

Reproductive Immunology at The Zita West Clinic

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In collaboration with

Clinical Immunology Laboratory
Rosalind Franklin University of Medicine and Science
(Formerly known as The Chicago Medical School, USA)

Chicago Blood Tests
Mon & Tues between 7:00am-7:00pm
Wed 8:00am-12:00pm

**Bloods are taken at The Doctors Laboratory following payment for the tests at Zita West Clinics.*

Introduction

The most common reason that IVF does not work is the failure of an embryo to implant. We also know that up to two-thirds of early pregnancies miscarry. We believe that whereas chromosomal abnormalities in embryos might be a major factor, a significant cause of these problems may relate to abnormalities in the woman's immune system which compromise successful embryo implantation.

Research has suggested that during a normal pregnancy, a unique type of immunity occurs that stops a woman rejecting an embryo and aids the growth and development of the foetus. If this immunity does not exist embryos may not implant, early pregnancies may miscarry or later complications may occur for the mother or baby. Special tests may identify couples that are at risk of these problems. Treatment that stimulates the proper immune response (immuno-modulation) in the mother may then improve the chances of a successful pregnancy.

However, clients must recognise and accept that this research is still in the experimental stages and must also recognise that some of the possible treatments (immuno-modulation) are not universally accepted. Clients are therefore urged to read this document, the Royal College of Obstetricians and Gynaecologists "Immunological Testing and Interventions for Reproductive Failure" document <http://www.rcog.org.uk/womens-health/clinical-guidance/immunological-testing-and-interventions-reproductive-failure> and the Zita West Reproductive Immunology Fee Schedule carefully.

While recognising that this is the frontier of our field, there are major practical difficulties in arranging suitable trials. Data from large randomised client studies is currently not available. Risks of treatments are also difficult to assess. As a result there is considerable controversy surrounding treatments in this field as none of these therapies are licensed for use in reproductive medicine. Zita West Clinics is committed to reviewing the available evidence, formulating clear and appropriate strategies and monitoring our results carefully. We also aim to provide clear information about the treatments, their efficacy and safety to enable clients to reach informed decisions.

Embryo implantation and early pregnancy loss have been Dr George Ndukwe's interest over the years. He was mentored by Professor Alan Beer and has developed arguably the largest and most successful Reproductive Immunology Programme in Europe for recurrent IVF failure/miscarriage in collaboration with the Immunology Laboratory at the Chicago Medical School.

Categories of Immune Problems

Listed below are four categories of immune problems that can cause pregnancy loss, IVF failures and infertility; and further in this document we describe the actual treatments and possible side effects. These will be discussed in detail at your consultation.

A- Lack of Blocking Antibody to Pregnancy

In normal pregnancy the part of the embryo derived from the man's sperm will cause the woman to develop antibodies that form a protective 'ring' (a blocking antibody) around the embryo. In couples that are a close genetic match there is a lack of the blocking antibody to pregnancy, the embryo or foetus is rejected and the pregnancy fails. The tests required are a blood test from the man and woman to determine if they are too closely linked genetically (called, 'DQ alpha matching' of the couple). We treat this with low dose Aspirin, steroids, low molecular weight heparin (Clexane or Fragmin) and Intralipid infusion. Some authorities recommend Lymphocyte Immune Therapy (LIT) for this.

B- Development of autoimmune antibodies

This category includes women who develop autoimmunity to phospholipids, thyroid molecules or other tissues. Phospholipids are the 'glue' molecules for implantation and development of the placenta. If antibodies attack them these processes cannot take place normally.

It also includes women who develop antibodies to the baby's DNA or DNA breakdown products and this problem is reflected by a positive Anti-nuclear antibody test (ANA). While we test for this specifically, tests can also be done for double-stranded DNA, single stranded DNA, polynucleotides and histones (DNA breakdown products). Some of these women have clinical manifestation of early mixed connective tissue disorders. The treatment for these problems includes the use of steroids (Prednisolone), low-dose Aspirin and Clexane.

Clients with thyroid antibodies and who have thyroid stimulating hormone (TSH) levels above 2 will require thyroxine supplements.

