delays the LH-peak for approximately two days behind the (calculated) commencement of acceptance (54).

In spontaneous ovulators, estrogen levels (102), or progesterone output (94, 95, 104), were thought to regulate the ovulatory LH-release

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and the length of the receptive period exclusively; now the overriding effect of neural, olfactory, or even emotional stimuli, has to be acknowledged.

### B. Neurohormonal Connections Between Genital Tract, Hypothalamus, Pituitary, and Ovaries in Animals and Man.

Fig. 1 is a schematic drawing, showing the neuroendocrine systems involved in spontaneous (I) and reflex-induced ovulation (II + I): the so-called hypothalamic-hypophysial-gonadokinetic system (I), and the neurohormonal pathways for coitomorphic stimuli (II). Since all the anatomical and functional prerequisites for reflex ovulation seem to exist in spontaneously ovulating species, it seems a logical step to assume that under certain programmed or unusual conditions, pathways for reflex ovulation are activated and assure conception.

In the spontaneously-ovulating rodents (rats, mice), the stimulus of coitus serves as an inducer for pseudopregnancy, i. e. the LTH-release necessary for progesterone production in the cyclic corpora lutea (86). The same pathways are responsible for oxytocin release.

The importance of the latter system for oxytocin release during parturition has been explored in detail in cattle, sheep, goats (105-106), and man (109), resulting in a change of the concept of the role of oxytocin in induction of parturition. Oxytocin is not initiating but supporting delivery: it is released in substantial amounts not before the forehead of the fetus starts to pass the cervix and to stretch the upper vaginal wall. This "Ferguson-Reflex" is mediated by afferent nervous pathways and results in oxytocin release from the posterior pituitary gland (105-108, 110, 111). It speeds up expulsion of the fetus after its entry into the birth channel, preventing asphyxiation (109, 112).

The "Ferguson-Reflex" is active also in nonpregnant lactating animals; oxytocin release is documented by an immediate let-down of milk (107, 108, 110, 111), which may result from coitus (113-115), from manual or mechanical manipulation of the vaginal tract (116-117), or the uterus (116, 117). Oxytocin discharge is achieved, for example, by blowing air into the vagina: an age-old method used even today by nomadic tribes in Africa to obtain milk let-down in primitive cattle (118). Neurectomy of the pelvic nerves in goats (107, 108) and in guinea-pigs (110, 111) abolishes this reflex entirely.

This oxytocin-releasing reflex is also well recorded in man. Coitus results, via afferent nervous pathways, in oxytocin and probably vasopressin secretion, as indicated by spontaneous milk let-down (93, 108, 110, 111, 119), antidiuresis (93, 119), and increase in mobility of oviduct and uterus (93, 108, 111, 119), the importance of which for sperm transport to the place of fertilization has been stressed (86). This phenomenon has inspired two artists of the Renaissance to remarkable, but quite different demonstrations: Leonardo da Vinci, in his famous sectional sketch depicting a man and a woman copulating, shows a direct connection between uterus and breast thought to transmit directly, increases in intravaginal and intrauterine pressure to the breast, resulting in a spill of milk (119). More artful and revealing is a life-size

painting by Paolo Veronese (1528-88) (Metropolitan Museum, New York), entitled "Venus and Mars United by Love". This title seems inappropriate since no copulation, not even an embrace, is depicted. But both figures are represented with the absent-minded stare of intimate involvement; Venus is spilling milk, while the right hand of Mars, concealed by a piece of clothing, is involved in caressing her vagina, causing clitoral orgasm. It is known that this response (let-down of milk) appears most frequently when there is a noticeable amount of the psychological component of orgasm as opposed to the purely frictional (93). Paolo Veronese might have intentionally depicted this aspect of love.

There is no doubt that nervous pathways exist for the transfer of coitomorphic stimuli in women between the distal part of the genital tract and the hypothalamic-pituitary system, which are activated at any coitus, masturbation, or mechanical stimulation of vagina and cervix.

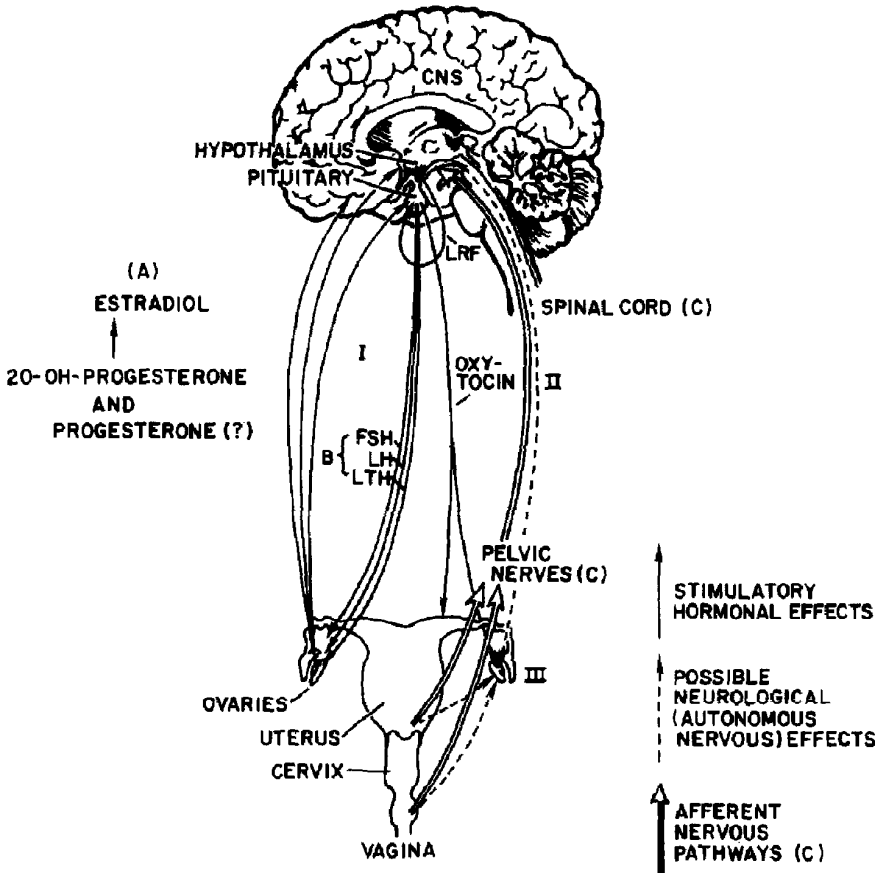
Little is known about the neural pathways in man, but animal data may substitute for defining those involved. The most detailed information has been collected in the rat, using as a model the phenobarbital blocked, cyclic rat, in which only coitus induced the ovulatory LH-surge (88, 120). Pelvic neurectomy blocks the genital stimulus for ovulation (88, 120). Posterior deafferentation of the hypothalamus at the level of the mammillary body did not block the coital stimulus, but anterior deafferentation rostral to the suprachiasmatic nucleus was successful in doing so (120), as well as disruption of the anterior basomedial hypothalamic fibres, at the posterior border of the optic chiasm (121). Electric stimulation of the median eminence in such rats did induce ovulation (120) as in the persistently estrous rat (122). It seems that the coital stimulus must ascend in the brain stem dorsal or lateral to the "half dome" of posterior hypothalamic deafferentation and must eventually reach the preoptic region with its cyclic ovulatory center, which it may activate, or it may descend independently into the median eminence areolate nucleus area (120).

