

The Role of Reproductive Surgeons/Surgery has Got Rekindled with Plateauing of IVF Results and Advances in Technology: A Comprehensive Narrative Review

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ABSTRACT

Earlier we have reviewed the role of surgery in need for fibroids removal prior to *In Vitro* Fertilization (IVF) in improving success rates, management of inoperable recurrent endometrioma presenting as severe incapacitating pain following leuprolide acetate depot by aspiration, recurring again at 2 years subsequently for sclerosing therapy presented as a case report updated advances in classification along with reproductive surgeries in mullerian anomalies. Updated management of oncofertility-does the use of vsels appear practical in the near future in human malignancies replacing cortical tissue and testicular tissue, autologous Platelet Rich Plasma (PRP) probability of it becoming a revolutionary therapy in the field of gynaecology and reproductive endocrinology and infertility, role of surgery in endometriomas and endometriosis, adenomyomas, tubal surgery. Here we have tried to outline how prior to the invention of IVF, reproductive surgeries which were believed to be fertility sparing were properly acknowledged, role of reproductive surgeons became obsolete. With the plateauing of IVF result interest has got rekindled with considerable advantages of reproductive surgeries is this field. Additionally, newer instrumentation as well as surgical procedure has evoked and made it attractive for reproductive surgeons for improvement of their expertise with regards to conservation of future fertility as well as train future Reproductive Endocrinology and Infertility specialist (REI) in view of solidifying this field of yielding pregnancies to maximum of infertile cases even in patients having cancer surgeries or earlier cryopreservation of oocytes in say patients with turners syndrome etc.

Keywords:

Reproductive surgeries, Fertility, Hysteroscopy, Laparoscopic ovarian drilling, Robotic surgery.

Introduction

The Origination of Reproductive Surgery

Prior to the invention of *In Vitro* Fertilization (IVF), reproductive surgeries which were believed to be fertility sparing were properly acknowledged. To start with fertility sparing surgeries like myomectomy was initiated. Subsequent to that surgery in the form of primary treatment for infertility (for instance tubal surgery) along with ultimately moved towards surgery for escalating fertility (for instance septoplasty). Once Assisted Reproductive Technology (ART) was introduced greater expansion of our capacity of tackling diseases of structural etiology was substantially escalated. This was followed by further evolution regarding treatment of non structural etiologies of infertility which has considerably resulted in the improvement of effectiveness of human reproduction. With the enhancement of efficacy in addition to ease of accessibility to ART, the part of reproductive surgeon was appearing to become redundant, with certain infertility specialists pointing that we should pay obituary to this topic [1]. Luckily advancements got attained apart from in case of instrumentation, as well as strategy in addition to in the scope. In case of its maximum

repetitiveness reproductive surgery is promoting fertility preservation at the time of considerable impact or damages to the ovarian reserve leading to Diminished Ovarian Reserve (DOR) as well as is influencing the probability of capacity of and aiding in continuation of pregnancy in addition to escalating the probability of a pregnancy in the cases of Mayer-Rokitansky Kuster Hauser syndrome with congenital lack of uterus. In view of the drastic escalation of outcomes obtained following ART have started reaching a plateau over the last 10 years, the part of reproductive surgeon is undermined in the form of being key for maximization of outcomes for the patients having a trial for conception, along with preserve this probability for future. Here we have attempted to review the historical aspect of reproductive surgery in addition to emphasizing the part of surgical strategy for the treatment of patients with infertility.

Surgery for Uterine Fibroids

The detailed description of historical aspect is available in reference 2. Only brief talk about subsequent to vaginal hysterectomy in year 120 and the abdominal hysterectomy in 1843 [3] came followed by myomectomy with the idea of preservation of fertility in 1845 [4]. Nevertheless, in preantibiotics era in addition to lack of blood transfusion escalation of mortality along with morbidity it took numerous decades till in 1922 Bonney made the invention of the uterine artery clamp which aided in the reduction of morbidity (Figure 1) [2].



Figure 1: Courtesy ref no. 2: Bonney clamp for uterine artery clamping.

Following this invention Bonney performed greater than 700 myomectomies with remarkable reduction of mortality(7;1.1%) [5]. Despite, the fame of Bonney was with regards to his pioneering work of fertility sparing radical surgery in case of cervical cancer he further gave recommendations apart from early myomectomy but further for Ovarian cystectomy for fertility preservation.. Bonney advocated utilization of this

advantageous surgery in case of a germane young woman stopping need for loss of lady's womb in a young woman getting utilized.

Gradually with the enhancement of survival in 1970's came the era of microsurgical techniques by Victor Gomel as well as Celso Ramon Garcia correlated with utilization of smaller bore sutures, careful tissue tackling in addition to heparinized saline-all of which aided in remarkable escalation of clinical outcomes. These all enhanced the acceptability of these fertility sparing surgeries in the form of safe along with efficacious strategies in correct choice of patients. Moving from abdominal myomectomy towards minimally invasive myomectomy then became the acceptable surgical approach in broad group of women from reproductive age.

The initial laparoscopic myomectomy was revealed by the German Kurt Semm in 1979 [6]. Subsequently came the introduction of the experience robotic assisted laparoscopic myomectomy in Michigan United States [7]. This minimally invasive strategy is correlated with substantially diminished hospitalization, lesser incidence of postoperative readmission, lesser surgical morbidity in contrast to abdominal myomectomy [8]. Although there are advantages still no clarification exists over the impact of fibroids on the reproductive capacity as well as if their removal does result in improvement of reproductive results.

Generally it has been acknowledged that the fibroids which are distorting cavity (FIGO 0,1,2 as well as 3) possess a negative influence over the reproductive results (Figure 2) [9].