C- Thrombophilia

Women in this category have a genetic or acquired thrombotic (blood clotting) tendency. This includes all thrombophilias including Platelet activation inhibitor gene polymorphism (PAI-1) and Methylene Tetrahydrofolate reductase gene mutation (MTHFR). Treatment includes low-dose Aspirin and low molecular weight heparin (Clexane/Fragmin). Women with MTHFR gene mutation however only need high dose folic acid (5mg) + Vitamin B6 and Vitamin B12. Femibion which contains Metafolin (a very active form of folic acid) and Vitamin B6 and Vitamin B12 may also be used.

D- Elevated Natural Killer (NK) Cells, elevated CD19 and CD19+, CD5+ immune cells and altered TH1:TH2 ratios

In women with elevated natural killer cells too much tumour necrosis factor (TNF) is produced which can attack the embryo and prevent implantation. Possible treatments may include steroids, low molecular weight heparin (Clexane or Fragmin) and Intralipid intravenous infusion. Intravenous immunoglobulin or Humira may be used in women allergic to egg or soya. Elevation of other CD cells can produce antibodies to hormones and neurotransmitters. Treatment may include steroids, low-dose Aspirin, Clexane/Fragmin, or selective Serotonin re-uptake inhibitors (SSRI) e.g. Prozac.

Elevated TH1:TH2 ratios are associated with recurrent embryo implantation failure and recurrent miscarriage. The treatment is Intralipid intravenous infusion, steroids and Clexane/Fragmin. Intravenous immunoglobulin or Humira may only be used in women allergic to egg or soya.

Indication for Immune Tests

The following couples would appear to be at increased risk of immune problems and should consider immune testing:-

- a) Women over the age of 35 who have had two or more miscarriages or two or more failed IVF/ICSI or GIFT cycles;
- b) Poor egg production from a stimulated IVF/GIFT cycle (less than 6 eggs);
- c) One blighted ovum (missed miscarriage);
- d) Unexplained infertility of over 3 years;

- e) Previous immune problems (Anti-nuclear antibody {ANA}, antithyroid antibodies, rheumatoid arthritis, and/or lupus, Crohn's disease, psoriasis, ulcerative colitis, etc);
- f) Previous pregnancies that have resulted in small babies (foetal growth retardation);
- g) One living child and repeated miscarriages while attempting to have a second child.

Immune Tests

A DQ Alpha

If the HLA DQ Alpha of the couple is too closely matched the mother's body does not offer enough protection to the new embryonic cells and rejects the embryo because it cannot identify the embryo as a developing foetus.

There are two different tests- the Alpha and the Beta test. Most clients are only tested for the Alpha. Depending on the results, sometimes the DQ Beta test is done. This can sometimes predict the occurrence of missed miscarriage. DQ Alpha incompatibility between mother and baby is found to be far more common in women who have had successful pregnancies and births.

DQ Alpha testing of both partners can also identify those women whose first baby activated the mother's natural killer (NK) cells and lowered her ability to produce blocking antibodies. This process prevents her from having another child without the use of immune modulation to reduce the NK cells and to increase the blocking antibodies.

B Reproductive Immunophenotype

This checks for the presence of Natural Killer Cells. In most cases, Natural Killer Cells are good because they stop the body from developing cancer. Up to 15% of women with recurrent pregnancy losses (3 or more) and 35% of women with 3 or more IVF failures have elevated NK cells. NK cells are one of the most primitive lymphocytes (white blood cells) in man. They have several useful functions. One of these is to produce a cytotoxic chemical called tumor necrosis factor (TNF). TNF is very effective in eliminating altered cells in our body e.g. cancer cells. Some women have higher than normal levels. The embryo can be misinterpreted as cancer cells and in pregnancy, NK cells increase in number and killing power, causing embryos to become damaged by the TNF. High NK levels are treated with Intralipid. At lower levels of NK Cells, steroids may be used.

C Natural Killer Cell Assay

This is a test-tube assessment that determines the killing power (activity) of a woman's NK Cells. NK Cells are placed in the test tubes with cells from embryo cell tissues and the results show the percentage of embryo cells killed. Abnormally high NK activity is treated with Intralipid. IVIg or Humira may be used only in women allergic to egg or soya.

