

PRIMARY AMENORRHOEA

by

PRATIBHA R. VAIDYA,* M.D., F.C.P.S., D.G.O., D.F.P.

A. G. KALE,** M.D., D.F.P.

V. G. KALE,*** M.D., D.G.O.

and

B. N. PURANDARE,**** M.D., F.R.C.S.E., F.C.P.S., F.I.C.S., F.R.C.O.G.,
F.A.M.S.

Amenorrhoea is a symptom complex which reflects some derangement in the hypothalamo-pituitary-uterine axis. The purpose of this paper is to present various aetiological factors encountered in our series of cases and to demonstrate the difficulties encountered in arriving at a proper diagnosis.

The age of menarche in India as investigated by Israel (1959) is 13.6 years. If the menstruation fails to occur by the age of 18 years, the condition is called primary amenorrhoea. This age limit is accepted by Israel (1967), Jeffcoate (1967) and many other authors. However, investigations on primary amenorrhoea can be started from the age of 16 years

for the problem of delayed menarche so that any obvious systemic diseases or stigmas of gross endocrine dysfunction or cryptomenorrhoea can be discovered at an early date (Jeffcoate 1967); Ramswami and Naidu, 1966).

Material and Method

One hundred and nine cases of primary amenorrhoea and delayed menarche attended the K. E. M. Hospital Gynaec. Endocrinological outdoor during the years 1968 and 1969.

A detailed history and careful clinical examination was done on all the patients. Serial vaginal smears, haemogram, erythrocyte sedimentation rate, urine and stool examinations, buccal smear, X-ray chest or screening were done for all the patients. X-ray skull and urinary gonadotrophin examination and thyroid study were done in selected cases. Endometrial biopsy was attempted in most of the cases.

*Lecturer, Gynec. & Obst. endocrinology.

**Registrar, Endocrinology, Gynec. & Obst.

***Research Student for Ph.D.

****Head of the Department of Obst. & Gynec., K. E. M. Hospital and Seth G. S. Medical College, Parel, Bombay-12.

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TABLE I
Distribution of Patients in Various Age Groups

Group	I	II	III	IV	V	VI
Age in years (completed)	16	17	18	19-20	21-25	More than 25
No. of patients	15	11	22	33	20	8

Total Number of patients : 109.

Table I indicates the distribution of these 109 cases in various age groups.

Twenty-eight patients attended the out patient department for primary amenorrhoea after the age of 20 years. The aetiological factors responsible for the primary amenorrhoea and sexual development of these 109 patients are summarised in Table II. Patients with normal breasts and external genitalia and with normal growth of pubic and axillary hair are considered as sexually mature (Oastler & Sutherland, 1956).

Lack of sexual maturation in these patients may be due to the hypothalamic, pituitary or ovarian factors. Patients

with lack of sexual maturation due to cretinism are usually referred to the medical endocrinological out patient department in our hospital and hence no case with obvious hypothyroidism is included here.

Table III indicates uterine development in these 109 patients.

Five patients had absent vagina in addition to absent uterus. Fifteen patients with tuberculosis of the genital tract had normal sized uteri.

Vaginal cytology judged by serial vaginal smears at the interval of 5-7 days are summarised in Table IV.

TABLE II
Classification of Etiological Factors and Sexual Developments

Aetiological factors	No. of patients	Sexual Development		
		Normal	Hypo-Sexual	Poor Development
Psychological disturbances	1	—	—	1
Hypopituitarism	5	1	1	3
Pituitary ovarian failure	25	1	7	17
Ovarian insufficiency	1	—	1	—
Ovarian agenesis	5	—	2	3
Ovarian teratoma (Bilateral oophorectomy)	1	1	—	—
Testicular feminisation syndrome	3	3	—	—
Faulty mullerian development	24	20	3	1
Tuberculosis	18	17	1	—
Severe malnutrition	8	1	1	6
Diabetes	1	—	—	1
Delayed menarche	17	5	6	6
Total	109	49	22	38

TABLE III
Uterine Development

Absent	Rudimentary	Small size	Normal size	Total
24	26	33	26	109

TABLE IV
Vaginal Cytology

No. of patients	Good	Oestrogen deficiency (atrophic smears)		
	oestrogenisation	Mild	Moderate	Severe
	38	23	28	16

Total : 105 patients studied.