In other species, details about the oxytocin-releasing pathways result from genital tract stimulations. In the ewe, spinoreticulo-hypothalamic fibres (123) transmit vaginal stimulation and cause oxytocin discharge (124) via the anterolateral columns of the spinal cord, through the subthalamus, the mesencephalic reticular formation, and finally the pituitary stalk (123). In the goat and the rabbit, similar pathways in the midbrain seem to involve the lateral tegmentum in association with the spinohypothalamic tract (125). Oxytocin release via these pathways in the goat reaches a maximum with the greatest distension of the vagina (126).

In cattle, artificial insemination techniques caused an oxytocin response at any time of the estrous cycle, with no significant difference between cycle phases (92), with the exception of the early luteal phase (Day 5), when cervical or vaginal stimulations did not elicit any detectable oxytocin release (127). In ewes (128) and goats (129), copulation causes, in addition, an elevation in LTH (prolactin) plasma levels.

The translation of vaginal stimulation into gonadomimetic humoral messages, released from the hypothalamus and/or the posterior pituitary, for the liberation of the gonadotrophins LH and LTH (prolactin), and possibly also FSH, still is not completely understood. Recent reviews

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**FIGURE 1:**

Ovulation-inducing, neurohormonal pathways for spontaneous (I) or coitus-induced (II and III) ovulation in mammalian species.

- I. A = Hormonal (steroids) and neurohormonal (LRF) interactions and stimulations preceding ovulation in normally cycling species with spontaneous ovulations, which result in B = ovulatory LH (and FSH, and possibly also LTH) release.
- II. C = Afferent nervous pathways, activated by coitus, causing B = ovulatory LH (and FSH, and possibly also LTH) and oxytocin release.
- III. Possible direct neurological (autonomous nervous) or biochemical effects which might be activated by or resulting from coitus.



(130-137) emphasize the activation of anterior hypothalamic neurones, some as far caudal as the paraventricular nucleus to vaginal stimuli (138); the stimulating effect of estrogens and the depressing effects of progesterone on the same neurones (139); the nervous sites of specific estrogen and progesterone action (133-137, 140, 141) and the enhancement (estrogen) or reduction (progesterone) of hypothalamic thresholds for ovulation (134, 142).

Increasing attention is paid to biogene amines located in the CNS and their role in translating neural stimulation into hormonal activities, their pharmacology (88, 130, 134, 135, 137, 143-145), and the topography of adrenergic and cholinergic neurones involved (132-134, 137). The variations in plasma monoamine oxydase activity in regularly menstruating women, with low pre-ovulatory and high post-ovulatory activity levels (146, 147), reflect those actions. The role of biogene amines as the actual transmitters of environmental influences on reproduction in man (seasons and menarche [148] and conception [149]) and animals is scarcely unveiled. But their activity might be involved in rather important phenomena, presently only recorded, but not yet understood: the pulsatile patterns of gonadotropin release (150), and the variations in the hypothalamic-pituitary sensitivity to feedback actions of estrogens during early and late positions of the follicular phase of the cycle (151), or the variations in the reactivity of the ovary to LH in the course of the cycle (152).

The modern insight into neurohormonal integration and transmission in the hypothalamic-pituitary complex, for the assurance of spontaneous and/or induced ovulations, corroborates the vision of the great contemporary of Paolo Veronese, Andreas Vesalius, who wrote in 1547: "... the amplitude of the [pituitary] infundibulum collects phlegm from above the corpus calosum and the sulci by its sides" (153).

### C. Direct Nervous, Biochemical and Pharmacological Influences of Ovarian Functions.

Nervous and/or biochemical influences, resulting from coitus, may even more directly affect ovarian functions: by local, sympathetic reflexes (Fig. 1) or by biochemical components of the ejaculate, respectively.

Prerequisites for these effects are the presence of an autonomous nervous system in ovaries and of their most likely target organs (beside blood vessels), smooth muscle fibres and exocrine glands.

In contrast to the voluminous literature on hormonal and central neural regulation of ovarian functions, and on ovarian histology and morphology in relation to follicle growth, atresia or ovulation, corpus luteum growth and regression, information on ovarian innervation and smooth muscle supply is sparse, and nearly all recent competent reviews on ovarian functions are devoid of any information or reflection in this respect.

(a) Extrinsic ovarian innervation, in accordance with the information reviewed by Marshall (154) and Hoftiger (155), originates from three sources: the superior ovarian nerves are descending from the inter-

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mesenteric nerves and the renal plexus along the blood vessels to the ovaries; the middle and the inferior ovarian nerves supply in addition the oviduct. About half of the ovarian nerves are post-ganglionic, while the remainder are preganglionic and synapse in ganglia located in or near ovaries and oviducts. Unlike the uterus and the vagina, the ovary is supplied by the vagus alone and is not connected with the sacral outflow (156).

