REPRODUCTIVE AND ENDOCRINE UNIT

STEVE BIKO ACADEMIC HOSPITAL

REPRODUCTIVE MEDICINE CLINIC:

Area: 82290, Level J 8 (Opposite Theatre)

Tel: (012) 354 2540/5337

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E-mail: Zozo.Nene@up.ac.za

Krushmee.Singh@gauteng.gov.za

REPRODUCTIVE BIOLOGY LABORATORY (RBL):

Area: 72351, Level 7

Tel: (012) 354 2208

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E-mail: Carin.Huyser@up.ac.za

Gerhard.Boshoff@up.ac.za

CLINIC TIMES

Monday – Thursday: 07:00-16:00

Friday: 7:00 – 13:00

STAFF:

Clinic

- Head of Unit: Dr LNZ Nene
- Consultant: Dr A De Bruin
- Consultant: Dr M Trouw
- Consultant: Dr J Biko
- Consultant: Dr H Kruger
- 3 Fellows
- Registrars (Department of Obstetrics and Gynaecology, University of Pretoria)

- Medical Officer: Dr K Singh
- Clinic Nurses
- Clinic Secretary

Reproductive Biology Laboratory (RBL)

- Head of the Laboratory: Prof C Huyser
- Assistant Director: Mr G Boshoff
- Embryologists (scientists and technologists)
- Laboratory Secretary

APPOINTMENTS

- All patients are seen by appointment only.
- Patients must allow sufficient time for parking, registration and opening of the unit file.
- Patients in the Semen Decontamination Programme: Appointments on a Thursday.
- Patients in Assisted Reproductive Techniques (ART) Programme must be at the Unit at 07:00 and no later than 07:30.
- Patients already in the ART programme or undergoing procedures may take precedence over New and Follow up patients.
- Every effort will be made to adhere to scheduled times.

PROTOCOLS FOR REFERRAL TO THE REPRODUCTIVE AND ENDOCRINE UNIT, STEVE BIKO ACADEMIC HOSPITAL

Gynae - Endocrine Clinic

Amenorrhoea

- All patients with Primary Amenorrhoea
- Secondary amenorrhoea, after a failed progesterone challenge test
- With abnormal Thyroid Function Tests
- With Hyperprolactinaemia

- Ambiguous genitalia
- Chromosomal abnormalities e.g. Turner's syndrome
- Polycystic ovarian syndrome (PCOS)
- Hyperandrogenism
- Premature Ovarian Dysfunction

Hysteroscopy Clinic

Post-Menopausal Bleeding

Recurrent pregnancy losses

Uterine abnormalities

Polyps

Sub mucous myomas

Removal of foreign body - Lost intrauterine contraceptive device (IUCD)

Secondary amenorrhoea with failed progesterone challenge test

Abnormal uterine bleeding – not responding to hormone therapy

Contraceptive Clinic:

Menopause Clinic:

Recurrent Pregnancy Loss Clinic:

Endometriosis Clinic:

Referral for Infertility

< 35 years

- with **1 year** of history of inability to fall pregnant after adequate, unprotected intercourse

>35 years

- with **6 months** history of inability to fall pregnant after adequate, unprotected intercourse

- Refer **immediately** in women

- 40 years old (not older than 41 years old)
- previous ovarian surgery
- exposure to cytotoxic drugs
- autoimmune disease
- strong family history of premature ovarian failure/early menopause
- suspected endometriosis
- known or suspected uterine/tubal disease/tubal surgery
- all patients requesting tubal re-anastomosis (reversal of sterilisation)

Cut-off age for referral is 41 years old.

- Women older than 40 may opt for IVF with an oocyte (egg) donor.
- Please see "Criteria for Suitable Egg Donor"
- The age cut-off for recipients is 50 years old.
- Please see "Criteria for Recipients"

BMI < 19 and > 35 kg/m^2

- Poor success rate
- Refer patient to dietician / weight loss programmes
- BMI to be between 19 – 30 before commencing ART

Age < 40

- Offer **3** Cycles only (if no history of other IVF treatment)

Age > 40 < 41

- Offer **1** Cycle only (if no previous History of other IVF treatment and if no evidence of low ovarian reserve)
- Patient to be advised on implications of Advanced Maternal Age

BASIC WORKUP

Women

FSH, LH, Estradiol, Anti-Mullerian Hormone (Day 2 menstruation)

Thyroid Function Test (TFT)

- In women with Thyroid disease
- In women with ovulatory disorders

Prolactin

- in women with ovulatory disorders
- galactorrhoea
- Symptoms and signs suggestive of pituitary tumours

HIV

Rubella IgG

Syphilis (RPR)

Hepatitis B & C

Pap smear

Men

HIV

Syphilis (RPR)

Hepatitis B & C

Semen Analysis (to be done at SBAH)

Single:

As above

LGBTQI:

As above

Test for tubal patency (where possible)

Hysterosalpingogram (HSG): if no history of Pelvic Inflammatory Disease or endometriosis

Or

Laparoscopy and chromopertubation as per indication

WHO DO WE SEE?