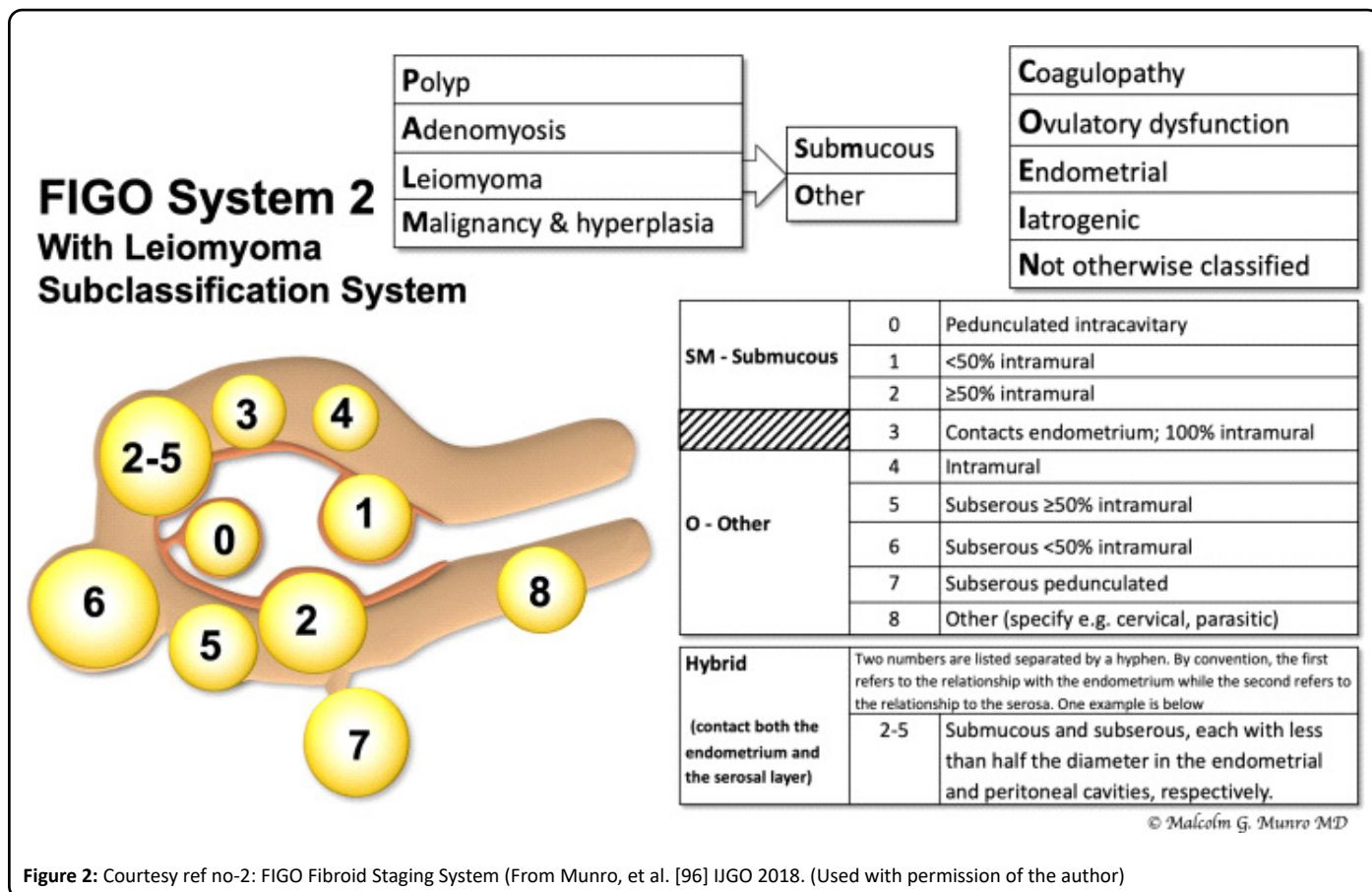


Figure 2: Courtesy ref no-2: FIGO Fibroid Staging System (From Munro, et al. [96] IJGO 2018. (Used with permission of the author)

On achieving pregnancy on the existence of fibroids which are distorting cavity possess a correlation with escalation of aberrant placement of placenta, Early Pregnancy Loss (EPL) abruptio placentae, malpresentations or Intrauterine Growth Restriction (IUGR) as well [10]. Retrospective studies pointed that removal of the fibroids encroaching the cavity by hysteroscopic strategy primarily might abrogate these risks [11].

The hysteroscopic myomectomy got generated subsequent to adapting urological instruments meant for resection with regards to treatment of prostate hyperplasia accessibility has been there since 1980. Neuwirth RS, along with Amin HK conducted first hysteroscopic myomectomy [12]. Subsequent to tackling initial problems advancements with regards to fluid management systems, shifting from monopolar to bipolar electrosurgery in addition to utilization of media which is isotonic possessing media meant for distension ensured events that had safety along with were efficacious [8]. Greater advances in instruments for instance hysteroscopic tissue morcellators, have aided the surgeons in being comfortable regarding taking place at the time of resection of large sized FIGO 0, as well as 1 kind uterine fibroids. In contrast to instruments meant for resection, morcellators aided in persistence of fragment removal for maximization for observing without utilization of electrosurgery that has the capacity of complications resulting in hands having lesser experience.

With regards to FIGO 3 or greater, minimally invasive strategy is usually believed to be the maximum accessible surgical route. Despite introduction of laparoscopic strategy, by Kurt Semm from Germany, Cameron Nezhat's adding of video with laparoscopy was the major reason of broad utilization of this approach in view of the other observers in the room having active part in the surgery. Additionally, utilization of diuted vasopressin, barbed surgical sutures in addition to power morcellation with regards to extracting tissues correlated with considerable reduced Operation Room (OR) time along with substantially diminished depletion of blood in contrast to earlier reiteration of this method [13].

As per its part in conservation of fertility apart from fertility escalating management, numerous uncontrolled studies have indicated with regards to laparoscopic myomectomy for fibroids which are distorting cavity has been correlated with lesser pregnancy loss in contrast to no surgery. Moreover, different large systematic reviews have revealed pooled pregnancy rates of 49-57% subsequent to laparoscopic myomectomy [14]. Nevertheless, no Randomized Controlled Trial (RCT), have been conducted for assessment of part of minimally invasive myomectomy regarding escalation of fertility. The heterogeneity of the uterine fibroids in addition to patients features present botheration for acquisition of the influence of fibroids on fertility. As long as RCT are fashioned in addition to conducted we can just presume with the causal interpretation regarding the resection of fibroids which are distorting cavity is a probably promising for women attempting to attain a pregnancy [15].

A matter which remains controversial is the part of myomectomy in case of FIGO 3 to 4 fibroids determined to be over 3-4 cm in size for escalating fertility. Despite, when fibroids are not distorting cavity, intramural fibroids might result in dysfunctional endometrial in addition to myometrial blood supply,

escalate uterine contractility as well as cause modification of local hormonal along with paracrine environment of the endometrium [16] (Figure 3).