(b) Intrinsic ovarian innervation is described by thick bundles of preterminal nerve fibres, entering the ovary together with blood vessels in the hilar region (154, 155). Catecholamine-containing nerves are seen in close proximity to blood vessels and stromal fibromuscular layers, forming a dense network which is well developed in cat, human and monkey (157-159), and which agrees well with the amount of norepinephrine detectable in ovaries (158). Acetylcholinesterase-staining nerve fibres were observed evenly distributed around blood vessels and interstitial tissue (157). In man, only less than 25% of all primary follicles show nerve fibres going underneath the follicle epithelium, although in ripening large follicles, many nerve fibres can be seen in theca and membrana propria (83, 84, 160, 161). In early phases of corpora lutea development, traces of this innervation are still recognizable, whereas mature corpora lutea always are devoid of nerve fibres. These observations seem to underline opinions that only innervated follicles may have a chance to ripen and to ovulate (83, 84, 161).

(c) Denervation experiments and ovarian transplants which might shed further light into the importance of nervous influences on ovarian functions, have been restricted mostly to small rodents: bilateral vagotomy (156), or abdominal ovarian denervation (156, 162), resulted in delay of puberty and erratic (162) or violently disturbed (156) cycles. Initially, enlarged corpora lutea are observed (156), which later completely disappear (162). The number of growing follicles (162) with large antra (156) is reduced, and consequently the ovarian weight (162). Unilateral abdominal denervation resulted in unilateral ovarian degeneration (162). Continuous administration of norepinephrine, either by implant into the ovarian bursa, or daily subcutaneous injections, completely reversed these denervation effects (162).

Transplanted ovaries, which may suffer from suboptimal reorganization (163), show corpora lutea atretica resulting from unovulated follicles with trapped egg cells (163), significantly reduced numbers of ovulations (163), or small follicles, together with corpora lutea, and prolonged vaginal estrus periods (164). Transplantation of the ovary to a jugulo-carotid skin loop in the neck of the ewe, together with its local uterine horn as a block of tissue resulted in cycles and estrous periods of normal length (165, 166). Separation of transplanted ovaries from their local uterine horns caused luteal retentions (167, 168). These observations lead to postulations of a luteolysine of uterine origin (169) and to the claim of prostaglandin  $F_{2\alpha}$  being this luteolysine in the ewe (170); an assumption which seems to have no validity in man (171).

(d) Spontaneous ovarian contractions and smooth muscle supply: Human and cat ovaries cultured in vitro display rhythmic contractions (172, 173), as the tunica vaginalis of the testes does in the rabbit rat (174, 175), and in man (176). Ovaries as well as testes have b-

shown to behave as smooth muscle preparations, having  $\alpha$ - and  $\beta$ -receptors and being, therefore, susceptible to autonomous nervous stimuli and to appropriate drug responses (173, 174, 175, 176).

The smooth muscle apparatus in the ovary, as described by many classical authors (155, 177), was until recently by modern research either denied in its existence or neglected (177). Only very recently, smooth muscle tissue was confirmed in ovaries of mice, rabbits and cats (177-181), sheep (182) and man (183). Smooth muscle cells are found in the ovarian stroma (cat: 177-179) and the follicular wall (cat: 180, 181, 183; sheep: 182). Cells surrounding corpora lutea show various changes of degeneration (sheep: 182), paralleling luteal regression. The fibromuscular tissue in the thecal regions (183) near ovarian follicles shows the presence of many nerve fibres (154). Contractions of the rabbit Graafian follicle have been observed in ovarian tissue transplanted to the anterior chamber of the eye (181).

Based on these observations, the following sequence of events is proposed for the mechanical events leading toward and achieving ovulation (172): the assumption is made that mammalian ovaries show spontaneous contractions *in vivo*. Contraction forces may increase the already existing intrafollicular pressure, working in mature follicles against the bulging stigma, its weakest area. There, progressive collagen breakdown decreases tensile strength. If the combined force of intrafollicular pressure and contraction is higher than tensile strength, the stigma is opened, follicular fluid extrudes and the follicular content is expelled (172). This concept, published first in 1865 (184), and already rejected in 1870 (185), was re-introduced in 1943 (186) and 1948 (155), but only now in 1972/73, it is again put forward for consideration (183).

(e) Pharmacological observations: Smooth muscles are classical responding organs to sympathetic nervous stimulation. At the ovarian site, their response to adrenergic stimulation seems to be uninhibited (173). However, contrary to the large body of information on the pharmacological effect of adrenergic, acetylcholinergic, or  $\alpha$ - and  $\beta$ -receptor stimulating or inhibiting drugs in laboratory animals (154) and man (187-189) on myometrial functions in uterus body, horns and tubes, little is known about their effect on ovarian smooth muscle. The  $\alpha$ -blocker dibenzylamine blocked ovulation partially when given in rabbits 7 to 10 hours after HCG, while the  $\beta$ -blocker propranolol was, at the dose levels supplied, inactive (190).

Exocrine glands in the ovary, another classical organ system responding to autonomous nervous regulation, are missing - if one does not want to call ovulation the conversion of an endocrine organ, the follicle, into an exocrine gland of the holocrine type. If one is willing to follow this train of thought, the astonishing information on  $\beta$ -adrenergic control of progesterone production (in bovine corpora lutea incubated *in vitro* [191]) no longer comes as a complete surprise. These data indicate strongly that the bovine corpus luteum synthesizes progesterone only in response to a  $\beta$ -adrenergic-like stimulus (LH; epinephrine; norepinephrine; isoproterenol), which can be inhibited by the  $\beta$ -blocking agent propranolol, but not by the  $\alpha$ -blocking compound phenoxybenzamine (191).

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Reserpin, given systemically at 5 mg/kg in rats, prevents ovulation which cannot be overcome by LH (10 mcg) and therefore seems to act at the ovarian level (192).

