increase towards term. No significant dif-
ference was seen in early pregnancy in one
anencephalic pregnancy studied.

The similar pattern of excretion of these
compounds in the Vervet monkey and man sug-
gests they may have an important physiologi-
cal role in the luteal phase of the menstrual
cycle and in early pregnancy.

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24. Mechanism of ovulation, H.R. LINDNER,
    Weizman Institute of Science, Rehovot,
    Israel

25. Induction of ovulation in chronic anovu-
    latory syndrome through a weak estrogen
    supplementation, P. KICOVIC[1], C. MASSA-
    FRA[2], G. D'AMBROGIO[2] and A.R. GENAZZANI[2],
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The chronic anovulatory syndrome mainly asso-
ciated with oligomenorrhoea is characterised
by estradiol (E2) values which vary very lit-
tle during the cycle, insufficiently to acti-
vate the positive feedback on gonadotropin
secretion but sufficiently to induce enough
modification of the endometrium for menstrual
bleeding.

9 subjects with the chronic anovulatory
syndrome as the primary cause of sterility
and/or oligomenorrhoea, were studied in de-
tail during a control cycle to define their
respective endocrine features. Two subjects
had moderately elevated basal LH levels while
the levels for others were normal. FSH was
normal in all cases. Non-chromatographed E2
was in the normal range (120-220 pg/ml) in
the follicular phase in 3 subjects while in
all the others it ranged from 70-150 pg/ml,
values significantly lower than expected but
lacking cyclic variation. All subjects were
given Epimestrol (3-methyl-ether-17-epi-
estriol) at a dose of 5 mg twice a day for 10
days, which induced ovulation and an adequate
luteal phase in 7 subjects, 3 of whom became
pregnant in the first cycle of treatment (2
did not desire pregnancy). In the 2 subjects

who failed to get an adequate luteal phase,
the treatment was changed to 5 mg x 3/day for
10 days in 2 cycles. One responded with a
short luteal phase and the other with an an-
ovulatory cycle. Treatment was then modified
to 5 mg x 4/day for 10 days in the first sub-
ject, who responded with an adequate luteal
phase and became pregnant; and 5 mg x 3/day
for 15 days in the second subject who re-
sponded with an adequate luteal phase for 3
cycles.

The hormonal pattern in all subjects indi-
cated that the LH ovulatory peak was always
related to the occurrence of an E2 peak indi-
cating follicular maturation. The LH peak
occurred either before, at or after the end
of treatment, but always related to the en-
dogenous E2 pattern. The day to day measure-
ment of FSH and LH during follicular matura-
tion in most cases failed to indicate in-
creased basal levels relative to the control
cycle, which suggests that Epimestrol, be-
sides having a positive effect on the intra-
pituitary synthesis and storage of gonado-
tropins, probably also potentiates the effect
of endogenous gonadotropins on the granulosa
cells, thus stimulating follicular growth and
maturation as found by the present results.

This study was partially supported by the
CNR project "Biology of Reproduction".

26. Oxytocin: a new effect, ovulation induc-
    tion, N.A. AL-HUSSARY and A.S. AL-JANABI,
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The role of oxytocin in controlling ovarian
function is still not clear. In the present
investigation the effect of injecting oxy-
tocin (Syntocinon®, Sandoz) intraperitoneally
on ovarian growth and ovulation was studied.
106 immature female Swiss mice were used.
They were injected with one of the following
doses of oxytocin: 10, 25, 50 and 75 mU,
given either on day 28 or 30 or 32 of age
repeated on the same day 3 h later and ani-
mals were sacrificed 48 h after the first in-
jection. Some of the animals injected with
50 mU oxytocin on 30 days of age were given
concomitantly a single dose of aspirin (200
mg/kg body weight). Another group underwent
hysterectomy on day 28 and was sacrificed 48
h later, while others were given a single
dose of Prostaglandin F2α (3 mg/kg) on day 30
and sacrificed 48 h later. The combined
ovarian weight (COW) of the animals injected
with 50 mU on day 28, 30 and 32 or 10, 25 and
75 mU on day 30 showed a significant increase
over the control (P < 0.001 and P < 0.005).
A significant decrease was seen in animals
who received aspirin on day 30 and in hyster-
ectomized animals both treated or untreated
with oxytocin in comparison with the intact
control. A significant increase in COW was
seen in animals injected with PGF2α. Ovula-
tion occurred in all groups treated with oxy-
tocin (25, 50 and 75) mU with highest rate
(80%) in animals receiving 50 mU. These re-
sults were confirmed histologically. These
results indicate that the ovarian effect of

oxytocin may be mediated through the release of uterine PGF2α.

