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Infertility and Diagnostic Study

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ABSTRACT: Direct evidence on age patterns of infecundity and sterility cannot be obtained from contemporary populations because such large fractions of couples use contraception or have been sterilized.Instead,historical data are exploited to yield upper bounds applicable to contemporary populations on the proportions sterile at each age.Examination of recent changes in sexual behavior that may increase infecundity indicates that sexually transmitted infections,the prime candidate for hypothesized rises in infertility,are unlikely to have added to infecundity to any great extent.These results imply that a woman in a monogamous union faces only moderate increases in the probability of becoming sterile (or infecund) until her late thirties.it appears that recent changes in reproductive behavior were guaranteed to result in the perception that infecundity is on the rise.Infertility is defined as the inability to conceive after one year of unprotected coitus and affects about 10-15% of couples.Obese women should be encouraged to lose weight by a combination of dietary modification and exercise.Even 5% weight loss has been reported to result in resumption of ovulation.Thus weight loss is definitely recommended.A common definition of sub- and infertility is very important for the appropriate management of infertility.Subfertility generally describes any form of reduced fertility with prolonged time of unwanted non-conception.Infertility may be used synonymously with sterility with only sporadically occurring spontaneous pregnancies.The major factor affecting the individual spontaneous pregnancy prospect is the time of unwanted non-conception which determines the grading of subfertility.Most of the pregnancies occur in the first six cycles with intercourse in the fertile phase (80%).After that,serious subfertility must be assumed in every second couple (10%) althoughafter 12 unsuccessful cyclesuntreated live birth rates among them will reach nearly 55% in the next 36 months.Thereafter (48 months), ~5% of the couples are definitive infertile with a nearly zero chance of becoming spontaneously pregnant in the future.With age,cumulative probabilities of conception decline because heterogeneity in fecundity increases due to a higher proportion of infertile couples.In truly fertile couples cumulative probabilities of conception are probably age independent.Under appropriate circumstances a basic infertility work-up after six unsuccessful cycles with fertility-focused intercourse will identify couples with significant infertility problems to avoid both infertility under- and over-treatment, regardless of age:Couples with a reasonably good prognosis (e.g. unexplained infertility) may be encouraged to wait because even with treatment they do not have a better chance of conceiving.The others may benefit from an early resort to assisted reproduction treatment.

LITERATURE REVIEW: In the review article we are diagnosis of infertility and easily known symptoms etc.These article basically helpful in research & developing technology.Infertility is defined as the inability to conceive after one year of unprotected coitus and affects about 10-15% of couples.Obese women should be encouraged to lose weight by a combination of dietary modification and exercise.Even 5% weight loss has been reported to result in resumption of ovulation.Thus weight loss is definitely recommended.Approximately 85% of infertile couples have an identifiable cause.The most common causes of infertility are ovulatory dysfunction, male factor infertility,and tubal disease.The remaining 15% of infertile couples have "unexplained infertility."Lifestyle and environmental factors,such as smoking and obesity,can adversely affect fertility.Ovulatory disorders account for approximately 25% of infertility diagnoses;70% of women with anovulation have polycystic ovary syndrome.Infertility can also be a marker of an underlying chronic disease associated with infertility.Clomiphene citrate, aromatase inhibitors such as letrozole,and gonadotropins are used to induce ovulation or for ovarian stimulation during in vitro fertilization (IVF) cycles.

03.INTRODUCTION: Infertility is defined as the inability to conceive after one year of unprotected coitus and affects about 10-15% of couples.[1]The chances of conception for a coupleat 12 months is 80% and at 18 months 90%.Reproductive failure can be attributed to the male or the female or both.This chapter will discuss the workup and management of the female.[4][1]The evaluation of the male partner including semen analysis and other diagnostic tests are reviewed in the next chapter.The couple should be seen together in an infertility clinic with

adequate time for counselling as well.Relevant tests should be performed in a proper order instead of doing a battery of investigations for all couples.[55]It is customary to wait for at least one year of unpro- tected intercourse before commencing investigations.However, there are exceptions such as when the woman is having irregular periods or the couple are elderly.In such cases it is best to start investigations and treatment early if the couple so desire.[53]

04.CAUSES OF INFERTILITY: The normal process of fertilisation can be interrupted at various levels resulting in infertility.

1. Male factor.
2. Ovulatory dysfunction.
3. Tuboperitoneal factor (including endometriosis).
4. Uterine factor.
5. Cervical and immunological factor.
6. Unexplained infertility.

05.CHECK BEFORE: It is important to do a detailed work up of both partners before invasive treatment as both may have problems.A proper history and clinical examination of both partners is a must.[9]The details of infertility age of the partners, type and duration of infertility-are considered.A coital and detailed menstrual history is important.Any evidence of infection in the past, previous pelvic surgery and details of previous infertility treatment are relevant.In the case of secondary infertility,the previous obstetric history is also taken.The clinical examination of the female should take into account BMI, examination of the thyroid and the breast,evidence of hirsutism and other signs of hyperandrogenism.The abdomen should be examined for any palpable masses.A thorough pelvic examination is a must and may pick up fibroids, endometriosis and infertility.[44][23][1]

06.INITIAL INVESTIGATIONS: The basic investigations that must be done before starting treatment are semen analysis,confirmation of ovulation,baseline ultrasound and documentation of tubal patency.[8]This will usually help us to arrive at a working diagnosis and decide on further treatment.Further tests may be needed in each section.Please refer to the chapter on examination of the gynaecological patient and imaging for a detiled description of ultrasound in evaluation of infertility.This includes details on the baseline scan,follicular monitoring and other uses of ultrasound in infertility.If there is amenorrhoea or irregular menstruation,the diagnosis is anovulatory infertility.Abnormal semen analysis indicates male factor infertility.[33]If the HSG shows tubal block it is tubal factor.Sometimes the clinical examination and ultrasound may show the presence of endometriosis or chronic PID.[41][23[12][9]Uterine factor like fibroids or congenital defects should be considered when the ultrasound or HSG shows an abnormality.The role of PCT and assessment ment of cervical factor is controversial.If all the tests are normal it may be unexplained infertility,but mild endometriosis is a possibility.[55][51][11][3][1]

07.MALE FACTOR: Male factor is the only cause in 20%, but may be a contributory factor in as much as 40%.Semen analysis is the basic test for evaluating the male factor and is an inexpensive and noninvasive test and so should form part of the very initial investigation.If the semen analysis is normal,there is no need to evaluate the male partner in detail.But if it is abnormal,a detailed clinical evaluation of the male is mandatory.[32][26][19][14][9]Assisted reproductive technology especially intracytoplasmic sperm injection (ICSI) has revolutionised the treatment of male infertility.The next chapter will elaborate on the investigation and treatment of male infertility including the details of the seminal fluid analysis.[44]

08.OVULATORY DYSFUNCTION: Ovulatory disorders account for about 30-40% of all cases of female infertility.They are also the most easily treated cause of infertility.If the woman is amenorrhoeic or oligomenorrhoeic,there is either anovulation or oligoovulation and treatment can be commenced at once.Women with regular menses are usu ally ovulatory,but very rarely some may be anovulatory.Hence they may need documentation of ovulation.[53]

08.01.CAUSES;

- PCOS
- Hpothalamic amenorrhoea
- Hyperprolactinaemia
- Other endocrinopathies
- Hypogonadotrophic hypogonadism
- Ovarian failure
- Decreased ovarian resers. (described at the end)