Prostaglandins, besides their luteolytic effects, cause *in vivo* contractile responses of human uterus, fallopian tubes and the ovaries as well (193). Site of their action possibly is the fibromuscular tissue of the theca interna.  $\text{PGF}_{2\alpha}$  is superior in this respect to  $\text{PGE}_2$  at the 100 mcg dose levels (193), but 50 mcg  $\text{PGF}_{2\alpha}$  and 50 mcg  $\text{PGE}_2$  combined are again fully active. Prostaglandins are known to be essential in the mechanism by which LH brings about follicle rupture during spontaneous ovulation (194-197); compounds with antiprostaglandin activities, given immediately after the cyclic (or coitus-induced) LH-release, block ovulation (194-197).

(f) Effects of biochemical components of the ejaculate: The decisive role endogenous prostaglandins seem to play in spontaneous ovulation make the possible effects of "exogenous" prostaglandins derived from the ejaculate (200-250 mcg  $\text{PGE}_2$ : 198) after coitus of special interest. Since, in an estrogen-dominated genital tract contraction, waves run from the cervix toward the ovary (199), PG-containing seminal plasma may reach the ovarian surface. Its effect on a ripe follicle, which has not yet received its ovulatory LH push, must remain speculative. Of interest is, in this respect, the observation that  $\text{PGE}_1$  stimulates testicular capsular contractions on the basis of which acetylcholine and serotonin exert increased contractility; both substances are otherwise inactive (200).

But prostaglandins are not the only components causing ovarian contractility. Human seminal plasma renders human ovaries, pulsating *in vitro*, tetanic (172, 201). If the compound(s) involved belong to the newly described group of prostaglandin-free spasmogens, i. e. uterine contractibility-inducing compounds derived from the prostate, this has to be clarified (202). These compounds found in seminal plasma of man, rat and guinea-pig, are supposed to be gangliosides, or prostaglandin carrier molecules (202).

In coitus-induced ovulation, central nervous and/or peripheral autonomic nervous involvement, or directly acting stimuli, may interact in the drive to push suitable ovarian follicles toward maturation and ovulation, or may help to ovulate nearly ripe or ripe follicles as a result of cohabitation.

### D. The Peculiar Follicular Phase in Humans.

Acceptance of reflex (coitus-induced) ovulation in humans renders any rhythm method of fertility control, based on the concept of "fertile" and "infertile" days within a given cycle, unreliable.

This threat requires a critical analysis of the primate menstrual cycle by using today's analytical tools, and a search for indications that may speak for or against the sole occurrence of a spontaneous, more or less precise mid-cycle ovulation.

Purposely, this analysis is not restricted to man, but embraces known data from primates. Since the 1920s, substantial information has

been collected from observation in primates and many details were understood only from studying primate cycles, ovulation, and gestation patterns in depth (72-74, 203-213). The striking similarities between the cycle in primates and man have masked the dissimilarities which, from certain viewpoints, seem to make these comparisons much less reliable or acceptable.

From an evolutionary point of view, man seems to hold the balance between species with an "abnormally" short follicular phase of about 4 days (cattle, sheep, swine: 214, 215), and those with an abnormally long one, up to 24 days in certain primates (203, 209, 210). In this respect, a remarkable observation, which has been hitherto overlooked, deserves strong emphasis: The common denominator of almost all species with a permanent or seasonal heat or menstrual cycle, in which after spontaneous or unsuccessful coitus-induced ovulation, a progesterone-producing corpus luteum is formed, which regresses due to (uterus born?) luteolysine, is a 14 (+ 2)-day corpus luteum period (214-216). Exceptions are dogs (55) and cats (217).

Another common denominator in many cycling animals is the "abnormal" or minimally short follicle phase of approximately four days' duration, for which the 4-day cycles of the small rodents, which is devoid of progesterone-producing corpora lutea and the ensuing endometrial secretory phase, could serve as a model. Its pattern probably results from two components: the follicle-growing phase, which, as it is known from observations in hypophysectomized or prepuberal animals, takes 60 hours from raising unstimulated follicles toward ovulation (218); and the "resetting"-time necessary for the central (151) and peripheral (152) organs in the system to overcome a postovulatory refractoriness in response to stimulations and for the restoration of normal positive and negative feedback actions. These components lend themselves to be formulated to computer simulations, as shown for the rodent cycle (219, 220), the follicular growth pattern in the bovine (221), and the human cycle (222). This 4-day follicle phase might be called the "standard follicular phase", and the 14 (+ 2)-day luteal phase, the "standard luteal phase".

Many species seem to employ for their cycle only the "standard follicular phase" plus the "standard luteal phase": "pseudopregnant" rats and mice; normally cycling cattle, sheep, pigs, goats, guinea-pigs.

The 8-day lasting follicular phase in the horse (223, 224) might be conceived as a "stretched" or doubled "standard follicular phase".

In humans, in an ideal cycle, the follicular phase consists of three (or four) "standard" phases - in which the wave-like growing follicles, due to lacking stimulation (or responsiveness to tonic LH-secretion) seem to become atretic during the first two or three of those phases.

In most monkeys, with a cycle length ranging from more than 28 days to 37 days (Rhesus: mean 28-day [225] cycles, but data indicating variations from 27-day [203] to 39-day [204] cycles; Baboon: 32 to 35 days [226]; Talapoin monkey: 33 days [209]; Ceropithecus mitis: 30 days [227]; Ceropithecus athiops: 33 days [227]; Chimpanzee: 37 days [210]), the follicle phase seems to consist of a multiple of "standard follicular phases", in which rules governing the one in humans seem to

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work even more persistently.

Only in the first 2-6 years post-menarche and in the last years before menopause, man seems to copy this pattern as well as another trait in which mature women and mature female primates differ: the high incidence of anovulatory cycles, seasonal or not, reported so frequently in monkeys (208) is observed only early or late during the reproductive life span in man (228).

The standard 14 (12-16)-day corpus luteum phase is recognized in the widely varying and in rather stable menstrual cycles in women. Modern methods of blood progesterone analysis in this respect only confirm what had been established decades ago with methods such as endometrial biopsy (229), cervical mucus viscosity (Spinnbarkeit) (229), basal temperature (229-231), and pregnanediol excretion studies (228). Much more variable is the follicular phase as indicated by the same methods and confirmed by modern plasma level hormone analysis, in women (231-239) as well as in primates (209, 213, 225).

