

INFERTILITY IN AFRICA: A REVIEW

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SUMMARY

Infertility is a worldwide problem today because of the psychological and physical suffering that it causes and also the economic consequences it has, both for the infertile couples who seek medical help and for the society as a whole.

The problem has therefore been critically looked into based on expert opinion and by extensive literature review highlighting the basic rudiments of the normal reproductive requirements, where damages, defects or lesions can occur and how best these can be remedied in order to restore as much as possible the reproductive potential of the afflicted couple.

Efforts have also been made to delve into the current approach to and discuss as much as possible the recent advances techniques in the management of infertility with particular emphasis on assisted reproduction. The ongoing controversy over the possibility of human cloning is also discussed.

KEY WORDS: Infertility, scope of problem, management, recent advances.

INTRODUCTION

Although infertility is not a disease in the classic sense, it is an extremely important personal concern for many couples and a significant health problem for the medical profession. It is a health problem with very definite psychological, emotional, physiological and social implications. It is a problem with a stigma which often leads to mental disharmony, matrimonial disharmony, divorce and ostracism.

According to the World Health Organisation (WHO)^{1,2} infertility is defined as the inability to establish a pregnancy within a specified period of time, usually 1 year, in couples of child reproductive age who are having regular intercourse without contraception.

In considering infertility as a health problem, the above definition is too restrictive and unrealistic for women aged 30-35 years, who have voluntarily delayed child bearing, to wait for 1 year before being attended to.²

In Africa where the premium is so much on pregnancy shortly after marriage and in Nigeria in particular where pregnancy is sometimes a precondition for marriage, the above definition is not only unrealistic, but is also psychologically unacceptable.^{3,9}

The problem of infertility in the developed and developing world has grown to the extent that it is now a

social concern. Evidence for this comes from the many reports on the subject in news magazines and some popular press. Gynaecologists and Obstetricians who are interested in reproductive health for women throughout the world cannot afford to ignore the problem.^{1,3,5,10-14}

The objectives of this review therefore are to highlight the basic requirements of normal reproduction (endowed by nature), what can go wrong, the scope of the problem, what remedies are available including the recent advances in assisted reproductive technologies.

Suggestions have also been proffered on the prevention and early treatment of sexually transmitted diseases STDs and pelvic inflammatory disease (PID) which have been clearly recognized^{12,4,20} worldwide as the main cause of primary and secondary infertility and also ectopic pregnancy.

The Scope of the Problem (Prevalence/ Epidemiology)

On the basis of the WHO study and other reports^{4,6,10,20-22} it is conservatively assumed that between 10 and 20 percent of couples, experience some form of involuntary infertility problem during their reproductive lives. Extrapolating this to the global population, it can be said that about 60-90 million people may be experiencing either primary or secondary infertility at the present time. Because of the high incidence of STD, PID and pregnancy related infections, the sub-Saharan Africa has the highest

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INFERTILITY IN AFRICA - M Anate, et al

prevalence of infertility of about 30-50% with the higher figure reported from Gynaecology clinic attendance in some parts of Africa including Nigeria.^{1,2,4-14,20-23}

In the USA, after excluding couples who have elected to be sterilized, it is reported that about 13.9% of married, potentially fertile couples, have infertility problem at some time in their lives^{19,21,22}. In the United Kingdom, the prevalence of infertility is reported to be 22% of all patients attending the gynaecology clinics^{1,20} and this is believed to be probably representative of most urban centres in the developed world.

From the most comprehensive study of infertility between 1979 and 1984^{1,5,19} it was demonstrated that infection-related diagnosis were clearly the most important factors among infertility patients world-wide accounting for up to 64% of female patients in the African centres and about 38% of patients in other areas of the world.

These studies have highlighted a somewhat paradoxical situation, internationally, infertility is greatest

in those areas of the world where fertility is the highest. This is likely due to the fact that those areas of highest fertility also have a high incidence of STDs which can cause infertility.

Centres for Disease control in the USA have shown that after a single episode of PID, about 12% of the patients will be infertile, after two episodes 25% will be infertile while after three episodes, the incidence is more than 50%²³. Delay in the treatment of the PID is reported to carry worse prognosis.^{19,20}

DIAGNOSIS OF INFERTILITY

The precise diagnosis of the cause(s) of infertility is the hallmark of the basis of the proper and possible successful management of the problem. The diagnosis of impaired fecundability depends largely on the knowledge of the requirements for normal fertility and the possible lesions that can impair these.

