CHAPTER - VI

REPRODUCTIVE PERFORMANCES IN FEMALE INFERTILITY
PART - A

PRIMARY AND SECONDARY INFERTILITY
Abortion denotes the termination of a pregnancy before the twenty-eighth week, that is, before the foetus is viable, according to English law. After this time the process is labour. The term abortion is also sometimes loosely applied to the products of conception which are passed; strictly, these are the abortus or conceptus. Miscarriage is a synonymous term which is preferred in case of deliberate termination of pregnancy.

There are many possible causes for abortion and more than one may operate at a time. In early weeks, mortality or disease of the foetus, often proceeds the expulsive action of the uterus. The most frequent single cause for abortion is malformation of the foetus and its membranes, it accounts for 50-60 per cent of early, 6-8 weeks abortions.

It is very important to distinguish between true infertility, unsuccessful pregnancies that is habitual abortions to a "child wish" which remains to be a serious problem of the woman who has borne live
children but has been unfortunate. In some cultures the problem is particularly serious because her whole social and personal security may depend on her fertility. Primary and secondary sterility can thus cause great anxiety, such woman are obviously apt to consult either doctors as well as some sort of quacks. Genuine infertility is the most difficult to investigate and can seldom be treated effectively.

The incidence of infertility, both primary and secondary varies from 10 to 30 per cent of all married couples. Menon et al. 1983 reports of 92 per cent females suffering from primary infertility and 8 per cent secondary infertility.

Primary infertility in a women is inability to achieve pregnancy after at least one year of unprotected coitus. Secondary infertility implies at least one year of infertility with proven fertility, including ectopic gestation. Recurrent abortions are considered to be a form of secondary infertility.

Causes of primary infertility in the female is not a topic of present thesis, but to evaluate the number of interviewed samples a little introduction has been given. Major causes of primary infertility in females are as follows; vaginal and cervical factors; uterine and endometrial factors; ovarian factors; tubal factor.
It is always a tragedy when a woman cannot conceive or bear children which she generally greatly desires and would cherish.

The term abortion denotes the termination of pregnancy after the embryo is implanted in the endometrium but before the foetus has attained viability, that is, before it has become capable of surviving the neonatal period with appropriate life support systems and eventually maintaining an independent extraterine life. Feotus is considered viable once it has attained 28 weeks of gestation and, or, weighs over 1000 gms. Menon et al. 1983.

It is impossible to establish precisely the incidence of abortion. A woman may abort without the knowledge that she is pregnant. Normally an early abortion might be mistaken for a delayed excessive menstrual period and vice-versa. To obtain information regarding the incidence of abortion in the community two approaches have been evolved Menon op.cit. Tietze, 1983. One relating the number of abortions to the population or the number of women at risk of having them, abortion rate/1000 total population, or abortion rate/1000 women of reproductive age; the second, relating the number of abortions to the number of pregnancies or live births, abortion ratio/1000 pregnancies or abortion ratio/1000 live births, Menon op.cit. Tietze 1983.
About 50% to 60% of spontaneous abortions results from ovular defects due to maternal and paternal (sperm) factors, 15 per cent are caused by maternal trauma, infections dietary deficiencies, diabetes, mellitus, hypothyroidism, poisoning or anatomic malformations, details have been given further.

Abortion is defined as termination of gestation before the fetus becomes viable. Viability is usually reached at 28 weeks, when infant weighs slightly more than 1 kg. Occurrence of about 3/4 th abortions before the 16th week of gestation is observed, of these 3/4th occur before the 8th week. At least 12% of all pregnancies terminates in spontaneous abortions, Novak et al. 1971.

There is no good evidence that abortions may be induced by psychic stimuli, such as severe, fright, grief, anger or anxiety. Causation of abortions in about 1/4th cases cannot be determined as a clinical diagnosis and a pathological one. Woman who are emotionally immature are prone to habitual or spontaneous abortions. Hormonal aberrations often seem to be responsible for these types of abortions, Krupp et al. 1977.

Pregnancies in human which is about 15% end by recognizable before the 22nd week, where the weight of the embryo is less than 500 grams, has been defined
as abortions. From the various evidences that are there of the human as well as the mammals many more zygotes are lost at an early stage of the development which are often malformed and remain unnoticed.