Vaginal cytology reflects the working of pituitary-ovarian axis. An atrophic vaginal smear may be due to the failure of pituitary or ovaries (Shah *et al.*, 1961). Patients showing good oestrogenisation of the vaginal cells belonged to the group of genital tuberculosis, malnutrition, psychological disturbances or delayed menarche.

Hypopituitarism

There were 5 cases with absent or very low levels of urinary gonadotrophins. Four patients had poor sexual development. One patient with hyposexual development had taken hormones. All these patients had selected deficiency of pituitary gonadotrophins only and there was no evidence of panhypopituitarism. Culdoscopy examination was done in two of these patients. One patient had both ovaries streak-like and other patient had one ovary smaller than normal and the other one was streak-like.

None of these patients in this series had space occupying intracranial lesion.

Pituitary-Ovarian Failure

There were 25 patients with pituitary ovarian failure but only one of these was sexually mature. Seventeen patients had poor sexual development. Culdoscopy examination was done in 3 cases. All had streak ovaries. One patient had ectopic kidney. Due to the lack of gonadotrophic hormone estimation they could not be labelled as definite pituitary or ovarian failure. Nearly all of them had moderate oestrogen deficiency in vaginal smears.

Ovarian Insufficiency

There was one case with hyposexual development and moderately hypotrophic vaginal smears in spite of normal urinary

gonadotrophic hormones. There was no evidence of any other abnormalities.

Ovarian Agenesis

There were 5 cases with ovarian agenesis. Their urinary gonadotrophins were abnormally high. This is considered a key to the diagnosis (Israel, 1967). All these patients used to get withdrawal bleeding with cyclical treatment. Typical changes of Turner's syndrome were not seen in any of these. They were sex chromatin negative. Jacob *et al.* (1959) showed the importance of sex chromatin in cases of primary amenorrhoea.

Ovarian Teratoma

One patient gave the history of laparotomy for ovarian teratoma, but accurate operation notes about unilateral or bilateral oophorectomy were not available. She was sexually mature because of previous hormonal treatment and used to get withdrawal bleeding after hormones. On investigations, vaginal smears were atrophic. However, urinary gonadotrophic hormones were abnormally high indicating bilateral oophorectomy.

Faulty Mullerian Development

Twenty-four patients with a faulty mullerian development had normosexual growth. Three patients had hyposexual development and only one patient had poor sexual development. The last patient was not investigated for urinary gonadotrophin estimation and she probably had hypopit-ovarian function in addition to mullerian agenesis. I. V. P. was done in a few cases for urinary tract abnormalities and only one case showed absence of one kidney.

Testicular Feminisation Syndrome

All these 3 patients had normosexual development. Pubic and axillary hair

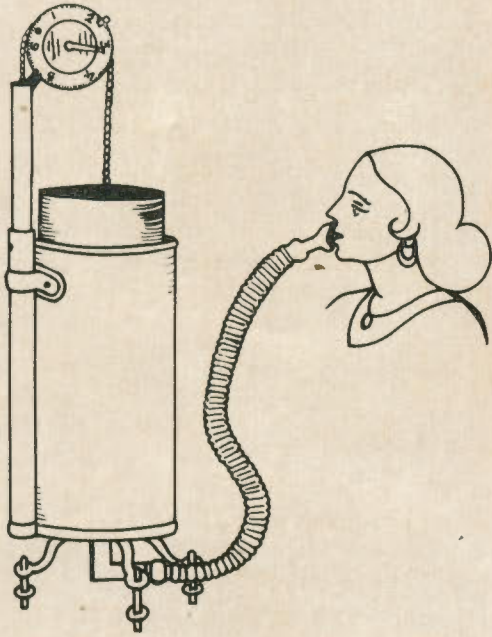


Fig. 1
Spirometer for testing pulmonary function.