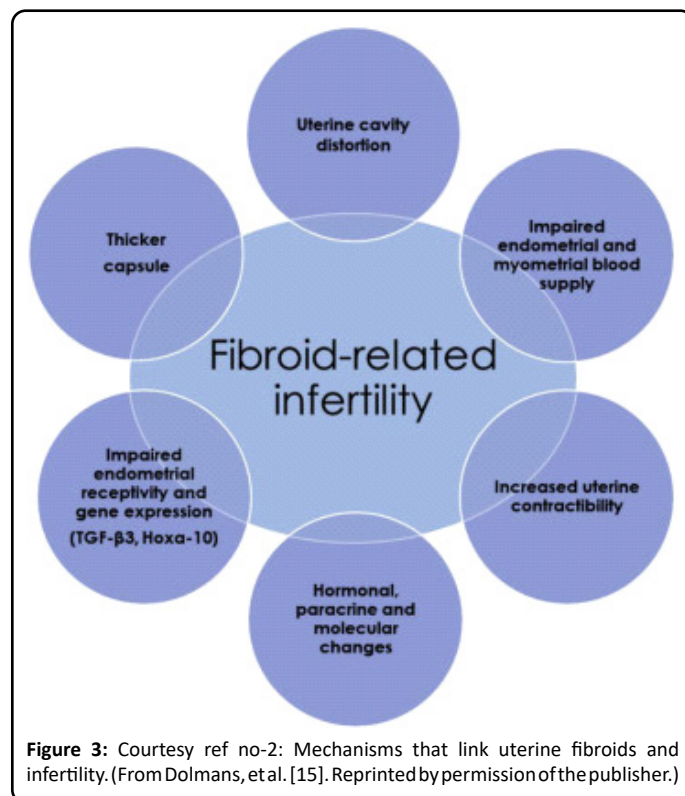


Figure 3: Courtesy ref no-2: Mechanisms that link uterine fibroids and infertility. (From Dolmans, et al. [15]. Reprinted by permission of the publisher.)

Of the outcomes obtained which corroborate their resection is the enhancement of quantities of Transforming Growth Factor- β (TGF- β) liberated by large intramural fibroids which possesses the capacity of changing bone morphogenetic protein-2 (BMP-2), along with HOXA 10 (member of the homeobox gene family) expression [17]. HOXA 10 portrays a key messenger in controlling endometrial receptivity continues to be persistently lesser once there is existent a submucosal fibroid pointing towards large intramural fibroids despite not distorting cavity, might be possessing inimical actions. Requirement of greater studies is there for attaining insight over the advantages of invasive myomectomy of non cavity distorting uterine fibroids. In the latter part we describe the more innovative in the form of non abating alternative to invasive myomectomy.

Surgery for Endometriosis Along With Adenomyosis

The isolation of endometrial glands with ectopic placement got initially observed in 1860 as well as got revealed by the pathologist Carl von Rokitansky in 1860 [18]. Subsequently in 1920 inimitable naming in addition to descriptions were made by Sampson along with Frankl respectively. In the same time period Cullen, et al. conducted surgeries for pain treatment for situations believed to be endometriosis along with adenomyosis currently; nevertheless, with considerable risks of mortality. Despite, a diagnostic laparotomy comprised the single approach to diagnose endometriosis in that era standardized therapy constituted of Total Abdominal Hysterectomy (TAH) with bilateral oophorectomy. Cullen failed to have realization dawned with regards to restricted resection are efficacious in case of milder disease. Furthermore, the 2 advances in these 100 years have been the advent of Combined Oral Contraceptives (COC) pill in

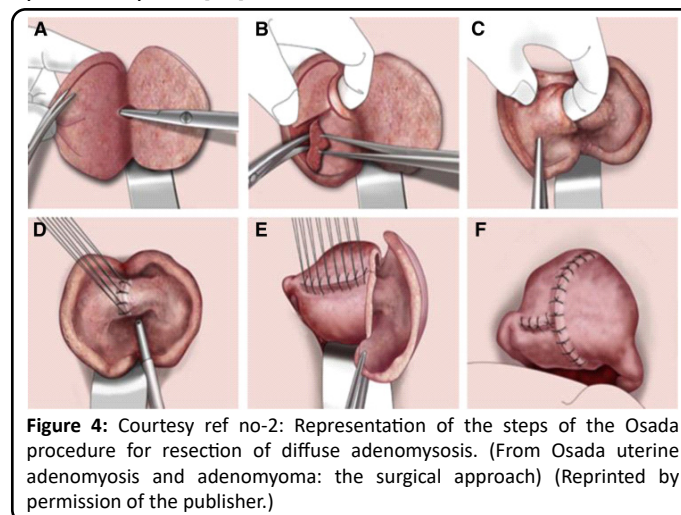
addition to laparoscopic surgery [19]. Now surgeons possess the capacity of treating pelvic pain or in case of tubal factor infertility with utilization of a minimally invasive strategy.

With regards to pelvic pain in view of endometriosis, despite the strategy in addition to techniques conducted have undergone advancements, surgery persists to be a significant part in the treatment of endometriosis. Regarding superficial areas destroying these damaged areas involved ablating such lesions in contrast to excising was illustrated to possess akin efficacy for treating pelvic pain in a Randomized Controlled Trial (RCT), nevertheless, in case of deep infiltrating endometriosis full excision is needed with it getting acknowledged with regards to depth of the lesions in addition to their usual intricate association with adjacent organs [20,21]. In the context of infertility fraction in view of endometriosis, the advantages of surgical diagnosis as well as destroying the disease is not clear. Marcoux, et al. [22], randomly enrolled patients with mild endometriosis into 2 groups 1 group for diagnostic laparoscopy/surgical ablation along with observations were that removal of disease by any means escalated pregnancy rates with regards to pregnancy which was unassisted. Nevertheless, on combination of outcomes obtained in an akin fashioned randomized study that was revealed 2 years later the patients number in an acknowledged endometriosis pointed that requirement for surgical ablation for achieving Live Birth Rates (LBR) unassisted was 12. Nevertheless, for patients who were having asymptomatic unexplained infertility with the presumption of 30% incidence of endometriosis observed at diagnostic laparoscopy were required to have laparoscopy for a single extra unassisted LBR, a quantity that has led to advocate no laparoscopy in such patients with *In Vitro* Fertilization (IVF) being given preference in the form of alternative for maximization of fertility [23-25].