Habitual abortion occur in 0.4 per cent pregnancies or spontaneous abortions are the resultant of 4 per cent pregnancies, these remain to be cause of recurrent or persistent rather than random or accidental factors. Many habitual abortions results from abnormal genetic disorders.

CLASSIFICATION OF ABORTIONS

Abortions based on various aspects have been classified into following types.

1. Depending upon the period of gestation: (a) early: upto 12 weeks, (b) late: 13 to 20 weeks.

2. Intervention: (a) spontaneous; (b) induced, could be (i) legal and (ii) illegal.

3. Clinical types: (a) threatened; (b) inevitable; this may be (i) complete, (ii) incomplete; (c) missed, (d) septic and (e) habitual.

Term septic abortion is often used to describe any of the above types of abortion which become complicated by infection Jeffcoate, 1983. A woman who sustains, 3, or, even 2 or, more spontaneous abortions of successive pregnancies is said to suffer from habitual or recurrent abortions.
A) Etiology of Spontaneous Abortions

Spontaneous abortions are believed to be due to a failure of several interrelated factors. The usual criterion for the diagnosis of spontaneous abortion is three or more pregnancies with consecutive losses generally in the third or fourth month. Bishop and Richards have indicated the incidence to be 0.41 percent of all pregnancies. The clinical symptomatology is not due to a single disease entity, but is characterized by many different etiological factors. These etiological factors can be classified under five major headings:

1. Genetic Factor: Repeated abortions where there is a history of foetal wastage interspersed with normal progeny, a genetic factor could then be suspected. Under these circumstances, the chromosomal karyotype for both husband and wife should be obtained. No known treatment at the present time for such a genetic defect is there, genetic counseling is all that could be offered to such cases.

2. Anatomical uterine and cervical defects: The incompetent cervical or, either traumatic or congenital, can be associated with repeated fetal loss. It is characterized by sudden expulsion of a normal sac and fetus between the 18th and 32nd week of pregnancy without prior cramps or bleeding.
3. The Luteal phase defect: This form of ovarian insufficiency is a relatively frequent cause of repeated miscarriage. It occurs in 34 per cent of patients studied by Jones and Delfs 1967. The etiology of the difficulty can be due to:

(i) Central factors, related to psychogenic neurogenic, or specific pituitary insufficiency.

(ii) Intermediate disturbances related to nutritional factors, drug toxicity, chronic disease processes, metabolic disease.

(iii) Specific ovarian insufficiency.

4. Blood Incompatibility: Although RH incompatibility are not a cause of repeated miscarriages. Certain ABO incompatibilities may be associated with this clinical syndrome. The history under these circumstances is characterized by one normal pregnancy, perhaps with a history of a jaundiced baby, then recurrent abortions at an earlier duration of pregnancy is obvious. This type of abortion is usually indicative of a tissue antibody. At the present time, there is no known treatment for this condition.

5. Sperm defects: Although probably a rare cause for repeated miscarriages, when increased numbers of abnormal spermatozoa are found in semen analysis of husbands of patients with repeated miscarriages this factor must be suspected, Novak et al. 1971.
B) Missed Abortion

When embryonic death occurs, the products of conception are generally expelled within a few weeks. When an early perished embryo is not expelled within two months, it is spoken of as a missed abortion.

When a woman, apparently pregnant, shows no sign of continued uterine growth, bleeding of some degree, often slight, muddy, and malodorous, may occur, but conversion of a definitely positive to a definitely negative pregnancy test is of course of decisive diagnostic point. The cause of the inability of the uterus to expel its contents is uncertain. Bengtsson has suggested that it results when death of the fetus occurs before placental failure. This deprives the uterus of a major estrogen source from the fetal adrenal precursors and causes an estrogen-progesterone-imbalance with an excessive progestrone effect. Thus the contractility of the myometrium is depressed and the repose to oxytocin inhibited.

C) Threatened and Inevitable Abortion

Menon op.cit. Tietze 1983, estimates the percentage of abortions in all pregnancy as 10 per cent, although others put the figure as high as 20 per cent. One or more missed periods followed by bleeding and sometimes cramps suggest that a pregnancy is threatened.
The persistence of a normal serum chorionic gonadotrophin titer is a good prognostic sign, while low titers are usually a signal of inevitable abortion. The symptoms sometimes subside and the gestation goes on uneventfully to term. In other instances the bleeding and cramps may increase with ultimate expulsion of the embryo. If there is no abortion, and the patient goes to term, the expectation of a normal baby is good, although abnormalities of the infant under these circumstances are slightly increased over those seen in the uncomplicated pregnancy.

