The IVF Comic Book

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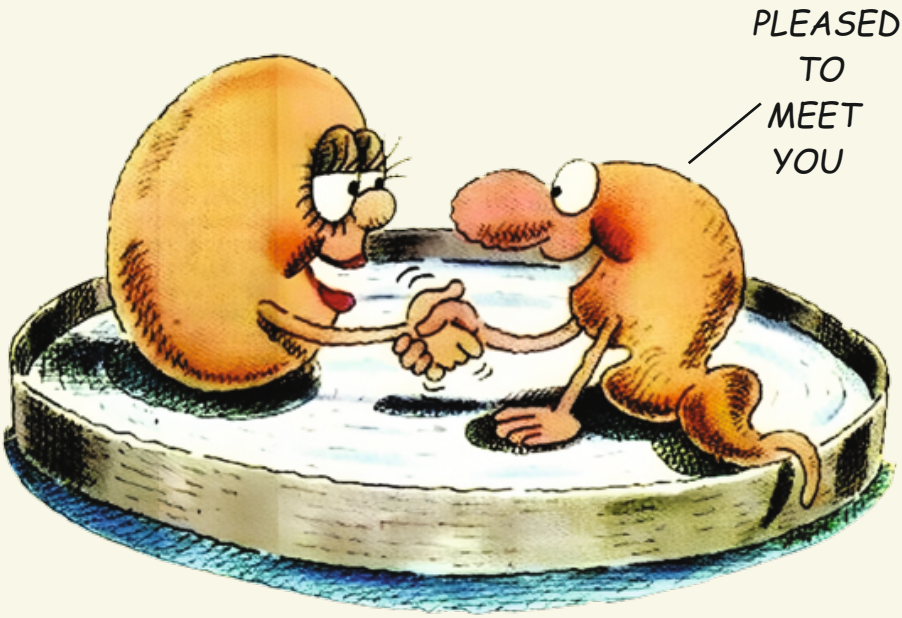
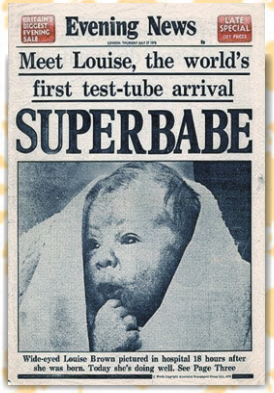


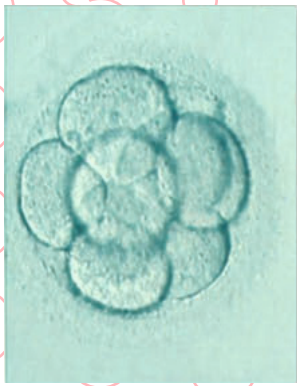
Art and design by : Syanne Djaenal


Evening News
Meet Louise, the world's first test-tube arrival
SUPERBABE
Wide-eyed Louise Brown pictured in hospital 18 hours after she was born. Today she's doing well. See Page Three

THE BIRTH OF LOUISE BROWN THROUGH IN VITRO FERTILIZATION (IVF) IN 1978 WAS A MAJOR MILESTONE IN INFERTILITY TREATMENT. IN A FEW DECADES, IVF HAS BECOME THE CORNERSTONE OF REPRODUCTIVE MEDICINE .AND IVF CLINICS TODAY ROUTINELY PERFORM TECHNIQUES WHICH WERE THOUGHT TO BELONG TO THE REALM OF SCIENCE FICTION A GENERATION AGO !

WHAT ARE THE ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) ?

ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) SUCH AS IVF AND ICSI WERE USED AS METHODS OF LAST RESORT. WHEN EVERYTHING ELSE WHICH HAD BEEN TRIED HAD FAILED. TODAY , SPECIALISTS WILL OFTEN RESORT TO THESE TECHNIQUES FIRST, SINCE THEY OFFER SUCH EXCELLENT RESULTS. TODAY, THANKS TO IVF TECHNOLOGY , THERE IS PRACTICALLY NO INFERTILE COUPLE WHO CANNOT BE OFFERED TREATMENT.



IVF IS A BASIC ASSISTED REPRODUCTION TECHNIQUE , IN WHICH FERTILIZATION OCCURS IN VITRO (LITERALLY, IN GLASS). THE MAN'S SPERM AND THE WOMAN'S EGG ARE COMBINED INA LABORATORY DISH, AND AFTER FERTILIZATION, THE RESULTING EMBRYO IS THEN TRANSFERRED TO THE WOMEN'S UTERUS. THE FIVE BASIC STEPS IN AN IVF TREATMENT CYCLE ARE SUPEROVULATION, EGG RETRIEVAL, FERTILIZATION, EMBRYO CULTURE AND EMBRYO TRANSFER.

IVF IS A TREATMENT OPTION FOR COUPLES WITH VARIOUS TYPES OF INFERTILITY, SINCE IT ALLOWS THE DOCTOR TO PERFORM IN THE LABORATORY WHAT IS NOT HAPPENING IN THE BEDROOM. WE NO LONGER HAVE TO LEAVE EVERYTHING UP TO CHANCE! IT IS A FINAL COMMON PATHWAY, SINCE IT ALLOWS THE DOCTOR TO BYPASS NATURE'S HURDLES AND OVERCOME ITS INEFFICIENCY, SO THAT WE CAN GIVE NATURE A HELPING HAND!

WHAT TESTS NEED TO BE DONE BEFORE STARTING IVF ?

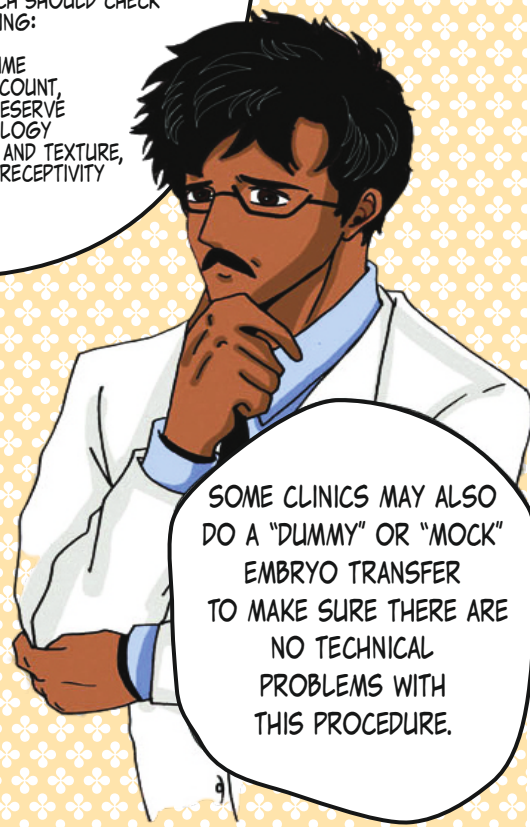
WE NEED THE RESULTS OF ALL THE FOLLOWING SIMPLE MEDICAL TESTS BEFORE DOING AN IVF CYCLE.

1. SEMEN ANALYSIS (TO CHECK THE SPERM COUNT AND MOTILITY);

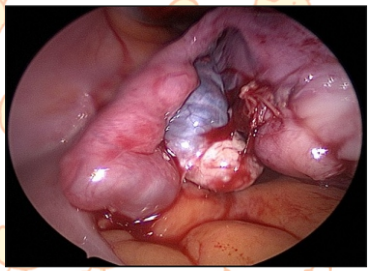
2. BLOOD TESTS FOR THE WIFE FOR THE FOLLOWING REPRODUCTIVE HORMONES - AMH (ANTI-MULLERIAN HORMONE), PRL (PROLACTIN) , AND TSH (THYROID STIMULATING HORMONE), TO CHECK THE QUALITY OF THE EGGS.

3. A VAGINAL ULTRASOUND SCAN ON DAY 2 OR 3 AND AGAIN ON DAY 10 OR 11 WHICH SHOULD CHECK FOR THE FOLLOWING:

A. OVARIAN VOLUME
B. ANTRAL FOLLICLE COUNT, TO CHECK OVARIAN RESERVE
C. UTERUS MORPHOLOGY
D. ENDOMETRIAL THICKNESS AND TEXTURE, TO CHECK ENDOMETRIAL RECEPTIVITY



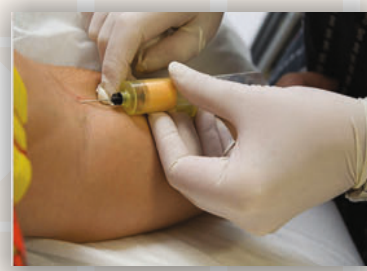
SOME CLINICS MAY ALSO DO A "DUMMY" OR "MOCK" EMBRYO TRANSFER TO MAKE SURE THERE ARE NO TECHNICAL PROBLEMS WITH THIS PROCEDURE.



IF A WOMAN HAS BLOCKED FALLOPIAN TUBES WITH LARGE HYDROSALPINGES , SOME CLINICS WILL REMOVE THESE PRIOR TO THE IVF CYCLE, BECAUSE THEY FEEL THAT THE PRESENCE OF A HYDROSALPINX DECREASES PREGNANCY RATES AFTER IVF.

FOR MEN WHO HAVE DIFFICULTY IN PRODUCING A SEMEN SAMPLE "ON DEMAND", THE CLINIC MAY ALSO FREEZE AND STORE THE SAMPLE PRIOR TO TREATMENT AS A BACKUP. THIS CAN HELP TO PREVENT THE TRAGEDY OF HAVING TO ABORT AN ENTIRE TREATMENT CYCLE BECAUSE THE MAN COULD NOT PRODUCE A SEMEN SAMPLE WHEN NEEDED.

BLOOD TESTS WHICH MAY BE DONE INCLUDE TESTS FOR IMMUNITY TO RUBELLA AND TESTS FOR HEPATITIS B AND HIV. DOCTORS ALSO ADVISE PATIENTS TO START TAKING 5 MG FOLIC ACID AS A PART OF PRE-PREGNANCY CARE TO REDUCE THE RISK OF BIRTH DEFECTS.



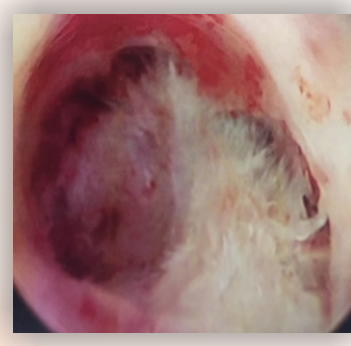
FOR PATIENTS WITH POOR OVARIAN RESERVE, WE ADD 75 MG DHEA (DEHYDROEPIANDROSTERONE) TO IMPROVE OVARIAN RESPONSE .

PATIENTS WITH PCOD ARE TREATED WITH METFORMIN (1500 MG) AND MYOINOSITOL (2 GM) DAILY TO IMPROVE EGG QUALITY.

MEN WHOSE SPERM COUNT IS VERY LOW

MOST CLINICS WILL CONSIDER DOING IVF ONLY FOR MEN WITH AT LEAST 3 MILLION MOTILE SPERM IN THE EJACULATE. IF THE SPERM COUNTS ARE LOWER THAN THIS, THEN ICSI IS A BETTER OPTION.

IT IS ALSO NOT ADVISABLE TO GO IN FOR IVF TREATMENT WITHOUT TRYING SIMPLER TREATMENT OPTIONS FIRST. IVF IS A COMPLEX PROCEDURE INVOLVING CONSIDERABLE PERSONAL AND FINANCIAL COMMITMENT. SO SIMPLER TREATMENT OPTIONS ARE USUALLY RECOMMENDED FIRST.



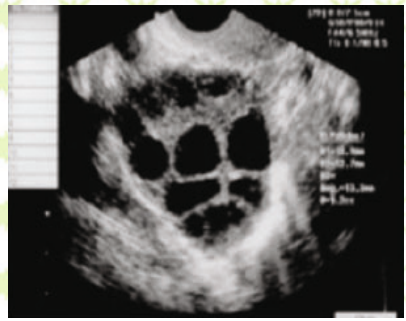
IVF IS NOT ADVISED FOR WOMEN WITH A DAMAGED UTERUS (FOR EXAMPLE, BECAUSE OF HEALED TUBERCULOSIS OR ASHERMAN SYNDROME) BECAUSE THE CHANCES OF SUCCESSFUL IMPLANTATION OF THE EMBRYO IN A DAMAGED UTERUS ARE VERY POOR.