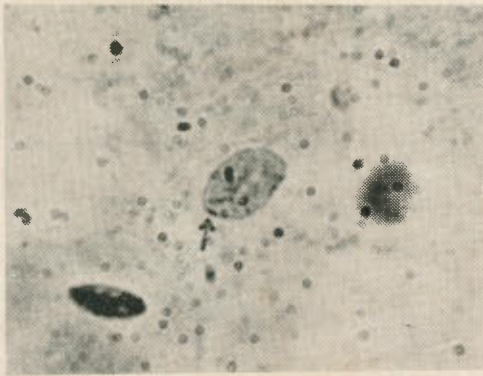


Fig. 2
A well spread amniotic nucleus showing typical sex chromatin body (arrow) X. O. I. L.

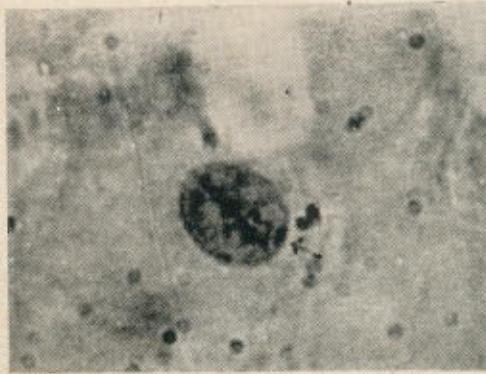


Fig. 1
An amniotic fluid nucleus showing a longitudinal fold in the centre and a typical, relatively larger, densely stained, marginal sex chromatin body (arrow) X. O. I. L.



Fig. 1
Squamous cell cancer with pearl formation.



Fig. 2
Epidermoid cancer of vulva.



Fig. 3
Malignant melanoma of urethral meatus showing
melanin pigments.



Fig. 4
Cancer vulva with leucoplakia.

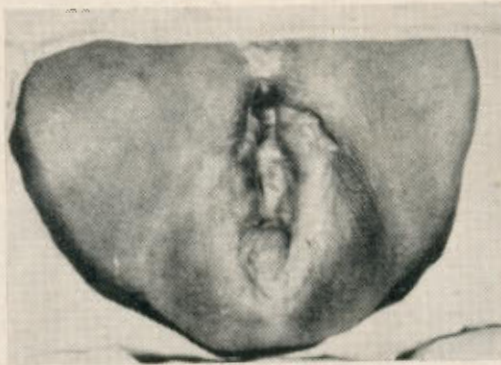


Fig. 5
Cancer of left labia majora extending up to
anal region.



Fig. 6
Cancer vulva arising at the fourchette and extending over the perineum and anal region of the left side.



Fig. 7
Block dissection of the inguinal region and upper part of femoral triangle of right side. Dissector is under femoral artery. X. Thin layer of superficial fascia left with the skin flaps.

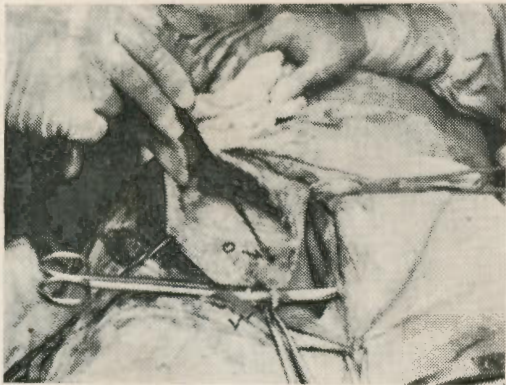


Fig. 8
Shows the great saphenous vein (V) and the fossa ovalis (O).



Fig. 9
Shows femoral artery (F) external iliac artery (I), external iliac vein (V) and obturator nerve (N).



Fig. 1
Patient lying in knee chest position preparatory to surgery.