**D) Incomplete Abortion**

In an incomplete abortion a significant portion of the pregnancy, usually a placental fragment, remains in the uterus. The patient suffers from a mild cramps, but the bleeding remains persistent and often starts flowing excessively.

Termination of pregnancy before 28 weeks is called abortion or miscarriage, Chauhan 1988, pretermination of pregnancy usually occurs between 28 and 36 weeks is a miscarriage. Abortion after 36 week any time is called still birth. Termination of pregnancy within three months or its multiple, are called as trimesters.

Blandau 1954 and Lanman 1968 observed marked effects on development when eggs and sperms are aged
before fertilization. In general it could be said that the aging of spermatozoas in the female genital tract usually gets accompanied by a gradual decrease in the fertilizing capacity. This decrease in fertility has not been reported to be accompanied by an increased frequency of abnormalities. Aging spermatozoa in the male genital tract usually gets accompanied by declined fertility without resulting defects in the offspring.

There are several reports suggesting that fertilization late in menstrual cycle may lead to abortions as well as malformations. Mikamo 1970 postulated fertilization of over ripe ova as a cause of abortion which was actually due to the cause of chromosomal anomalies. Basal body temperature has also shown to be correlated with ovulation, it has been generally accepted that ovulation takes place one or two days before the rise of temperature.

The present chapter deals with the various variabilities which actually leads a female to either remain infertile or abortions. Clinically diagnosed 209 infertile females with their various diagnosed variabilities by the physicians have been detailed in this part of the present work. About 89 females were infertile due to primary infections, whereas a few out of 120 had some other problems which has been briefly elaborated here.
Various factors are responsible for infertility in females. These have been distinctly categorised in table 6.1. It is quite evident from the table that the maximum percentage frequency for primary infertility due to vaginal and cervical factors is highest between the age group 20 to 25 years. This frequency subsequently decreases to 3.34 per cent between the age group 26 to 30 years, finally at frequency of 1.91 per cent and 0.96 per cent is seen to be observed between the age groups 31 to 35 years and 36 to 40 years respectively. Women affected by the vaginal infection cannot conceive until it is cleared, hence this infection does not occur at any particular stage but unhygienic conditions remain prevalent in such cases, Menon et al. 1983 (Table 6.1).

Primary infertility can also be caused by uterine and endometrial factors. Maximum percentage frequency of this trait was observed between the age group 20 to 25 years, this frequency is seen to decrease to a similar value of 1.44 per cent which was observed in the age groups 26 to 30 years and 31 to 35 years. A minimum percentage frequency of 0.96 and 0.48 in the age groups of 36 to 40 years and 41 and above, respectively was observed. The uterine and endometrial factors affecting infertility in females does not actually correspond to any particular age, but it has a relation to benign tumors, and uterine synechiae which causes failure in implantation, and can affect any individuals.
Ovarian factors are also a cause of primary infertility in females. It is observed from table 6.1 that the maximum percentage frequency of this factor was observed between the age group 20 to 25 years. There was observed to be a gradual decrease in percentage frequency for this infection, which was about 3.34 per cent between the age group 26 to 30 years. About 2.39 per cent frequency was observed amongst female individuals of 31 to 35 years of age and finally a minimum percentage frequency was noted between the age group of 36 to 40 years. Appropriate steriod hormones and ovulation are usually responsible for normal ovarian function, which may otherwise totally or partially affect its function. Frequency of this factor is not responsible for its affect on a particular age, but it varies due to many other physiological functions, Krupp et al. 1977.

Tubal dysfunction continues to be one of the major causes of infertility in females. Maximum percentage frequency was observed to be almost similar between the age groups of 20 to 25 years and 26 to 30 years. A percentage frequency of 4.78 was observed amongst the female of age group 31 to 35 years. The incidence of tubal factor is reported to be from 30 to 40 per cent in our country, Menon et al. 1983. Affect of this factor destroys the tubal integrity (Table 6.1).
<table>
<thead>
<tr>
<th></th>
<th>Primary Infertility</th>
<th></th>
<th></th>
<th></th>
<th>Secondary Infertility</th>
<th>Abortion</th>
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<td></td>
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<td>Uterine and</td>
<td>Ovarian</td>
<td>Tubal</td>
<td>Amenorrhea</td>
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<tr>
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<td>3.34</td>
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<td>2.87</td>
<td>8</td>
<td>3.83</td>
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<td>26 to 30</td>
<td>4</td>
<td>1.91</td>
<td>3</td>
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<td>7</td>
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<td>14</td>
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<td>31 to 35</td>
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<td>3</td>
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<td>41 and above</td>
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<td>TOTAL</td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>
Fig. No. 6.1 Infertility in female individuals