Surgery which is fertility sparing with regards to dysmenorrhoea in addition to menorrhoea in view of adenomyosis started getting escalatingly used subsequent to displaying successful wedge resections got revealed in 50's to 1960's [26]. Surgery which is fertility sparing gets lesser used in contrast to in other pathologies, partially in view of the restrictions imposed for precise diagnostic methodologies despite recent advancements in imaging modalities might aid in greater isolation of correct surgical subjects. Additionally, the absence of precise planes correlated with focal as well as diffuse kinds of this problem causes a greater complex resection in contrast to that with myomectomy. Although, there are such hurdles surgical innovations by Japanese surgeons generated numerous innovative strategies over last certain decades for maximization of the quantities of adenomyosis resected with concurrent fertility conservation. 2 noticeable approaches which have been posited having the aim of total adenomyosis getting excised are inclusive of asymmetrical dissection methodology in addition to triple flap one (Figure 4) [27].

Long term following of 2123 uterine adenomyomectomies which got reported from 13 Japanese centres was 449 pregnancies leading to 361 live birth delivery rates [30]. Nevertheless, the larger incision essential with these surgical strategies escalates the risks of uterine rupture in a subsequent pregnancy to 3-6% in contrast to baseline of 0.005% in case of a nonscarred uterus along with <1% of subsequent to a prior myomectomy/

hysterotomy scar [27].



Surgery for Adnexa

Polycystic Ovary Syndrome (PCOS)-ovaries: Another fertility sparing surgery not involving the uterus is conducted on the ovaries. Of the maximum previous ovarian techniques were inclusive of ovarian wedge resection in addition to drilling of ovaries. The goal of both of these surgeries was disturbance of the intraovarian androgen generation along with restoration of folliculogenesis in a substantially lesser androgenic milieu [29]. Stein as well as Leventhal originally detailed Ovarian wedge resection in their pioneering work over 7 patients whose presentation was having amenorrhoea as well as Polycystic ovaries [30]. On realization with regards to this strategy leading to remarkably escalated incidence of post surgical adhesion generation (in greater than 90% of patients) that could not be accepted, thereby ovarian drilling replaced it. The initial ovarian drilling got conducted in 1984 [31].

Ovarian drilling comprises of creation of numerous holes over the ovarian cortex with the utilization of electro-surgical instruments has been acknowledged to be the second line strategy for patients with resistance to agents meant for induction of ovulation [32]. To start with it was advocated to make 10-20 holes/ovary, in view of the illustration of the following ovarian failure, their was modification to creation of holes not more than 4/ovary with the utilization of particular electro-surgical fashion of energy delivered [33]. Patients having earlier failure of induction of ovulation, ovarian drilling portrays an efficacious manner with regards to restoration of ovulation function in addition to normalization of androgen quantities along with correlated symptoms with PCOS. Furthermore, pregnancy rates were apparently akin to those observed subsequent to gonadotropins treatment; however with considerably lesser risk of multiple pregnancy as well as Ovarian Hyperstimulation Syndrome (OHSS) [34].

Endometriomas-ovaries: William Wood Russell was the person who firstly detailed the existence of endometrial tissue amongst ovaries-alias ovarian endometriomas [35]. Subsequently considerable knowledge has been attained in the context of the manner by which endometriomas influence ovarian reserve.

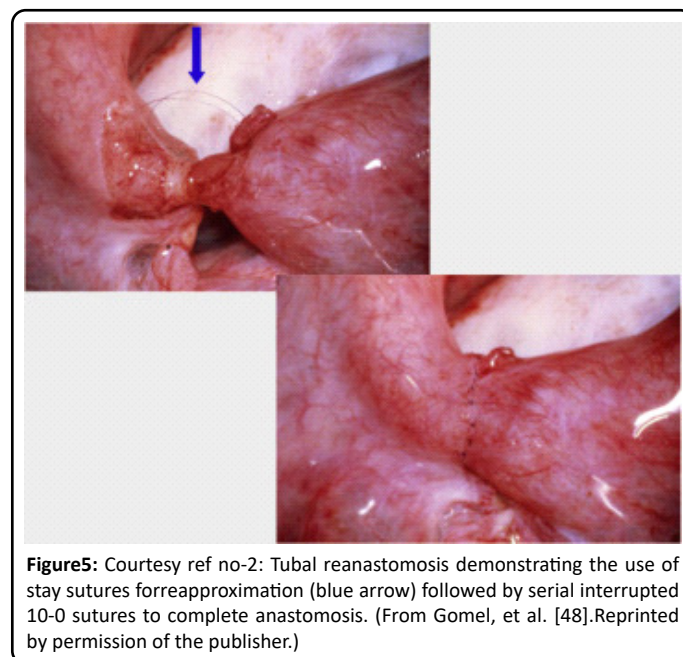
The chronic inflammatory injury which results secondary to endometriomas leads to propagation of tissue fibrosis that might

cause displacement in addition to reduction of ovarian follicles followed by reduction in oocyte quality in addition to ovarian reserve [36]. Moreover, endometriomas might further result in diminished ovarian reserve by evoking premature follicular generation along with atrophy, thus causing augmentation of ovarian insufficiency. Kitajima, et al. [37], recently illustrated that endometriomas might result in premature activation of Granulosa Cells (GCs) resulting in escalated follicular atresia with resultant diminished quality of remnant Primordial Follicles (PF).

Numerous methodologies have been detailed with regards to annihilation of ovarian endometriomas. Differentially from other cysts endometriomas being invasive possess a significant correlation with tissue fibrosis beneath its presence. Thereby laparoscopic drainage along with ablation portray early surgical strategy however were correlated with substantially greater rate of recurrence. Cystectomy, which implicates stripping of the cyst wall, partially or in its entirety portrayed a natural evolution; however in which significant expertise was the need of the hour. On contrasting with ablation, cystectomy was correlated with significant inimical influence over antral follicles count as well as Antimullerian Hormone (AMH) quantities [38]. What comprises of remarkable significance is the decision making with regards to initial surgical attempt is total excision of the ovarian endometrioma in view of repeated surgeries for recurrent cyst gets correlated with significant depletion of ovarian reserve in contrast to a single lone surgery [39]. Innovations by the laparoscopic surgeon with the utilization of hydrodissection in addition to laser vaporization have been illustrated to be safe with ovarian conservation strategies [40,41]. Earlier sclerotherapy utilizing ethanol or lidocaine has been considered an option in infertile cases who present with pain as an option [9] portrays another minimally invasive surgical attempt which might be attempted transvaginally by a Reproductive Endocrinology and Infertility specialist (REI) represents who are already accustomed to performing transvaginal needle procedures. Nevertheless, its part is restricted apparently to patients that represent poor surgical candidates whose cysts prevent safe oocyte recovery [42,43].