- Infertile couples (see "**Referral for Infertility"**)
- Couples where either partner has a history of fertility related problems
- Single and LGBTQI couples
- Partner has a low sperm count or abnormal semen parameters
- Endocrine problems associated with infertility
- HIV positive couples who wish to undergo risk reduction methods of Assisted Reproductive Techniques (ART). Certain criteria must be met before ART can be offered.
- All patients must have a referral letter with copies of the required recent results not older than 6 months. (Please see **"Basic Workup"**)
- Patients must follow the appropriate referral system from the Primary Health Care Facility or Medical Practitioner or Secondary Health Care Facility or Gynaecologist.
- Our Unit encourages openness of all medical conditions between partners prior to the initial consultation in order for the unit to provide the couple with the appropriate and optimal care.
- Partners are seen together at the initial and follow up appointments.

REQUIREMENTS FOR THE FIRST VISIT (BY THE HOSPITAL)

Appointment date: _____

1. Two (2) ID photos each of partner
2. Copies of ID / Passport documents of both partners
3. Proof of income (payslip) for both partners. If either or both partners are unemployed a 3 months bank statement or an affidavit from the SAPS is required
4. Proof of residence (e.g. Rates account statement, Rental agreement)
5. Referral letter and copies of previous results (mandatory). Not older than 6 months

6. **Please confirm your appointment (Tel: 012 354 2540) at least one (1) week beforehand**
7. Consultation fees charged as determined by income or as per tariff rates.
8. Accounts of the investigations performed will be forwarded to the person responsible for the payment.

   Private and Foreign patients will pay in cash on the day of the tests.
9. A semen analysis will be requested on the day of your appointment. A period of three (3) days abstinence is required. Results can take up to 2-3 weeks.
10. **Foreign Patients:**

    Foreigners need to follow the admission criteria of the hospital.

    Foreigners must follow-up and obtain clearance from the hospital's Finance Department.

    All legal documents must be in order and valid for at least 6 months from time of first appointment.

FIRST VISIT

- All patients requesting fertility treatment must be present for the first consultation
- A full history is taken from both partners
- Systemic as well as the gynaecological examination is performed
- A pelvic ultrasound is done
- Possible problems are identified and solutions offered
- The basic facts of Assisted Reproductive Techniques (ART) procedures and costs are explained
- A semen sample will be analysed by our staff at our Reproductive Biology Laboratory (RBL). This is important as our laboratory will be handling the semen and the embryos.
- Patients or couples may be referred to the Dietician, General Practitioner, Medical Specialist, Lawyer, Psychologist or social worker for further consultation and evaluation. The ART procedure of choice can only be discussed once all the reports become available.

- A multi-disciplinary team approach is adopted for holistic care

FOLLOW-UP VISIT

- Should be scheduled by the couple within 2-3 weeks of initial appointment. All results of investigations performed must be in the file. Follow up visits is subject to availability of appointments.
- Results are discussed.
- The relevant ART procedure will be discussed in detail with the couple.
- The procedure, success rates, approximate costs, risks, complications and cycle dates will be explained by the doctor and the nurse i.e. Rest of Team
- The couple is given the opportunity to ask questions
- The couple signs the Unit's informed consent form.
- Some patients may be required to repeat tests or consult with a Dietician, General Practitioner, Specialist, Lawyer, Social worker or the Psychologist before "Rest of Team" can be performed.

PROCEDURES

- Further infertility work-up if indicated (ultrasound examination / semen decontamination etc.)
- Office Hysteroscopy where indicated
- Laparoscopic and /or hysteroscopic surgery where indicated
- Assisted Reproductive Techniques (ART) procedures:
    - Intra-uterine insemination (IUI)
    - In-vitro fertilization (IVF)
    - Intra-cytoplasmic sperm injection (ICSI)
    - Intra-uterine insemination with donor sperm
    - IVF with donor sperm
    - IVF or ICSI with a known oocyte (egg) donor
    - IVF or ICSI with a surrogate mother.
    - Semen Decontamination in HIV positive men

LAPAROSCOPY

Laparoscopic surgery (L/S) is minimal invasive surgery involving the introduction of a "camera lens" into the abdomen through a small incision (0.5-1.5 cm).The abdomen is insufflated with carbon dioxide gas. L/S allows for the evaluation of the tubes, ovaries, the uterus and possible pelvic pathology.

Effort will be made to correct all abnormalities within the informed consent agreement between the surgeon and the patient at the time of the operation.