INDEX
- Vaginal and cervical factors
- Uterine and Endometrial factors
- Ovarian factor
- Tubal factors
- Amenorrhea
- Abortion → (Secondary infertility)
- Not affected
- Total

PERCENT (%)

28
24
20
16
12
8
4
0

20 to 25
26 to 30
31 to 35
36 to 40
41 & Above
Not affected

AGE IN YEARS

NIL
Amenorrhea is also a cause of primary infertility in female which has been dealt separately in the next part of the same chapter.

Secondary infertility in females is a cause of abortions. Usually abortion occurs with the increasing age of females. Maximum percentage frequency of abortion is observed between the age groups of 31 to 35 years, a percentage, less, of this trait was observed between the age group 36 to 40 years. There were some incidences of abortion at the age group of 20 to 25 years and 26 to 30 years of age which was subsequently lesser than the occurrence of the incidence at higher age group. Minimum percentage frequency was observed between the age group 41 and above. Occurrence of abortions is invariably observed at all ages due to variable infections as mentioned earlier, later age of the female has adverse affect of this trait, whether she herself may remain responsible or her counterpart may play, the, only role.

Trimester abortions varies considerably amongst the female individuals, particularly, its affects accounts for increasing age of the patient. The maximum percentage frequency for 1st Trimester abortion was observed between the age group 36 to 40 years, obviously the age factor remains dominant in this aspect. Observation of almost a constant percentage frequency of 4.78
and 4.31 between the age groups 26 to 30 and 31 to 35 years respectively was noticed. A minimum of 2.87 per cent was observed between the age groups 20 to 25 years, and on the contrary 3.34 per cent of frequency was noticed at much higher age level, that is 41 and above (Table 6.2).

From the table 6.2 the incidence of 2nd Trimester abortion is observed. Between the age group 31 to 35 years a maximum percentage frequency was observed, the incidence of its occurrence between the age groups 20 to 25 year and 36 to 40 year is observed to be similar in the present study. Only, one individual was observed at the age group of 41 and above, the incidence of its frequency is usually observed at later age of the female individuals, an occurrence of such type of abortions is usually after 24 weeks, an incidence could be named as miscarriages.

Observation of 3rd Trimester abortions were noticed amongst only three individuals. Between the age group 20 to 25 years the percentage frequency was higher, whereas, only one individual between the age group 26 to 30 was noticed. Occurrence of 3rd Trimester after 36 weeks is usually a still births.
Table 6.2

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Ab. No.</th>
<th>Pc</th>
<th>Ab. No.</th>
<th>Pc</th>
<th>Ab. No.</th>
<th>Pc</th>
<th>Ab. No.</th>
<th>Pc</th>
<th>T O T A L</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 to 25</td>
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<td>2.87</td>
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<td>0.96</td>
<td>11</td>
<td>5.27</td>
<td></td>
</tr>
<tr>
<td>26 to 30</td>
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<td>4.78</td>
<td>2</td>
<td>0.96</td>
<td>1</td>
<td>0.48</td>
<td>13</td>
<td>6.22</td>
<td></td>
</tr>
<tr>
<td>31 to 35</td>
<td>9</td>
<td>4.31</td>
<td>6</td>
<td>2.87</td>
<td>-</td>
<td>-</td>
<td>15</td>
<td>7.18</td>
<td></td>
</tr>
<tr>
<td>36 to 40</td>
<td>11</td>
<td>5.26</td>
<td>3</td>
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<td>-</td>
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<td>-</td>
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<td>-</td>
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<td>118</td>
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</tr>
<tr>
<td>TOTAL</td>
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<td></td>
<td></td>
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</table>
Fig. No. 6.2 Trimester abortion in the female individuals

INDEX

1st Trimester
2nd Trimester
3rd Trimester
Not affected
Total

Abortions

PERCENT (%)

72
68
64
16
12
8
4
0

20 to 25
26 to 30
31 to 35
36 to 40
41 & Above
Not affected

AGE IN YEAR
Table 6.3 deals with various variabilities which leads to spontaneous abortions. Causes of genetic factor which ultimately leads to this kind of abortion has been discussed in further chapter. Spontaneous abortions due to anatomical uterine and cervical factors is noticed to occur in the maximum percentage frequency of age group 36 to 40 years. A similar trend of frequency for this defect was observed between the two age group individuals, that is, 20 to 25 and 31 to 35 years. Occurrence of minimum percentage frequency was noticed between the age group 26 to 30 years and 41 and above years amongst the female individuals. The cause of this factor is basically dependent on cord abnormalities or congenital anomalies.