These are shown in Table 1.

TABLE 1: Requirements for and impairment of fertility in a couple

A. Male

	Requirements	Functions	Impairment (Lesions)
1.	Hypothalamus	Produces GnRH for the anterior pituitary gland	Tumour, inflammation (infection)
2.	Pituitary gland	Produces LH, FSH, Prolactin, ICSH, TSH	Tumour, hypopituitarism (hypogonadotropic-hypogonadism)
3.	Thyroid gland	Produces sex hormone binding globulin (SHBG), T ³ and T ⁴	Tumour, hyper- or hypo-thyroidism
4.	Liver	Regulates metabolism of endogenous & exogenous sex hormones	Cirrhosis
5.	Adrenal glands	Produce androgens & Corticosteroids	Tumour, adrenal hyperplasia or insufficiency
6.	Testes	Spermatogenesis, Produce androgens & little Oestrogen	Cryptorchidism, germinal cell hypoplasia, aplasia, sclerosis or atrophy of seminiferous tubules as in Klinefelters syndrome, infection (viral or bacterial), epididymo-orchitis.
7.	Vas deferens	Convey sperm from the testes	Congenital absence, ligation, occlusion (blockage) by infection

INFERTILITY IN AFRICA
- M Anate, et al

	Requirements	Functions	Impairment (Lesions)
8.	Prostate gland	Produces acid phosphatase and fibrinolysin for the liquefaction of seminal fluid	Infection
9.	Seminal vesicles	Produce seminal fluid in which the spermatozoa respire	Congenital absence, infection
10.	Penis	Deposit sperm in vagina	Hypospadias, phimosis, urethral stricture from STD, erectile dysfunction.

B. Female

	Requirements	Functions	Impairment (Lesions)
1.	Hypothalamus	Produces GnRH for the anterior pituitary gland, thyrotrophin	Inflammation, toxicity, tumour
2.	Pituitary gland	Produces FSH, LH, Prolactin and TSH	Adenoma (prolactin producing) necrosis.
3.	Thyroid gland	Produces T ₃ , T ₄ , (SHBG)	Thyrotoxicosis, hypothyroidism
4.	Adrenal glands	Produce androgens and some oestrogen	Hyperplasia causing hirsutism and masculinization
5.	Liver	Regulates metabolism of endogenous and exogenous sex hormones	Cirrhosis
6.	Ovaries	Produce ova, oestrogen, progesterone and some androgen	Congenital absence, polycystic, infection, (viral or bacterial), adhesions from infection or endometriosis
7.	Fallopian tubes	Collect and convey ova to uterus, site of fertilization, convey fertilized ovum to uterus	Congenital absence, blockage by infection, endometriosis and ligation
8.	Uterus	Sustains conceptus, expels it at term.	Congenital absence, didelphis, bicornute, subseptate, Asherman's syndrome, fibroids, adenomyosis.
9.	Cervix	Produce mucus, retains uterine contents	Congenital absence or poor development, hostile mucus to sperm, mucus sperm anti-bodies, damaged or incompetent OS
10.	Vagina	Site of sperm entry & depot	Congenital absence, infection, imperforate hymen or membrane vaginismus, gynatresia.

SIGNIFICANT AETIOLOGICAL FACTORS

Apart from the broadly based possible causes of infertility listed in Table 1, there are regional variations the world over in the causes of infertility.

Up to 64% of female patients in Africa particularly sub-Saharan Africa and about 38% of patients in other areas of the world are reported to have impaired fertility.^{2,5,10,11,20,22,23} In Africa, this is mostly due to STDs, pregnancy related infections and PID. Other ancillary causes are uterine fibroids, endometrial adhesions, septate uterus, etc.

In developed countries with relatively very low incidence of PID, anovulatory dysfunctions are the commonest causes of infertility accounting for about 21-30% of infertile women while endometriosis takes over from PID in these countries.^{14,19,25}

In industrialized countries, the WHO has reported that the incidence of infertility due to male factors is approximately the same as the disorders in the female^{2,5} but in Africa, male factors are believed to account for about 20-50% of couple infertility.^{4,9,13-18} Some of these male factors include azoospermia, oligospermia, seminal fluid infection and erectile dysfunction which may be due to testicular failure, congenital anomalies, varicocele, epididymo-orchitis, vas deference occlusion, chronic alcoholism, etc.