WHAT ARE THE 5 BASIC STEPS OF AN IVF TREATMENT CYCLE ?
1. SUPEROVULATION
2. EGG RETRIEVAL
3. FERTILISATION
4. EMBRYO CULTURE
5. EMBRYO TRANSFER

HOW IS SUPEROVULATION PERFORMED ?

DURING SUPEROVULATION, DRUGS ARE USED TO INDUCE THE PATIENT'S OVARIES TO GROW SEVERAL MATURE EGGS RATHER THAN THE SINGLE EGG THAT NORMALLY DEVELOPS EACH MONTH. SUPEROVULATION ALLOWS US TO GROW EGGS WHICH WOULD OTHERWISE HAVE DIED IN THE NORMAL COURSE OF EVENTS, WHICH IS WHY IT DOESN'T REDUCE OVARIAN RESERVE. MOST OFTEN, THE DRUGS ARE GIVEN OVER A PERIOD OF 9 TO 12 DAYS. DRUGS CURRENTLY IN USE INCLUDE; HUMAN MENOPAUSAL GONADOTROPIN (HMG), FOLLICLE STIMULATING HORMONE (FSH) AND FSH/LH COMBINATIONS.

TODAY, MOST IVF PROGRAMS USE GNRH ANALOGS IN COMBINATION WITH GONADOTROPINS DURING OVULATION ENHANCEMENT. TREATMENT WITH THE ANALOGS PREVENTS THE RELEASE OF LH FROM THE PITUITARY GLAND DURING TREATMENT AND THEREBY PREVENTS PREMATURE OVULATION, ALLOWING DOCTORS TO GROW EGGS TO SUIT THEIR CONVENIENCE. GNRH ANALOGS CAN BE USED EITHER IN THE FORM OF A LONG PROTOCOL; OR AS A SHORT PROTOCOL. ANOTHER OPTION IS TO USE THE NEWER GNRH ANTAGONISTS FROM DAY 7 TO SELECTIVELY SUPPRESS THE LH SURGE.



HOW IS SUPEROVULATION MONITORED ?

AN ULTRASOUND SCAN IS DONE ON DAY 3, TO CONFIRM THAT THERE ARE NO CYSTS IN OVARY, AND THAT DOWNREGULATION HAS BEEN ACHIEVED. A BLOOD TEST FOR ESTRADIOL CAN ALSO BE DONE, AND THE RESULT SHOULD BE LESS THAN 50 PG/ML. THE HMG INJECTIONS FOR SUPEROVULATION ARE THEN STARTED FROM DAY 3. THE DOSE OF HMG USED NEEDS TO BE INDIVIDUALIZED FOR EACH PATIENT. DEPENDING UPON THE ANTRAL FOLLICLE COUNT AND OVARIAN MORPHOLOGY. OUR STANDARD DOSE IS 225 IU DAILY FOR PATIENTS LESS THAN 35; 300 IU DAILY FOR PATIENTS MORE THAN 35; 450 IU DAILY FOR POOR RESPONDERS; AND 150 IU DAILY FOR PATIENTS WITH PCOD.

TIMING IS CRUCIAL IN AN IVF TREATMENT CYCLE, IN ORDER THAT THE DOCTOR RECOVER MATURE EGGS. TO MONITOR EGG PRODUCTION, THE OVARIES ARE SCANNED FREQUENTLY WITH VAGINAL ULTRASOUND SCAN , USUALLY ON A DAILY OR ALTERNATE DAY BASIS FROM DAY 10 ONWARDS. BLOOD SAMPLES ARE ALSO DRAWN IN SOME CLINICS, TO MEASURE THE SERUM LEVELS OF ESTROGEN, AND SOMETIMES LUTEINIZING HORMONE (LH). THE DOSE OF THE HMG IS ADJUSTED, DEPENDING UPON THE OVARIAN RESPONSE.

FOLLICLES USUALLY GROW AT A RATE OF 1-2 MM/DAY MATURE FOLLICLES HAVE A DIAMETER OF ABOUT 16-20 MM IN SIZE. THE ENDOMETRIUM SHOULD ALSO BE EXAMINED CAREFULLY ON THE VAGINAL SCAN, AND THIS SHOULD BE TRILAMINAR AND 8 MM IN THICKNESS. SOME CLINICS ALSO MEASURE THE BLOOD ESTRADIOL LEVEL AND EACH MATURE FOLLICLE PRODUCES ABOUT 200-300 PG/ML OF ESTRADIOL. WHEN THE FOLLICLES ARE MATURE, INJ. HUMAN CHORIONIC GONADOTROPIN (HCG) IS GIVEN TO TRIGGER OVULATION. THIS PRECISE CONTROL ALLOWS THE IVF TEAM TO HARVEST MATURE EGGS 35-37 HOURS AFTER THIS SHOT.

THIS IS WHAT A TYPICAL IVF TREATMENT PROTOCOL IN OUR CLINIC LOOKS LIKE. TREATMENT STARTS FROM DAY 1 (THE DAY THE BLEEDING STARTS) OF THE CYCLE. AT THIS TIME, WE DOWNREGULATE BY STARTING INJ LUPRIDE (GNRH ANALOG), 0.2 ML SC DAILY ON DAY 3, WE DO AN ULTRASOUND SCAN TO CONFIRM THERE IS NO OVARIAN CYST, AFTER WHICH WE START SUPEROVULATION WITH 225 IU OF GONAL-F (FSH) DAILY. MANY DIFFERENT BRANDS ARE AVAILABLE. THE DOSE OF FSH WILL DEPEND UPON THE OVARIAN MORPHOLOGY AND THE ANTRAL FOLLICLE COUNT. WE DO THE NEXT SCAN ON DAY 10, AFTER WHICH WE DO SCANS EVERY ALTERNATE DAY TO MONITOR FOLLICULAR GROWTH. THE DOSE OF FSH IS TITRATED ACCORDING TO THE OVARIAN RESPONSE.

THIS IS WHAT THE DAILY SCHEDULE WOULD LOOK LIKE.

DAY 1, INJ LUPRIDE 0.2 ML SC. (DOWNREGULATION STARTS)
DAY 2. INJ LUPRIDE 0.2 ML SC.

DAY 3. INJ LUPRIDE, 0.2 ML SC. VAGINAL ULTRASOUND SCAN TO CONFIRM THERE IS NO OVARIAN CYST. IF THERE IS NO CYST, WE CAN COMMENCE SUPEROVULATION. IF THERE IS A CYST LARGER THAN 30 MM, WE CAN ASPIRATE IT AND CONTINUE WITH TREATMENT.

DAY 4 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC
SUPEROVULATION STARTS

DAY 5 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC

DAY 6 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC

DAY 7 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC

DAY 8 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC

DAY 9 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC

DAY 10 INJ LUPRIDE, 0.2 ML SC. INJ GONAL-F, 225 IU SC

ALTERNATIVE TREATMENT PROTOCOLS

THIS IS A MINIMAL STIMULATION IVF TREATMENT PLAN

THE DAY THE PERIOD STARTS = DAY 1

TAB LETROZ, 2.5 MG, 2 TAB DAILY FROM DAY 2 TO DAY 6 TO HELP THE WOMAN PRODUCE MORE OF HER HORMONES.
INJ GONAL-F, 150 IU SC DAILY FROM DAY 2.

SCANS EVERY ALTERNATE DAY FROM DAY 8

THE GONAL-F CONTINUES AND WE ADD INJ CETROTIDE (GNRH ANTAGONIST), TO PREVENT PREMATURE OVULATION

WHEN THE FOLLICLES ARE MATURE, WE TRIGGER WITH HCG AND EGGS ARE RETRIEVED AFTER 36 HOURS.

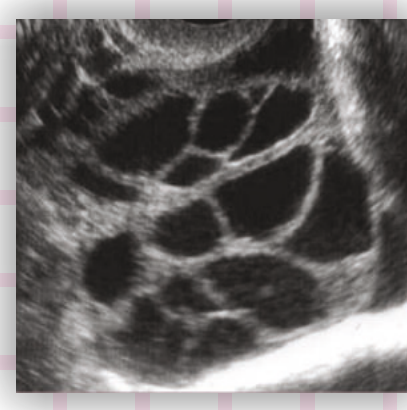
THIS IS APPROXIMATELY DAY 12 - 14 .

FOR PATIENTS WITH POOR OVARIAN RESERVE, HIGHER DOSES OF GONAL-F ARE USED TO HELP RECRUIT MORE FOLLICLES, SO THE OVARIAN RESPONSE IS BETTER. THIS OFTEN NEEDS TRIAL AND ERROR TO OPTIMISE OVARIAN RESPONSE. INJECTIONS ARE AVAILABLE IN MANY FORMS, INCLUDING PENS, PRELOADED SYRINGES AND VIALS.

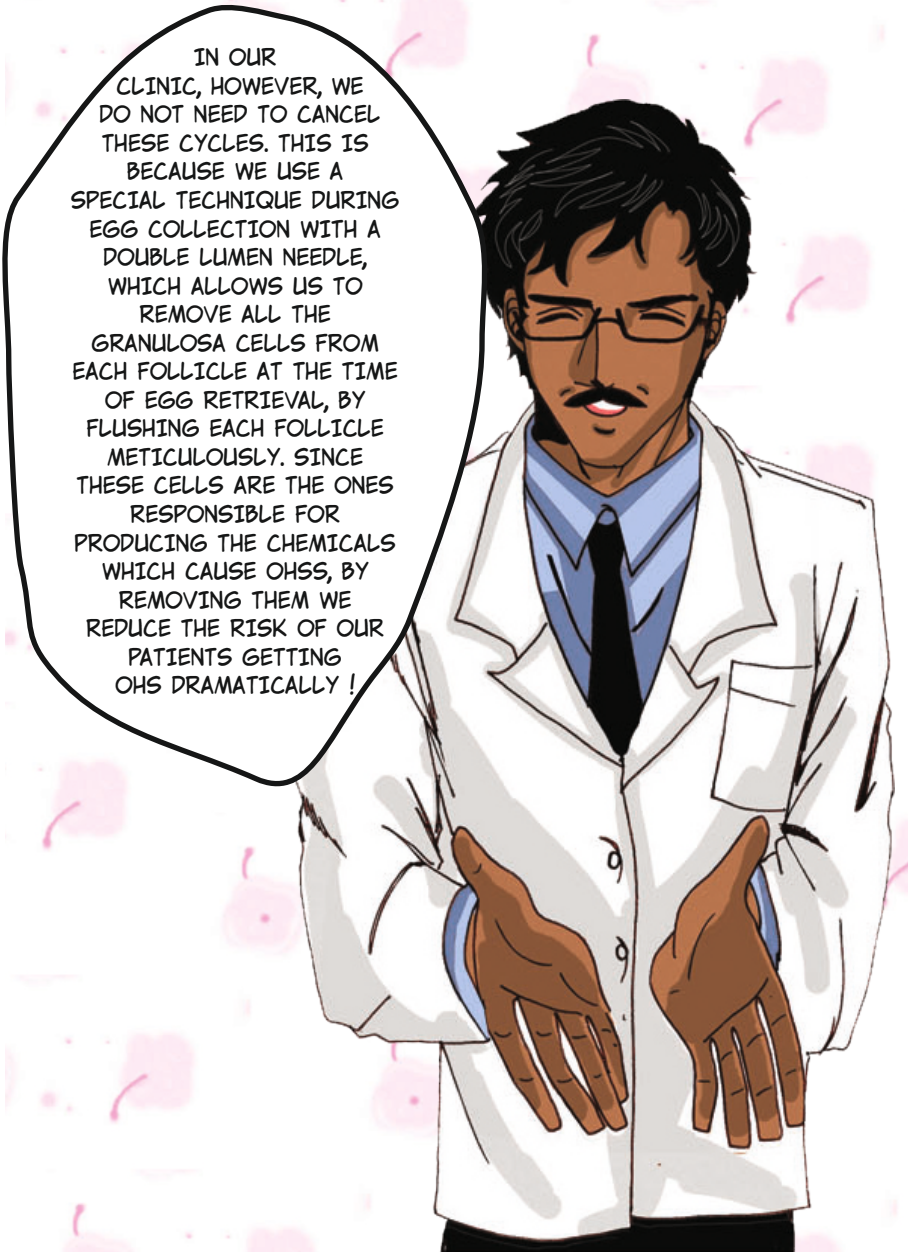
WHEN MAY AN IVF CYCLE BE CANCELLED ?