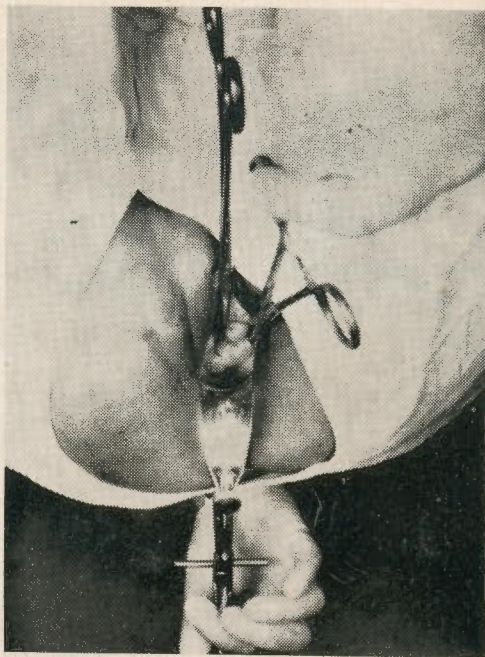


Fig. 2
Ovary held with sponge forceps and delivered in the vagina.

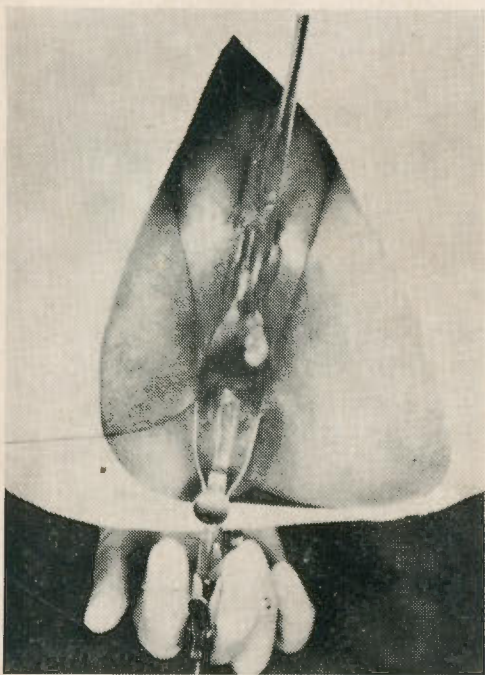


Fig. 3
Tied loop of tube seen in Vagina.

Premature Ovarian Failure
Vaidya & Purandare pp. 41-45

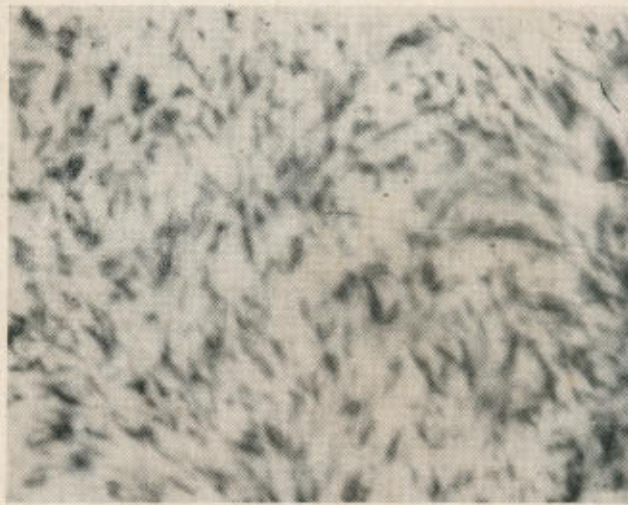


Fig. 1
Ovarian stromal tissue and absence of primordial follicles.