Tubal operations: In 1896 the first fallopian tubes reconstruction got attempted [44]. Nevertheless, not till introduction of microsurgical strategies in 60's and 1970's this procedure came in modern use. Previous attempts for salpingostomy used Mulligan hood-a silastic device which was sutured to the opening of tubes for sustenance of patency, however the requirement was a second look laparotomy 3 months subsequently to its removal [45]. In view of the production of considerable adhesions from the originating laparotomy as well as need for invasive methodologies, temporary tubal patency methodologies were not accepted. In 1967 Sweden's Swolin K subsequent to his observations of intraperitoneal delivered hydrocortisone diminished postoperative adhesions, with him conducting 33 salpingostomies through laparotomy for restoration of fertility [46]. 10 intrauterine pregnancies (30.3%) were revealed by him in addition to 12.1% rate of ectopic pregnancies. 3 years subsequently Leslie Brown who bore the First IVF child Louis Brown further underwent bilateral salpingostomies for attenuation of tubal blockade [47]. Nevertheless, to her

misfortune no success was attained however 8 years later it turned out to be the fortune of numerous infertile women (Figure 5) [48].



Additionally combination with surgical strategies for reduction of acute inflammatory response along with avoidance of postoperative adhesions initiated by Gomel V as well as Garcia C, there was drastic escalation of successful anastomosis. In case of modern date minimally invasive strategies in women amongst 18-30 years, 30-33 years in addition to 34-49 years might anticipate pregnancy rates of 73%, 64% as well as 46% respectively [49]. Besides, the kind of the sterilization done (84% with utilization of clips vis a vis with 41% using bipolar electrocautery) in addition to the extent of the residual tube (≥ 4 cm vs ≤ 4 cm) portion both factors of significance with regards to prognosis of reproductive success [50].

Just till 1990's tubal operations were believed to be treatment strategies for getting over tubal disease at the time when escalation of IVF success rates with regards to LBR moved from 14% to 31.6% [51]. In case of this time period of Assisted Reproductive Technology (ART), it is significant to take into account various factors for instance ovarian reserve, coexistent diagnosis for infertility, number of children wanted, apart from patients preference, religious thought processes along with accessibility of ART.

In contrast to IVF cumulative Live Birth Rates (LBR) over time period of 5 years were commensurate to ones having undergone tubal reanastomosis (52% vis a vis 60%) other than women <37 years who had >cumulative LBR with tubal reanastomosis (72.2% vis a vis 52.4%) [50]. The ART results in 2001 given by American Society of Reproductive Medicine (ASRM) in 2001 registry [51].

Mullerian Abnormalities

Other than the tackling of the uterine leiomyomas, endometriosis, as well as adnexal disorders reproductive surgeons have to tackle complicated mullerian abnormalities. An

updated classification of mullerian abnormalities was given by the American Society of Reproductive Medicine in 2021 (ASRM) [52]. This newer gadget with correlated interactive website gives a useful clinical gadget in aiding in differential diagnosis with regards to these abnormalities. In future this gadget would be aiding in surgical videos for aiding in better detailing of the surgical of these complicated mullerian abnormalities.

Presumably one of the most common abnormalities which we in the form of the REI specialist have to tackle is the uterine septum. Presentation of women having uterine septum is an escalation of risk of infertility, recurrent miscarriage as well as preterm birth [52]. Retrospective outcomes obtained have pointed that an incision might escalate pregnancy rates [53]. A recent multicentre Randomized Controlled Trial (RCT), The Randomized Uterine Septum Transaction Trial (TRUST) was not able to illustrate any escalation of successful reproductive outcomes in case of women who underwent septum excision [54]. Substantial restricting factors of their study was wide inclusion criteria, definition of uterine septum was considerably liberal, with significant time consumption in enrolment for instance 8 years for 80 patients getting enrolled were believed to be the significant restricting factors in view of generalization of their outcomes. Till trials that have been fashioned vigorously we have persistence of uncertainty with regards to the advantages in our thought perception of septum incision. Managing greater complicated abnormalities by surgical means are canonically conducted for abrogation of pain in addition to conservation along with restoration of fertility in case of obstructive abnormalities. Having the acknowledgement regarding broad kinds of pathologies are present with mullerian abnormalities, this newer classification would aid in diagnostic assessment along with surgical management of these complicated mullerian abnormalities (Figure 6) [55].

Furthermore vaginal abnormalities might be present alone or correlated with uterine aberrations for instance Mayer Rokitansky–Kuster–Hauser Syndrome is the diagnosis for an individual presenting with lack of mullerian development in a patient presenting with primary amenorrhea and no apparent vagina [56].

Regarding the patients with vaginal agenesis, neo vaginal generation by stretching the vagina, its replacement or approaches regarding its augmentation. Generation of a neovagina through its stretching with the utilization of dilators was first detailed by Frank Rin (1938) a reproductive endocrinologist in New York [57]. To start with one begins in the posterior direction and then after 2 weeks changing direction upwards towards the usual line of vaginal axis, pressure is applied with dilators available commercially for 20'/day to the point of modest discomfort. Gradually utilizing larger dilator a functional vagina can be created in several months [58-62]. Plastic syringe covers can be used instead of the expensive commercial glass dilators. A very easier and effective technique is to hold the dilator in place with a tight garment, maintaining pressure by sitting on a running bicycle seat (mounted on a special stool or even a bicycle) [63]. In case of women having unsuccessful dilation surgical vaginal stretching by utilization of Vecchiotti technique is remarkably successful obtaining a vaginal length of 8-9 cm in routine. Its basis is utilization of an