THE COMMONEST REASON FOR CANCELLING A CYCLE TODAY IS A POOR OVARIAN RESPONSE. IF A PATIENTS GROW LESS THAN THREE FOLLICLES, AND IF THE ESTRADIOL LEVEL IS LOW. THE CHANCES OF A PREGNANCY ARE POOR, AND PATIENTS MAY DECIDE TO ABANDON THE CYCLE. THE PROBLEM OF A POOR OVARIAN RESPONSE IS COMMONER IN OLDER WOMEN AND IN WOMEN WITH ELEVATED FSH LEVELS AND LOW AMH LEVELS.

THESE CAN BE DIFFICULT PATIENTS TO TREAT ! IN THE NEXT CYCLE, THE DOCTOR MAY NEED TO INCREASE THE DOSE OF HMG IN ORDER TO GROW MORE FOLLICLES, AND THIS IS OFTEN HELPFUL FOR YOUNG WOMEN.

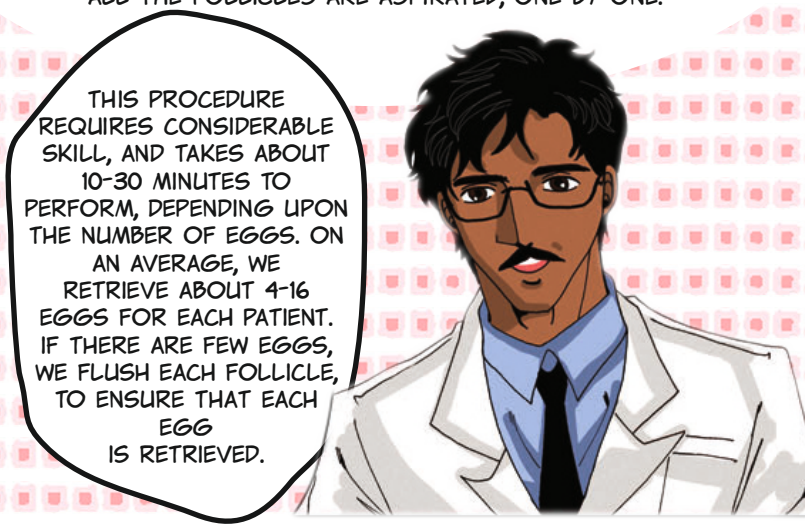


THE OTHER REASON TO CANCEL A CYCLE IS WHEN PATIENTS GROW TOO MANY FOLLICLES ! THESE ARE USUALLY PATIENTS WITH PCOD. AND IF THERE ARE MORE THAN 25 FOLLICLES, OR IF THE LEVEL OF THE ESTRADIOL IS MORE THAN 6000 PG/ML. MANY CLINICS WILL CANCEL THE CYCLE, BECAUSE THE RISK OF OVARIAN HYPERSTIMULATION SYNDROME (OHSS) IS VERY HIGH. AN ALTERNATIVE OPTIONS IS TO GO AHEAD WITH EGG COLELCTION, AND FREEZE ALL THE EMBRYOS.


IN OUR CLINIC, HOWEVER, WE DO NOT NEED TO CANCEL THESE CYCLES. THIS IS BECAUSE WE USE A SPECIAL TECHNIQUE DURING EGG COLLECTION WITH A DOUBLE LUMEN NEEDLE, WHICH ALLOWS US TO REMOVE ALL THE GRANULOSA CELLS FROM EACH FOLLICLE AT THE TIME OF EGG RETRIEVAL, BY FLUSHING EACH FOLLICLE METICULOUSLY. SINCE THESE CELLS ARE THE ONES RESPONSIBLE FOR PRODUCING THE CHEMICALS WHICH CAUSE OHSS, BY REMOVING THEM WE REDUCE THE RISK OF OUR PATIENTS GETTING OHS DRAMATICALLY !

EGG RETRIEVAL

EGG COLLECTION IS ACCOMPLISHED TODAY BY ULTRASOUND-GUIDED ASPIRATION. THIS IS A MINOR SURGICAL PROCEDURE. THAT CAN BE DONE EVEN UNDER INTRAVENOUS SEDATION. IN OUR CLINIC, WE PREFER GENERAL ANESTHESIA, AS THIS IS KINDER. THE DOCTOR GUIDES A NEEDLE THROUGH THE VAGINA INTO EACH MATURE FOLLICLE, UNDER ULTRASOUND GUIDANCE. THE FOLLICULAR FLUID CONTAINING THE EGG IS THEN SUCKED OUT THROUGH THE NEEDLE INTO A TEST TUBE, AND ALL THE FOLLICLES ARE ASPIRATED, ONE BY ONE.

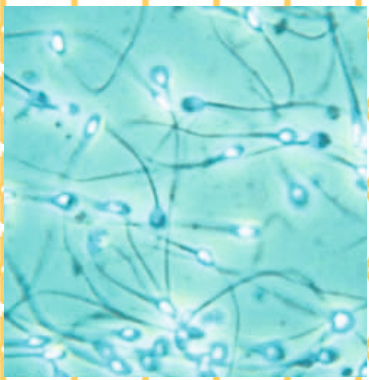


THE OLDER METHOD OF PERFORMING EGG RETRIEVAL INVOLVED A LAPAROSCOPY, AND THE EGGS AND FOLLICULAR FLUID WERE ASPIRATED UNDER DIRECT VISION. HOWEVER THIS METHOD IS RARELY USED TODAY. BECAUSE THE VAGINAL ULTRASOUND GUIDED METHOD IS MUCH QUICKER, EASIER AND SAFER.

HOW ARE THE EGGS INSEMINATED IN THE IVF LABORATORY ?

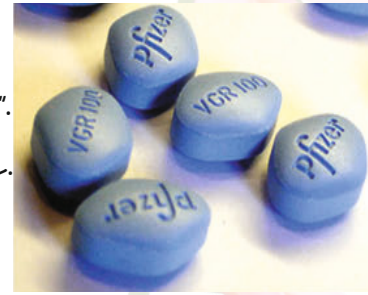
THE ASPIRATED FOLLICULAR FLUID IS THEN IMMEDIATELY CARRIED INTO THE ADJOINING LABORATORY WHERE IT IS EXAMINED BY THE EMBRYOLOGIST UNDER A STEREOZOOM MICROSCOPE, IN ORDER TO IDENTIFY THE EGG. EACH EGG IS SURROUNDED BY STICKY CUMULUS CELLS, AND IS CALLED AN OOCYTE-CUMULUS COMPLEX.

THESE ARE WASHED IN CULTURE MEDIUM, GRADED FOR THEIR MATURITY AND THEN TRANSFERRED INTO THE CO2 INCUBATOR. INSEMINATION (ADDING THE PROCESSED SPERM) IS USUALLY DONE AFTER 2-6 HOURS, TO ALLOW THE EGGS TO MATURE

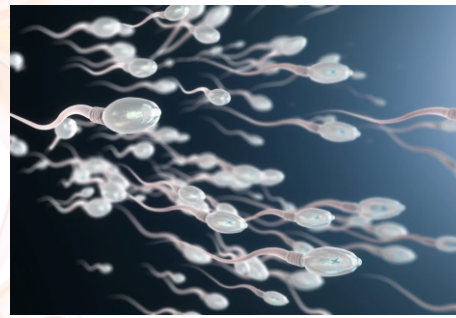


ON THE DAY THE EGGS ARE HARVESTED, THE HUSBAND PROVIDES A SEMEN SAMPLE. THE SPERM ARE SEPARATED FROM THE SEMINAL PLASMA IN A PROCESS KNOWN AS WASHING THE SPERM, AND THESE WASHED SPERM ARE USED TO INSEMINATE THE EGGS.

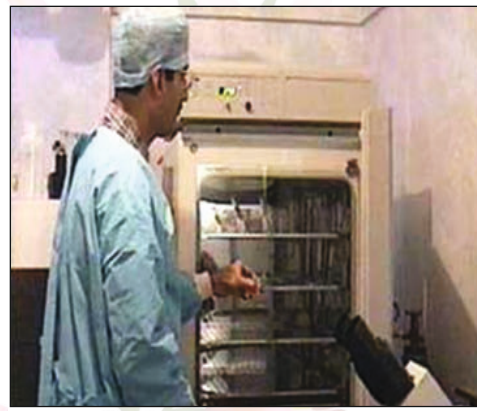
SOME MEN MAY HAVE CONSIDERABLE DIFFICULTY PRODUCING A SEMEN SAMPLE AT THE APPROPRIATE TIME, BECAUSE OF THE "PRESSURE TO PERFORM". FOR THESE MEN, USING A PREVIOUSLY STORED FROZEN SAMPLE CAN BE HELPFUL. VIAGRA (SILDENAFIL CITRATE) CAN ALSO BE USED TO HELP THEM TO GET AN ERECTION, AS CAN USING A VIBRATOR.

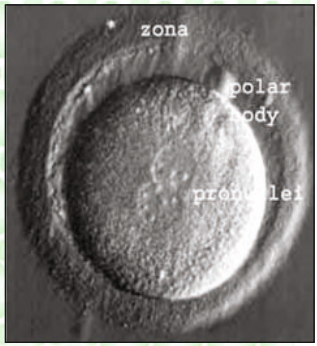


A DEFINED NUMBER OF SPERM (USUALLY 10000 SPERM PER EGGS) IS PLACED WITH THE EGGS IN A LABELED DISH CONTAINING IVF CULTURE MEDIUM. THE DISHES ARE PLACED IN A CO2 INCUBATOR WHICH HAS A CONTROLLED TEMPERATURE THAT IS THE SAME AS THE WOMAN'S BODY-37 C. THE CONDITIONS IN THE INCUBATOR AND THE CULTURE MEDIUM ARE DESIGNED TO MIMIC THE CONDITIONS IN THE FALLOPIAN TUBE, SO THAT THE EMBRYOS CAN GROW HAPPILY IN VITRO.



THE CULTURE MEDIUM, WHICH HAS TO BE VERY PURE, CONTAINS VARIOUS INGREDIENTS SUCH AS PROTEIN, SALTS, BUFFER AND ANTIBIOTICS WHICH ALLOW OPTIMAL GROWTH OF THE EMBRYO. THINK OF IT AS "CHICKEN SOUP FOR THE EMBRYO" !





HOW IS FERTILISATION CHECKED IN THE IVF LAB ?

ABOUT 18 HOURS AFTER INSEMINATION, THE EMBRYOLOGIST CHECKS TO SEE HOW MANY EGGS HAVE FERTILIZED. THIS IS CALLED A PRONUCLEAR CHECK, AND NORMALLY FERTILIZED EMBRYOS AT THIS TIME HAVE A SINGLE CELL WITH 2 PRONUCLEI. EACH PRONUCLEUS APPEARS AS A CLEAR BUBBLE WITHIN THE EMBRYO. THE MALE PRONUCLEUS REPRESENTS THE GENETIC CONTRIBUTION OF THE HUSBAND, WHILE THE FEMALE PRONUCLEUS REPRESENTS THE CONTRIBUTION OF THE WIFE . WHEN THESE FUSE, A NEW LIFE, WITH A UNIQUE GENETIC COMPOSITION IS FORMED. ABNORMALLY FERTILIZED EMBRYOS (FOR EXAMPLE, THOSE WITH THREE PRONUCLEI), OR THOSE WHICH HAVE FAILED TO FERTILISE, ARE DISCARDED, OR USED FOR RESEARCH.