Spontaneous abortions due to luteal phase defect usually relates to nutritional deficiency and metabolic diseases. In the present work between the age group 36 to 40 years the maximum percentage frequency was observed. There was the observation of this factor to be similar in the individuals belonging to the age group 26 to 30 and 31 to 35 years. A little higher frequency was also observed amongst 3 individuals between the age group 20 to 25 years. Incidence of spontaneous abortions due to this factor is obviously not related to age but many physiological factors along with malnutrition and severe metabolic diseases are responsible for its occurrence.
### Table 6.3

Infertility Due to Spontaneous Abortions

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Genetic factor</th>
<th>Anatomical uterine and cervical defects</th>
<th>Luteal phase defects</th>
<th>Blood Incompatability</th>
<th>Sperm defects</th>
<th>TOTAL</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<td>26 to 30</td>
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<td>2</td>
<td>1</td>
<td>1</td>
<td>7</td>
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<tr>
<td>31 to 35</td>
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<td>2</td>
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<td>36 to 40</td>
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<td>-</td>
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<td>8</td>
</tr>
<tr>
<td>41 and above</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>180</td>
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**TOTAL**

<table>
<thead>
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<th>Ab. No.</th>
<th>Pc</th>
</tr>
</thead>
<tbody>
<tr>
<td>209</td>
<td>100.00</td>
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</tbody>
</table>
ABO system incompatibility appears to be associated with higher incidence of spontaneous abortions. Pande, et al. 1973. In the present study similar percentage frequency was noticed between the age groups, 20 to 25, 26 to 30 and 31 to 35 years. This type of abortion is usually indicative of a tissue antibody, which can obviously occur due to immunological rejection of the foetus.

From table 6.3 it can be inferred that occurrence of spontaneous abortion due to sperm defect has some relation, as incidence of two similar percentage frequency between the age group 20 to 25 years and 26 to 30 years was observed, Novak et al. 1971, when a female suffers from recurrent miscarriages the factor of her husbands abnormal spermatozoas ought to be considered.

Patients suffering from primary infertility were not taken for karyotyping as the infertility in them was quite obvious. Those female individuals who were suffering from primary and secondary amenorrhea were karyotyped inspite of the fact it was quite clear from their diagnosis the reason, so as to why they were actually having the problem.

Female individuals who had abortions, whether first trimester, second or third were considered for the karyotyping so as to evaluate the chromosome findings in them, along with the ones who were aborting
on account of infections. There were 4 female individuals who were probably aborting on account of genetic factor, which has been dealt further.

Female individuals suffering from abortions were, a few, due to spontaneous abortions, while some of them had miscarriages and still births. There had been a few who had, had, habitual abortions. All these individuals were considered for karyotyping so as to do the analysis of their chromosomes.
PART - B

PRIMARY AMENORRHEA
The second part of this chapter, "Reproductive Performances in Infertile Females" deals with those female individuals who were infertile due to either primary amenorrhea or secondary amenorrhea. Apart from clinical diagnosis by the physician for the cause of infertility in them they were finally included for laboratory detection. Amenorrhea, primary or secondary, leads a female to remain infertile. Many facts relating to the endocrine factors in puberty and to the endocrine relationship of menstrual cycle have been studied during past few years.

The influence of food, body build, nutrition and social origin has relationship with menarche, and it has been studied intensively world wide. Occurrence of menarche is basically governed by genetic factors, but most important factor being the environmental socio-economical and, of course, nutritional.

Roberton in the year 1830 and 1840 was the first one to relate menarche with the climatic conditions.
According to him in hot zone menarche occurs as early as 8 or 9 year, and in temperate climatic region it is usually seen to occur between the age of thirteen or fourteen year. In arctic regions the occurrence of menarche is noticeable only between 18 and 19 years of age. Roberton later revised his opinion and attributed to racial factors also.