MANAGEMENT STRATEGY

For a rational approach to the proper management of the infertile couples, the recent advances in this field take into account a comprehensive history, physical examination and relevant tests like semen analysis, tubal patency test by HSG or laparoscopy dye test, post-coital test, cervical mucus penetration test, antisperm antibody assay, hysteroscopy, the zona-free hamster egg penetration tests, endometrial dating, basal body temperature (BBT) chart, varicocele assessment, pituitary gland and ovarian ultrasonography, laboratory assessment of ovulation by midluteal phase progesterone levels (normal 5-36 ng/ml), serum prolactin levels (normal 6-24 ng/ml), TSH level (normal 0.2-5.0 µu/ml), FSH level (normal 4-20 mlu/ml), LH level (normal 4-20 mlu/ml), oestrogen level (normal 50-150 pg/ml) and T₄ level (normal 50-135 ng/ml).

Table 2 shows the WHO criteria for normal semen analysis.

Following the necessary investigations appropriate for each couple, the correct diagnosis would have been made and the appropriate treatment of the couple instituted which could be medical or surgical.

TABLE II: WHO criteria for normal semen analysis

Standard Tests	Results
Volume	>2.0mls
PH	7.2 - 8.0
Sperm concentration	>20 x 10 ⁶ /ml
Total sperm count	>40 x 10 ⁶ /ejaculate
Motility	>50% with forward progression or 25% with rapid progression within 60 minutes of ejaculation
Morphology	>30% with normal forms
Pus cells (WBC)	<1.0 - 10 ⁶ /ml or <2/HPF
Immunobead test	<20% spermatozoa with adherent particle
Mixed agglutination test	<10% spermatozoa with adherent particle.
Optional Tests	
Alpha glucosidase	>20mlu/ejaculate
Zinc	>2.5 µ mol/ejaculate
Total citric acid	>52 µ mol/ejaculate
Total fructose	>13 µ mol/ejaculate
Total acid phosphatase	>200u/ejaculate

In the past 2-3 decades, there is no doubt that there have been some advances in the management of infertility. These have been brought about by better understanding and application of reproductive neuroendocrinology with increasing use of hormonal immunoassay in gynaecology practice, improvement and regular use of endoscopy for key-hole procedures, improved ovarian ultrasonography for assessing the growth of follicles (follicular tracking) and oocyte recovery/harvesting and improvements in the various assisted reproductive technology (ART).

These are discussed further below.

SELECTED ASPECTS OF SURGICAL AND MEDICAL THERAPY

1. Macroscopy

In women with infertility due to tubo-peritoneal factors, macrosurgery still has a limited place in the management of infertility in the developing countries of Africa where facilities for microsurgery are grossly inadequate or non-existent.

In a series of 317 women who had macrosurgery for tubo-peritoneal infertility in Ilorin, Anate *et al*⁷ reported a pregnancy rate of 14.7% with a total cumulative

pregnancy rate of 19.2%. This low yield was attributed to many factors like late hospital consultation by the patients, traditional medication which often causes more damage, high and gross incidence of PID and high male infertility factors.

2. Microsurgery

For patients with post infectious infertility, the two aspects of surgical therapy that are of particular interest are microsurgery to treat tubal disease and hysteroscopy to treat intrauterine adhesions and the uterine septum.

The introduction of microsurgery into gynaecology practice in 1974 provided a useful high technology tool to aid in the surgical therapy of the infertile female. The initial hope was that pelvic and tubal diseases could be corrected with reasonable success using this technique. After almost 26 years experience (1974-2000) with microsurgery, the expectations that this will dramatically improve the chances of pregnancy in women with tubal disease have been most disappointing. Conception rate after salpingostomy is no more than 30-40% with very high percentage of the pregnancy being tubal ectopic gestations. Generally, the prognosis for fertility with microsurgery is inversely proportional to the extent of tubal disease present.