SOMETIMES, EVEN THOUGH THE EGGS AND SPERM MAY LOOK EXCELLENT, THERE MAY BE A TOTAL FAILURE OF FERTILIZATION. THIS CAN BE A MAJOR BLOW, BECAUSE IT MEANS THAT THERE ARE NO EMBRYOS TO TRANSFER. POOR FERTILIZATION RATES MAY BE BECAUSE OF POOR SPERM, LAB PROBLEMS OR AN EGG PROBLEM. IF ONLY ONE PATIENT HAS POOR FERTILIZATION ON A PARTICULAR DAY IN A GOOD LAB, THEN IT'S USUALLY THE SPERM WHICH ARE HELD TO BE RESPONSIBLE.

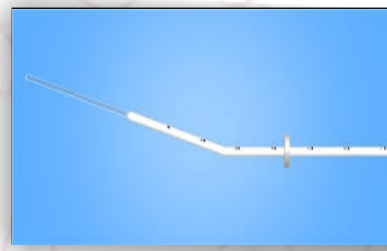
HOW ARE EMBRYOS CULTURED IN THE IVF LAB?

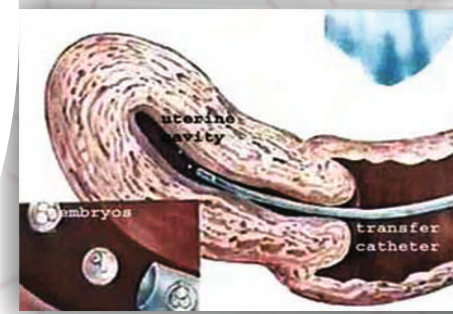
THE NORMALLY FERTILIZED EMBRYOS ARE LEFT IN CULTURE, WHERE THEY CONTINUE TO DIVIDE, AND THEIR QUALITY GRADED AFTER ANOTHER 24 HOURS. GOOD QUALITY EMBRYOS DIVIDE RAPIDLY: AND HEALTHY EMBRYOS HAVE 2-4 CELLS, OF EQUAL SIZE, WITH CLEAR CYTOPLASM AND FEW FRAGMENTS ON DAY 2 (ABOUT 48 HOURS AFTER EGG RETRIEVAL).

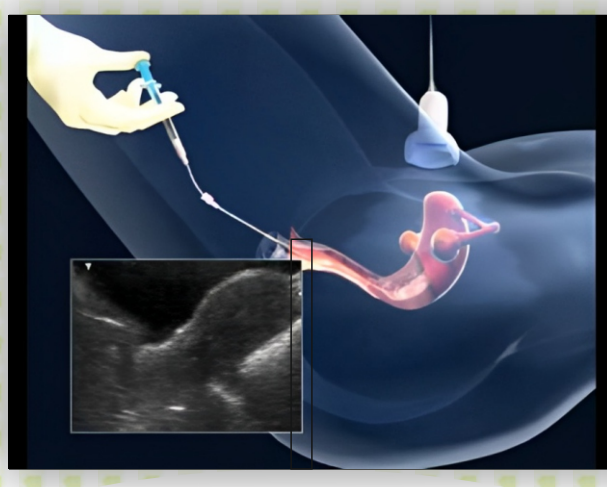
THE IVF LAB IS THE HEART OF THE IVF CLINIC TODAY, AND AN IVF CLINIC IS ONLY AS GOOD AS ITS LAB! THE EMBRYOLOGIST IS THE UNSUNG HERO OF IVF TREATMENT WHO DOES ALL THE IMPORTANT WORK BEHIND THE SCENES.

MANY PATIENTS ARE WORRIED THAT THEIR EGGS, SPERM OR EMBRYOS MAY GET MIXED UP WITH SOMEONE ELSE'S. WHILE THIS CAN HAPPEN, THE PROBABILITY OF IT HAPPENING IN A WELL-RUN LABORATORY IS VERY LOW, BECAUSE GOOD LABS HAVE QUALITY CONTROL MECHANISMS TO PREVENT SUCH MIXUPS FROM OCCURRING.

IN THE PAST, AFTER 72 HOURS, WHEN EMBRYOS USUALLY CONSIST OF EIGHT CELLS EACH, THE DOCTOR WOULD TRANSFER THEM INTO THE UTERUS USING A FINE STERILE PLASTIC HOLLOW TUBE CALLED AN EMBRYO TRANSFER CATHETER. THIS PROCEDURE IS KNOWN AS A DAY 3 EMBRYO TRANSFER. TODAY, GOOD CLINICS CULTURE EMBRYOS ROUTINELY TO DAY 5 AND DO ONLY BLASTOCYST(DAY 5) TRANSFERS.



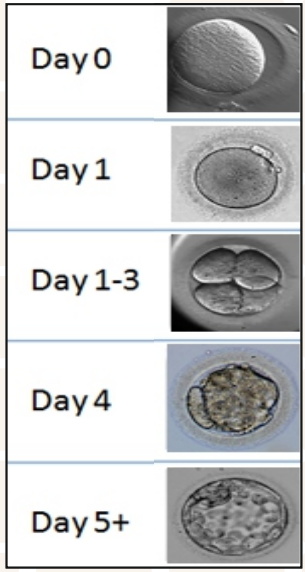




HOW IS EMBRYO TRANSFER PERFORMED ?

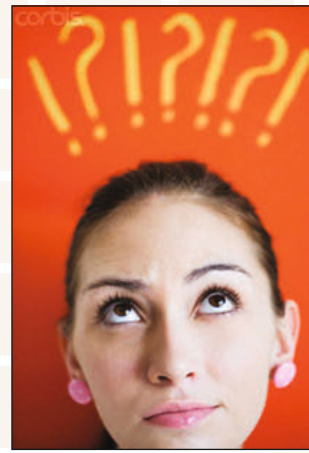
EMBRYO TRANSFER IS DONE ON AN OUTPATIENT BASIS. NO ANESTHESIA IS USED, ALTHOUGH SOME WOMEN MAY WISH TO HAVE A MILD SEDATIVE. ONE OR MORE EMBRYOS SUSPENDED IN A DROP OF CULTURE MEDIUM ARE DRAWN INTO A TRANSFER CATHETER, A LONG, THIN STERILE TUBE WITH A SYRINGE ON ONE END. GENTLY, THE DOCTOR GUIDES THE TIP OF THE LOADED CATHETER THROUGH THE CERVIX AND DEPOSITS THE FLUID CONTAINING THE EMBRYOS INTO THE UTERINE CAVITY.

THE PROCEDURE SHOULD BE DONE WITH CARE AND TAKES BETWEEN 10 AND 20 MINUTES. DOCTORS PERFORM THE TRANSFER UNDER ULTRASOUND GUIDANCE, TO ENSURE PROPER PLACEMENT OF THE EMBRYOS IN THE UTERINE CAVITY. MOST DOCTORS ADVISE A FEW HOURS OF BED REST AFTER THE TRANSFER.

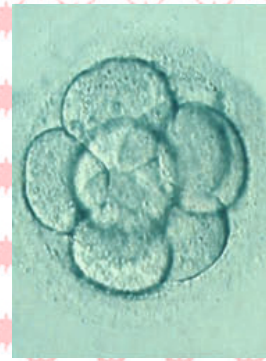


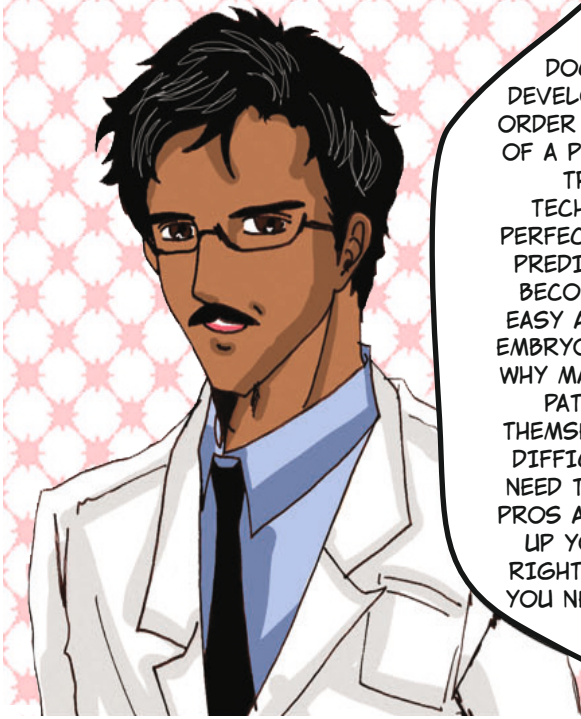
CLINICS TODAY TRANSFER 1-2 GOOD QUALITY EMBRYOS ON DAY 3 OR DAY 5. WE TRANSFER ONLY ONE DAY 5 BLASTOCYST IN OUR CLINIC. EMBRYOS ARE GRADED ACCORDING TO THEIR APPEARANCE . TOP QUALITY EMBRYOS HAVE A HIGHER CHANCE OF IMPLANTING AND LOWER GRADE EMBRYOS HAVE A LOWER CHANCE OF IMPLANTING. HOWEVER, THE BABIES WHICH RESULT FROM LOWER GRADE EMBRYOS ARE COMPLETELY NORMAL, IF THEY DO IMPLANT SUCCESSFULLY. YOU SHOULD ASK THE DOCTOR TO PROVIDE YOU WITH PHOTOGRAPHS OF YOUR EMBRYOS. THIS IS IMPORTANT DOCUMENTATION AND CONFIRMS YOU HAVE RECEIVED HIGH QUALITY TREATMENT.

HOW MANY EMBRYOS TO TRANSFER IS ONE OF THE MOST DIFFICULT DECISIONS FACING AN IVF PATIENT TODAY. THE MORE THE EMBRYOS TRANSFERRED, THE GREATER THE CHANCES OF GETTING PREGNANT. SINCE THE PURPOSE OF AN IVF CYCLE IS TO ACHIEVE A PREGNANCY, THEN WHY NOT TRANSFER AS MANY AS POSSIBLE? HOWEVER, THE PRICE YOU PAY FOR TRANSFERRING MORE EMBRYOS IS THAT THE RISK OF A MULTIPLE PREGNANCY INCREASES AS WELL.

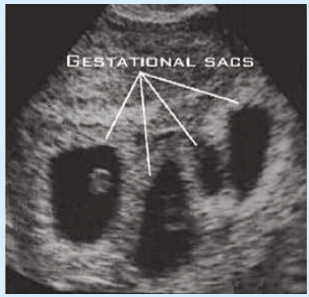


IN SOME COUNTRIES, SUCH AS THE UK, DOCTORS ARE ALLOWED TO REPLACE A MAXIMUM OF ONLY 2 EMBRYOS TO REDUCE THE RISK OF HIGH-ORDER MULTIPLE BIRTHS .SOME CLINICS IN SCANDINAVIA HAVE NOW STARTED TRANSFERRING ONLY ONE EMBRYO (SET, SINGLE EMBRYO TRANSFER) IN YOUNG WOMEN , IN ORDER TO REDUCE THE RISK OF A MULTIPLE PREGNANCY. IN USA, THERE ARE NO LAWS, AND SOME CLINICS WILL TRANSFER 4 EMBRYOS FOR YOUNG PATIENTS AND UPTO 6 FOR OLDER WOMEN ,AND THIS NUMBER IS QUITE ARBITRARY.