HYSTEROSCOPY AND OFFICE HYSTEROSCOPY

Hysteroscopy is the introduction of the "camera lens" inside of the uterus to evaluate the uterine cavity. Hysteroscopy can be done in theatre or as an office procedure in the unit.

Effort will be made to correct all abnormalities within the informed consent agreement between the surgeon and the patient at the time of the operation.

INTRA-UTERINE INSEMINATION (IUI) OR ARTIFICIAL INSEMINATION

Can be described as the introduction of a processed sperm sample into the uterine cavity (womb). In order to perform this procedure, the fallopian tubes must be patent and the semen sample must be within the normal parameters.

IN-VITRO FERTILIZATION (IVF)

A procedure whereby the female undergoes controlled ovarian stimulation. The eggs (oocytes) are harvested and fertilized naturally with the partner's sperm in a "dish". The embryos are transferred into the uterine cavity (womb) under ultra-sound guidance. IVF is performed when the woman has blocked or damaged fallopian tubes that may interfere with the egg and the sperm uniting. Another indication for IVF would be if the partner's semen analysis has abnormalities that may preclude the couple from undergoing an IUI or spontaneous pregnancy.

INTRA- CYTOPLASMIC SPERM INJECTION (ICSI)

A procedure whereby the female undergoes controlled ovarian stimulation. The eggs (oocytes) are harvested and each mature egg is injected with partner's sperm and cultured in a "dish" (one sperm per egg). The embryos are transferred into the uterine cavity (womb) under ultra-sound guidance. ICSI is performed when semen has abnormalities that will preclude the couple from undergoing an IUI, IVF or spontaneous pregnancy.

TRANS - EPIDIDYMAL SPERM ASPIRATION (TESA) OR TESTICULAR BIOPSY

This procedure is performed on male patients where the testes seem to be functioning normally but there is an obstruction preventing the sperm from being released. A small needle is introduced in the epididymis and sperm is aspirated. Sometimes the clinician may resort to testicular biopsy in order to retrieve sperm.

Patients with suspected obstructive azoospermia are referred to the **Andrology Clinic, Level 7 Bridge C. (Tel: 012 354 2377).** The patient is referred back to us. This is done to evaluate if the patient is a suitable candidate for Trans-Epididymis Sperm Aspiration (TESA) or Testis Biopsy for ART.

A patient undergoing testis aspiration or biopsy may consider the use of Donor Sperm as a back up if no sperm is retrieved either via TESA or Testis biopsy. This "back up" option should be discussed by the couple ahead of the planned procedure and clear directives should be given to the doctor at the unit. The TESA/testis biopsy is performed by the Registrars from the Department of Urology.

SEMEN DECONTAMINATION

A procedure whereby blood-borne pathogens (organisms) e.g. HIV are removed from the semen sample in order to reduce the risk of transmission of the infection to the partner or the prospective baby.

Requirements:

All patients must have a **referral letter with the copies of the required recent results.**

Blood results not older than six (6) months (RNA viral load and CD4 count) is required at the initial visit.

ID photos for administrative purposes.

Semen viral validation pathology tests are self-funded.

Process

- At the couple's initial visit, the male partner will be scheduled for a semen evaluation on the first available Thursday.
- A referral letter for decontamination should be obtained from the clinic and provided to the laboratory staff, along with the semen sample for first evaluation
- With the couple's follow-up visit, the decontamination procedure and relevant costs will be discussed.
- The couple contact the clinic when ready to proceed with ART treatment and a semen decontamination procedure is scheduled through the clinic with the laboratory (which will be on the first available Thursday).
- A semen sample is produced on the scheduled day and provided to the laboratory in order to proceed with the decontamination and cryopreservation procedures.
- A portion of the purified sperm sample will be submitted for HIV-1 DNA and RNA testing.
- Semen decontamination and pathology results will be available from the clinic within two weeks after the decontamination procedure.

ADOPTION:

In some instances, we may not be able to offer the couple Assisted Reproductive Techniques.

Adoption is a viable option in childless couples and couples wanting more children. Please contact the social workers for more information (Private social workers or The Child Welfare Society).

CRITERIA FOR GAMETE DONATION AND SURROGACY[2]

The Criteria for the RECIPIENT in an egg donor cycle:

- Younger than 45
- Medical assessment by the obstetrician who will be providing ante-natal care with regards to pregnancy and the risks involved
- Physician's assessment of general health, specifically diabetes, hypertension, coronary heart disease
- Psychological evaluation required (together with partner)
- An ECG and mammogram may be performed.
- Informed consent from recipient and partner
- Legal binding agreement between the couple and the egg donor (and her partner if married) once the donor is found to be suitable. The couple needs to provide the clinic with a copy of the document.