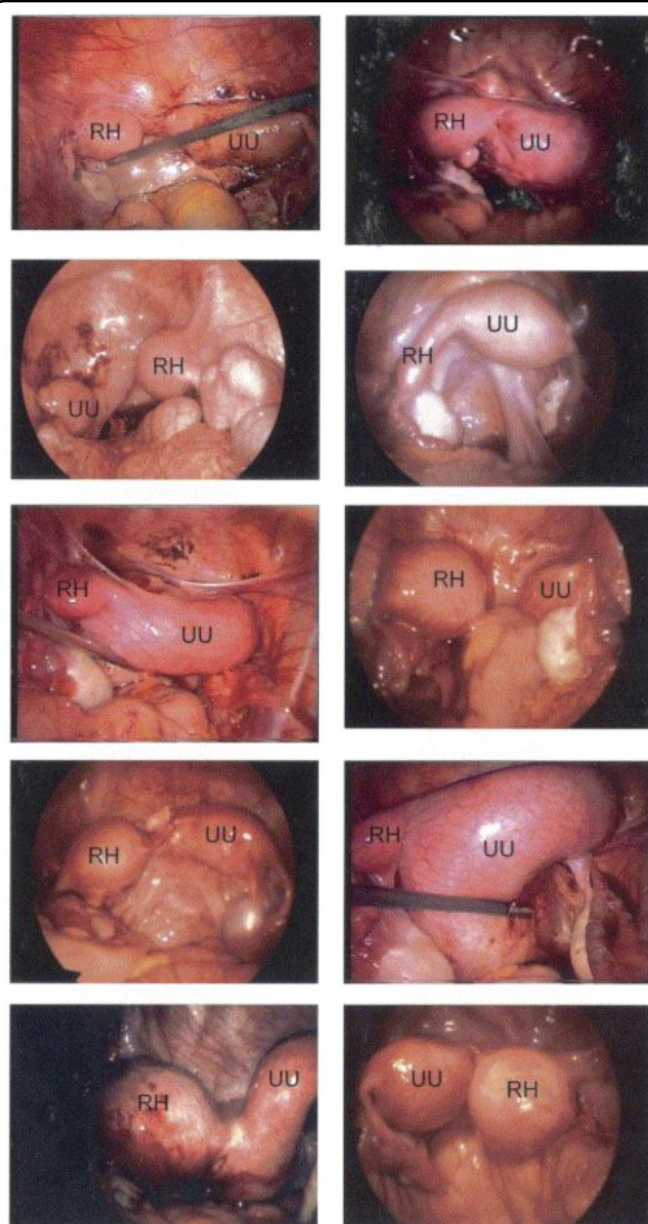


Figure 6: Courtesy ref no-2: Wide range of surgical findings at the time of laparoscopic management of noncommunicating rudimentary horns. (From Fedele, et al. [55]. Reprinted by permission of the publisher.) UU $\frac{1}{2}$ Unicornuate uterus; RH $\frac{1}{4}$ rudimentary horn.

olive with its placement in the perineum using an abdominally tensioning gadget with application of cranioventral tension at the time period of 4-7 days. Besides stretching techniques neovagina generation is feasible by utilization of replacement tissues [64]. The McIndoe in addition to Davydov techniques are dependent on either a split thickness skin graft or use of peritoneum respectively. Innovative strategies implicate use of novel tissues like buccal mucosa, tilapia skin fish or use of placental membranes that aid in augmentation of the tissues present in the manner which further escalates tissue characteristics as well as their functional working.

Ectopic Pregnancies

Apart from escalating surgeries reproductive surgeons possess the part in surgical treatment of ectopic pregnancies, particularly cervical in addition to caesarean scar implantation pregnancies.

About 2% of the total pregnancies in the United States are ectopic, out of which 10% have implantation in non tubal areas [65]. Advancements in Imaging technologies REI's have produced innovative minimally invasive methodologies for tackling the patients who are stable basically by Ultra sonography-driven local injection. REI's have sufficient expertise for performing these techniques in view of routine utilization of Trans Vaginal Ultra Sonography (TVS) for oocyte retrieval. Injection of methotrexate or potassium chloride have been substantially detailed earlier [66]. Incidence of caesarean scar pregnancy apparently has been escalating in view of escalation of number of caesarean deliveries throughout the world with a study quoting an incidence as high as 1 in 531 women possessing a caesarean scar would generate a caesarean scar pregnancy [67]. First line treatment usually comprises of direct injection of methotrexate or potassium chloride as well as aspirating with a needle with/ without systemic methotrexate delivery. Operative removal by a laparoscopic strategy or USG driven or vacuum aspiration are believed to be the first line surgical strategies where a gestation sac is present in which case either methotrexate or potassium chloride availability is not there or are contraindicated [68]. Furthermore, REI's possess remarkable skills with regards to diagnosis in addition to management of early pregnancies in view of earlier determination of pregnancy through TVS amongst 5-7 wks is correlated with remarkably lesser risk of maternal morbidity to contrast to diagnosis in addition to treatment initiation at over 9 weeks GA (5.9 vs 32.4%, odds ratio 0.14; 95% CI:0.1-0.4) [69].

On successful resolution of caesarean scar pregnancy is attained need for caesarean scar defect repair is there in case the patient wants a further pregnancy. Handling of these kind of patients is preferably done by the REI's in view of their surgical experience with the acknowledged fact of escalated bleeding along with need for hysterectomy occasionally as well.

Besides, the risk of implantation in the following pregnancy caesarean scars niches have been known to be correlated with a considerably diminished successful IVF along with Intracytoplasmic sperm injection (ICSI) cycle (15.9% vis a vis 23.3% OR:0.6; 95% CI :0.5-0.9) [70]. It has been posited to take place in view of alterations in endometrial receptivity, tough embryo transfer, dysfunctional myometrial contractility as well as embryotoxic blood components getting trapped within this niche. There is no clarification regarding the revision has any correlation with escalation of reproductive outcomes, reduction in recurrence rates or alterations in placenta accreta spectrum condition.

Reproductive Surgery Future

Transplanting uterus: Absolute Uterine Factor Infertility (AUI) impact less than 5% of women are in the reproductive age [71]. Of those having presentation in the form of AUI earlier other than IVF with the utilization of a gestational carrier used to be the exclusive manner of attaining a biologically correlated child. Nevertheless, utilization of a gestational carrier is not legal throughout the world, expensive where legally allowed in addition to not aiding the woman to get the satisfaction of bearing a pregnancy in her own body. Transplanting uterus was illustrated to be a plausible manner for getting over this problem, giving a newer archetype for patients with AUI.

Despite, the first uterine transplantation was conducted in Saudi Arabia in the year 2000 (a patient who had a hysterectomy in view of Post Partum Haemorrhage (PPH), practically 14 years subsequently the first live birth was obtained in Sweden by Branstrom M, et al. [72]. Subsequently it has been attempted to decline surgical morbidity to living donors by obtaining organs from either demised or brain dead both of which have yielded live births [73]. It has been determined that greater than 60 uterine transplantations have been conducted leading to greater than 20 live births as detected by May 2020 [74]. Uterine transplantations in US (n=33) one year survival of the graft had been 74% (23/31 recipient) of which 58% (19/33 recipient) had borne 21 live births [75]. The average GA at birth of neonates was 36 weeks 6 days (30 ± 1 -38 weeks) as well as average birth weights 2860 (1310-3940), median (range) (58th-6th-98th) percentile. Once the morbidity the recipient as well as obstetrical/neonatal results escalate it has been pointed that enhanced interest would be evoked in utilization of uterine transplantations in aiding in chance for pregnancy in case of AUI as well as those who had a hysterectomy, patients having presentation in the form of androgen insensitivity syndrome, robust Ashermans Syndrome in addition to transgender female patients.

