Sheets Physiology

Number	17
Doctor	Mohammad
Done By	Rawan Mohammed
Correction	Rama Al-Ashqar

In this sheet, we are talking about two extremes related to the ability to reproduce. These are: when it starts (at Puberty) and when it ends (at Menopause/Andropause).

Puberty

-The transition from quiescent reproductive endocrine system (inability to reproduce) to state of reproductive function (ability to reproduce).

-The ability to reproduce means: the ability to form germ cells in the male and the female, the ability to **nurse** the zygote formed after fertilization, and the ability to **form nutritional** material after delivery.

-Begins with pulsatile GnRH/LH secretion during REM sleep.

-Range of onset: 9-14 years.

-Completion of pubertal development: 2-4.5 years.

-In males: certain biochemical and physical factors and signs will appear.

1) Biochemical signs: spikes of LH and FSH , a continuous increase in testosterone, night emission and spermatogenesis (the production of sperms) also starts at puberty.

2)Physical signs: the first sign is the enlargement of testis, due to increase in size of seminiferous tubules and Leydig cells. Other secondary sex characteristics will develop due to androgens secreted from the testis (the driving force), adrenal testosterone also plays a role.

-In females: the first sign is breast development, but the landmark sign is Menarche which is the first menstrual cycle (menstruation is a reflection of previous physiological parameters). So, menstruation means that we had previous follicular development followed by associated hormonal development reflected on the endometrium causing the menstruation (Menarche).

Menarche has been occurring earlier in the past few decades in US, Europe.(distance from equator, higher altitudes.)

-What determines age at puberty?

Genetics is the most important factor but there are other factors: psychology, nutrition, geographic location, exposure to light, body composition, fat deposition and exercise.

Menopause- Andropause

-The cessation of the ability to reproduce (cessation of menstrual cycle and androgenic function so, no more shedding of the endometrium) by obsolescence (state of no longer being used) of ovaries, no estradiol production, no ova, only occasional secondary follicles, few primary follicles.

-Occurs in females, but **not in males.**

In males, there is no reduction or loss in the ability to reproduce. They don't have an absolute Andropause, they can still form spermatozoa and produce testosterone. But in literature, other physiological parameters that occur with aging play a role in the production of testosterone and spermatozoa (not directly) some are: cardiovascular, respiratory, joint, vascular, blood vessel variables , clotting, closure and atherosclerosis.

Some say that we should increase the level of androgen but in fact we already have enough amounts to maintain normal function so we don't need more. (fig1) The body always has a great reserve of hormones of all kinds, but only small amounts are needed to bind to receptors, when these receptors are saturated, any excess hormones won't function.

-Occurs at 50 years of age on average.

-Can occur naturally (normal physiological pattern), due to surgery (no ovaries, no follicles) or as a result of chemotherapy.

-Ovarian aging can be: physiologic or premature.

Premature Ovarian Failure: is the loss of ovarian function and menstrual cycle at a young age(below 40), could be due to neurological or chemical reasons, or from chemotherapy. Studies found that the absence of a certain tumor suppressor gene in rats results in recruitment of all follicles (so; no remaining follicles) and the ovary becomes exhausted and fails to function.

-Recalling the sequence that occurs in females:

During intrauterine life and after delivery, we have a lot of follicles in the ovaries, they start to decrease in number with aging and so, the probability of recruitment will decrease and eventually become close to zero. Also, with aging, the function of the follicles will decrease and they will become abnormal follicles (non-responsive follicles) which can't be recruited by LH/FSH. These abnormal poor follicles secrete less amount of estrogen during proliferative phase compared to the normal follicles.