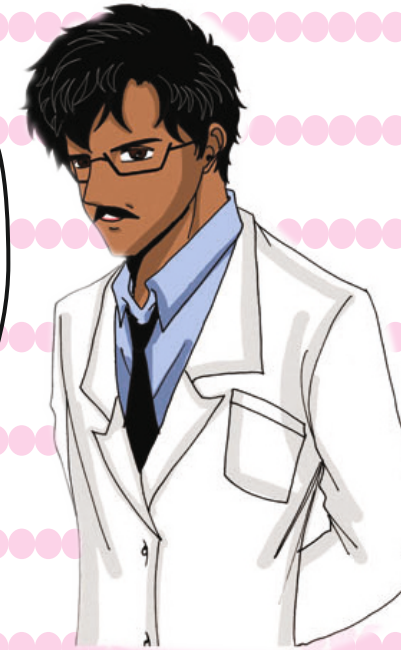
DOCTORS HAVE TRIED TO DEVELOP AN EMBRYO SCORE IN ORDER TO PREDICT THE CHANCES OF A PREGNANCY AFTER EMBRYO TRANSFER . SINCE THE TECHNOLOGY IS STILL NOT PERFECT , AND WE STILL CANNOT PREDICT WHICH EMBRYO WILL BECOME A BABY, THERE IS NO EASY ANSWER AS TO HOW MANY EMBRYOS TO TRANSFER . THIS IS WHY MANY CLINICS WILL ALLOW PATIENTS TO DECIDE FOR THEMSELVES. THIS IS ALWAYS A DIFFICULT DECISION, AND YOU NEED TO CAREFULLY WEIGH THE PROS AND CONS BEFORE MAKING UP YOUR MIND. THERE IS NO RIGHT OR WRONG NUMBER AND YOU NEED TO TAKE THE PATH OF LEAST REGRET.



TRANSFERRING MORE EMBRYOS INCREASES THE CHANCES OF GETTING PREGNANT AND ALSO INCREASES THE RISK OF A MULTIPLE PREGNANCY. HOWEVER A HIGH -ORDER PREGNANCY IS A COMPLICATION FOR WHICH THE DOCTOR CAN PERFORM A SELECTIVE FETAL REDUCTION IN ORDER TO REDUCE THIS TO TWINS. NOT GETTING PREGNANT MAY BE A WORSE OUTCOME FOR SOME PATIENTS! WE SUGGEST THAT PATIENTS TRANSFER ONLY A SINGLE TOP QUALITY BLASTOCYST , AND FREEZE THE REST. IN MOST CYCLES WE FREEZE ALL THE EMBRYOS ON DAY 5 AND TRANSFER THEM IN SUBSEQUENT CYCLES, ONE AT A TIME UNTIL THE PATIENT GETS PREGNANT.

WHAT HAPPENS AFTER THE EMBRYO TRANSFER ?

THE TERRIBLE 2 WEEK WAIT (2WW) NOW STARTS! THE EMBRYO TRANSFER COMPLETES THE MEDICAL TREATMENT IN THE IVF CYCLE AND MOST CLINICS PROVIDE "LUTEAL PHASE SUPPORT" AFTER THE TRANSFER, USUALLY WITH ESTROGEN TABLETS AND PROGESTERONE SUPPOSITORIES TO INCREASE THE CHANCES OF IMPLANTATION. HOWEVER, THIS PERIOD IS OFTEN THE HARDEST PART OF AN IVF CYCLE FOR THE PATIENT BECAUSE OF THE AGONY AND SUSPENSE OF WAITING TO FIND OUT IF A PREGNANCY HAS OCCURRED. THIS CAN BE DETERMINED BY THE BETA HCG BLOOD TEST WHICH MEASURES THE LEVEL OF THE HORMONE BETA HCG , ONLY 10 TO 14 DAYS AFTER THE TRANSFER. FOR MOST PATIENTS, THESE 14 DAYS ARE OFTEN THE LONGEST DAYS OF THEIR LIFE!



IT IS NORMAL TO BLAME YOURSELF FOR SOMETHING YOU MAY OR MAY NOT HAVE DONE DURING THIS TIME IF YOU DO NOT CONCEIVE. THEREFORE, TRY NOT TO DO ANYTHING FOR WHICH YOU WILL BLAME YOURSELF IF YOU DO NOT GET PREGNANT. IN GENERAL THE FOLLOWING GUIDELINES ARE OFFERED.

'NO INTERCOURSE OR ORGASMS UNTIL THE FETAL HEARTBEAT IS SEEN ON ULTRASOUND, OR THE PREGNANCY TEST IS NEGATIVE'.

'DO NOT UNDERTAKE EXCESSIVE PHYSICAL ACTIVITIES SUCH AS JOGGING, AEROBICS OR TENNIS'.

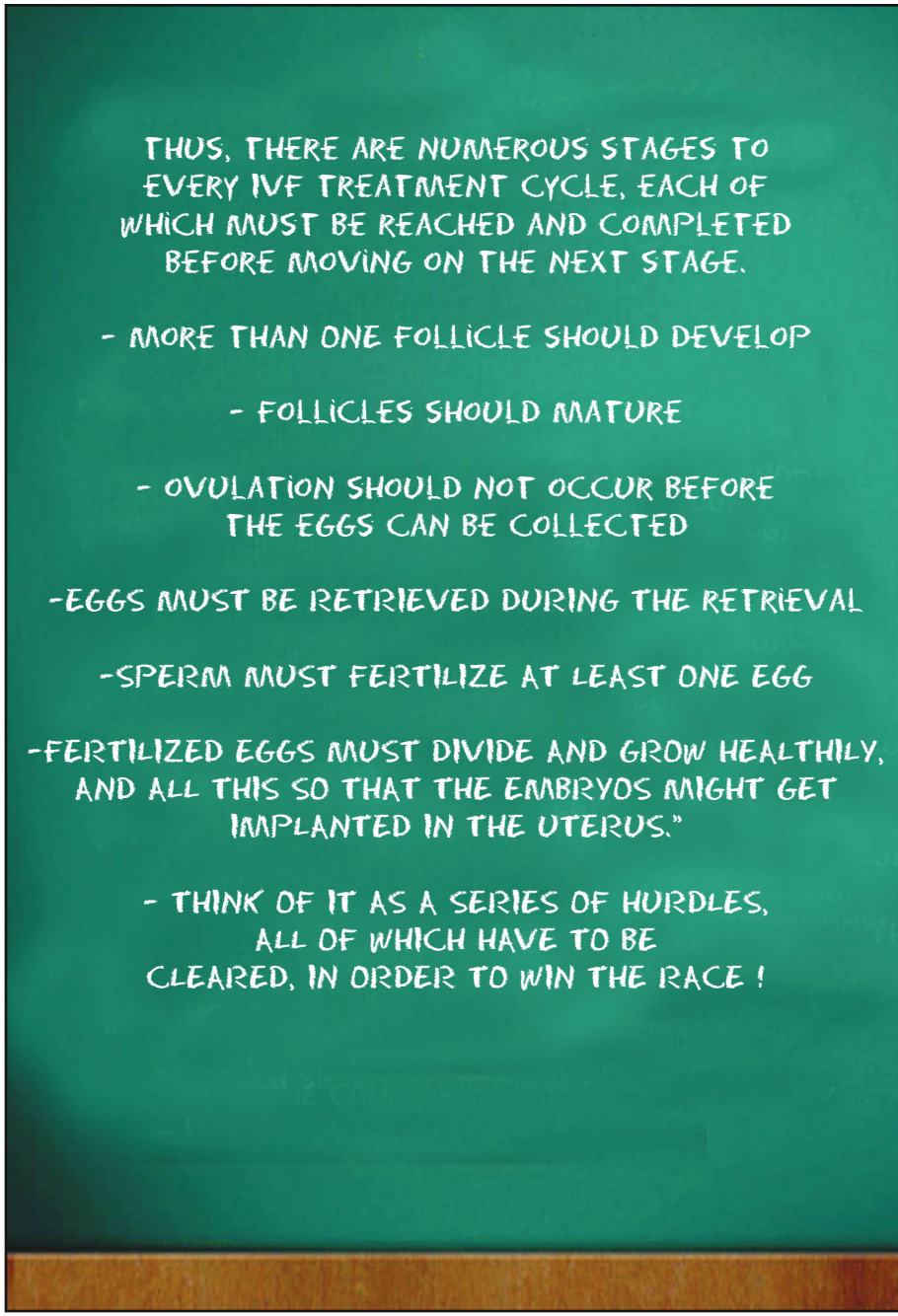
'NO HEAVY LIFTING'

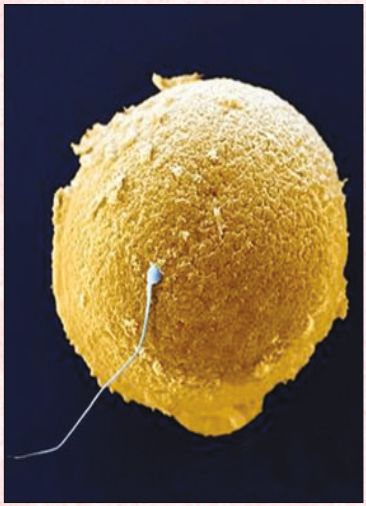
YOU MAY RETURN TO "WORK" AFTER 24 HOURS OF BED REST (GETTING UP FOR BATHROOM AND MEALS ONLY) AND ONE TO TWO DAYS OF LIGHT ACTIVITY. IT IS SAFE TO TRAVEL 1-2 DAYS AFTER THE TRANSFER.

IF YOU ARE UNSURE WHETHER OR NOT TO DO SOMETHING, TAKE THE "PATH OF LEAST REGRET". ASK YOURSELF - IF I DON'T GET PREGNANT, WILL I BLAME MYSELFFOR DOING THIS ? AND IF THE ANSWER IS YES, DON'T DO IT ! YOU MAY HAVE SOME VAGINAL SPOTTING OR BLEEDING PRIOR TO YOUR BETA HCG BLOOD TEST. HOWEVER, YOU MUST HAVE THE BLOOD TEST DONE. EVEN IF YOU THINK YOUR PERIOD HAS STARTED.
THERE ARE NO SYMPTOMS OR SIGNS WHICH WILL BE ABLE TO TELL YOU WHETHER OR NOT YOU ARE PREGNANT. YOUR EMBRYO IS SAFE IN YOUR UTERUS, LIKE A PEARL IN AN OYSTER, SO PLEASE DON'T LET YOUR MIND PLAY GAMES WITH YOU!

MANY DOCTORS USED TO ADVISE "STRICT BED REST" AFTER AN EMBRYO TRANSFER. HOWEVER, PHYSICAL ACTIVITY DOES NOT AFFECT YOUR CHANCES OF GETTING PREGNANT. FORCED BED REST WHEN YOU ARE PHYSICALLY WELL CAN BE VERY EMOTIONALLY TAXING AND WE ENCOURAGE PATIENTS TO LEAD A NORMAL LIFE AS POSSIBLE.

I REMIND PATIENTS THAT IT'S FINE FOR THEM TO DO WHATEVER NORMAL COUPLES WOULD DO AFTER HAVING SEX - AFTER ALL, HOW DOES IT MATTER TO THE EMBRYO THAT IT ARRIVES IN THE UTERINE CAVITY IN THE NORMAL COURSE OF EVENTS AFTER HAVING SEX IN THE BEDROOM, OR AFTER SPENDING 5 DAYS IN THE IVF LABORATORY, AND THEN BEING TRANSFERRED INTO THE CAVITY WITH A CATHETER?


THUS, THERE ARE NUMEROUS STAGES TO EVERY IVF TREATMENT CYCLE, EACH OF WHICH MUST BE REACHED AND COMPLETED BEFORE MOVING ON THE NEXT STAGE.
- MORE THAN ONE FOLLICLE SHOULD DEVELOP
- FOLLICLES SHOULD MATURE
- OVULATION SHOULD NOT OCCUR BEFORE THE EGGS CAN BE COLLECTED
-EGGS MUST BE RETRIEVED DURING THE RETRIEVAL
-SPERM MUST FERTILIZE AT LEAST ONE EGG
-FERTILIZED EGGS MUST DIVIDE AND GROW HEALTHILY, AND ALL THIS SO THAT THE EMBRYOS MIGHT GET IMPLANTED IN THE UTERUS."
- THINK OF IT AS A SERIES OF HURDLES, ALL OF WHICH HAVE TO BE CLEARED, IN ORDER TO WIN THE RACE !