09.DOCUMENTATION OF OVULATION:

09.01.Clinical methods: Ovulation pain (mitthelschmerz) and mid cycle spotting occur in some women and is suggestive of ovulation.Cervical mucus at the time of ovulation is another clinical marker and appears copious and watery.But these are not definite proof of ovulation.[33][22][14][9][1]

09.02.Basal body temperature: This is a very simple and inexpensive method whereby the woman checks her temperature by a basal thermometer daily in the morning,before getting out of bed and before she consumes food.The principle is based on the thermogenic effect of progesterone.The secretion of progesterone by the ovary post ovulation causes a rise in temperature of about 0.5° C over the bascline recorded in the follicular phase of the menstrual cycle.[34][23]This temperature elevation lasts for about 10 days.So the chart is biphasic.A nadir may also be recorded at the time of the LH surge just prior to ovulation. The advantages are that it is inexpen sive and simple.There are several drawbacks.Firstly, ovulation can only be identified retrospectively and hence BBT cannot direct the timing of intercourse.Other causes of pyrexia may interfere with test interpretation.In a few ovulatory women the chart may be monophasic.Taking the temperature in the morning may create stress,which itself may contribute to infertility.Hence it is not much used today.[34][27][9]

09.03.Urinary LH or serum LH: Urinary LH kits are available over the counter and detect the midcycle LH surge in urine.This LH peak occurs between 8-20 hours before ovulation.They are usually detectable for only 12 hours and so twice daily sampling may be needed.The problem is again that it may create stress for the woman.In 10% women the urinary test may not be positive and serum LH may be necessary.[56][31][30][6]

09.04.Midluteal serum progesterone: This is the best and simplest method in women with regular menstruation.It is typically performed on day 21-23 of a 28-day cycle to coincide with peak proges- terone production.If oligomenorrhoeic, the measurements are repeated weekly from day 21 till menses.An absolute threshold has not been settled upon.Most clinicians would consider levels of 10 ng/ml.As indicative of ovulation and an adequate luteal phase.[11][4][2][1]

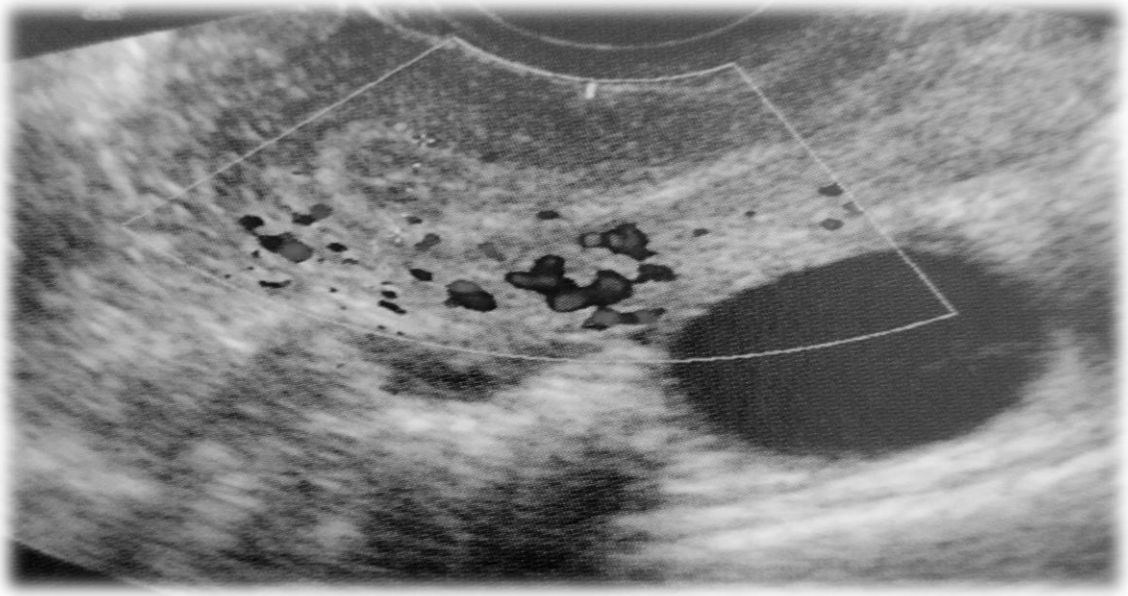

Fig.01.TVS showing a preovulatory fomcle and the typical trilaminar endometrium just prior to ovulation.

09.05.Endometrial biopsy: An endometrial biopsy showing secretory endometrium has been previously used for documenting ovulation and luteal phase defect.Subnuclear vacuolation is pathognomonic of ovulation.An enometrial histology showing a lag of more than 2 days was considered suggestive of luteal phase defect.But this is now mainly of historical interest due to the invasive nature of the test.[16][9]

09.06.Ultrasound monitoring: Ovulation can be documented by ultrasound visualisation of the dominant follicle and monitoring it until ovulation takes place.At this time the size of the follicle decreases and fluid appears in the cul de sac.It usually occurs when the dominant follicle is between 17-25 mm.It is also useful in detecting the rare condition of a luteinised unruptured follicle. Here typical rupture of the follicle does not occur, although serum progesterone rises into the ovulatory range.The endometrial thickness is also measured, and just prior to ovulation, the endometrium has a typical trilaminar appearance due to the effect of oestrogen (Fig.01).Routine use of ultrasound to documemt ovulation is not popular because of the inconvenience.It use is mainly in ovulation induction or superovulation.[14][9][3][1]

10.HORMONAL TESTS IN AMENORRHOEA OR OLIGOMENORRHOEA:

Progesterone challenge test

- FSH
- TSH
- Prolactin

The various differential diagnosis of anovulatory infertility should be considered in this group and further testing is indicated.For a more detailed description refer to the chapter on amenorrhoea.A progesterone challenge test is done in amenorrhoea and if there is a withdrawal bleed,it indicates that there is endogenous oestrogen and then the most likely diagnosis is PCOS.If the test is negative,then FSH testing is done to differentiate between hypogonadotrophic amenorrhoea and hypergonadotrophic amemorrhoea.If the FSH levels are high it indicates ovarian failure.If the levels are low it may be hypogonadotrophic amenorrhoea which could be due to hypothalamic or pituitary causes.A TSH and prolactin levels is indicated in all cases of amenorrhoea and oligomenorrhoea.By means of these tests usually the specific type of anovulation will be determined.A day 3 FSH level is also useful in assessment of ovarian reserve especially in women above 30.[55][23][17][13][11]

11.MANAGEMENT OF OVULATORY DYSFUNCTION:

The management of ovulatory dysfunction is by ovulation induction.Ovulation induction aims at the release of one egg per cycle in a woman who has not been ovulating regularly or has not been ovulating at all.In contrast,superovulation or controlled ovarian hyperstimulation (COH) aims at causing more than one egg to be ovulated and is indicated in the treatment of unexplained infertility and also in IVF cycles.[32][22][17][1]

11.01.PCOS:

This is the commonest cause of ovulatory dysfunction and accounts for 90% cases of oligomenorrhoea and 30% cases of amenorrhoea.This condition is discussed in detail in the chapter on PCOS and only ovulation induction is discussed here.[12][11][4][1]