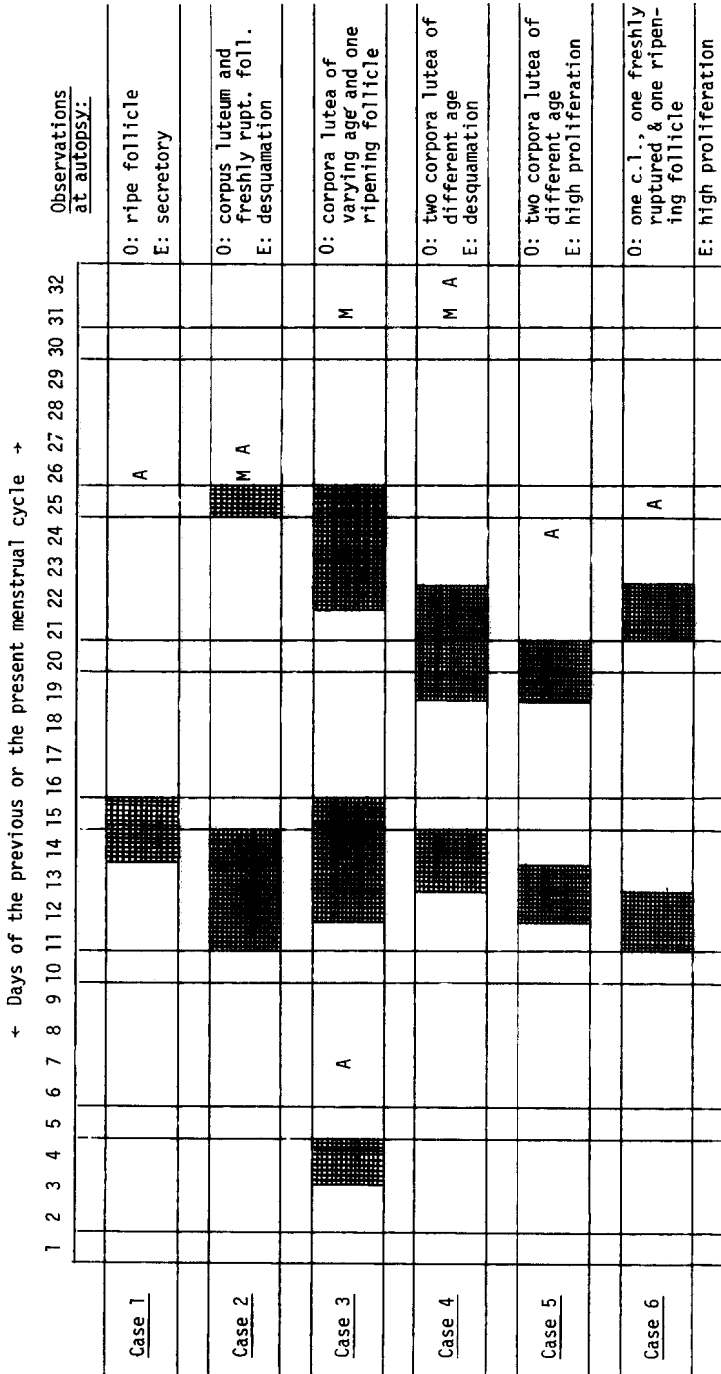
One is tempted to assume that during this curiously enlarged follicle phase, which is initiated in man by a rather sharp postmenstrual FSH (and LH?) increase (232, 233, 236, 240) (an evolutionary reminiscence to the hormonal sequence after progesterone withdrawal with its "standard follicular phase" in other species?) and which is characterized by generally elevated FSH and LH levels (232, 235-237, 241-244), a tendency for induced ovulation or for acceleration of follicle growth exists, similar to the one reported in animals with a much shorter follicular phase, as in cattle, sheep and swine (see also Table 1). Even the most critical observers concede that monkeys can conceive as early as Day 6 after onset of the last menstruation (73), or up to 8 days before mid-cycle (226), and women from Day 8 (latest Day 9) on up to Day 20 (202, 206, 245-247). From a large number of artificial inseminations, it is known that 2% of those women conceived only if inseminated before Day 7 (248). Palpation and direct observation have revealed that, like the rabbit, development of a Graafian follicle from an inconspicuous tertiary follicle to ovulation in monkey and man (207, 211, 212), does not last longer than 20 hours - a time well spent for sperms to capacitate, if necessary, and to accumulate at the oviductal ovulation site, if this growth was coitus-induced or hastened.


Biologically, the stretched out follicle phase in man can be conceived not only as a period necessary to restore an adequate uterine environment post-menstrually, but also to invite coitus-induced stimulation to follicle growth or ovulation. Interestingly enough, "removal of a biopsy specimen (from human ovaries) can affect the duration of the preovulatory but not of the post-ovulatory phase of a cycle" (227).

### E. Paracyclic Ovulations in Women.

Do paracyclic ovulations occur in women independently from coitus, and may conception result from a chance encounter of egg and sperm cells in oviduct? Stieve (84) has presented evidence as shown in Fig. 2, which clearly seems to indicate that paracyclic follicle growth, ovulation, and corpus luteum formation, besides the mid-cycle ovulation, can appear at any time at any regular cycle. Greulich, Morris & Black (230)

FIGURE 2: Paracyclic ovulations in women: From autopsies made immediately post mortem (adapted from 84).



LEGEND:  = Time interval in which ovulations must have occurred.  
 A: day of autopsy (day of death)      0: ovarian status at autopsy  
 M: day menstruation commenced      E: endometrium at autopsy

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TABLE 2: Distribution of Conceptions From Rape; From Short-term Exposure; During Undisturbed Menstrual Cycles (in %).