D TH1:TH2 Intracellular Cytokine Ratios

The ratio between the TH1 and TH2 groups of immune cells correlates with recurrent embryo implantation failure and miscarriage. TH1 dominance prevents implantation and causes miscarriage. TH2 dominance leads to a successful pregnancy. In this test the TH1:TH2 intracellular cytokine ratios are measured. The treatment of choice is Intralipid. IVIg or Humira may be used only in woman allergic to egg or soya. However, Humira may not be successful in about 20% of women. The aim is to restore TH2 dominance, thereby facilitating implantation and preventing miscarriage. It is important to

understand that appropriate immunotherapy simply restores the chances of a successful pregnancy. It is not 100%.

E ANA (Antinuclear Antibody)

This test checks for problems similar to lupus, rheumatoid arthritis and other immunological diseases that can also result in pregnancy losses or infertility. This test becomes weakly positive in women with infertility and in women with recurrent pregnancy losses.

F Anti-DNA/Histone Antibodies

If a woman reacts to the broken down DNA (histones), this test can identify if she has a reaction to her own embryos.

G APA (Antiphospholipid Antibodies)

When this test is positive, the woman's blood clots too fast cutting off support to the baby. These antibodies also cause the embryo to attach too weakly to the uterus. The treatment includes the use of low dose Aspirin, steroids and low molecular weight heparin. These medications are started during the cycle of conception.

H Other Common Tests for Treatment Failure

Other tests that are widely available in all laboratories may be required. These include thyroid function tests (TFTs), antithyroid antibodies and full thrombophilia screen.

I Anatomical tests: (May sometimes be required)

- Detailed ultrasound to exclude hydrosalpinx (fluid in the Fallopian tube), uterine abnormality, fibroid or polyps.
- Hysteroscopy.

*appropriate tests will be recommended by Dr George Ndukwe

Treatments for Immune problems

It is important to understand that some of these treatments remain experimental and that some of these drugs are not licensed for the immune treatment of infertility or for use in pregnancy. There are potentially serious adverse reactions to some of the medication, e.g. IVIg or Humira (no longer used routinely) if not used with due care under strict supervision. They are also very expensive. A separate consent form will be required for some of the medication.

1 Aspirin Therapy

Low dose Aspirin (75mg/day) is often used in women with antiphospholipid antibody syndrome, recurrent pregnancy losses or infertility caused by immunity. Low dose Aspirin is prescribed alone or combined with heparin or steroid treatment. Aspirin 75mg tablets can be purchased over the counter and do not require a prescription.

Side Effects

The possible side effects of full dose Aspirin are not seen with low dose Aspirin treatment. These side effects are nausea, heartburn, upset stomach, decreased appetite and microscopic amounts of blood in stools, On very rare occasion, allergic reactions have been observed following Aspirin ingestion. If you have any history of Aspirin sensitivity, please inform our Fertility Nurse Specialist or Dr George Ndukwe. The above-mentioned side effects are mainly experienced in clients taking a normal adult dose or high dose of Aspirin therapy. Low dose Aspirin treatment is reported to have minimal, if any, side effects.

Aspirin intolerance manifested by exacerbation of asthma (bronchospasm) and rhinitis may occur in a client with a history of nasal polyps, asthma, allergic skin reactions or rhinitis. If you have any past history of any of the above, please notify us before starting Aspirin.

Enteric coated Aspirin is also available for women with a history of gastrointestinal side effects of plain Aspirin or conditions requiring chronic or long-term Aspirin therapy.

Interaction

When you start to take low dose Aspirin, moderation in taking the following food is recommended: Curry powder, paprika, liquorice, prunes, raisins, gherkins, tea and other than the occasional use of antacids. Phenobarbitone decreases Aspirin efficacy.

Usage During Pregnancy

The use of Aspirin during pregnancy, especially chronic or intermittent high doses, may affect the maternal and fetal blood clotting mechanisms, leading to an increased risk of bleeding. High-dose Aspirin may be related to increased perinatal mortality, intrauterine growth retardation, and congenital defects. Luckily, only low-dose Aspirin is used for immune treatment. Recent evidence suggests that Aspirin may increase the relative risk of early miscarriage and for this reason clients are now advised to stop low-dose Aspirin just before embryo transfer and not to take it in early pregnancy.