Of course, we would see some **abnormal follicles even before menopause** because this process does not happen at once but happens **gradually**. This means females start to lose the ability to reproduce gradually even before menopause (cessation of menses) because they are having worse and worse types of follicles as they age and eventually fertility declines. (fig2, fig3)

-No recruitment means there is no oocyte, so **no fertility**.

no recruitment ---> no ovulation----> infertility and no secretory phase ----> no progesterone

-The prolongation of menstrual cycle before menopause is due to decrease in progesterone levels. Less menstrual cycles (They become less frequent, and instead of occurring every month, they will occur maybe every 6, 8, 10... weeks and so on)

-Low levels of inhibin, less steroids (estrogen and progesterone), **more gonadotropins (LH/FSH).**

Low hormonal levels of estrogen and progesterone means no negative feedback of LH and FSH, so, high levels of LH and FSH, the curve would show a continuous rise with no peaks. (LH/FSH high levels theoretically mean recruitment of follicles, but then again, the follicles are non-responsive).

- Less **AMH** (Anti-Mullerian Hormone) which is a marker for follicular development and is **only secreted by small-to-medium size follicles**, these follicles start to decrease with age due to less steroids, so less AMH. (fig4)

less steroid hormones----> less follicular development

Fertility period during life span:-

- At puberty: the first menstrual cycles are anovulatory, so the fertility is low.
- After complete puberty: we have normal fertility (fertility period of the female has a certain time during the month).
- At a certain age close to menopause >35yrs: fertility starts to decline as the pool of normal follicles start to decline, too.
- At menopause >50yrs: infertility (0)

For example, at 20-25 years old maybe the probability of pregnancy is 40% but at a group age of 45-50 years old the probability would be 2% and for more than 50 years old the probability would be zero.

fig1

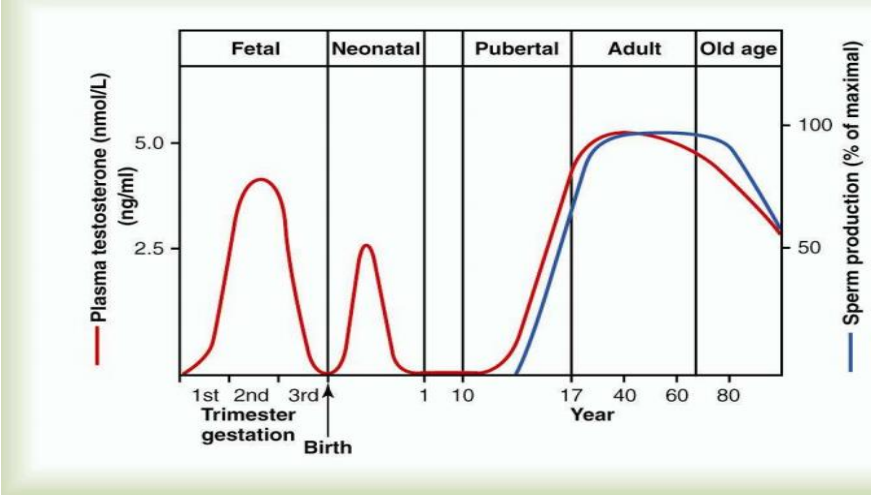
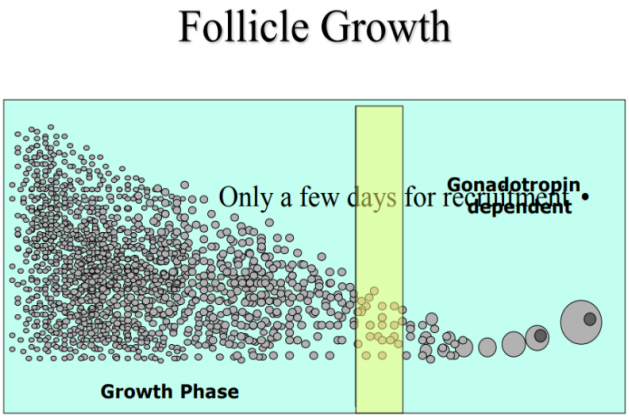
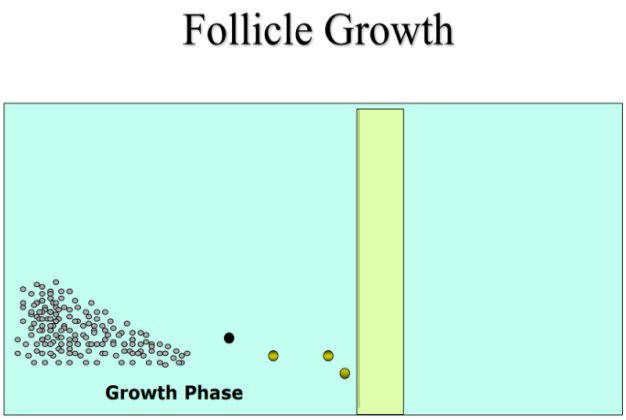