CONDITION	n	DAYS OF THE MENSTRUAL CYCLE											29-30	REF.									
		1-2	3-4	5-6	7-8	9	10	11	12	13	14	15			16	17	18	19	20	21-22	23-24	25-26	27-28
I. Rape	214	3.3	11.4	13.1	7.5	4.2	7.8	3.7	4.2	5.1	5.6	2.3	4.2	6.1	2.3	2.8	1.9	4.2	2.8	1.9	1.4	-	77
II. Rape	36	2.8	28.0	5.6	5.6	5.6	-	11.1	8.3	8.3	2.8	2.8	5.6	2.8	-	-	-	8.3	5.6	2.8	2.8	5.6	81
III. Rape	79 (89)*	-	3.6 (5.6)	11.4 (20.0)	13.9 (21.1)	12.6 (1.1)	5.1 (-)	3.8 (-)	11.4 (-)	5.1 (1.1)	5.1 (-)	6.3 (-)	7.6 (-)	7.6 (-)	6.3 (-)	1.3 (-)	2.5 (2.2)	2.5 (5.6)	2.5 (13.3)	2.5 (16.7)	2.5 (7.8)	-	80
IV. Rape	214	0.9	0.9	5.6	13.1	5.6	2.8	6.5	5.1	7.0	4.7	5.1	6.5	4.7	4.7	4.2	4.7	2.8	5.1	4.7	2.8	1.4	82
V. Rape	108	11.1	33.4	31.5	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	251
Rape Cases I-IV	543	1.8	7.2	9.3	10.3	4.2	6.1	4.8	4.8	7.2	4.9	3.8	5.7	5.5	3.7	2.9	2.6	3.7	4.4	2.7	1.8	1.0	288
Conceptions during short leaves of absence W. War I	838	43.9	26.2	23.1	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	253
Conceptions during short leaves of absence W. War II	100	3.0	20.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	252
Conception Risks in % **	393	17.7	29.9	23.7	33.0	32.6	40.8	28.3	26.5	10.5	4.8	2.5	3.1	2.8	2.0	4.7	1.9						

Legend:  
 n = Total number of conceptions  
 \* = Cases in which rape but not conception occurred  
 \*\* = Risk of conception on different days of the menstrual cycle, calculated from 1898 cycles: % = cycles with conception from coitus at this day, of all cycles with coitus recorded for this day (Adapted from 255).



have reported another clear case of an ovulation on Day 6 in an otherwise normally cycling, institutionalized virgin with no copulatory experience; from surgical observations by Sevitt (249), ovulation can occur on any day of the first half of the cycle.

Recent gonadotrophin release studies, although limited to a rather small sample of the female population, are not devoid of evidence of ovulatory LH-release-like LH-peaks at unusual timings (240, 250). In one case, a spontaneous double surge of LH-FSH was observed three days after the mid-cycle LH-FSH peak. As judged by the fast increase in plasma progesterone levels, this mid-cycle peak was an ovulatory one (250). At the day of the second gonadotrophin peak, progesterone levels had reached the 10 ng/ml mark, defying Speroff's and Vande Wiele's assumption (on which their computer model [= engineering analysis] of the human menstrual cycle is resting) that any plasma LH surge is inhibited by progesterone plasma levels larger than 1 ng/ml (222).

#### F. Coitus-induced Ovulation (Conceptions) in Women.

(a) Conceptions resulting from rape: In the years after World War II, a number of German gynecologists (77, 80-82, 251) recorded a total of 720 rape cases, out of more than 1700 cases they were exposed to between 1945 and 1947. Only those patients were selected from whom reliable information could be obtained about the menstrual cycle, its pattern, the last menstruation prior to the rape itself, as well as assurance that no other cohabitations took place. This, in many cases, had to satisfy the courts for the granting of abortions. The distribution on the coitus-induced pregnancies in relation to the day of the menstrual cycle on which rape was committed for 543 out of 720 cases, is shown in Table 2. According to the author's calculations, between 32.5% and 45.9% of all conceptions took place during the "safe" period after menstruation, between 10% and 29.7% during the "safe period" before menstruation, and 44 cases (8.1%) during menstruation (77, 81-82, 192). As a control, Linzenmeier (80) gives the number of rape cases during the same periods that did not result in pregnancies (Table 2). Schrank & Koch (82) report that 64.1% of all the 732 women violated became pregnant from rape. Seven amenorrhoeic women, who conceived as a result of rape and its emotional turbulence, had previously experienced no menstruations for 1, 6, 18, 20, 2 x 24 and 25 months (77). The rather equal distribution of conceptions observed by Ibrdgger (77) during the first 18 days of the cycle seems important (Table 2). The 543 cases shown in Table 2 confirm a fertility elevation during most of the first half of the cycle and not just a midcycle fertility peak, which obviously was not prominent during the prevailing condition.

(b) Conceptions resulting from limited exposure: Information on conceptions resulting from limited exposure bear similar risks as those collected from rape cases: reliability of the patient's claims that no other exposures have been experienced, and dependency on the physicians' or researchers' critical capabilities to report only on cases in which he is sufficiently satisfied that the patient's claims can be accepted and confirmed, if possible, by clinical evidence (for example calcula-

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tions based on the duration of the gestation period). The tendency to discriminate against the patients' claims has prevented critical appraisal of probably useful evidence. In the light of female emancipation, the wholesale disqualification of the patients' reports as exercised in the past (206) seems unjustified.

Two sources for information on conceptions from limited exposure exist: Data from World War I and World War II, when German soldiers, transferred from one war theater to the other, always had to cross their country and were customarily granted a 24 to 48-hour "leave of absence" to visit their families. Conceptions resulting from these "conjugal" visits are shown in Table 2. Koller (252), in evaluating 100 carefully selected cases from World War II, calculated conception risks during the first and the last 4-day period of the cycle still as high as 5 to 10% of the risk of conceiving during the mid-cycle period.

In 241 married British women, participating in a field trial investigating the basal-body-temperature method of birth regulation (254), the risk of conception on different days of the menstrual cycle, in a total of 1,898 cycles, was calculated (255). The data are shown in the bottom line of Table 2. Quite striking is the high risk of conceptions (ratio of conception cycles to all cycles, resulting from recorded coitus on given days of the cycle) during the follicular phase, versus the very low risk after mid-cycle. Interestingly enough, a first maximum is seen on Days 7-8 (end of the second "standard follicular phase"?), which is only approximately 27% below the maximum risk on Day 12 (third "standard follicular phase"?); although markedly reduced, the chance to conceive during the corpus luteum phase nevertheless seems to exist.