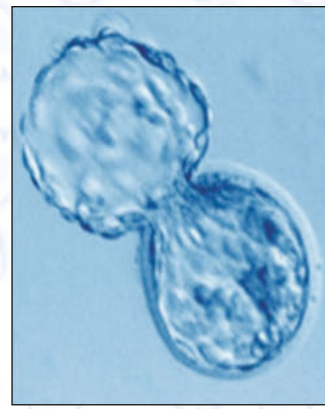


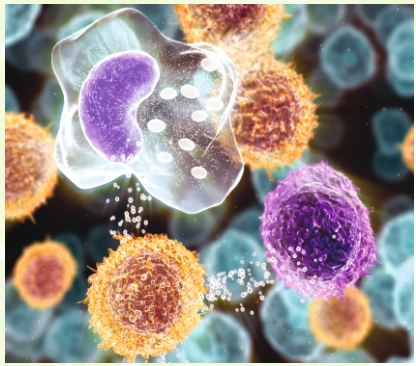
WHY DOESN'T EVERY EMBRYO BECOME A BABY?

WHILE MODERN TECHNOLOGY IS VERY GOOD AT MAKING EMBRYOS IN THE LABORATORY, WE STILL CANNOT CONTROL THE IMPLANTATION PROCESS. WE DO NOT KNOW WHICH EMBRYO WILL BECOME A BABY AND THIS CAN BE VERY FRUSTRATING, FOR BOTH PATIENTS AND DOCTORS!

MANY PATIENTS WHO DO NOT GET PREGNANT AFTER AN EMBRYO TRANSFER START BELIEVING THAT THEIR BODIES ARE DEFECTIVE, AND THAT THEY HAVE "REJECTED' THE EMBRYO. THEY FEEL THAT IF THEY FAILED TO BECOME PREGNANT EVEN AFTER THE DOCTOR TRANSFERRED GOOD QUALITY EMBRYOS, THAT THEIR UTERUS IS FLAWED. HOWEVER, YOU NEED TO REMEMBER THAT EMBRYO IMPLANTATION IS A VERY COMPLEX PROCESS, WHICH CONSISTS OF A SERIES OF PHASES IN WHICH THE EMBRYO HAS TO APPOSE AND ATTACH ITSELF TO THE MATERNAL ENDOMETRIUM AND INVADE INTO IT.

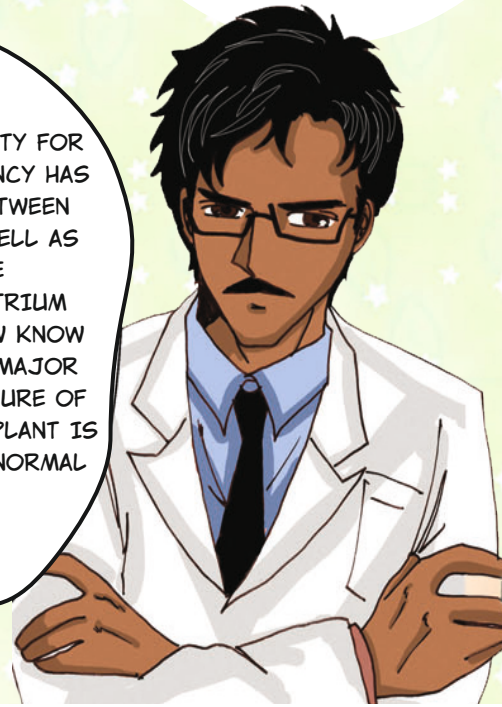
FIRST, THE EMBRYO HAS TO UNDERGO FURTHER DEVELOPMENT, TILL IT REACHES THE BLASTOCYST STAGE. THEN IT HATCHES FROM ITS SHELL, KNOWN AS THE ZONA. THE HATCHED BLASTOCYST THEN NEEDS TO IMPLANT IN THE ENDOMETRIUM, AND THE THREE PHASES OF IMPLANTATION ARE KNOWN AS APPOSITION, ADHESION AND INVASION, AND THEY OCCUR DURING THE PERIOD OF TIME KNOWN AS THE IMPLANTATION WINDOW.





MANY MOLECULES, SUCH AS CYTOKINES, GROWTH FACTORS AND CELL ADHESION PROTEINS CALLED INTEGRINS PLAY AN IMPORTANT ROLE IN THIS COMPLEX PROCESS DURING WHICH THE BLASTOCYST AND MATERNAL ENDOMETRIUM MUST UNDERGO AN EXQUISITE DIALOGUE. HOW IMPLANTATION IS REGULATED REMAINS AN ENIGMA, BUT WE NEED TO REMEMBER THAT THE IMPLANTATION PROCESS IS SURPRISINGLY WASTEFUL. IN HUMANS, EVEN NATURAL REPRODUCTION IS NOT VERY EFFICIENT! AFTER IVF, IT'S ONLY ABOUT 40%, WHICH MEANS THAT ONLY UPTO 40% OF TOP QUALITY BLASTOCYSTS IMPLANT SUCCESSFULLY TO BECOME A BABY.

THE RESPONSIBILITY FOR THIS LOW EFFICIENCY HAS TO BE SHARED BETWEEN THE EMBRYO AS WELL AS A DEFECTIVE EMBRYO-ENDOMETRIUM DIALOGUE. WE NOW KNOW THAT ONE OF THE MAJOR REASONS FOR FAILURE OF THE EMBRYO TO IMPLANT IS A GENETICALLY ABNORMAL EMBRYO.



MANY PATIENTS BLAME THEMSELVES WHEN THEY DON'T GET PREGNANT AFTER AN EMBRYO TRANSFER. THEY FEEL THAT THE FACT THAT THE EMBRYO DID NOT IMPLANT MEANS EITHER THAT THEIR BODY IS DEFECTIVE ; OR THAT IT "REJECTED" THE EMBRYO ; OR THAT THEY DID NOT REST ENOUGH. HOWEVER , PLEASE DO REMEMBER THAT EMBRYO IMPLANTATION IS A COMPLEX BIOLOGICAL PROCESS, WHICH YOU CANNOT INFLUENCE BY YOUR DIET OR PHYSICAL ACTIVITY, SO THERE IS NO NEED FOR YOU TO BLAME YOURSELF IF THE EMBRYOS DO NOT IMPLANT.

HOW CAN YOU MAXIMISE YOUR CHANCES OF SUCCESS AFTER IVF?

AVOID ALL UNNECESSARY MEDICATIONS OTHER THAN PARACETAMOL (TYLENOL). IF YOU ARE TAKING OTHER PRESCRIPTION MEDICATIONS, CHECK THAT THESE ARE SAFE WITH YOUR DOCTOR

NO SMOKING OR ALCOHOL USE. STUDIES SHOW BOTH CAN RESULT IN LOWER PREGNANCY RATES AND A GREATER RISK OF MISCARRIAGE. WHY PUT YOURSELF THROUGH THIS IF YOU ARE NOT DOING EVERYTHING YOU CAN TO INSURE YOUR SUCCESS?

NO MORE THAN TWO CAFFEINATED BEVERAGES PER DAY.

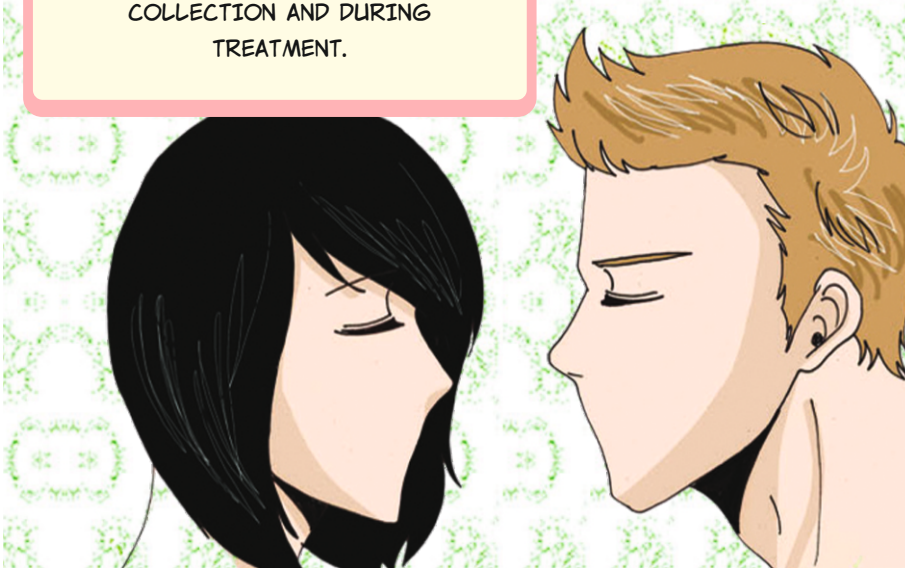
AVOID ANY CHANGES IN YOUR DIET. DURING AN IVF CYCLE , A HEALTHY WELL BALANCED DIET WORKS BEST.

REFRAIN FROM INTERCOURSE FOLLOWING EMBRYO REPLACEMENT UNTIL THE PREGNANCY TEST IS DONE.

NORMAL EXERCISE MAY CONTINUE UNLESS ENLARGEMENT OF YOUR OVARIES PRODUCES DISCOMFORT.

AVOID HOT TUBS OR SAUNAS.

ABSTAIN FROM INTERCOURSE FOR AT LEAST THREE DAYS, BUT NOT MORE THAN SEVEN DAYS PRIOR TO COLLECTION OF SEMEN FOR EGG COLLECTION AND DURING TREATMENT.

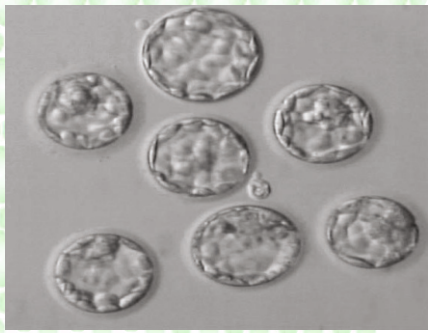


HOW MUCH DOES IVF COST?

THE COST OF A SINGLE IVF TREATMENT CYCLE VARIES WIDELY FROM APPROXIMATELY RS 70,000 TO MORE THAN RS 200,000 DEPENDING ON THE PROGRAM AND THE ITEMS INCLUDED IN THE FEE. IT IS IMPORTANT TO GET AN ITEMIZED LISTING FROM THE SELECTED PROGRAM OF WHAT COSTS ARE INCLUDED IN THE TREATMENT CYCLE. TRY TO FIND YOUR "TOTAL" MEDICAL COST - HOW MUCH YOU WILL HAVE TO SPEND OUT OF YOUR OWN POCKET FOR THE ENTIRE TREATMENT. MANY CLINICS DO NOT INCLUDE THE COST OF CERTAIN PROCEDURES (SUCH AS ULTRASOUND SCANS) AND THESE CAN THEN ADD UP TO QUITE A BIT! OTHER EXPENSES TO BE AWARE OF INCLUDE TIME MISSED FROM WORK AND TRAVEL AND LODGING EXPENSES.

WHAT IS EMBRYO FREEZING ?
SINCE MOST IVF PROGRAMS SUPEROVULATE PATIENTS TO GROW MANY EGGS, THEY OFTEN HAVE MANY EMBRYOS. SINCE THE RISK OF MULTIPLE PREGNANCIES INCREASES WITH THE NUMBER OF EMBRYOS TRANSFERRED, MANY PATIENTS ARE LEFT WITH SUPERNUMERARY OR 'SPARE' EMBRYOS. THESE CAN BE STORED; DISCARDED; OR USED FOR RESEARCH.