Oncofertility: For the female cancer patients having requirement for gonadotoxic chemotherapy or pelvic radiotherapy, various surgical strategies are present for conservation of future fertility further than oocyte along with embryo cryopreservation. Despite, certain are beyond the REI's, usual practice, procedures like radical trachelectomy however others for instance cryopreservation of ovarian tissue, ovarian transpositions in addition to uterine fixations, can be well tackled by the reproductive surgeons.

McCall from the Louisiana States University documented the first patient ovarian transpositions for a patients with Cervical Cancer in 1958 [76]. It has been well acknowledged that the oocyte possesses substantial sensitivity to ionizing radiation with just 4-6 Gy sufficient for the depletion of a minimum of 50% of all ovarian follicles [77]. The degree of injury to ovarian reserve is basically based upon the full radiation dosage delivered to the ovary, baseline ovarian reserve as well as age of the patient. In case of ovarian transpositions movement of 1 or both ovaries out of the pelvis has been implicated canonically as lateral along with as cephalic the extent the full anatomy aids in a void of total bulk of the anticipated radiation field of the pelvic radiotherapy (Figure 7) [78].

Subsequent to 1958 patients with colorectal cancer as well as pelvic lymphomas who are posted for pelvic radiotherapy. In a recent meta-analysis where 892 patients underwent ovarian transpositions with subsequent brachytherapy, 94% illustrated conservation of ovarian function following radiotherapy, how diminished to 65% in the ones who had external beam radiation therapy, with/without brachy therapy [79]. Subsequent to gonadotoxic therapy ovaries are canonically left back in the transposed localization with regards to ovarian stimulation in view of migration back towards the radiated region is correlated with escalated rates of ovarian insufficiency [80]. Although, it yields substantial success in conservation gone through of future fertility less than 10% of women below the age of 35

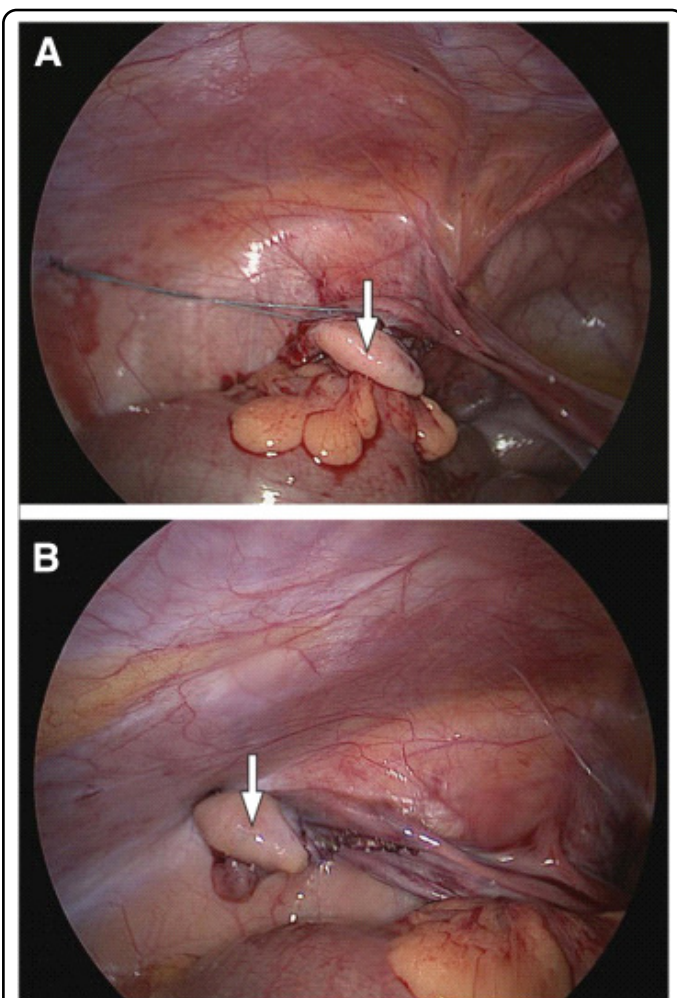


Figure 7: Courtesy ref no-2: Demonstration of ovarian transposition in a prepubescent girl. (A): Demonstrates the left ovary that is sutured to the abdominal wall with a non-resorbable suture; and (B): demonstrated the ovary after transposition to the left paracolic gutters. (From Irtan, et al. [78]. Reprinted by permission of the publisher.)

having gone through pelvic radiotherapy for cervical, anal or uterine cancer had gone through ovarian transpositions [81].

Apart from ovaries the other organs in the pelvis that are radiation sensitive are inclusive of injury to the uterus along with endometrium in particular myometrial fibrosis, uterine vascular injury as well as endometrial injury that might restrict successful implantation in addition to live birth [82]. The first patient who had uterine transposition as well as fixation was conducted in case of a 26 year old patient having rectal adenocarcinoma by Ribeiro R of Brazil in 2017 for conferring protection to both uterus along with ovaries from adjuvant pelvic radiotherapy prior to rectosigmoidectomy [83]. Total mobilization of uterus along with ovarian pedicles, colpotomy in addition to placement in the upper abdomen was implicated in this procedure. Subsequent to fixation to the anterior abdominal wall, the cervix was anastomosed with the fascia of the umbilicus with regards to aiding in the efflux of the menstruation. In this particular early patient reported uterus was reimplanted into the pelvis 18mths subsequent to pelvic radiotherapy when her menstrual cycle resumption occurred regularly. Despite, this surgical procedure might be out of the realm of REI's, a simpler procedure where involvement of uterine fixations to the anterior abdominal wall

with utilization of resorbable interrupted sutures with out need of the colpotomy in addition to mobilization of pelvic vessels might be possible from technical angle [84].