11.02.Lifestyle modification: Obese women should be encouraged to lose weight by a combination of dietary modification and exercise.Even 5% weight loss has been reported to result in resumption of ovulation.Thus weight loss is definitely recommended.[45][3][1]

11.03.Clomiphene citrate:

This is traditionally the first line method of ovulation induction in women with PCOS.[32][22][14][9]

Mechanism of action: Clomiphene citrate is a selective oestrogen receptor modulator which binds to oestrogen receptors.This causes the hypothalamus to be unable to recognise the endogenous oestrogen level and mistakenly interpret it as low.[44][12]This interferes with the negative feedback resulting in increased GnRH and FSH.This increased FSH initiates folliculogenesis.Ovulation rates are about 80% but pregnancy rates are only 40%. This discrepancy is mainly due to the antioestrogenic effects of clomiphene on the cervical mucus and endometrium,which extend to the secretory phase.This is because the half-life of clomiphene citrate is high and may continue up to weeks.[45][2]

Dosage and monitoring: Clomiphene is usually com- menced at a dose of 50 mg daily for 5 days commenc ing from day 2-5 of the cycle.If ovulation does not occur,the dose can be stepped up to 100 or even 150 mg daily.Many gynaecologists do not increase the dose above 100 mg as higher doses increase the antioestrogenic side effects.If ovulation does not occur after three courses of clomiphene citrate,it is best to switch over to another drug. Once ovulation occurs the ovulatory dose is continued for as much as 6 cycles.Ultrasound monitoring can be commenced at least 5 days after the last day of clomiphene. Ideally a baseline scan should have been done on day 2 to exclude any preexisting cysts.[44][52][32][1]

Side effects: The main side effects are hot flushes.Other problems like visual symptoms,headaches,breast tenderness, abdominal bloating etc.Can also occur.The other problem is persistence of follicular or corpus luteal cysts.If any pre-existing cysts are present,it is best to wait for one month to allow the cyst to regress.The other main issues are multiple pregnancy in about 6% and ovarian hyperstimulation syndrome in 5%.[9][3][1]

Relationship with ovarian cancer: This is a controversial topic.It has been suggested that clomiphene citrate induces ovulation,disrupting the ovarian epithelium,thereby rendering the epithelial cells more vulnerable to malignant transformation.But this has never been substantiated by evidence.However the RCOG recommends that not more than 12 cycles of clomiphene citrate must be given.[34][23][18]

Clomiphene and adjuvants:Treatment:[GYNECOLOGY BOOK]

Metformin: Metformin and clomiphene had been found to result in higher ovulation rates than clomiphene alone.But recent RCTs show no such advantage.[41][7][2]

Bromocryptine: Some women with PCOS may have borderline hyperprolactinaemia and in such cases bromocryptine or cabergoline may have to be combined.

Human chorionic gonadotrophin (hCG): This is used as an adjuvant to clomiphene to cause ovulation in the dose of 5000-10000 units.It is given when the follicle attains a size of 18-25 mm and the endometrial thickness is at least 7 mm.[53][1]

Glucocorticoids: Glucocorticoids are now uncommonly used along with clomiphene as they increase insulin resistance further. If at all, the use is limited to women with high levels of the adrenal androgen DHEAS (Dehydroepiandrosterone (DHEA) is a hormone that your body naturally produces in the adrenal gland.DHEA helps produce other hormones, including testosterone and estrogen.Natural DHEA levels peak in early adulthood and then slowly fall as you age).[Google]

Human Menopausal Gonadotrophins (HMG): Clo-5 miphene citrate is administered as usual along with or followed by injections of HMG.Careful ultrasound monitoring is essential to minimise risk of multiple pregnancy and ovarian hyperstimulation syndrome (OHSS).[45][21][2]

Aromatase inhibitors:

The aromatase inhibitor letrozole is effective in inducing ovulation in clomiphene resistant patients.The aromatase enzyme is the final step in the formation of oestrogen.[7][2][1]

Letrozole will block the aromatase enzyme suppressing oestrogen synthesis resulting in low oestrogen levels.This in turn will increase the pituitary release of FSH and causes follicular development.The main advantages are that the half-life is very short (about 48 hours) and so the hypo-oestrogenic effects do not extend into the luteal phase as in the case of clomiphene.Also there is no depletion of oestrogen receptors as with clomiphene.So the endometrial response is better than with clomiphene.The dosage is 2.5-5 mg daily from day 3 onwards for 5 days.But letrozole is still not licensed for use in ovulation induction in many countries.[45][21][11][9]

Gonadotrophins:

Some women with PCOS will not respond to clomiphene citrate and aromatase inhibitors.These women require gonadotrophins for ovulation induction,either alone or in combination with clomiphene citrate or letrozole.Various preparations are available in the market.HMG is a combination of FSH and LH.Pure FSH and recombinant FSH are also available and are more useful in PCOS as these women already have LH hypersecretion.Careful monitoring with ultrasound and if necessary oestradiol levels are essential to optimise pregnancy rates while avoiding complications (Fig.02).The multiple pregnancy rates are about 20% and the incidence of mild hyperstimulation is about 20%.Severe hyperstimulation is seen In 1-2%.PCOS patients have a high number of small antral follicles which are potentially capable of stimulation by exogenous gonadotrophins leading to the above complications.[54][31]

Laparoscopic ovarian drilling (Fig.03):Initially surgical management was by wedge resection of the ovaries to reduce the androgenproducing tissue.Today laparoscopic ovarian diathermy is the surgical method of choice.Not only do the women have higher rates of ovulation following the procedure,there is also a lowered resistance to ovulation inducing agents.Also in comparison with gonadotrophins the miscarriage rates are less.In addition,it is a one-step procedure and multiple pregnancy and OHSS risks are eliminated.The main disadvantage is that it is an invasive procedure with all the attendant risks of general anaesthesia.A rare sequel is the risk of surgically induced premature menopause due to disruption of the ovarian vascular supply.[44][39][2]A commoner problem is the formation of periadnexal adhesions which may further compromise fertility.[29][23][1]

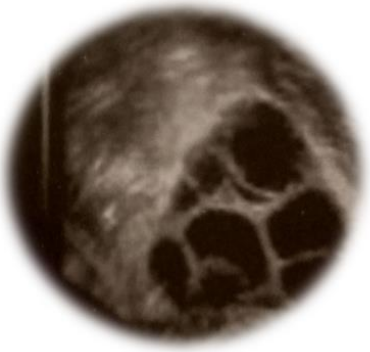

Fig. 02.USS appearance of hyperstimulated

Fig. 03.Laparoscopic ovarian drilling in PCOS.

In vitro fertilisation: This is the final stage in the management of PCOS.

Insulin sensitisers: Insulin resistance is thought to have a major role in the pathogenesis of PCOS.Hence insulin sensitisers were widely used in PCOS.Metformin is the drug which has been most studied and can be given in the dose of 1000-1500 mg in divided doses. Metformin inhibits glucose production without producing hypoglycaemia,while enhancing glucose uptake by the skeletal muscle.Side effects are gastrointestinal symptoms like nausea,vomiting,bloating and diarrhoea.Lactic acidosis can occur in those with impaired renal function.The contraindications are liver and renal failure.Gastrointestinal symptoms can be minimised by taking the drug with meals,increasing the dose slowly or using sustained release formulations.