Hannover 1865, confirmed Roberton's results by pointing out the low age of menarche for Greenland and Eskimos. Nevertheless, studies of menarche in Czechoslavakia, Poland and else where have been reviewed by Valsik 1965, which showed that geographical location of the dwelling place and particularly its elevation above the see level, affects the seasonal rhythm of menarche.

The beginning of menstruation remains to be an outstanding feature of puberty, the first period being called the menarche. It was Gessel et al. 1956, who defined menarche as an important episode in a woman's life which later in the life is followed by sequence of manifestations of adolescence.

The three terms being synonymous namely adolescence, puberty and menarche are sometimes used loosely. Jeffcoats 1983, described menarche as the onset of menstruation and merely a manifestation of puberty.
Much earlier, that is, in the year 1950 Selye recognised menarche as one of the many prerequisites of fertility and also as an objective indicator for the onset of puberty. Selye 1950, explains the phenomenon of puberty as an increase in the gonadotrophin secretion of the anterior lobe of the pituitary. This secretion of gonadal hormone in turn affects the causation of menstruation and also brings about the development of accessory organs as well as somatic and psychic in general.

Clinically menstruation is uterine bleeding which occurs at intervals of 24 to 32 days in a normal woman during her reproductive years. The pituitary gonadotrophins and estrogens are responsible, although progesterone, thyroid hormones and the adrenocortico steroids also influence menstruation.

Ovulation and the resulting production of estrogen and progesterone result in bleeding that is, ovulatory menstruation, from a secretory endometrium when pregnancy does not occur. In the absence of ovulation bleeding also known as anovulatory menstruation, is from a non secretory endometrium.

Menarche which generally, occurs between the age 11 to 14 years, initially marks the onset of menstrual period. Menstruation ceases with the menopause at 45 to 55 years of age, Krupp et al. 1977.
The average duration of menstrual bleeding is for about 3 to 7 days, and a blood loss of an individual woman mounts to about 50 to 100 ml normally, unless, one happens to suffer from phyomenorrhrea, which is the unusual prolong bleeding, a matter of concern, to almost, every woman.

Characteristically, menstrual blood does not clot because it already gets clotted in the uterine cavity and has later reliquified. Many a woman suffer from uterine cramping with the ovulatory cycle, but anovulatory bleeding is generally more painful, Novak et al. 1971.

Menstrual aberrations are often an indication of a disease or a deficiency state, emotional tension and pregnancy. Abnormal menstrual cycles deserves close analysis, it is not enough to know whether the loss is slight or more, but its exact duration an periodicity has to be determined, Jeffcoate, 1983.

Amenorrhea or absence of menstruation is a symptom and not a disease. Normal menstruation is the end result of coordinated cycle events in the hypothalamo-pituitary-ovarian-uterine axis, Menon et al. 1983. Amenorrhea is a reflection of an interruption in the function of this chain or may be due to mechanical aberrations in the genital tract.
Amenorrhea may be physiological or pathological. Physiological amenorrhea occurs during pregnancy, lactation and after menopause. Pathologically, it may be primary or secondary. Primary amenorrhea is the failure of menses to appear initially by the age of 18 years after which the diagnosis ought to begin. Cryptomenorrhea signifies the occurrence of menstrual cycle but does not appear externally, because of an obstruction of the lower genital tract. A reduction in the frequency of menses, the interval being as long as 38 days but less than three months is oligomenorrhea. Hypomenorrhea is the reduction in the number of days or the amount of menstrual cycle. And finally secondary amenorrhea implies to the cessation of menses after the initial menarche, Novak et al. 1971.

As mentioned earlier if menarche is not achieved by the age of 18 years a girl is considered to have primary amenorrhea. Menon et al. 1983 describes primary amenorrhea as a restricted term as it conveys the absence of menstruation. Delayed puberty includes some or all aspects of the physiological process of puberty development, development of breast, increased rate of physical growth-height, pubic and axillary hair and skeletal maturation. The causes of delayed puberty or primary amenorrhea are as follows:
Diagrammatic representation of factors determining sex in utero, showing operational indicative sites by arrows, denoting connections of one with other, (i) sex chromosomes; (ii) genes on autosomes; (iii) organizer influence of the gonad directly in ducts; and (iv) hormones of the fetus.
(i) **Outline tract defects**: which causes crypto-menorrhea and haemocolpos.