2 Heparin Therapy

Low molecular weight heparin is often used in treatment for women with inherited or acquired thrombophilia (clotting tendency) – with the presence of factor V (Leiden) mutation, abnormalities in Protein C or S and in PAI-1-gene polymorphism. It is also used empirically as a “suppressor” of the immune and clotting systems. Several commercial preparations are available, e.g. Fragmin and Clexane. It is known that regular heparin (or high molecular weight heparin) does not cross the placenta in pregnant women. This seems to be the same for low molecular heparin.

A Clexane (Enoxaparin)

Clexane is a low molecular weight heparin. Clexane will usually be prescribed as 20mg or 40mg, subcutaneously, once daily.

B Fragmin (Dalteparin)

Fragmin is a low molecular weight heparin. Fragmin is often prescribed as 2500 IU or 5000 IU, subcutaneously daily.

Dosage and injection can be changed based on the clients’ need.

Contraindication to low molecular weight heparin

Clients with the following concerns should not use Clexane/Fragmin injections:

- Known hypersensitivity
- Active bleeding
- Thrombocytopenia (decrease in the number of platelets)
- Hypersensitivity to heparin or pork products
- Severe hypertension
- Osteoporosis

Warnings for low molecular weight heparin

- Clexane and Fragmin are not intended for intramuscular administration.
- Clexane and Fragmin cannot be exchangeable with heparin or other low molecular weight heparin.
- In clients with a history of low platelet count either induced by heparin or other reason it should be used with extreme caution.
- As with other anticoagulants, there have been rare cases of neuraxial hematoma reported with the concurrent use of Clexane and spinal/epidural anaesthesia resulting in paralysis.

Common Side Effects

Mild local irritation, pain, bruising, ecchymoses (small purple skin patch) and erythema (redness, flushing of skin) may occur at the injection site. Osteoporosis after prolonged use, hair loss (very rarely).

Calcium supplementation

To minimise the bone thinning effect of heparin, we advise clients taking Fragmin/Clexane to use a calcium supplement (500mg tablet, twice a day). These can be purchased over the counter and do not require a prescription.

Monitoring

Periodic full blood count and platelet count should be considered for long-term usage.

Important Points To Remember

1. Preferred site of injection is the abdominal area. Injections must be given 2 inches away from the umbilicus (belly button). If you need another area to give your heparin, you may use your thighs or buttocks, but this is only if there is no other place in your abdominal area.
2. Rotate your sites of injections. Never inject in the same place as a previous injection or in a bruised area.
3. Some bruising at the site of injection is normal (less than 2p size). If increased bruising occurs, you may use ice before you clean the area for injection and/or after you have given yourself the injection.
4. Notify your doctors that you are taking heparin before any medication or surgical procedure.
5. Contact your doctor if any of the following symptoms occur:
 - Nose bleeds
 - Blood in the urine or stool

- Excessive bleeding lasting greater than 15 minutes and not controlled by direct pressure
- Unusual bruising not at the site of injection

Possible Side Effects

- Bleeding
- Local irritation – redness, mild pain, and itching at site of injection
- Nausea and vomiting, chill and fever (rare)

3 Steroid Treatment

Indications:

a) Immune modulation

Prednisolone and Dexamethasone are two commonly prescribed steroids. Prednisolone is prescribed to suppress abnormal autoimmunity such as ANA and autoantibodies to DNA and/or histones. Prednisolone treatment can be combined with Aspirin or heparin, or both.

b) 'Poor responders'

Dexamethasone is also used in the stimulation phase of an IVF cycle to try to increase egg numbers. We prefer not to use Dexamethasone in early pregnancy as most of it can cross the placenta.