Probably the maximum attractive surgical gadget for conservation of fertility would be cryopreservation of in addition to transplantation. The first frozen thawed ovarian tissue transplantation was conducted in 1999 [85]. As detected by 2019 it has been determined that greater than 130 live births have been attained [86]. From technical angle this procedure implicates laparoscopic excision of the ovarian cortex strips which undergo processing followed by cryopreservation. The tissue which has been thawed its implantation can be done orthotopically into the remnant of ovary or other regions in the pelvis for instance ovarian fossa or broad ligaments/heterotopically. Canonically heterotopic transplantation is conducted in the retroperitoneum with in the pelvis or abdominal wall with the clearcut benefit of easy accessibility for ultimate ovarian stimulation or when, robust pelvic adhesions or disease is present which results in avoidance of heterotopic transplantation. Just 1 live birth has been documented subsequent to heterotopic transplantation in a patient in which bilateral oophorectomy had been conducted [87]. One of the problems with heterotopic transplantation is viability of graft with regards to tissue tension, temperature along with blood supply of the rest.

Finally, the future endeavour for ovarian tissue transplantation would be the capacity of safe conservation along with transplantation of whole ovaries-specifically in case of prepubertal women who usually do not possess enough tissue mass for conservation of ovarian cortex strips. Two significant problems that are having requirement for overcoming for its viability:

- we need improvement of our capacity of processing as well as cryopreservation of solid organs in the manner which ensures least tissue injury.
- requirement for generating greater successful manner for ensuring revascularization of the tissues at the time of transplantation. The utilization of extracellular tissue matrix scaffolds are getting actively evaluated with regards to ensuring least reperfusion injury in addition to maximizing tissue viability as well as growth during transplantation time .

Innovative Upcoming Procedures Along With Gadgets

Vaginal natural Orifice Transluminal Endoscopy (vNOTES): The invention of Bonney's clamp with regards to uterine artery ligation aided the reproductive surgeons in their capacity of surgical performance in the presence of a considerably vascular uterus aided in the generation of numerous innovative surgical strategies. In these modern days innovative minimally invasive surgical approaches have made it further indiminishing the already least scar strategy to a single scar or further no abdominal scar. Laparoscopy with a single port in addition to Vaginal Natural Orifice Transluminal Endoscopy (vNOTES) represent innovative procedures whose indications are enhancing. Furthermore vNOTES possesses remarkable probability in surgical tackling of ovarian torsion, Ectopic pregnancies in the tube along with ovarian cystectomy as well.

Radiofrequency ablation: Apart from innovative newer strategies, further innovative treatment models for instance utilization of Radiofrequency Ablation (RFA) for uterine leiomyomas. Additionally, RFA tries to stimulate coagulative necrosis amongst a myoma for attaining reduction in volume of the myoma, thereby myoma correlated symptoms [88]. At present 2 gadgets accessibility is in US namely—Acessa (Hologic) as well as Sonata (Gynesonics) systems, where utilization of laparoscopic in addition to transcervical strategy respectively. Nevertheless, these gadgets are just acknowledged for utilization in symptomatic fibroids in case of patients who do not want any future fertility. Moreover RFA portrays an intriguing procedure, in view of no requirement for myometrial incisions/sutures; however in an akin fashion tissue diagnosis is also not aided or resection of the myoma tissue. There are scarce outcomes accessible with regards to reproductive results in reproductive aged women wanting fertility. Recently, Polin, et al. [89], conducted a systematic review, where they isolated 50 pregnancies subsequent to 923 RFA patients (10 transcervical as well as 40 laparoscopic). Of these there were 6 spontaneous miscarriages (12%) along with 44 full term pregnancies (88%) with just 2 revealed complications, placenta praevia, along with, Post Partum Haemorrhage (PPH), with degenerated myoma getting expelled. There were no uterine ruptures, no invasive placentation or documented preterm delivery. Greater outcomes are required for making sure with regards to safety in addition to effectiveness of RFA for patients with uterine fibroids who want any future fertility. Till we manage to get such outcomes, their part in reproductive aged women continues to be restricted. Their part in case of adenomyomas or diffuse adenomyosis also continue to be probable answers where present surgical procedures are substantially morbid as well as medical treatment inefficacious for women who want future fertility.

Regenerative medicine: Another field which is the attractive is the utilization of regenerative treatment for instance stem cells for abrogating endometrial damage. Intrauterine adhesions occur in view of injury to the regenerative layer of the uterine lining/endometrium. On robust injury, there is depletion of the capacity of endometrium to heal in addition to lead to regrowth of the normal overlying stratum functionalis. The present standard of hysteroscopic breakdown of adhesions got generated by REI's, with the idea of restoration of the normal architecture of the uterine cavity. Stem cell treatment in combination with tissue engineering 3D scaffolds possess the capacity of restoration of the basal layer which got injured from dilatation and curettage/myomectomy. At present, endometrial, mesenchymal, bone marrow, along with umbilical stem cells have been documented to possess a positive action on the healing of the damaged endometrium [90]. It has not been acknowledged with regards to use of these therapies would be for primary avoidance subsequent to surgery for patients with susceptibility to adhesions formation or in the form of secondary avoidance for the ones already having prior disease. Attempts have been made in regenerating other reproductive tissues is attractive in restoration of normal reproductive working on advancement of age. Active assessment of Mesenchymal Stem Cells (MSC's) in their utilization in case of Premature Ovarian.

Insufficiency (POI), or conditions like turners syndrome patients oocyte cryopreservation might help. In view of their angiogenic in addition to anti apoptotic characteristics [91]. Besides MSC's therapies for POI, other workers are evaluating the part of Platelet Rich Plasma (PRP) for restoration of the ovarian working along with enhancement of IVF success rates [92-95]. Requirement for gaining insight in generating greater safety along with effectiveness of these innovative procedures prior to their utilization in the form of therapeutic strategies is there.

Conclusion

In the past 2 centuries in addition to Specifically past 20-30 years reproductive surgery used to be the only strategy being accessible therapies for patients with infertility however were thought to be obsolete with the advent of IVF/ART. Remarkable advancements in these surgeries, procedures, strategies have drastically escalated both with enhancement of technologies as well as greater information sharing. Concurrently there was an upsurge in the ART results, thereby our thought process with regards to need for surgery reduced. Nevertheless, at present reproductive surgery has attained newer premature ovarian failure which has again brought reproductive surgery to the forefront for tackling patients with infertility. In case of reproductive surgeons possessing expertise for performing these techniques might aid in conservation of reproductive working in addition to might aid in enhancement of ART results as well. The initiation of reproductive medicine possess roots in reproductive surgery, that represents a skill which will continue to be an integral part of our capacity of optimizing ART results. Furthermore, passing on these skills to our next generations of Reproductive Endocrinology and Infertility specialists (REI) is significant.

Conflict of Interests

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