(ii) **Uterine Causes**: caused by genital tuberculosis which is very much prevalent in our country.

(iii) **Mullerian agenesis**: the condition includes absence of uterus, cervix and the upper part of vagina. Malformation in such cases are seen in even an adult girl but she fails to menstruate.

(iv) **Gonadal dysgenesis**: or dysgenetic gonads are those which are imperfectly formed or differentiated. This term is used collectively for a clinical entity that has a spectrum of causes. Frequently it is caused by abnormalities of sex chromosomes and it is of five kinds.

a) **Turner syndrome**: a syndrome of infantilism, the patient is short with a small chin, low posterior hair line, webbing of neck, deformed carrying angle, abroad shielded chest with laterally placed nipples, poorly developed breasts, absent or scanty axillary and pubic hair, immature Mullerian ducts, streak gonads, 45; XO, chromosomal pattern on karyotyping.

b) **Pure gonadal dysgenesis**: patients belonging to this group are phenotypic females with dysgenetic gonads, primary amenorrhea, absent or poorly developed secondary sexual characteristics and eunuchoid habitus. Menon op cit. De Court et al. 1960, described in a
19 year old female with gonadal dysgenesis and a 46, XX complement. The exact cause of a patient with pure gonadal dysgenesis and 46, XX karyotype remains to be unknown, Menon et al. 1983.

c) Swyer's syndrome or XY gonadal dysgenesis:
individuals with XY chromosome constitutions have normal female external genitalia but hypoplastic internal genitalia. The pathogenesis of this normal XY sex chromosome complement could be testicular degeneration which is usually total but incomplete, hence Mullerian inhibition are lost and individuals have female external and internal genitalia. The streak gonads undergo neoplastic changes which can turn malignant.

d) Gonadotrophin resistance syndrome: in this condition there is a good development of breast, axillary and pubic hair, hypergonadotrophic status, normal karyotype, normal Mullerian tract development and normal follicular apparatus on ovarian histology, but primary amenorrhea.

e) Testicular feminization syndrome or androgen insensitivity syndrome: in this the patient appears a typical female with normal breast normal external genitalia but no axillary or pubic hair, a blind vagina with no Mullerian structure. The gonads (testes) are mostly inguinal or labials, rarely intra-abdominal, karyotypes is 46, XY, with normal FSH and testosterone levels, as for males, on hormonal analysis, Menon et al. 1983.

(iv) Cause in other areas like hypothalamus, higher CNS, pituitary, other endocrines like thyroid and
adrenals are similar to those in secondary amenorrhea.

Primary amenorrhea may provide an important indication of systemic disorder; it could be due to a chromosomal anomaly such as Turner's syndrome as already mentioned or it could also be due to an autoimmunity reaction against antigens, Novak et al. 1971.

Novak et al. 1971 evaluated cytohormonal pattern in relation to primary amenorrhea.

The evaluation of women in the reproductive age who have never menstruated should include cytohormonal pattern, presence of ovulation, and chromosomal sex. They thus can be considered in four significant clinical categories.

**Normal Hormonal Pattern with Positive Chromatin**

This is found in anatomic variants with XX sex chromosome constitution (e.g. congenital atresias, absence of portions of the generative system other than ovaries) or otherwise normal females with systemic disease or endocrinopathies insufficient to place the hormonal pattern outside the normal range. In the former, a normal ovulatory shift in the cytohormonal pattern (M.I.) is present if there are normally functioning ovaries. In the latter the shift is usually absent or abnormal. Very few or very small sex chromatin bodies
Non-disjunction of the sex chromosomes of the ovum at the time of reduction division. Possible combination of sex chromosomes after fertilization are XXX; XO; XXY and YO, which has never been found clinically.
may indicate mosaicism, translocation or other genetic abnormalities whose exact nature can be determined only by thorough cytogenetic studies.

**Abnormal Hormonal Pattern with Positive Chromatin**

These individuals have a normal XX sex chromosome constitution and significant endocrinopathy. One must rule out artifacts (hormonal therapy inflammation, cervical or vulvar contamination of the specimen) and then consider disease such as dysfunctions of the ovary (agenesis, hypofunction, primary or metastatic tumors) primary (dwarfism, simond's disease, tumors), thyroid (marked hypothyroidism, cretinism), adrenal, (hyperplasia, tumor), endometrium, (hyperplasia, tumor), breast (hyperplasia, tumors) and chromosomes (mongolism, miscellaneous somatic trisomy). An XXX individual has "double positive chromatin".