Possible Side Effects

The principal complications resulting from prolonged therapy with steroids are fluid and electrolyte disturbances, hyperglycemia (high blood sugar levels), glycosuria (abnormal amounts of glucose in urine), increased susceptibility to infection, peptic ulcer, osteoporosis, behavioural disturbance, e.g. nervousness, insomnia, changes in mood, cataracts, and striae (skin stretch marks). Cushingoid features consisting of moon face, buffalo pads (fatty pads at back of neck and along the collar bone), central obesity, ecchymoses, acne, and hirsutism (excessive hair growth) can occur. Your features will return to normal following cessation of steroids.

Diet Restriction

Average and large doses of Prednisolone can cause elevation of blood pressure, salt and water retention and increased excretion of potassium and calcium. Dietary salt restriction, potassium supplementation and regular blood pressure monitoring is advised if steroids are used in high dose for long periods. Only moderate doses are, however, used in reproductive immune therapy.

Diabetes

Prednisolone can induce diabetic tendency. If Prednisolone is indicated, your blood sugar level will need to be monitored, especially during pregnancy.

Other Cautions

Prednisolone should be used with caution if you have ulcerative colitis, abscess or other pyogenic (pus forming) infection, diverticulitis, peptic ulcer, hypertension, congestive heart failure, history of blood clots, osteoporosis, Cushing syndrome or convulsive

disorder. Osteoporosis can be prevented by calcium supplementation, which is reported to suppress bone resorption without detectable suppression of indices of bone formation in steroid treated clients.

Notify your doctor that you are taking steroids before taking any medication or having a surgical procedure and carry an identification card in your wallet stating that you are on steroids.

Withdrawal

Too rapid withdrawal of Prednisolone during the weaning process may cause nausea, fatigue, anorexia (loss of appetite), dyspnea (laboured breathing), hypotension (low blood pressure), hypoglycaemia (low blood sugar), myalgia (muscle pain), fever, malaise, arthralgia (joint pain), dizziness, skin sloughing off and fainting. If you have any of these unusual problems, contact our clinic immediately. For clients on Prednisolone we advise a gradual step-wise reduction by 5mg every 3 days, ending with 5mg every other day for 3 doses.

There are a number of studies in which pregnant clients received Prednisolone and have shown little, if any effect on the developing foetus. The drug does not cross the placenta to the foetus. Please talk to us and ask questions during your consultation if you have any concerns.

4 Intravenous Intralipid 20% Solution Infusion Treatment

Intralipid is an emulsion of soya bean oil, egg phospholipids and glycerine. It has been used since the 1970s to provide essential fatty acids as part of intravenous feeding for patients who cannot get their nutrition orally. Evidence from both animal and human studies suggests that Intravenous Intralipid administration may enhance embryo implantation. Although the exact mechanism of this beneficial action has not been completely elucidated, it has been suggested that Intralipid stimulates the immune system to remove "danger signals" that can lead to pregnancy loss. Also, recent evidence has confirmed the ability of Intralipid to suppress Natural Killer (NK) cytotoxicity for a sufficient duration of time to enhance implantation and maintain pregnancy. It has also been known to be the most effective treatment to correct TH1/TH2 abnormalities.

Clinical studies using Intralipid have shown improved pregnancy and live birth rates in recurrent embryo implantation failure after IVF and recurrent miscarriage in women with elevated NK activity and TH1/TH2 abnormalities. Studies comparing IVIg, Intralipid and sHLA-G confirmed they all suppressed NK cell cytotoxicity with equal efficacy. However, Intralipid has the advantage that it is relatively inexpensive and it is not a blood product. Intralipid treatment is not yet licensed for use in reproductive failure or pregnancy and is considered investigational. You will be responsible for the cost of all treatment, including Intralipid administration.

Nature and Duration of Procedure

Treatment is given intravenously and dosage and infusion protocols are determined based on laboratory testing and clinical responses. Treatment is usually given while you are attempting to achieve a pregnancy and during pregnancy. The infusion is given as a drip in the arm and is administered and supervised at your home by a "Healthcare at Home" nurse. The procedure takes a minimum of two hours.

Potential Risks

Clients allergic to eggs or soya bean oil MUST NEVER have Intralipid.