Although the previous studies showed benefit,recently the results of some large RCTs have come to light where no obvious benefit is shown.Hence at the moment metformin is not considered a first line agent in the management of infertility.Hence its use is mainly in women with obvious insulin resistance and glucose intolerance.Further studies are needed to definitely establish its place in PCOS.Metformin is a category B drug and many continue

the drug in pregnancy,but the safety in pregnancy needs more studies to be definitely established.Other insulin sensitisers like rosiglitazone and pioglitazone whch are thiazolidinediones have also been found to be effective in PCOS,but are category C drugs and hence not much used.[44][39][9][1]

12.SOME OTHER CAUSE:

12.01.Hyperprolactinaemia:

This is also a cause of anovulatory infertility.Dopamine agonists like bromocryptine or cabergoline are used to counter the hyperprolactinaemia.Bromocryptine is commenced at a dose of 2.5 mg and the dose is slowly stepped up to even 15

mg daily.The main side effect is postural hypotension and hence the drug is best given at bed time.Long acting dopaminergic drugs are now becoming very popular.An example is cabergoline which is available as 0.5 mg tablets and can be given twice weekly.The response to treatment is usually prompt with ovulation rates of more than 90% and pregnancy rates of 70%.If the use of dopamine agonists alone does not result in preg- nancy,they can be combined with clomiphene citrate or gonadotrophins.The drug is usually stopped once pregnancy is diagnosed.In women with visual symptoms a pituitary macroadenoma must be excluded by CT scan or MRI.Surgery by transsphenoidal adenectomy is rarely indicated in case of drug resistance and intolerable side effects.Surgery may be indicated in case of suprasellar extension also.[45][22][14][9][6]

12.02.Hypothyroidism: This is another cause of anovulatory infertility and can be treated with thyroxine.Once the woman becomes euthyroid,ovulatory cycles ensue spontaneously.[4]

12.03.Hypogonadotrophic amenorrhoea: This condition is associated with low levels of FSH and LH and is usually due to hypothalamic or pituitary dysfunction.These women will not respond to a progesterone challenge and hence drugs like clomiphene citrate are not effective.Either pulsatile GnRH therapy or gonadotrophins can be used for inducing ovulation.Imaging studies are essential to exclude intracranial lesions.[6][1]

12.04.Hypergonadotrophic amenorrhoea: These are usually cases of primary or premature ovarian failure and have no oocytes.They are candidates for ovum donation and IVF.[3][1]

12.05.Hypothalamic amenorrhoea:A common cause of hypothalamic amenorrhoea is a low BMI as in anorexia nervosa and malnutrition.In such women,weight gain is the ideal treatment.

13.COMPLICATIONS OF OVULATION INDUCTION:

13.1.Ovarian hyperstimulation syndrome (OHSS): This is a life-threatening complication of medical induction of ovulation.Any patient undergoing ovulation induction is at risk,but there are certain impotent risk factors.Even though OHSS can occur with clomiphene citrate,gonadotrophins are much more implicated especially in the severe varieties of OHSS.The risk of mild OHSS is 20%,moderate OHSS 6% and severe OHSS 2%.Hence close monitoring with ultrasound and if necessary oestradiol levels are needed.The other main risk factor is PCOS especially the young and lean women with PCOS.Pregnancy is another risk factor due to the continuing stimulation by the endogenous hCG OHSS is 4 times more common in conception cycles.[12][3][1]

13.01.01.Classification:OHSS can be mild,moderate or severe.In mild OHSS,there may be abdominal bloating or pain and the ova ries are usually less than 8 cm in diameter.In moder ate OHSS,the ovarian size is 8-12 cm in diameter and there is associated ascites.In severe OHSS,the ovarian size is more than 12 cm in diameter with asciteshydrothorax,haemoconcentration,oliguria and anasarca.There may be complications like renal failure and thromboembolism.[43][2][1]

13.01.02.Pathophysiology:

Pathophysiology The main pathophysiology is abnormal accumulation of fluid in the third space, i.e.the peritoneal,pleural and rarely the pericardial space,resulting in intravascular volume depletion and haemoconcentration.The main factor implicated in the increased capillary permeability and leakage of protein rich fluid into the third space is vascular endothelial growth factor(VEGF).Interleukins are also implicated.[4][1]

13.01.03.Prevention: Prevention is very important by detecting high risk factors and careful monitoring.It is essential to start with the lowest dose of gonadotrophins in PCOS and stringent monitoring with ultrasound and oestradiol.It is best to cancel the cycle and withhold HCG if there are more than 3 mature follicles.Coasting or delaying the dose of HCG is also possible and may be helpful.An alternative is to use the initial agonis tic effect of GnRH agonists like leuprolide in place of hCG.[43][2][1]If possible, conversion to an IVF cycle is the best choice,in which case aspiration of the follicles may be protective.In such cases the embryos can be cryopreserved for transfer in a later cycle.Cabergoline is also being found useful to prevent severe OHSS.[2]

13.01.04.Management: The treatment is mainly supportive to produce symptomatic relief to the woman,maintain circulatory and renal function volute must beromboembolism.The intravascular volume fluids he maintained with oral fluids or intravenous fluids if there is hypovolaemia.Colloids are better and albumin is the volume expander of choice.Diuretics are to be avoided.Severe cases may require prophylactic heparin to be com menced.The ascitic fluid can be drained for symptomatic relief.[47][41][39]

13.01.05.Multiple pregnancy: This is another complication of ovulation induction,which increases the risks to the mother and fetuses,Those candidates at high risk are carefully monitored and if there are more than three

follicles,cycle cancellation may be considered.Or conversion to an IVF cycle and transfer of only 2 embryos is an option.Multifetal reduction can be tried, but carries a lot of risks.[36][33][1]

14.TUBOPERITONEAL FACTOR: Tubal and peritoneal factors are responsible for about 30-40% cases of female infertility.Tubal factors are usually due to previous pelvic inflammatory disease (PID),tuberculosis,post abortal or puerperal sepsis,appendicitis or previous pelvic surgery.Other causes are salpingitis isthmica nodosa,benign polyps and intratubal mucous debris.Peritoneal factors include peritubal and periovarian adhesions and can result from PID,endometriosis or surgery.[5][3][1]The risk of infertility after a single episode of PID is 12%,which increases to 23% and 53% after two and three episodes.Many women would have no definite history and in such cases subclinical chlamydial infection may be the cause.Symptoms like deep seated pelvic pain congestive dysmenorhoes and deep dyspareunia are suggestive of endometriosis,but may aho be found in chronic PID.[23][1]

Causes of tubal factor infertility:

- PID-Intratubal mucous debri
- TUBERCULOSIS-Following pelvic surgery
- APPENDICITIS-Cornual polyps

14.01.EVALUATION OF TUBAL PATENCY AND PERITONEAL FACTOR: An evaluation of tubal patency is usually part of the initial investigations.In women with anovulatory in fertility this can be deferred for some time.But usually if the woman does not conceive cycles of successful ovulation inddespite at least 6 tubal patency is indicated.In cases of secondary in fertility it is very important.The different methods of assessing tubal patency are discussed below.[32][12][6][1]

14.01.01.Hysterosalpingograpy[Timing]: This is the commonest method in vogue today for assessment of tubal occlusion.It is usually done within 10 days of the period and after cessation of flow.This is in order to reduce retrograde flow of the menstrual endometrium which can result in infection and endometriosis.Also during menstruation the uterine veins are much dilated and this can cause increased vascular intravasation.After 10 days of periods the chance of pregnancy is there and hence radiation is best avoided.[21][18][2][1]