However, the best results with microsurgery are unquestionably in the tubal reanastomosis for the reversal of surgical sterilization.^{2,10,11,21}

3. Hysteroscopy

An area where results have been slightly more encouraging has been the hysteroscopic treatment of patients with intrauterine adhesions (Asherman's syndrome) and the uterine septum (hysteroscopic metroplasty). Most of the patients with Asherman's syndrome present with secondary infertility, with the primary insult being postabortal or postpartum trauma and infection. Following hysteroscopic lysis of the adhesions followed by a period of hormonal therapy (oestrogen) to encourage endometrial proliferation, normal menstruation can be restored in 88% of the patients and a subsequent pregnancy rate of 32-81% has been reported depending on the severity of the condition.^{20,26,27}

The separate uterus is a condition that now lends itself to hysteroscopic metroplasty. In a situation where the uterus is completely or partially divided by a longitudinal septum, pregnancy wastage can often occur. In a series of 367 patients with poor reproductive history treated by dividing the uterine septum with a semi-rigid scissors under hysteroscopic control, Sciarra and Siegler *et al*²² reported almost 59% full term pregnancy rate among the patients.

4. Uterine Leiomyomata and GnRH agonist (buserelin acetate or suprecur)

Uterine fibroids remain a recognised predisposing factor to infertility mostly in the third decade of life in both developed and developing countries particularly among the black women, and are of concern to the gynaecological surgeon who is trying to preserve fertility. In this situation, after a preoperative hysterosalpinogram (HSG) and a thorough endocrine evaluation of the patients, myomectomy is often indicated for the preservation of the reproductive function.

The current availability of gonadotrophin-releasing hormone (GnRH) agonists (Buserline or Suprecur) to effectively block GnRH secretion, creating a hypoestrogenic environment, has added a new dimension to the preoperative treatment of patients with uterine fibroids. Patients so treated with this compound usually become amenorrhoeic within 4 weeks of treatment with a significant reduction of uterine size/volume of about 10-57% within 3 months of the onset of therapy⁸.

The therapy is also reported to result in an 11% increase in the treated patients hematocrit and an obvious decrease in the uterine vascularity¹⁰.

With the GnRH agonists, we now have the possibility of medical therapy to reduce the uterine volume and vascularity prior to surgery, thus allowing for less hazardous surgical myomectomy and the preservation of many patients' fertility potential.

5. Falloposcopy (Fallopscopy or Tuboscopy)

This is another recent advancement in tuboplasty and fertility enhancement. With improvement in endoscopic technology, both transuterine or retrograde fallopscopy are now feasible. The ability to visualize the tubal lumen via a transuterine microendoscopic system (fallopscopy) can allow therapeutic manoeuvres like the removal of microcellular plugs, intratubal adhesiolysis with a small plastic inflatable balloon and probing of tubal lumen with a fine plastic probe to secure tubal patency, thereby enhancing the fertility potential of many patients with tubal blockage. Fallopscopy may also be used to select cases for microsurgery, IVF and for placing gametes or embryos in the fallopian tubes in assisted reproductive procedures.^{10,14,28-31}

6. Anovulatory Infertility

This is another area of infertility where a lot of advances have been made in recent years. Listed in table

3 are the major causes of anovulation.

TABLE III: Major causes of anovulation

A. Primary ovarian failure	
1.	Genetic
2.	Autoimmune disease
3.	Cytotoxic chemotherapy
4.	Pelvic radiotherapy
B. Secondary ovarian dysfunction	
1.	Specific abnormal gonadotrophin regulation
a.	Hyperprolactinaemia
b.	Kallman's syndrome (hypogonadotrophic, hypogonadism and anosmia)
2.	Functional abnormal gonadotrophin regulation
a.	Weight loss
b.	Excessive exercise
c.	Drugs (combined oral pills, cytotoxic drugs, injectable contraceptives)
d.	Idiopathic
C. Gonadotrophin deficiency	
1.	Pituitary tumour
2.	Pituitary necrosis (infection), thrombosis or ablation
D. Disorders of gonadotrophin action	
1.	polycystic ovarian syndrome (PCOS)

(a) **Normogonadotrophic anovulation:** In this, the majority of the patients have polycystic ovarian syndrome (PCOS) characterized by normal plasma levels of FSH, elevated levels of LH giving LH/FSH ratio > 1, obesity (BMI > 25) and presence of polycystic ovaries on ultrasonography.