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27. Disturbances of menstrual cycle ,
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The regulation of the menstrual cycle and ovulation is the result of the balanced and coordinated effects of the hypothalamic gonadotrophin releasing hormone (GnRH), the pituitary gonadotrophins, and ovarian response.

The GnRH, secreted by the hypothalamus in a specific quantity must impinge upon a responsive pituitary. The information carried by the releasing hormone must be received and interpreted by the target cell of the pituitary, and these cells, in turn, must be capable of synthesizing and releasing gonadotrophins in adequate quantities and with a specific rhythm. The gonadotrophic hormones then act on the ovary and stimulate three balanced and appropriately coordinated processes, namely, growth of the follicle, differentiation of the follicular cells, and steroid production. The steroidogenic function of the ovary resulting in the release of appropriate steroids at the proper time and in the correct amount constitutes a multipurpose system. It acts as a messenger system in the feedback mechanism which regulates the secretion of the gonadotrophins and it modulates follicular responsiveness to gonadotrophins, exerts specific action upon the various functional compartments of the ovary, including the vascular apparatus; it stimulates changes in the genital organs in preparation for the transport of the ovum and the sperm cells, and prepares the endometrium for implantation of fertilized eggs.

Any interruption of the complex feedback system regulating the function of the hypothalamic-pituitary-ovarian axis may lead to anovulation.

Roughly one-third of the infertile population seeking advice at sterility clinics present with cycle disturbances and/or ovulation failure.

Anovulation may be accompanied by a variety of menstrual disorders, the nature of which is directly related to the level and type of fluctuation of the ovarian steroids, or interfering hormones, metabolites or other substances.

We will not consider in depth in this paper studies oriented to assessing the diagnosis and treatment of systemic diseases (e.g., cirrhoses, hematochromatosis, sickle cell anemia, renal failure) or endocrinopathies associated with cycle disturbances, but not directly related to the hypothalamic-pituitary-gonadal-axis (adrenal, thyroid, diabetes).

Rather, we will focus on the endocrine pathology resulting in anovulation, cycle disturbances and the so called "luteal insufficiency" which may benefit from treatment with gonad-regulating agents.

Such patients may be classified into distinct groups depending on the aetiological origin of the disturbance.

a. Hypothalamic-pituitary failure. Amenorrheic women with little or no evidence of ovarian oestrogen production, non-elevated prolactin levels, low or non-measurable gonadotrophin levels, and no detectable space-occupying lesion in the hypothalamic-pituitary region.

b. Hypothalamic-pituitary dysfunction. Women with a variety menstrual cycle disturbance (luteal phase insufficiency, anovulatory cycle or amenorrhea) with distinct evidence of ovarian oestrogen production and with non-elevated prolactin or gonadotrophin levels.

c. Hyperprolactinaemic patients with a space-occupying lesion in the hypothalamic-pituitary region. Women with a variety menstrual cycle disturbances (luteal phase insufficiency, anovulatory cycles or amenorrhea) with elevated prolactin levels and evidence of a space-occupying lesion in the hypothalamic-pituitary region.

d. Hyperprolactinaemic patients with no detectable space-occupying lesion in the hypothalamic-pituitary region. Women with a variety of menstrual cycle disturbances (luteal phase insufficiency, anovulatory cycles or amenorrhea) with distinct evidence of ovarian steroid production and with elevated prolactin levels.

A number of effective drugs and hormones are available for regulating ovarian function in such patients. These can be classified into three groups: 1. Human gonadotrophins; 2. Clorotrianisene analogues; and 3. Ergoline derivatives. Each group of these agents acts through a different mechanism. Gonadotrophins stimulate the ovary directly, chlorotrianisene analogues stimulate the hypothalamic-pituitary system, and ergoline derivatives inhibit excessive prolactin secretion which interferes with the normal reproductive function.

Each of these agents may be used at various dosage levels and in different treatment schemes sometimes in combination, or in conjunction with oestrogens or anti-gonadotrophins, and all of them carry risks of various, sometimes severe, complications.

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28. Effect of epimestrol treatment on endocrine and clinical features of short and inadequate luteal phase, A.R. GENAZZANI[1], G. D'AMBROGIO[1], C. MASSAFRA[1] and P. KICOVIC[2], [1]Department of Obstetrics and Gynaecology, University of Siena, Via P. Mascagni 46, 53100 Siena, Italy, and [2]Reproductive Medicine Programme, Medical Unit, Organon, Oss, Holland

A short luteal phase is characterised by an adequate rise of plasma progesterone levels after the mid-cycle LH ovulatory peak which rapidly decline after a few days to follicular phase levels. In an inadequate luteal phase, progesterone plasma levels after ovulation show only a small rise, reaching levels which are normally less than half those expected. The aetiopathogenesis of these conditions has until now been poorly under-