14.01.02.Contraindications: There is a risk of infection after HSG and so current or past PID are both contraindications.In fact if there is clinical or sonological evidence of an adnexal mass or tenderness on bimanual examination,it is best to avoid a HSG and opt for a laparoscopy to assess the tubes and the pelvis.All patients are given a prophy lactic antibiotic like doxycycline.In summary,if pelvic pathology is suspected,a HSG is bypassed and a laparoscopy done.[57][33][23][21][3]

14.01.03.Procedure: After cleansing the vagina,a catheter or cannula is introduced into the cervix and iodinebased contrast is injected into the uterus,preferably under fluoro scopic guidance.The dye should fill the uterus and pass into the tubes and then spill freely into the peri toneum.The dye can be water soluble or oil soluble,Oil based dyes give better details of the tubal architecture,but there is a risk of lipid embolism and lipid granuloma formation.First,about 3-4 ml.of contrast is injected slowly in order to outline the uterine cavity.After that,about 5-10 ml. is injected to demon- strate tubal fill and spill or tubal obstruction. Hence usually two films are sufficient. Some take a delayed film after 20 min to check for pooling of the dye near the tubal fimbriae which may indicate peritubal adhesion.Proximal tubal block or distal tubal occlusion with or without hydrosalpinx may be seen.The commonest cause of proximal occlusion is tubal spasm and to alleviate this possibility,an antispasmodic can be given prior to the procedure.Other causes of proximal Block are tubal or cornual polyps,intratubal mucous debris and salpingitis isthmica nodosa.Most cases of tubal disease affect both tubes.Hence unilateral block is usually not pathological and is due to the dye following the path of least resistance.The commonest cause of distal occlusion with or without hydrosalpinx is PID.Sometimes the tubes may be patent,but there may be loculations of dye near the fimbriae and this may indicate peritubal adhesions due to PID or endometriosis.In tuberculosis the tubes may show a beaded appearance.[6][3][1]

Fig.04.HSG showing a normal uterine cavity and tubes with bilateral fill and spill.

14.01.03.Therapeutic benefit: Even though the HSG is a diagnostic method,it has some therapeutic value as well.This is possibly due to flushing of any inspissated mucus and debris from the tubal lumen allowing fertilisation and pregnancy to occur.[34][4][2]

14.01.03.Problems and limitations: Pain and discomfort is a problem.There is always the risk of reactivation of latent infection,especially tu berculosis.HSG for evaluating the uterine cavity is much less sensitive than three-dimensional ultrasound and hysteroscopy.Tubal spasm may give the false appearance of proximal occlusion.Again even if the tubes are patent, peritubal adhesions may not be evident in all cases.[11][3][1]

15.SELECTIVE SALPINGOGRAPHY: This is a radiological procedure which can be used to further evaluate proximal occlusion.Under fluoroscopic guidance,a small guidewire is used to allow selective tubal cannulation.

15.01.Sonosalpingography or Sion's test: In this method saline is infused into the uterus at the time of transvaginal ultrasound. Sonohysterography or visualisation of the uterine cavity is excellent for confirming small polyps and submucous fibroids.Sonosalpingography for visualising the tubes is less effective than sonohysterography,but can be tried as it is less invasive than HSG.It may be useful especially in young couples with a short duration of infertility.Recently albumin mixed with saline or echogenic particles like Echovist has been used and colour doppler employed to evaluate the tubes.When sonographic contrast medium like Echovist is used it is termed hysterosalpingo contrast sonography or HyCoSy.[32][11]

Fig. 05.HSG showing bilateral hydrosalpinges.

15.02.Laparohysteroscopy and chromotubation

15.02.01.Procedure: Laparoscopy is the gold standard to evaluate the fallopian tubes.In addition, peritoneal disease can also be evaluated and it allows visualisation of all the pelvic organs.A double puncture technique must be employed under general anaesthesia.Additional punctures can be used if any operative procedure is to be carried out.Hence laparoscopy can be both diagnostic and therapeutic.At the end of the procedure a detailed description of all the findings should be made.Some units provide videorecording.Chromotubation at the time of laparoscopy involves the transcervical instillation of a dye like methylene blue.Direct laparoscopic visualisation of the dye escaping through the fimbrial openings confirms tubal patency,A hysteroscopy must be combined with the laparoscopy and will detect any cornual polyps or uterine problems and is discussed further below.For more details refer to the chapter on endoscopy.[23][1]

15.02.02.Advantages: An advantage over HSG is that at laparoscopy,the external surface of the tube can be assessed espe cially the fimbria.Peritubal and periovarian adhesions can be picked up.Perihepatic adhesions may suggest previous PID.The other main advantage of laparoscopy is that endometriosis can be detected.A careful search must be made for endometriosis in the ovaries, uterosacral ligaments and peritoneum.In the case of tuberculosis,tubercles may be seen over the tube and the intestines.The external surface of the uterus can be assessed to differentiate between a bicornuate and a septate uterus. Other anomalies like didelphys and unicornuate uterus can also be picked up.In addition subserosal and intramural fibroids can be detected.At the same sitting most of these problems like endometriosis and periadnexal adhesions can be corrected.Polycystic ovaries can be punctured with cautery to increase the chance of ovulation.[45][23][1]

When is laparoscopy indicated?

Some are in favour of routine diagnostic laparoscopy for all patients.The argument for this is that minimal endometriosis can be detected and treated at the same sitting.Usually because of the anaesthetic risks involved, most gynaecologists would prefer to do laparoscopy when any abnormal findings suggestive of endometriois or PID are detected in the clinical or sonological work up, or when tubal occlusion or peradnexal adhesions are suspected on the HSG.In the former category,laparoscopy would be the first line diagnostic method bypassing a HSG.

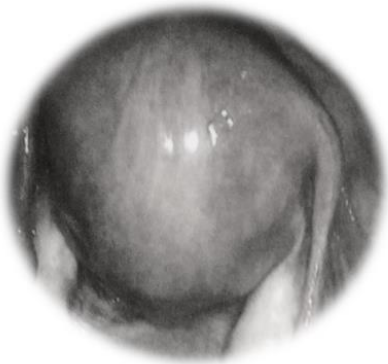

Fig.06.Normal pelvic anatomy at laparoscopy

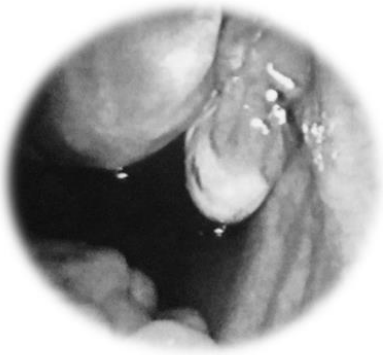

Fig.07.Laproscopic chromotubation showing the fill and spill of dye through the tubes.

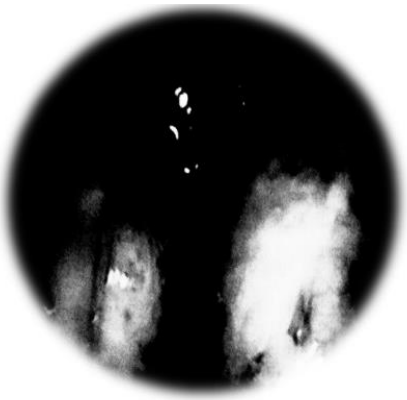

Fig.08.Bilateral chocolate cysts in endometriosis kissing ovaries.