In this disorder, after weight reduction, treatment is by ovulation induction with clomiphene citrate (50-250mg), human menopausal gonadotrophin (150 units i.v. daily) or recombinant FSH (75 units sc). The other alternative treatment for this disorder is by laparoscopic laser "drilling" of the ovaries (modern equivalent of ovarian wedge resection) and pregnancy rates of 50-60% have been reported after 6 ovulatory cycles of treatment.^{14,22-25}

(b) **Hypogonadotrophic Hypogonadism Anovulation:**

This may be due to weight loss, excessive exercise or could be idiopathic. If the pituitary failure is secondary to hypothalamic dysfunction, then treatment can either be by pulsatile GnRH (15 µg per pulse i.v.), daily injection of hMG (150 units) or recombinant FSH to induce ovulation while using sonographic follicular tracking or serial serum estradiol level measurement to avoid superovulation and multiple pregnancy.^{14,24}

(c) **Hypergonadotrophic Hypogonadism Anovulation:**

Women in this group may have the so-called resistant ovarian syndrome (which is rare) in which the ovary contains thousands of premodial follicles or premature ovarian failure. Pregnancy for this group of patients lie in oocyte donation programme.^{14,28,31,34,35}

Such patients can also benefit from recent ovarian surgical transplant (replacement) technology which has been successfully carried out at New York Methodist Hospital, USA by Dr Kutluk Oktay.

Though the technique was initially to delay or prevent menopause, it is envisaged that it can restore normal reproduction. Hence it is not recommended for women aged 30 years and above.

Those at the root of the technology have postulated the possibility of taking a good biopsy of ovary of young women and subject the specimen to cryopreservation for future use. It is however stressed that in thawing the frozen ovary before transplant about 30% of the follicles could be lost.

(d) **Hyperprolactinaemic Anovulation:** This is mostly due to pituitary adenoma. Hence images of the pituitary gland with CT scan or magnetic resonance imaging should be performed to exclude an adenoma. If the pituitary gland is normal, treatment with bromocriptine (2.5 - 25mg daily) has been found effective in inducing ovulation and successful pregnancies achieved.^{14,24,25,34,35}

(e) **Hypothyroidism Anovulation:** About 4% of hypothyroid women are afflicted with infertility characterized by amenorrhoea and hyperprolactinaemia.^{26,36-38} Such women usually present themselves when the hypothyroidism is compensated, that is, the plasma levels of T₃ or T₄ are normal or marginally low while the TSH level is elevated. Also the prolactin level is elevated while the FSH and LH levels are within normal limits.

The treatment of such women with thyroxin (0.05 - 0.15 mg daily) has been reported to result in normoprolactinaemia, ovulatory menses and

successful pregnancies^{24,34,36} It is necessary to state that in the absence of proven hypothyroidism, thyroid therapy has no place in the management of anovulatory infertility.

Table 4 shows the summary of the methods used for treating infertility due to ovulatory dysfunction.

TABLE IV: Methods of treating anovulatory infertility

1. Clomiphene citrate (clomid)
2. Human menopausal gonadotrophin (hMG)
3. Human chorionic gonadotrophins (hCG)
4. Purified (recumbitant) FSH
5. Gonadotrophin releasing hormone₄ (GnRH)
6. GnRH agonists
7. Bromocriptine (parlodel) for hyperprolactinaemia
8. Ovarian wedge resection or cautery
9. Ovarian laser drilling or macroscopic drilling at laparotomy

7. Male infertility:

Despite the great advances made in recent years in the field of andrology, the aetiology of male infertility in most cases is still evasive. There is, however, increasing evidence that environmental factors play an important role in male infertility. In the investigation of sub-fertility in males, semen analysis still remains the first port of call. The details of this are shown in Table 2 of this write up. When there are two consecutive abnormal semen analysis at 3 months apart, the diagnosis of male infertility is made.^{14,16,17}

If sperm number and motility are reduced, mesterolone (a weak synthetic androgen) can be used (50 – 100mg daily). In patients with normal sperm count but reduced motility, fluoxymesterone (another synthetic androgen) can be used (5 mg daily) in the second half of the wife's menstrual cycle.

In moderate oligospermia and motility, split ejaculate or concentrating the more motile sperm by a "swim-up" technique (using 2 mls of Ham's F-10 solution) can be used for artificial insemination.