Side effects are rare and include febrile episodes (fever) and less frequently shivering, chills and nausea/vomiting (less than 1%). The infusion should be discontinued in such cases. Other adverse effects are extremely rare, occurring in less than 1 in 1 million infusions e.g. hypersensitivity reactions (anaphylaxis, skin rash & urticaria), respiratory symptoms (rapid breathing) circulatory effects (high or low blood pressure), abdominal pain, headache and tiredness. These side effects are mainly seen in clients having Intralipid daily for intravenous feeding. The safety profile for Intralipid is regarded as extremely good.

5 Immunoglobulin G (IVIg) Infusion Treatment

IVIg infusion treatment alone or in conjunction with conventional immunotherapy such as anticoagulation or immunosuppression may be indicated in some women with recurrent spontaneous miscarriages or infertility caused by immune problems who are allergic to egg or soya and, therefore, cannot have Intralipid.

IVIg consists of concentrated human immunoglobulins, primarily IgG (immunoglobulin G), prepared from pooled human donors (8,000-13,000 donors per lot), screened free of blood-borne disorders. Dosage and infusion protocol will be determined based on laboratory testing and clinical responses.

Before IVIg can be given, all clients must have a blood test to check their Immunoglobulin Panel to rule out deficiency in Immunoglobulin A. This is because in such women there is a risk of severe reaction.

Side Effects

Side effects to IVIg infusion tend to be related to the rate of infusion. Possible side effects include malaise, a feeling of faintness, fever, chills, headaches, nausea, and vomiting. Shortness of breath, chest tightness, thrombosis and joint pains have also rarely been reported.

Viral Safety

No cases of human immunodeficiency virus transmission have been related to the administration of IVIg. Hepatitis B and C virus transmission have been reported in IVIg improperly prepared. However, there are still concerns about possible viral transmission. It is recommended to use only IVIg products that have been prepared with an additional viral inactivation procedure.

Hypersensitivity

Anaphylactic reactions may occur during IVIg treatment in clients with IgA (Immunoglobulin A) deficiency. Before IVIg infusion, serum IgA level should be checked. Clients with IgA deficiency need further workup before IVIg infusion.

6 Adalimumab (Humira)

Humira belongs to a new class of drugs that block the effects of the products of NK cells (tumour necrosis factor-alpha-TNF-a). It is only used in women with immune abnormalities causing recurrent IVF failure or miscarriage, who are allergic to egg or soya and, therefore, cannot have Intralipids. It is licensed for the treatment of clients

with rheumatoid arthritis or Crohn's disease. Recent work done at the Chicago Medical School indicated that it may be useful in the treatment of recurrent miscarriage and recurrent embryo implantation failure. Although it is not licensed for this purpose, it can be used after proper investigation if there is a clear indication for use. This drug will be used preceding fertility treatment or pregnancy cycle only. The aim is simply to bring TNF- α levels back to normal prior to treatment or pregnancy, thereby reducing any potential adverse effects from the raised levels. We do not advise its use in pregnancy. Treatment with anti TNF- α drugs should not be initiated in clients with active infections, including tuberculosis, chronic or localised infections until infections are controlled. We have showed that Intralipid is more effective than Humira as Humira may not reduce TH1:TH2 abnormalities in up to 20% of women.

Before starting Humira, clients must rule out Tuberculosis by TB Gold test

TNF- α may be important in immunological defence against cancer. There is, however, no clinical evidence that anti TNF- α drugs increase the risk of cancer.

Administration of Humira (Adalimumab)

Humira comes as a single dose (40mg), pre-filled syringe and is given as a subcutaneous injection once every two weeks. Complete elimination of Humira may take up to five months. Clients usually need 2 to 4 doses, dependent on severity of immune abnormality.

Side Effects

In placebo-controlled studies 20% of clients treated with Humira developed injection site reactions (redness and/or itching, bleeding, pain or swelling) compared to 14% who received placebo. The incidence of serious infections was extremely low. The infections were primarily upper respiratory tract infections, bronchitis and urinary tract infections. In clinical trials with Humira for up to 53 months no increase in rates and incidences of malignancies were observed. After 24 weeks of Humira 12.6% of clients with negative anti-nuclear antibodies tested positive compared with 7.3% of placebo-treated clients. The significance is unclear. A drug-induced lupus-like syndrome may occur and the drug must be discontinued in that case. Although development toxicity study in monkeys showed no maternal toxicity to embryos and no developmental abnormalities, we do not advise the use of Humira in pregnancy.