Fig.09.Flimsy adhesions in the cul de sac in chronic PID.

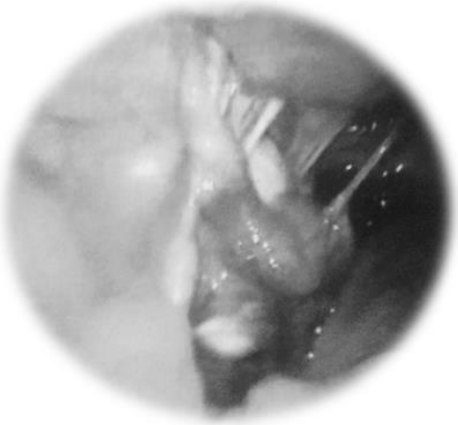

Fig.10.Peritubal adhesions.

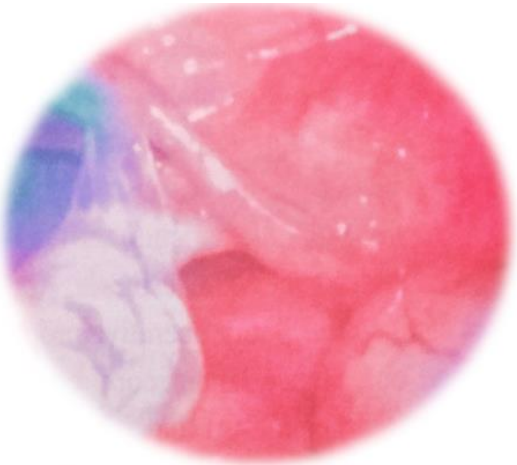

Fig.11.Periovarian adhesions.

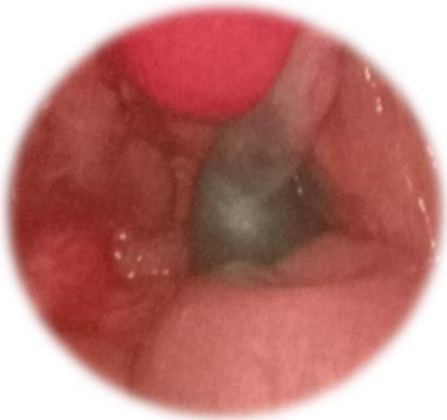

Fig.12.Distal tubal occlusion detected at chromotubation at laparoscopy.

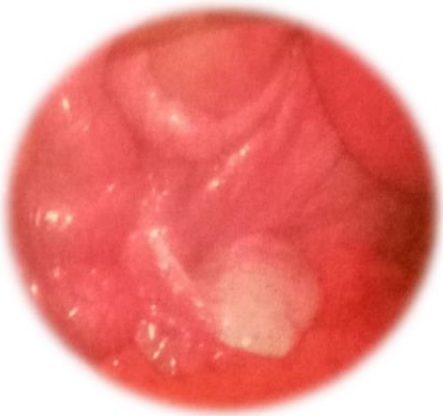

Fig.13.Tuberculosis showing the typical beaded appearance of the tubes.

15.02.03.Risks:

There are the risks of general anaesthesia,bleeding.Damage to the adjacent organs and infection.

15.03.Falloposcopy and salpingoscopy:
Salpingoscopy is the passage of a very fine endoscope through the fimbriated end of the tube at laparoscopy.Falloposcopy is much more complicated and involves the passage of a fine flexible fibreoptic device from the uterine cavity through the tubal ostia distally to the fimbriae.This allows direct fibreoptic visualisation of the tubal ostia and intratubal architecture.Both these procedures may allow visualisation of the inner lining of the tube,but the increasing use of IVF as a treatment for tubal disease makes such evaluations unnecessary and impractical.[45][43][38][1]

16.MANAGEMENT OF TUBOPERITONEAL FACTOR

16.01.Proximal tubal occlusion: Tubal spasm is the commonest reason for a false positive finding of proximal occlusion.The main causes are intratubal mucous debris,salpingitis isthmica nodosa and intratubal polyps (Fig 11).Selective salpingography and fluoroscopic cannula tion can be tried at the same time when the occlusion is diagnosed on HSG if there is a good radiology back up.Otherwise hysteroscopic cannulation of the tube can be attempted.If these fail,IVF is the usual resort.Tubocornual anastomosis using mi crosurgical procedures is an alternative.[47][3][1]

16.02.Distal tubal occlusion: Distal tubal occlusion is usually due to any post inflammatory condition like PID,tuberculosis,dometriosis and prior pelvic surgery.There may or may not be a hydrosalpinx.A hydrosalpinx can cause infertility not only due to the tubal occlusion;the fluid within the hydrosalpinx is directly embryotoxic and may prevent implantation.Cases of distal tubal occlusion can be corrected laparoscopically by fimbrioplasty or salpingostomy.Fimbrioplasty involves lysis of fimbrial adhesions or dilatation of the fimbrial phimosis.Salpingostomy or salpingoneostomy involves creating a new opening in case of distal tubal occlusion.Peritubal adhesions can also be surgically excised.However,IVF is generally the recommended treatment for distal tubal occlusion with hydrosalpinx.Removal of a hydrosalpinx has been shown to significantly increase IVF pregnancy rates.A simpler alternative to salpingectomy is proximal tubal occlusion by a clip device.Patients with both proximal and distal occlusion are also best treated by IVF.[3][2][1]

16.03.Endometriosis: Laparoscopic excision of endometriotic cysts.Adhesiolysis and fulguration of endometriotic deposits by diathermy or laser can be done.There is usually no place for postoperative medical therapy as this is the best time for conception to occur.If she fails to conceive,intrauterine insemination is tried,followed by in vitro fertilisation.The management is discussed in detail in the chapter on endometriosis.[4][1]

16.04.Reversal of sterilisation: Microsurgical principles should be adhered to usually laparotomy is used for reversal of sterilisation.But recently excellent reports are reported with laparoscopic tubal anastomoses The results depend on the method of sterilisation,site of anastomosis and presence of other pelvic pathology.The best results are following isthmic isthmic anastomosis and in cases where the sterilisation was done using clips.IVF is a viable alternative and is best if there are as sociated adverse prognostic factors.Also if there is no success following the reversal procedure.[41][33][1]

17.UTERINE FACTOR:
Submucosal fibroids,endometrial polyps,uterine anomalies and intrauterine synechiae can interfere with implantation leading to infertility.All of these are commonly associated with early recurrent pregnancy loss but can also contribute to infertility.However it is imperative that all other causes of infertility are ruled out before labelling as uterine factor infertility.[5][2]

NOTE

Proximal tubal occlusion is managed by hysteroscopic cannulation and if it fails, IVF Distal tubal occlusion and hydrosalpinx is best managed by IVF.Endometriosis best managed by operative laparoscopy and if it fails, IVF

17.01.EVALUATION OF UTERINE CAVITY

17.01.01.Hysterosalpingography: This has already been described under tubal factor and in many cases may help to delineate the uterine anatomy as well.Submucous fibroids may be seen as filling defects.Intrauterine synechiae also appear as irregular filling defects.widely separated in a bicornuate uterus,but usually 3D ultrasound or laparoscopy is needed to ascertain the diagnosis.For further details and HSG pictures refer to the chapter on congenital uterine anomalies.