EMBRYOS CAN BE FROZEN AND STORED IN LIQUID NITROGEN. THESE STORED EMBRYOS CAN THEN BE USED LATER FOR THE SAME PATIENT, SO THAT SHE CAN HAVE ANOTHER EMBRYO TRANSFER CYCLE DONE WITHOUT HAVING TO GO THROUGH SUPEROVULATION AND EGG COLLECTION ALL OVER AGAIN. FROZEN EMBRYO TRANSFER CAN BE DONE IN A NATURAL CYCLE; OR IN A 'SIMULATED NATURAL CYCLE', IN WHICH THE ENDOMETRIUM IS PRIMED TO MAXIMIZE ITS RECEPTIVITY TO THE EMBRYOS BY USING ESTROGENS AND PROGESTERONE.

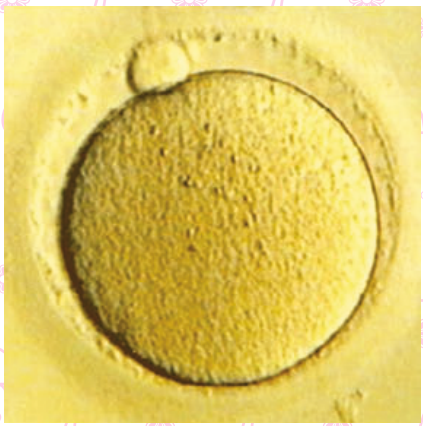


SINCE PREGNANCY RATES WITH GOOD-QUALITY FROZEN- THAWED EMBRYOS ARE AS GOOD AS WITH FRESH EMBRYOS, WE ENCOURAGE ALL OUR PATIENTS TO FREEZE AND STORE THEIR SUPERNUMERARY EMBRYOS, RATHER THAN DISCARD THEM. FREEZING IS VERY COST-EFFECTIVE, SINCE TRANSFERRING FROZEN-THAWED EMBRYOS IS MUCH LESS EXPENSIVE THAN STARTING A NEW CYCLE, SO THAT IT SERVES AS A USEFUL "INSURANCE POLICY" IN CASE PREGNANCY DOES NOT OCCUR. HOWEVER, SINCE IT IS WORTHWHILE FREEZING ONLY GOOD QUALITY EMBRYOS, , THE OPTION OF FREEZING IS A "BONUS" WHICH IS AVAILABLE TO ONLY ABOUT 50% OF ALL IVF PATIENTS-THOSE WHO ARE GOOD OVARIAN RESPONDERS AND GROW LOTS OF EGGS.

IN A GOOD CLINIC, NEARLY ALL FROZEN EMBRYOS SURVIVE THE FREEZE-THAW PROCESS. IT IS REASSURING TO KNOW THAT THE RISK OF DEFECTS IS NOT INCREASED AS A RESULT OF FREEZING. THESE FROZEN EMBRYOS CAN BE STORED FOR AS LONG AS IS NEEDED - EVEN FOR MANY YEARS. WHEN THEY ARE IN LIQUID NITROGEN, AT A TEMPERATURE OF -196 C. THEY ARE IN A STATE OF SUSPENDED ANIMATION, AND ALL METABOLIC ACTIVITY AT THIS LOW TEMPERATURE STOPS, SO THAT A FROZEN EMBRYO IS LIKE SLEEPING BEAUTY!

IN THE PAST, EMBRYOS WERE FROZEN USING SLOW FREEZING TECHNIQUES UTILIZING SPECIAL CHEMICALS CALLED CRYOPROTECTANTS. A NEWER TECHNIQUE CALLED VITRIFICATION OR FLASH FREEZING IS NOW PREFERRED. THIS ALLOWS MORE EFFICIENT FREEZING, AND VITRIFIED EMBRYOS HAVE A NEARLY 100% SURVIVAL RATE AFTER THAWING. THE EXPERIENCE OF THE EMBRYOLOGIST PLAYS A KEY ROLE IN THE SUCCESS OF FREEZING EMBRYOS.

ONCE STORED, EMBRYOS CAN BE USED BY THE COUPLE DURING A LATER TREATMENT CYCLE, DONATED TO ANOTHER COUPLE OR REMOVED FROM STORAGE. THESE OPTIONS SHOULD ONLY BE UNDERTAKEN AFTER CONSIDERABLE DISCUSSION AND WRITTEN CONSENT FROM THE PARTIES CONCERNED.



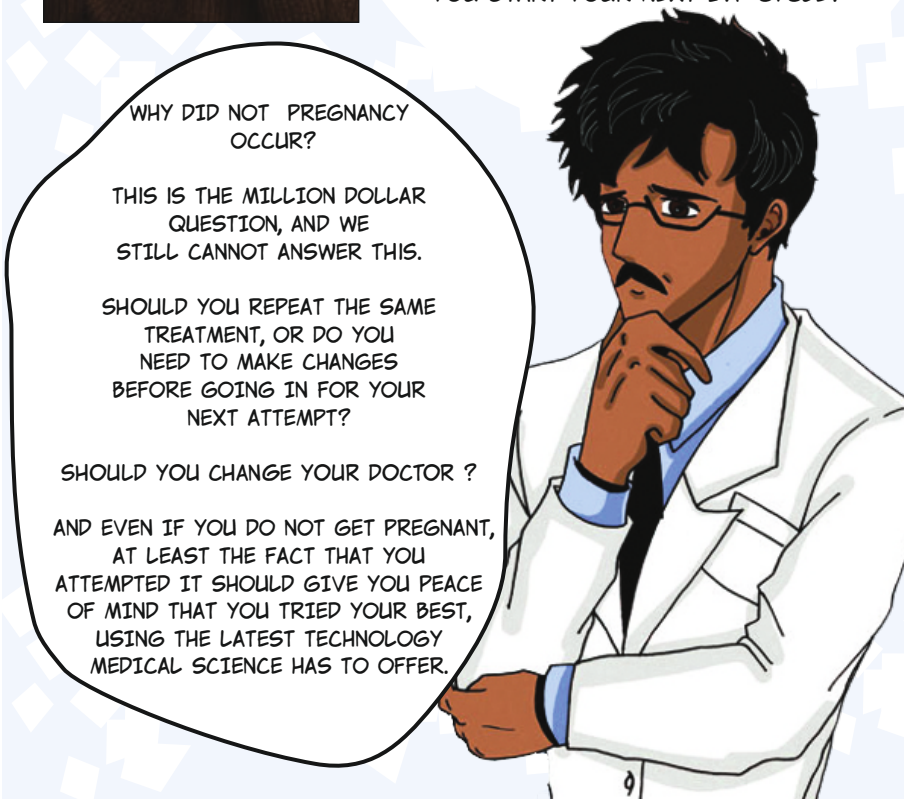
EGG FREEZING

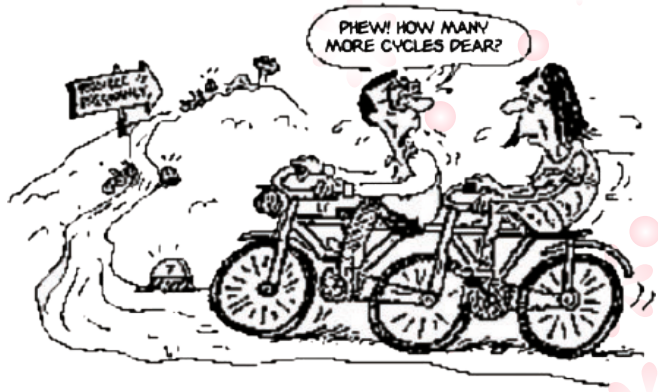
A NEW TECHNIQUE CALLED VITRIFICATION (WHICH USES ULTRA-RAPID COOLING TOGETHER WITH AN INCREASED CONCENTRATION OF CRYOPROTECTANTS) NOW ALLOWS US TO FREEZE UNFERTTILIZED HUMAN OCCYTES AS WELL. THIS ALLOWS THE FACILITY OF EGG STORAGE AND EGG BANKING.

WHAT HAPPENS IF THE IVF CYCLE FAILS?

IF YOU DON'T GET PREGNANT AFTER AN IVF ATTEMPT, YOU ARE LIKELY TO BE DISAPPOINTED AND DISHEARTENED. HOWEVER, THIS IS NOT THE END O THE ROAD - IT'S JUST THE BEGINNING OF A NEW JOURNEY!

AT THE END OF THE IVF CYCLE, YOU NEED TO SIT DOWN WITH YOUR DOCTOR AND ANALYSE WHAT YOU LEARNT FROM IT. WAS THE OVARIAN RESPONSE GOOD? WAS THE ENDOMETRIUM RECEPTIVE? DID FERTILIZATION OCCUR? WAS THE EMBRYO TRANSFER EASY AND ATRAUMATIC? WHEN CAN YOU START YOUR NEXT IVF CYCLE?

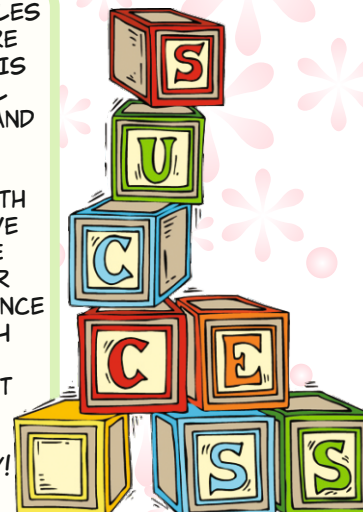




WHAT ABOUT YOUR NEXT IVF CYCLE?

MOST DOCTORS WOULD ADVISE YOU TO WAIT FOR A MONTH BEFORE STARTING A NEW CYCLE. WHILE IT IS MEDICALLY POSSIBLE TO DO THE NEXT CYCLE BACK TO BACK, MOST PATIENTS NEED A BREAK TO MARSHAL THEIR EMOTIONAL STRENGTH BEFORE STARTING AGAIN. YOUR DOCTOR MAY NEED TO MODIFY YOUR TREATMENT, DEPENDING UPON AN ASSESSMENT OF YOUR PREVIOUS CYCLE. HOWEVER, IF THE CYCLE WAS SATISFACTORY, THE DOCTOR WILL OFTEN ADVISE YOU TO REPEAT EXACTLY THE SAME TREATMENT AGAIN - AND ALL THAT IT MAY TAKE TO ACHIEVE YOUR IVF SUCCESS IS TIME, PATIENCE, AND ANOTHER ATTEMPT.

INTERESTINGLY, WE OFTEN FIND THAT COUPLES GOING THROUGH A SECOND IVF CYCLE ARE MUCH MORE RELAXED AND IN CONTROL. THIS MAY BE BECAUSE THEY ARE AWARE OF ALL THE MEDICAL AND PROCEDURAL MINUTIAE, AND ARE BETTER PREPARED FOR THESE; AND BECAUSE THEY HAVE HAD A CHANCE TO ESTABLISH A PERSONAL RELATIONSHIP WITH THE MEDICAL TEAM. ALSO, SINCE THEY HAVE ALREADY FACED FAILURE THE FIRST TIME AROUND, MANY OF THEM ARE MUCH BETTER ABLE TO COPE WITH THE STRESS OF IVF, SINCE THEY ARE PREPARED FOR THE WORST. WITH TODAY'S IVF TECHNOLOGY, WE CAN CONFIDENTLY REASSURE ANY PATIENT THAT WE CAN HELP THEM TO GET PREGNANT PROVIDED THEY HAVE INEXHAUSTIBLE RESOURCES OF TIME, MONEY AND ENERGY!



WHAT ARE MY CHANCES OF GETTING PREGNANT ?