Lymphoid Follicle in Endometrium
—Mehrotra et al. pp. 76-79

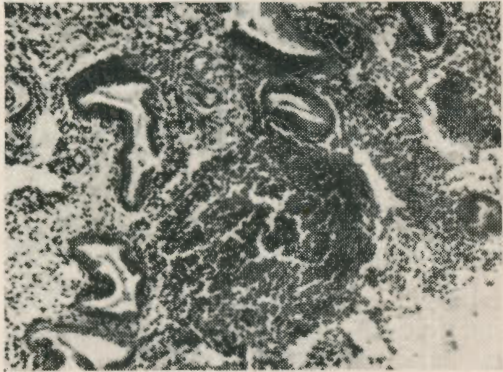


Fig. 1
Showing lymphoid follicle in the phase of
endometrium.

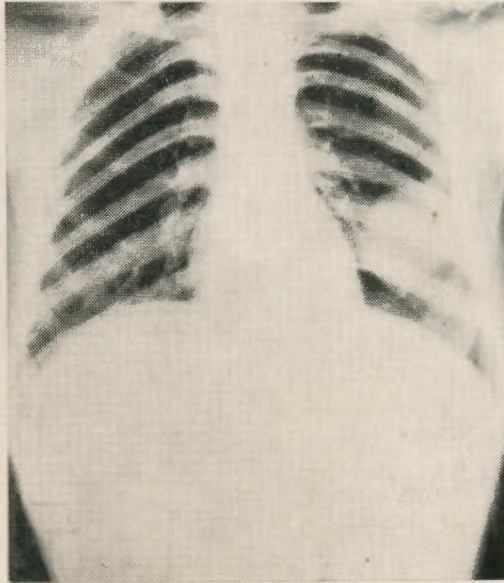


Fig. 1
Chest X-Ray P. A. View Left Lung shows
cannon ball shadow in the lower-lobe.



Fig. 2
Two hard nodules on the under-surface of the
Liver by the side of the gall-bladder.



Fig. 3
Operated specimen Uterus with fallopian tubes
and bilateral theca lutein cysts of the ovaries.

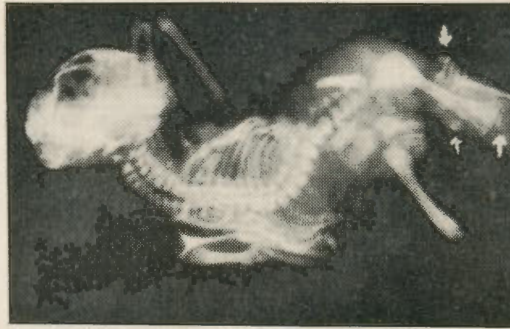
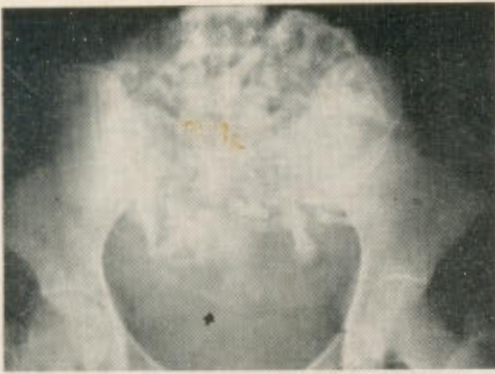


Fig. 1

X-Ray abdomen showing the foetus and calcified membrane at the arrow.

Fig. 2

X-Ray of the foetus removed at operation. Note the ossification centres of lower end of femur and calcaneum.

Cyclopia—Sainaba et al. pp. 87-89

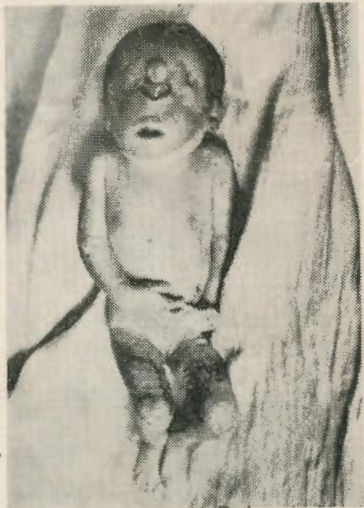


Fig. 1

Cyclops-frontal view showing the central eyes and proboscis.