17.01.02.Transvaginal sonography and sonohystero graphy: Transvaginal ultrasound will help in assessing the pelvis and the uterine cavity sonohysterography if done along with it is superior to HSG in both sensitivity and specificity for assessing the uterine cavity.This procedure has also been described as sonosalpingography under

tubal factor whereby saline is instilled into the uterine cavity along with transvaginal ultrasound.Sonohysterography is a very good method for delineating the endometrial cavity and may pick up small polyps and fibroids.

17.01.03.Three-dimensional ultrasound:3D ultrasound is fast becoming a very accurate method of assessing uterine anomalies and is almost replacing hysteroscopy for the diagnosis.Refer to the chapater on congenital uterine anomalies for de tails and pictures.[43][21]

18.MANAGEMENT:

Endometrial polyps can be easily removed hystero scopically.Large fibroids,submucous fibroids and those which distort the endometrial cavity are best removed.The role of other fibroids in infertility is generally not proven.Submucous fibroids can be removed hysteroscopically if more than 50% is pro truding into the cavity.Other fibroids can be removed at laparotomy or laparoscopy.If per formed laparoscopically,the surgeon's experience is a critcal factor as appropriate closure of the defect is necessary to prevent rupture in a subsequent pregnancy.Intrauterine synechiae can be lysed hysteroscopi-cally and if necessary, Foley catheter can be kept in the uterine cavity for 1 week after the procedure.Conjugated oestrogen 2.5 mg daily can be given for about 2 months to regener ate the endometrium.Pregnancy rates are very good,Uterine anomalies are more often associated with recurrent pregnancy loss than infertility.Hysteroscopic septal resection under laparoscopic guidance is recommended for women with recurrent miscarriage.Many gynaecologists would prefer to remove the septum even if infertility is the presenting symptom,as the possibility of a live birth is increased by reducing the chance of miscarriage and preterm labour.Surgical correction of a bicornuate uterus may be indicated in repeated pregnancy loss,but not if in fertility is the presenting complaint.[32][11][2]

19.CERVICAL AND IMMUNOLOGICAL FACTOR:

1. Hostile cervical mucus.
2. Antisperm antibodies in cervical mucus.

Cervical factor is thought to be a cause of infertility in less than 5% couples.Nearing ovulation,the cer vical mucus becomes thin,watery and elastic.This stretchability is termed spinnbarkeit and can be assessed by using two glass slides to pull the sample apart.At ovulation the spinnbarkeit should be at least 8 cm.Ovulatory mucus will also show a char acteristic fern ing pattern on microscopic examination of a dried sample.All these effects are due to the action of oestrogen.Antisperm antibodies can be found in semen,cervical mucus or in the male or female serum.[23][1]

19.01.Timing and procedure: This is historically the method which has been in vogue to assess the cervical factor in infertility.The PCT should be done just before the anticipated time of ovulation when the mucus is stretchable and allows the passage of sperm.Home LH kits can be used to time the test.A period of abstinence of 2-3 days is recommended.The couple to have coitus before the test.The timing of the PCT in relation to coitus is not agreed upon.2-12 hours has been suggested.A small amount of cervical mucus is withdrawn by means of a syringe.The amount clarity and spinnbarkeit is assessed.The mucus is pulled between two slides to assess spinnbarkeit and it should be at least 8 cm.Ferning is then assessed after drying.Then the number of sperms per high power field and motility are assessed by examining several fields.Usually at least 5 motile sperms must be seen per high-power field.[44][25][15][11][1]

19.01.01.Abnormal PCT

There are several reasons for an abnormal PCT.The commonest is incorrect timing of the test causing the cervical mucus to be thick and of poor quality.In such cases the test can be repeated in the next cycle.Other causes of poor mucus are anovulation,infections,prior surgery on the cervix and use of medica tions like clomiphene citrate.Clomiphene citrate may result in thick scanty mucus because of its antioes trogenic action.If there is absent sperm despite normal cervical mucus,coital problems must be suspected.Azoospermia or severe oligoasthenospermia can also cause the same result.The presence of immotile sperm or sperm which show the'shaking phenomenon suggests the presence of antisperm antibodies.[9][1]

ADVANCED MATERNAL AGE AND DECLINING OVARIAN RESERVE

Ovarian reserve indicates the quantity and quality of the oocytes in the ovary.The quality of the oocytes determines their fertilisation potential.Advanced maternal age may be associated with decreased ova a rian reserve or aging of the ovary.This is especially important in the case of women above 35.But chronological age is not always a good predictor of ovarian reserve.Various tests are available to assess ovarian reserve.These tests may be useful in that they may indicate a diminished chance for success in both spontaneous conception and IVF.They may also indicate a poorer response to gonadotrophins and increased chance of cycle cancellation.They may help in counselling women prior to IVF regarding their chance of success.No one test is considered ideal.There are passive and dynamic tests.

CLOMIPHENE CITRATE CHALLENGE TEST

This is an advancement upon the basal FSH test.Basal FSH levels are taken and then clomiphene citrate 100 mg/day is given from day 5-9 of the cycle and repeat FSH levels are again taken on day 10.If the woman has a good ovarian reserve,there will be a normal cohort of follicles producing adequate oestradiol and inhibin levels.These will be able to suppress the FSH levels back into the normal range by day 10.This test is more sensitive than basal FSH 5.If the ovarian reserve is poor,the FSH levels on day 10 will be high.This is especially useful in unmasking poor ovarian reserve in women with a normad.

19.01.02.Limitations of the PCT: Recently the role of the PCT has declined in important tance due to various factors.The reproducibility is less and the positive predictive value is poor.It is not uniformly predictive of pregnancy and many women with an abnormal PCT go on to achieve a pregnancy.The literature gives a variety of values and there is no consensus as to what constitutes a normal test.The main problem is incorrect timing.In such situations,even if the semen quality is good.The PCT may be abnormal.Another problem is that as the treatment for unexplained infertility is primarily intrauterine insemination (which bypasses the cervix and removes the antibodies from the sperm by washing) the routine assessment of cervical factor is not useful.The couple will have to IUI to due course whether the test is normal or abnormal.Hence there is no valid reason to perform the test.[14][12][8][3][1]

19.02.Antisperm antibodies: Both men and women can mount an antibody response to sperm.In men it may be in the semen and in women in the cervical mucus.Both men and women can exhibit antisperm antibodies in the serum.IgG can be found in serum,cervical mucus and semen.IgA antibodies are seen in cervical mucus and seminal plasma.The large IgM antibodies are only seen in serum and not in local secretions.Antisperm antibodies can be of IgG,IgM and IgA types.It must be remembered that ASA are present in about 10% infertile couples, but also in about 2-5% of fertile men and women.Hence the exact significance of antisperm antibodies in infertility is not definitely proven.The mechanism by which ASA may lead to infertility is not clear.The semen quality could be affected.There may be interference with capacitation,acrosome reaction,fertilisation and cleavage of the embryo.The aetiology of ASA is again unclear.In women,coital trauma has been proposed as a hypothesis leading to formation of ASA.But why they are not seen in all women is not clear.In men the blood-testes barrier protects the serum from exposure to sperm.Any condition which causes a break in this barrier like testicular trauma or torsion,reversal of vasectomy and genital tract infection can lead to autoimmunity.For detecting ASA in the semen,we have the immunobead test and the mixed agglutination reaction.Even if ASA is positive,the treatment is the same as of unexplained infertility,i.e,superovulation and IUI.Hence,the clinical relevance of testing for ASA is uncertain and it is not routinely performed.[7]

20.UNEXPLAINED INFERTILITY:

In about 15% couples,in spite of routine investigations,no obvious cause for the infertility may be found.This is termed unexplained infertility.The frequency of unexplained infertility will depend on the use of diagnostic

laparoscopy in the infertility work up.In centres where routine diagnostic laparoscopy is being performed there is more chance of minimal and mild endometriosis being picked up and so naturally the proportion of cases of unexplained infertil.Ity will be less.*Probable causes of unexplained infertility:*

- Minimal and mild endometriosis.
- Peritubal adhesions.
- Luteinised unruptured follicle.
- Occult defects in the ovum.
- Occult defects in sperm.
- Oxidative stress injury to sperm.