A "swim-up" sample or split ejaculate of $0.3 - 1 \times 10^6$ /ml or more sperm density at 95% motility can also be used for the conventional IVF.^{14,28,37}

If the sperm count is less than 0.3×10^6 /ml or the semen sample is azospermic, some spermatozoa can often be obtained either by percutaneous epididymal

sperm aspiration (PESA) or testicular biopsy.^{14,37} This can be used for IVF combined with intra-cytoplasmic sperm injection (ICSI or micro insemination). If the man has erectile dysfunction, viagra (sildenafil 50mg daily) is the current drug of choice. In the presence of vas deferens blockage, surgical resection with end-to-end anastomosis is the treatment of choice and the success rate is about 80 – 90%.³⁸

8. In vitro fertilization (IVF) and assisted reproductive technology:

Since 1978, IVF has been an option for couples with infertility.^{2,28,37,39} Originally limited to patients with tubal disease, the assisted reproductive technology have been liberalized to many other types of infertility including male infertility. However, appropriate patient selection and appropriate counselling are essential bearing in mind that female reproductive ability is at its best during their early twenties, falling in the late twenties and early thirties and dropping sharply over the age of 35 – 40 years.^{2,10,14} Patients should not be considered candidates for assisted reproduction until all standard infertility treatments have been applied.

IVF treatment begins with controlled ovarian stimulation by hMG or recombinant FSH in combination with a GnRH analogue and human chorionic gonadotrophin (HCG). Oocytes are recovered from mature ovarian follicles by laparoscopy. Usually, up to two thirds of the recovered oocytes are fertilized in-vitro (test tube or dish) with the partner's sperm. The fertilized oocytes (embryo) are either implanted in the uterine cavity or undergo cryopreservation for future use. In general, 15-20% of patients who undergo embryo transfer may expect a clinical pregnancy. About 20% of these clinical pregnancies will abort spontaneously and about 5% will result in tubal ectopic pregnancies. While the remaining 75% will result in viable births with a substantial number of these being multiple pregnancies.^{2,10,14,28,37}

IVF and assisted reproductive technologies have been a great hope for many couples, primarily in the industrialized countries. The technology is expensive and requires a high degree of technical skill. The procedure need to be simplified and results improved so that these procedures can be applied to larger numbers of deserving patients in a cost-effective manner worldwide.

Apart from IVF, the other methods of assisted reproduction or assisted fertility technology are as follows:

- (a) AI — Artificial insemination using husband's sperm or donor sperm. This has been in use for decades.
- (b) GIFT — Gamete intra-fallopian transfer which involves the placement of oocytes and sperm into the fallopian tube by laparoscopy. Many cases of successful pregnancies by this technique have been reported.^{10,14,30,31,37}
- (c) ZIFT — Zygote intra-fallopian transfer. This involves in-vitro fertilization of oocytes and then transferring them to the fallopian tubes by laparoscopy.^{28,37}
- (d) TET — Tubal embryo transfer which involves the placement of cleaving embryos into the fallopian tube by laparoscopy.
- (e) POST — Peritoneal oocyte and sperm transfer. This is the placement of oocytes and sperm into the peritoneal cavity by laparoscope. This and (d) have not been widely used in assisted reproductive technology.³⁷
- (f) SUZI — Subzonal insertion of sperm by micro injection or micro-insemination. Presently this technique (SUZI) relies on laser-assisted thinning of the zona pellucida and microinjection of sperm under the zona.
- (g) ICSI — Intracytoplasmic sperm injection. This is a microinjection of a single spermatozoon directly into an oocyte followed by transcervical transfer of the resulting embryos into the uterus. This is most often used in cases of male infertility due to impaired sperm penetration of oocytes zona layer. Many full term pregnancies have been achieved by this technology the world over.^{10,14,40} The Nigerian credit in this regard could go to the Bridge Head Clinic, Lagos.

ICSI was first introduced in 1993 as a new form of in-vitro fertilization (IVF) and is now accepted as the treatment of choice for severe male infertility in many centres around the world.

However, there is little information about the long-term outcome of the children conceived by ICSI. From the studies carried out by Bowen *et al*,⁴⁰ there was no significant difference in the incidence of major health problems or major congenital malformations in the first year of life between the children conceived by ICSI and

those conceived by routine IVF or naturally. Both produced babies of good health and normal development though there is an increased risk of mild delays in the mental development index at 1 year in ICSI children compared with children conceived by IVF or conceived naturally.

9. Human Cloning:

Since the cloning of the sheep Dolly in Scotland just over 4 years ago, it has been envisaged that it should be possible to clone human being. This has provoked a lot of controversy both ethical/moral and political/religious the world over to the extent that some countries in Europe and the USA have legislated against it.