Fig. 2

Cyclops-lateral view showing the short webbed neck.

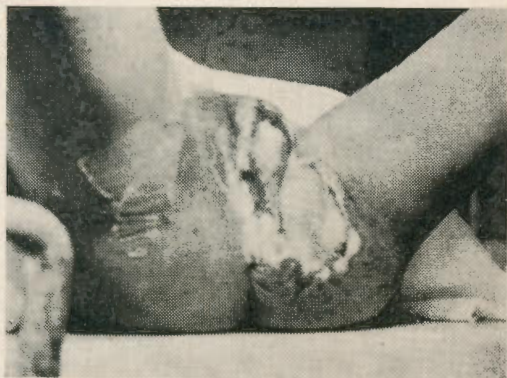


Fig. 1

Photograph shows an extensive area of ulcer on the vulva after sloughing of the necrosed area at the sight of injection.



Fig. 2

The guinea pig shows development of coloured patch and oedema at the site of injection.

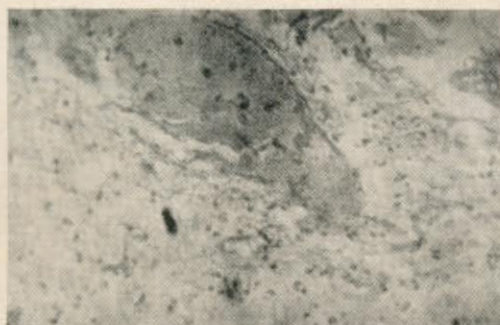


Fig. 3

Photomicrograph showing dilated venules with intravascular thrombosis and extravasation of large number of neutrophils at the site of reaction in the guinea pig.

**THE FEDERATION OF OBSTETRIC AND GYNAECOLOGICAL
SOCIETIES OF INDIA**

**VII INTERNATIONAL CONGRESS OF OBSTETRICS AND
GYNAECOLOGY**

The VII International Congress of Obstetrics and Gynaecology will be held in Moscow, August 12-18, 1973, at the Kremlin palace of Congresses at the Moscow University on Lenin Hills. The All-Union Scientific Society of Obstetrics and Gynaecology will participate in preparation and conducting of the Congress. Professor L. S. Persianinov, Academician of the USSR Academy of Medical Sciences is the President of the Congress.

In the Scientific Programme of the Congress the following subjects are approved for discussion:

- (i) Uterine contractility, normal and abnormal.
- (ii) Biochemistry of the amniotic fluid, the fetus and Newborn.
- (iii) The influence of Hormones on the development and growth of tumours in the female.
- (iv) Gynaecological Problems in Adolescence.
- (v) Recent progress in Obstetrics and Gynaecology.

These problems will be discussed at the plenary and section sessions and in the discussion groups.

The working language at the congress will be: Russian, English, French and German. During plenary sessions a simultaneous translation into Russian, English, French and German will be available. At symposia and section sessions a simultaneous translation into Russian and English will be provided.

Please remember the last date of submission of application forms is 31st December 1972. Federation is sending a copy of first announcement of the above congress to its member bodies along with form which is to be filled by the participant. Please contact the Honorary Secretary of your Society for the same.

If you desire to have further detailed information regarding this congress please contact the General Secretary Federation of Obstetrics and Gynaecological Societies of India 31/c Dr. N. A. Purandare Marg, Purandare Griha, Bombay-7. All the inquiries will be promptly attended to.

C. L. JHAVERI
VILAS M. MEHTA
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28-10-1970.

was very scanty in two patients and absent in one patient. All of them had negative sex chromatin, absent cervix and uterus and shallow vagina. However, only one of these 3 patients was diagnosed by gonadal biopsy which confirmed the presence of testicular tissue. Jacob *et al.* (1959) have stressed the importance of chromosomal abnormality in cases of primary amenorrhoea.