Ovulation is usually absent, but if it is present, it may provide key evidence of the site of abnormalities. Intermediate maturation (M.I. $0/100^\circ$) indicates lack of ovarian function. Parabasal maturation (M.I. $100^\circ/0^\circ$) or a pattern approaching this, is found in pituitary or adrenal dysfunction or in extreme hypothyroidism. One must also consider the rare case of extreme hypospadias in klinefeller's syndrome with vaginal formation (XXY in mosaic pattern usually) and of a mosaic Turner syndrome (e.g. XX/XO).
Normal Hormonal Pattern with Negative Chromatin

This may be present in testicular feminization with an XY sex chromosomal constitution (feminizing male pseudohermaphroditism). When estrogen production is adequate, the cytohormonal pattern may be well within normal limits, when it is extreme the maturation index may shift excessively to the right, past normal, and at times even with exfoliation of anucleate superficial cells. Ovulation is absent, and thus, so is the cytohormonal shift.

Abnormal Hormonal Pattern with Negative Chromatin

This is found in the usual Turner's syndrome (XO) and in masculinizing male pseudohermaphroditism (XY). In patients with Turner's syndrome, intermediate cell maturation or parabasal cell maturation is present, depending upon the age of the patient. Male pseudohermaphrodite may have an androgenic cytohormonal pattern, or may approach intermediate cell or parabasal cell maturation depending on their age. Ovulation and its cytohormonal shift are absent in such cases, Novak et al. 1971.

The second part of this chapter deals with amenorrhea a cause of primary and secondary infertility in females. Two female individuals suffering from primary amenorrhea and three due to secondary amenorrhea have been taken an account off, keeping in mind their actual reason for
Table 6.4

Infertility due to Amenorrhea in female individuals

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Amenorrhea</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>20 to 25</td>
<td>Primary</td>
<td>Secondary</td>
<td>TOTAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>26 to 30</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>1.44</td>
<td></td>
</tr>
<tr>
<td>31 to 35</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>36 to 40</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
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<td>41 and above</td>
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<td>-</td>
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</tr>
<tr>
<td>Not affected</td>
<td>-</td>
<td>-</td>
<td>204</td>
<td>97.60</td>
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</tr>
</tbody>
</table>

TOTAL: 209 100.00
Table 6.5

Percentage distribution of female sample for amenorrhea

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Outflow tract defects</th>
<th>Uterine causes</th>
<th>Mullerian agenesis</th>
<th>Gonadal dysgenesis</th>
<th>Causes in other compartments</th>
<th>Uterine causes</th>
<th>Ovarian causes</th>
<th>Gonadotrophin resistant syndrome</th>
<th>Polycystic ovarian syndrome</th>
<th>Hypothalamo-pituitary lesions</th>
<th>TOTAL</th>
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</thead>
<tbody>
<tr>
<td>20 to 25</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>0.96</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>26 to 30</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>0.96</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>31 to 35</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>0.96</td>
<td>1</td>
<td>0.48</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>36 to 40</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>41 and above</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Not affected</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>209</td>
</tr>
</tbody>
</table>

209 100.00
the affected conditions, (From 209 infertile female individuals.

Cause of infertility due to primary amenorrhea and secondary amenorrhea has been dealt in table 6.4. Incidence of primary amenorrhea was observed between the age group 20 to 25 years, the incidence was observed to be very low in this factor. Many factors are related in the occurrence of primary amenorrhea which has been dealt in table 6.5.

Three female individuals were observed to suffer from secondary amenorrhea. The incidence of this occurrence was noticed at the age group of 26 to 30 years. Table 6.5 deals with the various factors which are related to primary and secondary amenorrhea. From the table the percentage frequency for primary amenorrhea is about 0.96. The incidence of uterine cause due to which the patient was affected has been discussed in prior part of this chapter.

Secondary amenorrhea was observed to be affected in three individuals, due to uterine and ovarian causes. The incidence of uterine cause was between the age group 26 to 30 years, while the incidence of ovarian cause was 0.48 per cent.

The sample of these 5 primary and secondary infertile female individuals were specifically karyotyped, to evaluate, in case any chromosomal abnormality could be observed, in them.
REFERENCES