Despite all these opposition, some eminent scientist, including Severino Antinori a renowned Italian Obstetrician, are pressing to go ahead with the technology, they believe that human cloning has a place in the management of infertile couple who have no chance of reproduction using other available methods known to mankind. Even of recent, there are already female volunteers wanting to be surrogate mothers to cloned human embryos.

However, the moral and medical concerns of this technology and possibly other assisted reproductive technologies is the establishment of pregnancy in women biologically beyond the usual age of pregnancy. Meanwhile the controversy over human cloning lingers on while two genetically modified human beings have been produced in America recently (May, 2001).

CONCLUSION

Infertility is a serious health problem in the whole world today. This is because of the psychological and physical suffering that it causes and also the economic consequences it has for both infertile couples and the society as a whole.

Researchers and clinicians need to aggressively fight the spread of STDs, by diagnosing and treating asymptomatic infectious disease in its earliest stages, by conservative gynaecologic surgery and by developing new contraceptive options that resist the spread of the common pathogens that cause pelvic infection and tubal disease (PID).

With this aggressive approach and with the recent advances in assisted reproductive technology, it should be possible to make great strides in solving the problem of infertility in the years ahead.

ACKNOWLEDGMENT

To Mr IA Anomi, the authors are grateful for the efficient secretarial services.

REFERENCES

1. World Health Organization (WHO): Infections, pregnancies and infertility: perspectives on prevention. *Fertil Steril* 1987; 47: 964-966.
2. Sciarra JJ: Infertility: An International Health Problem. *International J Gynecol Obstet* (Special issue) 1994; 46(2): 155-163.
3. Anate M, Akeredolu O: Attitude of male partners to infertility management in Ilorin, Nigeria. *Niger Med Pract* 1994; 27(5): 46-49.
4. Akande EO: Problems of infertility in Sub-Saharan Africa. *DOKITA* 1987; 16: 23-27.
5. Cates W, Farley TMM, Rowe PJ: Worldwide patterns of infertility: Is Africa different? *Lancet* Sept. 1985; 14: 596-598.
6. Ladipo OA: The epidemiology of infertility. *DOKITA* 1987; 16(1): 1-5.
7. Aimakhu VE: Surgery to restore fertility -- Personal experience. *Trop J Obstet Gynaec* 1980; 1(1): 45-49.
8. Otolorin EO: management of female infertility: The tubo peritoneal factor. *DOKITA* 1987; 16(1): 13-19.
9. Anate M, Akeredolu O: Surgical management of female infertility: The Ilorin experience, Nigeria. *Niger Med Pract* 1996; 32(3/4): 39-43.
10. Sciarra JJ: Selected topics of international interest, 1988. In: *Advances in Gynaecology and Obstetrics* (eds P Belfort, JA Pinotti, TKAB Eks) P. 1-15. The proceedings of the XII World Congress of Gynecology and Obstetrics, Rio de Janeiro, October, 1988.
11. WHO: Programme on the diagnosis and treatment of infertility. *International J Andrology* 1989; 12: 254-264.
12. Chukwudebelu WO: Esege N, Megafu U: Etiological factors in infertility in Enugu, Nigeria. *Infertility* 1979; 2: 183-200.
13. Glwa-Osagie OF, Ogunyemi D, Emuveyan EE, Akinla DA: Etiological classification and sociomedical characteristics of infertility in 250 couples. *Int J Fertil* 1984; 29: 104-108.
14. McVeigh E: Assisted Fertility. *Postgraduate Doctor Africa* 1998; 20(3): 82-88.
15. Nwabuisi C, Onile BA: Male infertility among sexually transmitted diseases clinic attendants in Ilorin, Nigeria. *Niger J Med* 2001; 10(2): 68-71.
16. Ajabo LN, Ezimokhai M, Kadiri A: Male contribution to sub-fertility in Benin-City, Nigeria. *Trop J Obstet Gynaecol* 1981; 2: 23-36.
17. Ladipo OA: Semen analysis in fertile and infertile Nigerian men. *J Nat Med Ass* 1980; 72: 785-789.
18. Oforofuo IAO, Onakehwo JUE, Enuman I: Fructose concentration in seminal fluid and the deoxyribonucleic acid content of spermatozoa from infertile human males. *Afr J Reprod Health* 1997; 1(1): 89-96.
19. Nandi E, Ory SJ, Herrmann R, O'Brien PS, Melton III LJ: fertility after ectopic pregnancy. *Fertil Steril* 1993; 60: 231-234.
20. Hull MGR, Glazener CMA, Keller NJ, Conway DI, Foster PA *et al*: Population study of causes, treatment and outcome of pregnancy. *Brit Med J* 1984; 291: 190-299.
21. Rowe PJ: Epidemiology of infertility. In: *Advances in Gynecologic Endocrinology. Proceedings of the 1st congress of the international Society of Gynecological Endocrinology* (eds AR Genazzani, F Petraglia, A Volep, F Pacchinctti) Vol 1. Parthenon. Carnforth, Lancashire, UK 1988.
22. Hillis SD, Joesoef R, Machbanks PA, Wassenaar JN, Westrom L: Delayed care of pelvic inflammatory disease as a risk for impaired fertility. *Am J Obstet Gynecol* 1993; 168: 1503-1505.
23. Cates W Jr, Rolfs RT Jr, Oral SO: Sexually transmitted diseases, pelvic inflammatory disease and infertility: An epidemiologic update. *Epidemiol Rev* 1990; 12: 199-220.