The Criteria for a suitable EGG DONOR

- Couples can decide between a known egg donor and an anonymous egg donor.
- There are egg donor agencies that can assist with anonymous egg donation.
- Our unit works with known egg donors.

Known donors:

- Healthy with sober habits, no known genetic abnormalities or risk factors for Sexually Transmitted Infections (STIs)
- Ideal body mass with a BMI < 30kg/m^2
- Minimum age : 18 years (as per National Health Act)
- Preferably between the ages of 21-34 years.

- If donor is younger than 21, the donor should have a psychological evaluation
- If donor is older than 34, the recipients should be informed regarding risks of aneuploidy and effect of donor age on the success.
- Established fertility is desirable but not essential
- The recipient can request the following tests: Cystic fibrosis carrier status, karyotype of the donor, Fragile X mutation.
- Psychological evaluation by a social worker or psychologist (with partner if married or in a stable relationship)
- History of previous egg donations at other infertility units.
- **RISKS**: Ovarian Hyper stimulation Syndrome, Infection, Bleeding, injury to organs, ovarian torsion, pregnancy

Procedure:

The donor is evaluated at the clinic.

Investigations:

- HIV type 1 and 2,
- Hepatitis B surface Ag,
- Hepatitis C Ab,
- RPR,
- blood group and Rhesus status and
- Anti-Mullerian Hormone.

Once the doctors are satisfied, the couple and the donor (and partner) will be referred to the social worker for consultation.

A full report should be forwarded to the doctor.

Once all the criteria have been met, the procedure is discussed with the participants.

Couples consult their own lawyers to discuss the implications of egg donation.

A legally binding document will need to be drawn up, signed and a signed copy handed to the clinic prior to treatment.

The Regulations for the National Health Act states that the donor oocytes may not be used in the following situations:

- Where five children exist who have been conceived from artificial fertilization using her gametes
- Where 2 or more pregnancies exist as a result of artificial fertilization using her gametes
- The possibility exists that after the intended artificial fertilization procedure; more than 2 pregnancies may exist simultaneously as a result of artificial fertilization with the donor's gametes.

Criteria for suitable SPERM DONOR

Our patients acquire the cryopreserved samples from anonymous donors from the Sperm Bank.

Donor sperm may be used if:

- The male partner does not have any sperm due to for example, testicular failure
- As a back up if Trans-Epididymal Sperm Aspiration (TESA) or Testis Biopsy is unsuccessful
- If the cost of ICSI is beyond the patients means and IUI is a viable option
- If the male partner is HIV positive and the couple wish to eliminate risk of HIV transmission.

SPERM BANK (Anonymous sperm donor)

Ampath Andrology Laboratory: Address: 1171 Stanza Bopape Street (previously known as Church Street), Hatfield, Pretoria.

Tel: 012 423 0560

Known sperm donors:

- Minimum age: 18 years
- Sperm should not be taken from donors aged 40 years or older.

- Healthy with sober habits, no known genetic abnormalities or risk factors for Sexually Transmitted Infections (STIs)
- Established fertility is desirable but not essential
- Psychological evaluation may be performed (donor and partner as well as the recipients)
- Couples consult their own lawyers to discuss the implications of sperm donation.
- A legally binding document will need to be drawn up, signed and a signed copy handed to the clinic prior to treatment.

Investigations:

- HIV type 1 and 2,
- Hepatitis B surface Ag,
- Hepatitis C Ab,
- RPR,
- Semen evaluation and Microscopy, Culture and Sensitivity

Criteria for a suitable SURROGATE

- Healthy with sober habits
- No risk factors for Sexually Transmitted Infections (STIs)
- Responsible and trustworthy
- Ideal body mass with a BMI < 30kg/m^2

Investigations:

- HIV type 1 and 2,
- Hepatitis B surface Ag,
- Hepatitis C Ab,
- RPR,
- Rubella IgG,
- CMV IgM,

- HTLV 1 and 2,
- Neisseria gonorrhoea,
- Chlamydia,
- Blood group and Rhesus status.

Once the doctors are satisfied, the couple and surrogate (and partner) will be referred to a social worker for consultation and to facilitate the surrogacy application to the High Court.

Couples consult their own lawyers to discuss the implications of surrogacy.

According to current Children's Act Legislation, ART with a surrogate mother cannot be instituted without a High Court Order. The social worker or lawyer (sourced by the couple) should be able to assist with this.

A copy of the High Court Order needs to be handed to the unit prior to commencing ART.

The prospective child should be genetically related to at least one of the commissioning parents.

Commissioned adoption is not currently practiced.

REFERENCES:

1. http://guidance.nice.org.uk/CG156
2. www.fertilitysa.org.za/Guidelines/ReproductiveMedicine