(c) Conceptions during amenorrhoea: Seven cases of conceptions resulting from rape during amenorrhoea have been quoted earlier (77). Five more cases of conceptions reported during amenorrhoea were found when screening for literature on psychological influences on reproductive functions in women (256-258). It seems that gynecologists harbour a treasure of information, which they in distrust to the patients' credibility, or in forestalment of the ridiculing by medical circles, either try to dispose or do not want to share.

Of the many case reports received in personal discussion, one outstanding but illuminating case deserves mentioning: An 18-year old girl, well protected by her family, engaged and due to be married, is seen by the gynecologist with the report of having never commenced to menstruate. Investigations confirm an intact hymenal membrane, small, but normally built genitalia and ovaries, a normal female phenotype, and a female karyotype. Slightly less than 10 months after consummation, and without menstruating before conception, a child was born and nursed subsequently. Within 3 months, without commencement of the cycle, the young woman conceived again. This pattern was repeated throughout a total of five subsequent gestations in a little more than six years. Voluntary abstinence after the fifth gestation triggered the first menstrual bleeding 6 months post partum, and a normal cycle developed (259).

(d) Malformations related to conceptions outside the safe period. Another indicator for either coitus-induced paracyclic ovulation or the chance fertilization of egg cells ovulated spontaneously at any time dur-

ing the "safe" period is the high incidence of anencephalus and spina bifida reported in Orthodox Catholic circles (257, 258) and the prevention of it in a number of cases by restricting intercourse to the mid-cycle period only (75, 76). It is reasonable to assume that the "rhythm method" of family planning, which is common in all Catholic countries, could be accounted for the high incidence of anencephaly and foetal abnormalities in Catholic populations (75, 76, 78, 260); especially, if one considers that not 80%, as determined by widely used calculation methods, but only 30% of all cycling women really qualify as candidates for the rhythm method (261). In discussing the possible causes for malformation, overripeness of the ovum is blamed. Two mechanisms of action are put forward: "Postovulatory" overripeness is thought to result from spontaneous ovulation at mid-cycle, but a delayed conception from intercourse at the first safe day (260) since the egg cell remains fertilizable far longer than it retains its capacity to give rise to a normal embryo (262); or "preovulatory" ripeness in which the ovum is retained in the follicle beyond the normal time (247, 260). As a result of the missing copulatory stimulants? As Hertig (247) puts it: "... if an oocyte lingers longer than Day 14 in the follicle, it has an increasing chance of becoming a 'bad egg' when fertilized". He links preovulatory overripeness convincingly with abnormal embryonic development (247). Postovulatory overripeness, if it is a reality, takes place in an internal milieu known (from studies in pigs [264]) to cause polyspermic fertilization, since progesterone effects during the corpus luteum phase inhibit polyspermy preventing mechanisms (265). Trisomie, monosomie or sporadic occurrence of mosaic aneuploidies are thought to result from aging of egg cells between ovulation and fertilization (262, 263).

(e) Duration of pregnancy as evidence for other than mid-cycle conceptions. Any student of the duration of human gestation length is impressed by the high variability reported, which only expresses the influence of overlooked biological facts, such as conceptions after abortions and pregnancies, with no menstruation having intervened (266-268). Information on conceptions even before menarche has long and unduly been discounted (269, 270). Probably many gynecologists have seen multipara who have never menstruated before or between their pregnancies (83, 84, 260, 268).

For the forensic definition of gestation length, the last menstrual period (LMP) as well as isolated coitus can be used as a starting point. Treloar et al. (267) does not follow the common attitude of relying entirely on LMP and disqualifying isolated coitus. After careful evaluation, he allows for two studies on isolated coitus to represent valid information, spreading successful conceptions from coitus on Day 1 to Day 34 after LMP, with 2/3 of 167 cases having conceived in the first two weeks after LMP (267).

Indirect evidence for exogenous factors influencing conception in man, possibly by disposing the female organism in a more receptive mood for induced ovulation, comes from the birth rate maximum 268 days after Pearl Harbor (271) and the significant minimum 269 and 270 days later (a depletion of fertile ova?); from the significant birth peak 270 days after the blackouts in New York (272) and Göteborg (273), and the rather amazing fact that in the United States a weekly parturition maxi-

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mum on Wednesdays and a minimum on Sundays exists (30% difference) which makes the assumption of fertilization occurring on weekends in a Christian country a reasonable one (271). On the other hand, if one takes the well documented figure of a gestation length of 278.64 to 279.89 (calculated from LMP) (274) as a standard, then the pregnancies related to events like Pearl Harbor and the blackouts seem to have commenced rather early in the follicular phase.

### G. Psychology and Reproduction in Women.

Female animals are, during proestrus, estrus or early pregnancy, subject to sensuous influences which may hasten ovulatory LH-release and/or ovulation (see Table 1), or may terminate the standing heat period (96-100, 102-103, 275), or may even terminate gestations (240-242). These influences may result from copulatory behavior (Table 1), even if it is only mimicked without coitus (54, 102), or solely from the exposure to olfactory signals (275-277). However, environmental influences completely unrelated to the reproductive sphere, but with marked impact on the animal's well-being and social status, can also imprint severe reproductive functions, as shown by the massive follicular development seen in prepuberal cattle (278), gilts (279), and anestrus ewes (280) as a result of transport or social stress situations (transfer into a new environment). This stress-related response resembles the follicle growth (and subsequent ovulation) seen after electrical stimulation of the genital tract in anestrus cows (281). Excitement and anxieties play an important role in triggering a spectrum of physiological responses, one sector of which seems to interfere with reproductive processes, stimulating, inducing or abolishing conditions for ovulation, conception and nidation.

Similar responses are seen in the human female under pressure, under the stress of a threatening physical, psychic or socially depressing environment. Subtle interrelations with purely sensuous influences may exist, which might be difficult to separate from psychological or physical effects.