24. Anate M, Olatinwo AWO: Anovulatory infertility: A report of four cases in Ilorin and literature review. *Niger J Med* 2001; 10(2): 85-91.
25. Olatinwo AWO, Anate M: Induction of ovulation: A review. *Niger J Med* 1999; 8(3): 93-98.
26. Valle RF, Sciarra JJ: Intrauterine adhesions: Hysteroscopic diagnosis, classification, treatment and reproductive outcome. *Am J Obstet Gynecol* 1988; 158: 1459-1463.
27. Siegler AM, Valle RF, Lindemann HJ, Mencagha L: Therapeutic hysteroscopy: Indications and techniques. CV Mosley company, St Louis, 1990.
28. Chang YS, Kim SH, Moon SY, Lee JY: Current status of assisted reproductive technology in Asia and Oceania. *J Obstet Gynecol Research* 1996; 22(4): 305-330.
29. Evans MI, Hume RF, Polack S, et al: The Geriatric gravida: Multifetal pregnancy reduction, donor eggs and aggressive fertility treatments. *Am J OBSTET Gynecol* 1997; 177: 875-878.
30. Hannoun A, Abu-Musa A: Gamete intrafallopian transfer (GIFT) in the treatment of severe male factor infertility. *Internal J Gynecol Obstet* 1998; 61(3): 293-295.
31. Ranieri M, Beckett VA, Marchant S, Kinis A, Serhal P: Gamete intrafallopian transfer or in-vitro fertilization after failed ovarian stimulation and intrauterine insemination in unexplained infertility. *Hum Reprod* 1995; 10: 2023-2026.
32. Henderson SR: The management of Dysovulatory infertility. In: Bonnar J (ed) Recent advances in obstetrics and gynaecology No 14, Churchill Livingstone (Publisher), Edinburgh, London, New York. P 241-258, 1982.
33. Gidoff PR, Jewelewicz R: Polycystic Ovarian Disease. *Obstet Gynaecol Clinic North America* 1987; 14: 931-953.
34. Shearman RP: Secondary Amenorrhoea. In: Whitfield CR (ed) Dewhurst Textbook of Obstetrics and Gynaecology for Postgraduates. 5th Edition. Blackwell Scientific Publications, Oxford. London P. 31-42. 1995.
35. Hamilton M: Treatment of anovulatory infertility in women. *Medicine Digest* 1996; 2(6): 10-17.
36. Edwards CR, Forsyth IA, Besser GM: Amenorrhoea, Galactorrhoea and Primary Hypothyroidism with high circulating levels of prolactin. *Brit Med J* 1971; 3: 462-464.
37. Keith L, Oleszczuk JJ: Iatrogenic multiple birth, multiple pregnancy and assisted reproductive technologies. *International J Gynecol Obstet* 1999; 64(1): 11-25.
38. Harrison RF: Infertility in women. *Brit J Hosp Med* 1977; 17: 45-54.
39. Wood C, Trounson A: In vitro fertilization and embryo transfer. In: Bonnar J (ed). Recent advances in obstetrics and gynaecology. No. 14. Churchill Livingstone (Publisher), Edinburgh. London. New York P. 259-282. 1982.
40. Bowen JR, Gibson FL, Leslie GI, Saunders DM: Medical and developmental outcome at 1 year for children conceived by intracytoplasmic sperm injection. *LANCET* 1998; 351/9115: 1529-1534.