Figure 80-9; Guyton & Hall

fig2, fig3





AMH

Termellen KP et al: Australian NZ J Obstet Gynecol 2005; 45:20-24

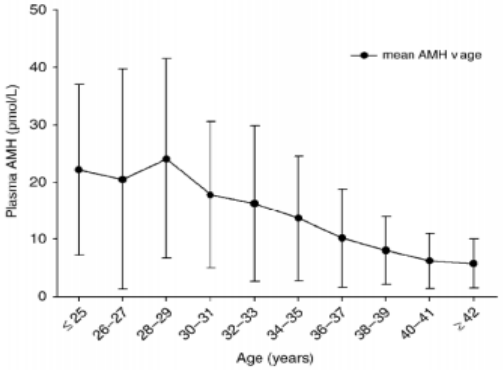
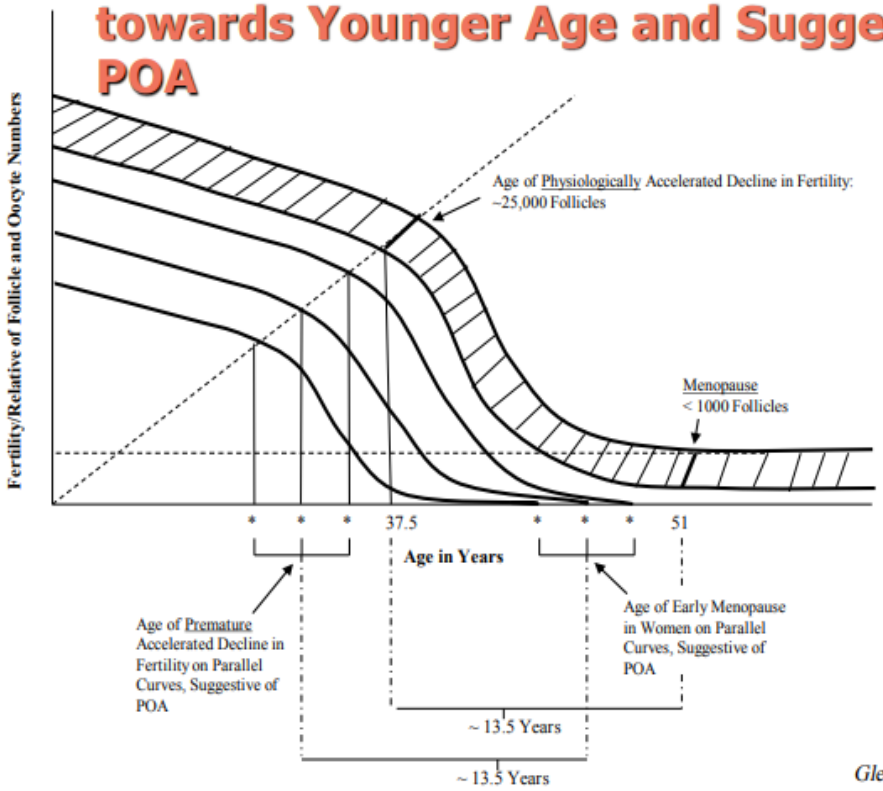


Figure 1 Early follicular phase (day 3–5) anti-müllerian hormone (AMH) over the reproductive age range. Mean ± standard deviation plotted.

AMH decreases with age

Physiological Age-Related Fertility Curve (Range) and Parallel Curves Shifted towards Younger Age and Suggestive of POA



Gleicher N. Contemp Ob/gyn 2004