The clinical conditions best known as resulting from these influences are functional amenorrhea (282) and pseudocyesis (283, 284). Psychogenic amenorrhea has been classified (285) into:

1. Major psychiatric disorders
2. Anorexia Nervosa
3. Pseudocyesis
4. Simple anxieties or stress -
  - (a) due to external catastrophe
  - (b) due to separation
  - (c) due to fear of becoming pregnant.

World War II, world-wide, and for some countries the immediate period thereafter, due to occupations, refugees, displaced persons, service in the armed forces, concentration or labor camps, provided a huge laboratory for the study of wide-spread epidemic amenorrhea due to external catastrophe and separation (256-258, 285-291). Initially, hun-

ger was thought to play an important role, but its importance has been downgraded or rejected in retrospect (289, 291).

Drew (291), in her review on the epidemiology of secondary (psychogenic) amenorrhea, shows an impressive correlation between external influences and the extent of amenorrhea in a given population. The scale ranges from below 5% in college students and waves to 50-70% in German and Japanese concentration camps, and 100% in condemned prisoners before execution (84). Of revealing consequence is the observation that of all the groups that comprised Dutch East Indies prisoners in Japanese concentration camps, the nuns were the only group that did not become amenorrheic (292). Of interest is the observation that of those rape cases causing amenorrhea (293), those experienced during the follicle phase were of longer lasting consequence than those violations suffered during the second half of the cycle, in which recovery (toward a normal cycle) was seen faster (293).

The World War II experience has aroused interest in the remaining category of cases, mostly belonging in the group of patients with anxieties or stress, due to the conscious (or even subconscious) fear of becoming pregnant (296-301). Two striking factors have been reported from those patients: Hormone resistance (294, 295), even to dose levels several times those effective in post climacteric women (295), resulting in the inability to cause menstruation, for which excessively rapid metabolic destruction of administered steroids or metabolic abnormalities were discussed (294); and extremely fast return to bleeding (and to a regular bleeding pattern) sometimes within hours (299) when the cause, for example the anxiety about being pregnant, is authoritatively resolved (296, 297, 299). This rapidity of response seem to support contentions that an autonomic nervous influence persists throughout the course of amenorrhea (302). It seems not unlikely that the same influence may render the genital tract tissues temporarily unresponsive to endogenous or exogenous steroids.

Pseudocyesis, known since the times of Hippocrates, has been reported as frequently as one case per 250 pregnancies (283). Its recurrent appearance in the same patient made its imprint in the world's history (the case of Mary Tudor: 284). Its name in French (*grosesse nerveux*) reveals the early insight into its psychosomatic origin.

Emotions are, as it has been shown, not without consequences on reproduction. In the case of psychogenic amenorrhea, this interrelationship and the nervous dominance over endocrine regulations is accepted.

The psychosomatic effects of emotions may not necessarily be restricted to the grave consequences quoted. Emotions may well play a role in facilitating or even predisposing to what is called coitus-induced ovulation. The possibility cannot be discounted that the rhythm method, with its emotional problems and its periods of voluntary abstinence, conditions for coitus-induced ovulations. This is supported by the high coital rates observed (in general) after periods of abstinence (which most couples seem to exercise during all or part of the menstrual bleeding period: 303). Stockpiled with emotions, a similar conditioning situation may prevail for unprotected first exposures in teenagers (79, 205) and premenarchal conceptions (304), the first extramarital in-

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tercourse, and probably for any cohabitation surrounded by excitement (207). This might have been a strong supportive force in facilitating conceptions resulting from rape, and limited exposures during the safe periods, as shown in Table 2. Another facilitating factor for other than mid-cycle conceptions during and after the two world wars might have been progesterone deficiencies during the luteal phase due to lack of protein in the diet. In monkeys kept temporarily on a protein-deficient diet, low progesterone production levels were observed (305). A similar situation in humans might allow nervous stimuli to override endocrine regulation.

Emotions surrounding cohabitation might play a role equal to the direct effect of coitus in inducing ovulations in situations where cycles supposedly are anovulatory: at menarche and menopause (306); it also may explain the increasing incidence of adolescent pregnancies (306, 307), and the stimulation of some of the remaining follicles in the ovary of early post-climacteric women (306). These emotions may even play a role in one of the oddities found when environmental influences on human fertility were studied: the "infamous" Christmas conception peak observed in Europe (308-311) may result from a release of tension, "...a more carefree attitude when people are in a festive mood" (309).

### H. Conclusions.

Martin (312), in a sweeping survey of the possible course of evolution of reproduction toward man indicates that primates have retained many ancestral features that were hitherto frequently regarded as "specializations" and that all living primates can be traced to a common stock characterized by a number of synapomorph characters. Maintenance of reproductive efficiency by more than one mechanism for triggering ovulation seems to be of evolutionary importance, and to be an advantage for the survival of the species. We have not - beyond situations such as rape, periods of enforced sexual abstinence and high public excitement - learned to understand which exogenous factors may activate endogenous neuroendocrine pathways that exist but are not normally or routinely employed for ovulation. The possibility of coitus-induced ovulation in man should no longer be denied, just because acceptance of its existence causes uncomfortable and far-reaching consequences. The case made and the facts presented indicate its existence. It makes one very skeptical that the cry for more rhythm research (313), and the attempts to perfect the rhythm method by environmental (314) or hormonal means (315), or by detecting biochemical changes accompanying ovulation (in advance: 316, 318) will ever lead to success. The remarkable traits observed during a careful study on the psychology of the misuse and rejection of contraception (317) make the need for simple, but "totally protecting" contraceptive methods evident. The remarkable success of "totally protective" anticonceptive means or methods, like the anticonceptive pill or the IUDs, can easily be explained by preventing conceptions from ovulations at any time. It should not be too difficult with the modern biochemical, statistical and demographic tools to establish existence, frequency and sociological importance of coitus-induced ovulation in man. However, this task needs abandoning of concepts which are more than often not scientifically, but either socially or ethically motivated (206, 207, 319).

Research into many details is required, without forgetting about the psychosomatic entity in man.

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