Genital Tuberculosis

Chronic diseases like tuberculosis anywhere in the body can cause amenorrhoea and is not related to debility (Jeffcoate, 1967). As late as 1955, primary amenorrhoea was considered a rare manifestation of genital tuberculosis (Barnes, T., 1955).

A girl is likely to develop genital tuberculosis if she acquires the infection during adolescence, when blood supply to the genital organs is good. Oastler and Southerland (1956) included genital tuberculosis as a cause of primary amenorrhoea.

Nine patients gave definite evidence of tuberculosis on histopathological examination. Endometrial biopsy revealed Koch's infection in only 5 cases. Four other patients had histopathological evidence of tuberculous salpingitis or mesenteric lymphadenitis. The tissue was obtained at the time of exploration. Four patients had evidence of tuberculosis elsewhere in the body. Five patients had tubo-ovarian masses and adhesions demonstrated by culdoscopy. No endometrium was obtained in 9 out of these 18 patients.

This stresses the importance of endometrial biopsy or dilatation and curettage in cases of primary amenorrhoea (Deshpande *et al.*, 1966; Bhargav and Madan, 1969). Reiss (1958), Netter *et al.* (1955) consider intrauterine bands and adhesions as strongly suspicious of tuberculosis.

Severe Malnutrition

Among 8 patients with severe malnutrition, 6 had poor sexual development. Most of these patients also had moderate or severe anaemia, i.e., haemoglobin below 8 gms.

Diabetes

This patient of juvenile diabetes required 70 units of Insulin daily, was mentally retarded and had a history of amenorrhoea. This patient was asked to take intermittent cyclic hormonal therapy.

Delayed Menarche

All the patients who had started with spontaneous menstruation or secondary sexual developments without any obvious pathology are grouped under the heading of delayed menarche. These patients belonged to different age groups upto 25 years and were not confined to the age of 16 to 20 years. Out of 17 patients with delayed menarche, 15 patients started spontaneous menstruation, 2 patients conceived. They belonged to the age group of 19-20 years. Two patients gave history of tuberculosis elsewhere in the body (tuberculosis of spine and tuberculous glands). One patient had jaundice and hepatomegaly and another patient gave past history of schizophrenia.

Treatment And Results

Almost all patients received a high protein diet, vitamins and minerals for 3 to 6 months. Deshpande *et al.* (1966) noticed encouraging response with this therapy in 70% of patients. Patients with poor secondary sexual characters received in addition cyclic line of treatment after investigation. Most of the patients with genital tuberculosis came very late. Patients with faulty Mullerian development were explained about the prognosis. Only one patient with a very shallow vagina underwent vaginoplasty.

Twenty-three patient started having

spontaneous menstruation. Fifteen of these were from the group of delayed puberty. All these patients received general line of treatment. Three patients from the group of malnutrition and anaemia started having spontaneous menstruation after correcting the nutritional deficiency. Three patients with the genital tuberculosis started spontaneous and regular periods. One patient aged 21 years attended the out door for sterility and primary amenorrhoea. She was diagnosed as a case of hypopituitarism by low urinary gonadotrophins, and vaginal smears revealed low ovarian oestrogen. She started spontaneous regular menstruation after only one course of Clomid 50 mgms. for 5 days. She failed to come for second and third courses. One year after menarche, the endometrial biopsy on the 1st day of the period revealed anovulatory cycle. One patient started spontaneous menstruation after controlling the schizophrenic attacks. Many patients failed to attend the out patients department for a repeated follow-up, so essential for definite conclusions and better results.

Summary

One hundred and nine cases of primary amenorrhoea were studied for the causative lesions.

Important causative factors were faulty Mullerian development, tuberculosis and delayed menarche, often due to malnutrition.

Twenty-five patients with pituitary ovarian failure without any other obvious endocrinopathy could not be grouped into any definite ovarian or pituitary group due to lack of urinary gonadotrophin hormone estimation.

Twenty-three out of 109 cases were known to have spontaneous regular menstruation. Better follow-up of the

patients will help to improve the results of this treatment.

Acknowledgement

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