In up to 20% of clients, elevated TNF- α levels may not be successfully reduced with Humira.

Infections

Severe infections, sepsis and re-activation of tuberculosis have been reported with TNF- α blockers. These drugs should not be started and should be discontinued if the client develops serious infection. These drugs are used cautiously in clients with a history of recurrent infections or medical conditions that predisposes to infections. Live vaccines should not be given concurrently with these drugs. The recommendation is that all clients should be screened for tuberculosis before starting the drugs. If symptoms develop suggesting tuberculosis, e.g. persistent cough, weight loss and low-grade fever, medical advice should be sought. Also, because of this slow elimination of the drugs, infections should be reported while on the drugs and for at least 6 months afterwards. Severe leukopenia (reduction of white blood cells), pancytopenia (deficiency of all blood cells) and aplastic anaemia and onset of demyelinating disease of the central nervous system including multiple sclerosis and optic neuritis have been rarely associated with some anti TNF alpha drugs. The drug should be used with great caution in clients with a history of these disorders or discontinued if the problems occur.

For medico-legal reasons we cannot organise Reproductive Immunology investigations and/or Immunotherapy for any clients who are not having assisted fertility or Recurrent miscarriage treatment at The Zita West Clinic.

An Integrated approach to Reproductive Immunology

We strongly recommend that anyone diagnosed with a reproductive immunological issue should consider having a nutritional consultation at The Zita West Clinic. Nutrition and lifestyle factors can influence the immunologic response of your body. Many of the immunological medications can cause a drug-nutrient interaction for example Aspirin can cause loss of Folic Acid and Vitamin C, Heparin can interfere with Potassium levels and Vitamin D levels, Steroids may interfere with the absorption of Vitamin D, Calcium, B6 and Zinc. As some of the drugs used in reproductive immunology tend to suppress the immune system it is important to support the immune system as much as possible with your diet. At a nutritional consultation one of our nutritionists will do an assessment of your current dietary intake and will formulate a nutrition plan specific to your Individual needs as well as suggesting appropriate supplements if required, a nutritional consultation cost £125.00 and can be booked through reception on 0207 224 0017

Complementary Therapies and Reproductive Immunology

Most women having reproductive immunology tests will have experienced the stress of either unexplained infertility, IVF failure, or miscarriage. Stress, over-work, fatigue and even getting a cold can have a powerful impact on their immune system. Complementary therapies such as Acupuncture and Hypnotherapy may help you physically and emotionally in achieving optimum mind-body balance. If you would like any of these treatments please contact our reception for more details on 0207 224 0017.

Immune Tests – Price List

Level 1 £ 780

(FBC, fasting blood glucose, LFT's, U&E's, thyroid function – TSH, FT4, thrombophilia screen – anticardiolipin antibodies (IgG and IgM), antithrombin 111, factor V Leiden, factor II prothrombin gene, PAIP polymorphism, activated protein C resistance, Protein C/Protein S, lupus anticoagulant, MTHFR, autoimmune antibodies – including anti-nuclear antibodies, thyroid peroxidase and anti-mitochondrial antibodies);

Thrombotic Risk Screen – FBC, anticardiolipin antibodies (IgG and IgM), antithrombin 111, factor V Leiden, factor II prothrombin gene, MTHFR, activated protein C resistance, Protein C, Protein S, lupus anticoagulant, £ 600

PAIP polymorphism £ 150

Autoimmune antibodies £ 120

Chromosome karotype (female) £ 220

Chromosome karotype (male) £ 220

Level 2

a) (NK assay, TH1:TH2- intracellular cytokine ratio, HLADQ alpha) - *female* £ 740
 HLADQ alpha – male £ 100

b) (NK assay, TH1:TH2) – *for female partner only* £ 680

HLADQ alpha £ 100

NK Assay £ 420

Follow-up NK Assay £ 340

TH1:TH2 £ 340

Leucocyte antibody – *for female partner* £ 190

Leucocyte antibody – *for male partner* no charge