20.01.Role of diagnostic laparoscopy: The role of laparoscopy in the evaluation of unexplained infertility is controversial.If diagnostic ity.Laparoscopy is routinely performed,endometriosis and periutubal adhesions can be picked up and treated.There is no doubt that more of occult pathology can be detected if laparoscopy is performed rounal tinely,but the value of laparoscopy will depend on whether it influences treatment or pregnancy out in comes.Whether the treatment of mild endometriosis due and peritubal adhesions improves fertility rates is not yet clear.The alternative to doing a diagnostic laparoscopy initially is to proceed straight to empirical treatment of unexplained infertility,i.e.controlled ovarian hyperstimulation and intrauterine insemination.This is a rationale approach in women with unexplained infertility and normal TVS and HSG findings considering the debatable value of diagnostic laparoscopy,the surgical risks involved and the proven efficacy of empirical treatment in unexplained infertility.If the initial treatment is unsuccessful, diagnostic laparoscopy can be performed.The best approach is to involve the couple to actively participate in the discussion as to whether to go for empirical therapy or diagnostic laparoscopy.Whenever diagnose laparoscopy is performed there is no doubt.That the visible endometriotic lesions must be ablated and adhesions,if present, released.[57][54][4][1]

21.MANAGEMENT OF UNEXPLAINED INFERTILITY: Expectant management yields very low pregnancy rates in women with unexplained infertility.Hence empiric therapy in the sequence described below is commenced.

21.01.Clomiphene citrate and intrauterine insemination (IUI): This is the initial treatment adopted.Clomiphene citrate is used to increase the fertility rate in ovulating women with unexplained infertility.Along with this,IUI will increase the number of motile sperms and will also bypass the cervical factor.An alternative is the use of the aromatase inhibitor letrozole and IUI.Intrauterine insemination (IUI) is the initial step in managing male factor infertility and unexplained infertility.This procedure involves the placement of about 0.3-0.5 ml of washed,processed and concentrated sperm into the intrauterine cavity by means of a transcervical catheter. Washing will remove the seminalplasma and isolate the pure sperm. If unwashed semen containing the seminal plasma is introduced the uterine cavity,it may result in severe cramping to the prostaglandins. Additional methods to improve sperm motility are by centrifugation through density gradients or sperm migration methods.The success rates are about 8-9%.[45][43][34][1]

21.02.Gonadotrophins and IUI: Controlled ovarian hyperstimulation with gonadotrophins and IUI is employed when there is no success with the above.Traditionally the IUI is timed at about 34-36 hours following the hCG injection.Gonadotrophins can be given for superovulation in normally ovulating women and combined with IUI they increase the chance of conception.The success rate are around 16-20%.[32][12]

21.03.In vitro fertilisation: The question of how many IUI cycles should be attempted before switching over to IVF is not easily answered,as financial considerations should also be taken into account.Other factors such as the age of the woman will also be important.Probably after about 6 cycles of IUI failure,the next logical step would be to opt for in vitro fertilisation.[12][1]

22.TESTS TO ASSESS OVARIAN RESERVE:22.01.Basal FSH level: This is done on day 2 or 3 of the cycle.Most centres would consider a normal value to be < 10 mIU/mL..

ULTRASOUND ASSESSMENT OF THE OVARY

Total ovarian volume has been suggested to be as sociated with decreased ovarian reserve.Another ultrasound feature is the basal antral follicular count before starting stimulation.This is the number of fol licles on day 2 measuring 4 mm or less in diameter by TVS.If the number is between 6 and 10 it indicates a good responseless than 6 may indicate a poor responder.A high number of antral follicles should alert the clinician to the possibility of OHSS.

22.02.Inhibin B: This is also a measure of diminished ovarian reserve Inhibin B is a peptide growth factor produced by the granulosa cells.Diminished inhibin B is the basis of the increased basal FSH and the clomiphene citrate challenge test.This may be a very early sign of di minished ovarian reserve.[32][14[12]

22.03Antimullerian hormone: Also called mullerian inhibiting factor.This also has role in embryonic sexual differentiation.Low levels indicate poor ovarian reserve.

23.CONCLUSION: Infertility is defined as the failure to achieve pregnancy after 12 months of regular unprotected sexual intercourse.Approximately 85% of infertile couples have an identifiable cause.The most common causes of infertility are ovulatory dysfunction, male factor infertility,and tubal disease.The remaining 15% of infertile couples have "unexplained infertility."Lifestyle and environmental factors,such as smoking and obesity,can adversely affect fertility.Ovulatory disorders account for approximately 25% of infertility diagnoses;70% of women with anovulation have polycystic ovary syndrome.Infertility can also be a marker of an underlying chronic disease associated with infertility.Clomiphene citrate, aromatase inhibitors such as letrozole,and gonadotropins are used to induce ovulation or for ovarian stimulation during in vitro fertilization (IVF) cycles.Adverse effects of gonadotropins include multiple pregnancy (up to 36% of cycles,depending on specific therapy) and ovarian hyperstimulation syndrome (1%-5% of cycles),consisting of ascites,electrolyte imbalance,and hypercoagulability.For individuals presenting with anovulation,ovulation induction with timed intercourse is often the appropriate initial treatment choice.For couples with unexplained infertility,endometriosis, or mild male factor infertility,an initial 3 to 4 cycles of ovarian stimulation may be pursued;IVF should be considered if these approaches do not result in pregnancy.Because female fecundity declines with age,this factor should guide decision-making.Immediate IVF may be considered as a first-line treatment strategy in women older than 38 to 40 years.IVF is also indicated in cases of severe male factor infertility or untreated bilateral tubal factor.Approximately 1 in 8 women aged 15 to 49 years receive infertility services.Although success rates vary by age and diagnosis,accurate diagnosis and effective therapy along with shared decision-making can facilitate achievement of fertility goals in many couples treated for infertility.60–80 million couples suffering from infertility every year worldwide, probably between 15 and 20 million (25%) are in India alone.According to a report by the World Health Organization (WHO),one in every four couples in developing countries is affected by infertility.[CURRENT NEWS]

The 7% of women were childless in India in 2015-2016 which increased to 12% in 2019-2021;the increase was statistically significant.Childlessness was positively associated with level of education, age at marriage,body mass index (BMI) level,and presence of thyroid.[INCLUDING RESEARCH REPORT]

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