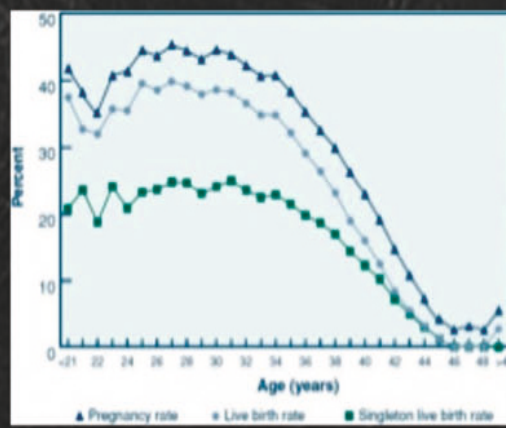
-THE WIFE'S AGE. CHANCES DECLINE WITH INCREASING AGE - PRECIPITOUSLY SO OVER THE AGE OF 40

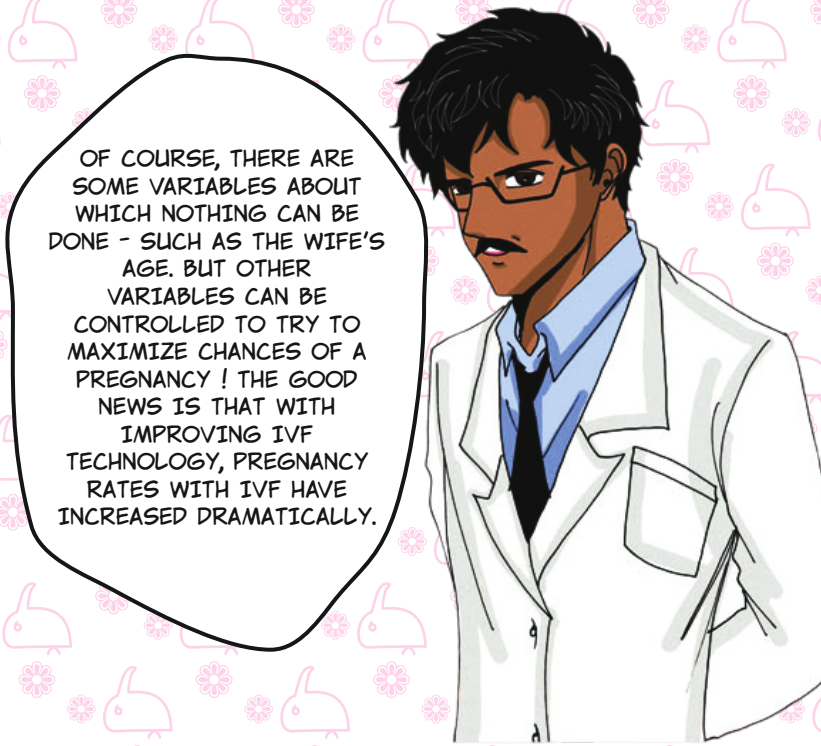
-THE MEDICAL REASON FOR THE IVF TREATMENT - CHANCES OF PREGNANCY DECLINE WHEN IVF IS DONE FOR SEVERE ENDOMETRIOSIS

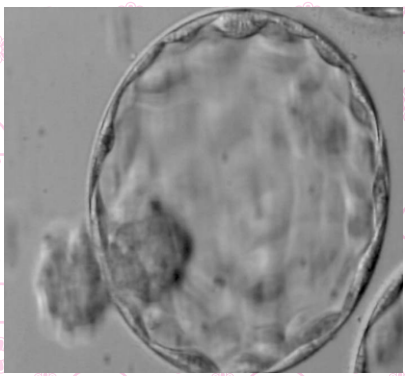
-THE QUALITY OF THE IVF CLINIC AND ITS SERVICES

-THE NUMBER OF EMBRYOS /EGGS TRANSFERRED

-THE SUPEROVULATION REGIME USED



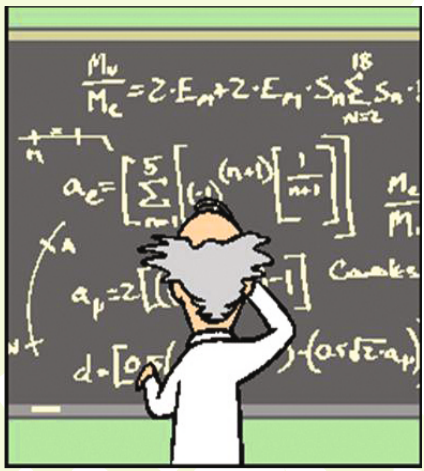




PREGNANCY RATES ARE RELATED DIRECTLY TO HOW MANY EMBRYOS ARE TRANSFERRED. FOR EXAMPLE, WHEN ONE TOP QUALITY BLASTOCYST IS TRANSFERRED, THE CHANCE OF PREGNANCY IS ABOUT 40% IN THAT CYCLE. THE NUMBER OF EMBRYOS TRANSFERRED NEEDS TO BE BALANCED AGAINST THE RISK OF MULTIPLE PREGNANCY WHICH NATURALLY INCREASES WITH MORE EMBRYOS.

,

WITH THIS IN MIND, MANY COUNTRIES NOW RECOMMEND THAT NO MORE THAN 2 EMBRYOS BE TRANSFERRED DURING ANY TREATMENT CYCLE. IN OUR CLINIC, WE TRANSFER ONLY ONE TOP QUALITY BLASTOCYST AT A TIME AND FREEZE THE REST TO MAXIMISE YOUR LIVE BIRTH RATE



HOW CAN A PATIENT INTERPRET IVF SUCCESS RATE FIGURES ?

FOR EXAMPLE, LET US CONSIDER A 30 YEAR OLD PATIENT WITH IRREPARABLE TUBAL DAMAGE WHO GOES THROUGH ONE IVF CYCLE. SHE CAN LOOK AT A PREGNANCY RATE OF 40% IN TWO WAYS. A SUCCESS RATE OF 40% MEANS THERE IS AN 60% CHANCE SHE WILL NOT GET PREGNANT. ON THE OTHER HAND, IF SHE TAKES NO TREATMENT. HER CHANCE OF GETTING PREGNANT IS ZERO. THE IVF CYCLE HAS INCREASED THIS TO 40% - NO ONE CAN DO ANY BETTER THAN THIS TODAY !

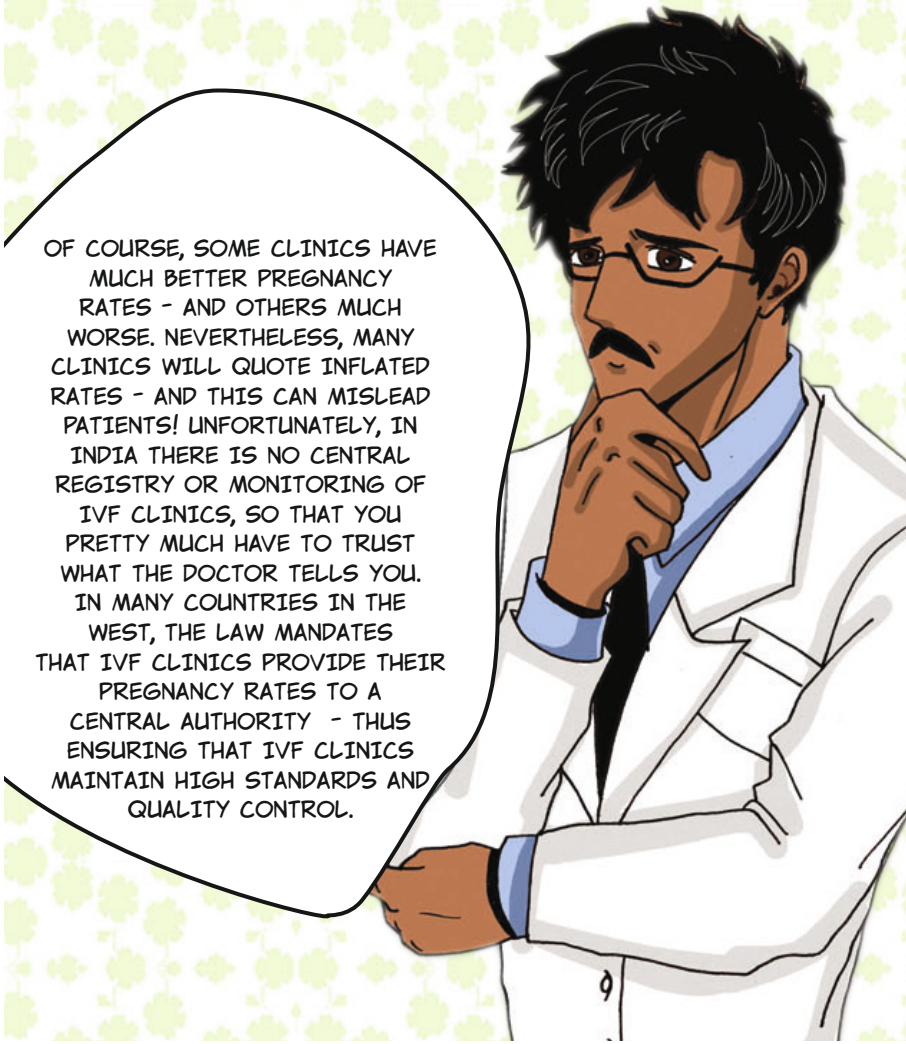
OF COURSE, FOR THE COUPLE WHO GETS A BABY, ITS A 100% BABY - AND FOR THE ONE WHO FAILS, ITS 0% - SO FOR THE INDIVIDUAL PATIENT, IT'S REALLY NOT A QUESTION OF STATISTICS! EACH IVF TREATMENT CYCLE IS A BIT LIKE TAKING A GAMBLE - AND YOU NEED TO HOPE FOR THE BEST AND PREPARE FOR THE WORST!

IVF TREATMENT SHOULD NOT BE CONSIDERED TO BE A SINGLE SHOT AFFAIR. PATIENTS SHOULD PLAN TO GO THROUGH AT LEAST 3 TO 4 CYCLES TO GIVE THEMSELVES A FAIR CHANCE OF GETTING PREGNANT. WITH 3 TREATMENT CYCLES, THE CHANCE OF GETTING PREGNANT IS ABOUT 80%. WHAT THIS MEANS, IS THAT EVEN THOUGH THE CHANCE OF GETTING PREGNANT IN A SINGLE CYCLE MAY NEVER BE MORE THAN 40%, OVER 3 CYCLES, THE CHANCES INCREASE TO 80% BECAUSE THE SUCCESS RATE IS CUMULATIVE.

THUS, LET US ASSUME THE PREGNANCY RATE FOR IVF AT A CLINIC IS 30%. IF 10 PATIENTS START AN IVF CYCLE, 3 WILL GET PREGNANT, LEAVING 7 PATIENTS. IF THESE 7 DO ANOTHER IVF CYCLE, ANOTHER 30% WILL CONCEIVE. IF THE REMAINING 5 DO ANOTHER CYCLE, 1 MORE WILL GET PREGNANT: AND AT THE END OF THE 4TH CYCLE, 1 MORE WILL CONCEIVE; SO THAT OF THE 10 PATIENTS WHO STARTED 7 WILL HAVE GOT PREGNANT IN 4 ATTEMPTS. THIS IS BECAUSE THE CHANCES OF GETTING PREGNANT IN THE NEXT IVF CYCLE DO NOT DECREASE JUST BECAUSE A PREGNANCY HAS NOT OCCURRED IN THE PREVIOUS CYCLE - SO THE BEST BET WOULD BE TO KEEP ON TRYING.

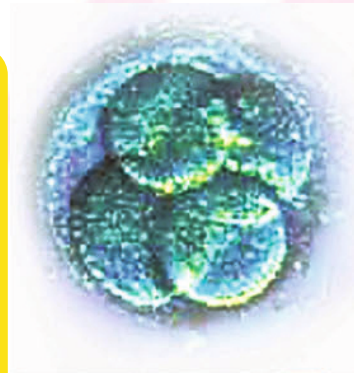
THEORETICALLY, WE COULD REASSURE EVERY COUPLE TAKING IVF TREATMENT THAT THEY WOULD GET PREGNANT - PROVIDED THEY WERE WILLING TO GO THROUGH AS MANY CYCLES AS WERE REQUIRED, TILL THEY HIT THE JACKPOT! OF COURSE, ONE HAS TO SET A LIMIT SOMEWHERE, AND THE DECISION WHEN TO STOP IS SOMETHING WHICH ONLY THE COUPLE CAN MAKE FOR THEMSELVES. AFTER MORE THAN 6 FAILED IVF CYCLES, THE CHANCE FOR A PREGNANCY WITH IVF DOES DECLINE.

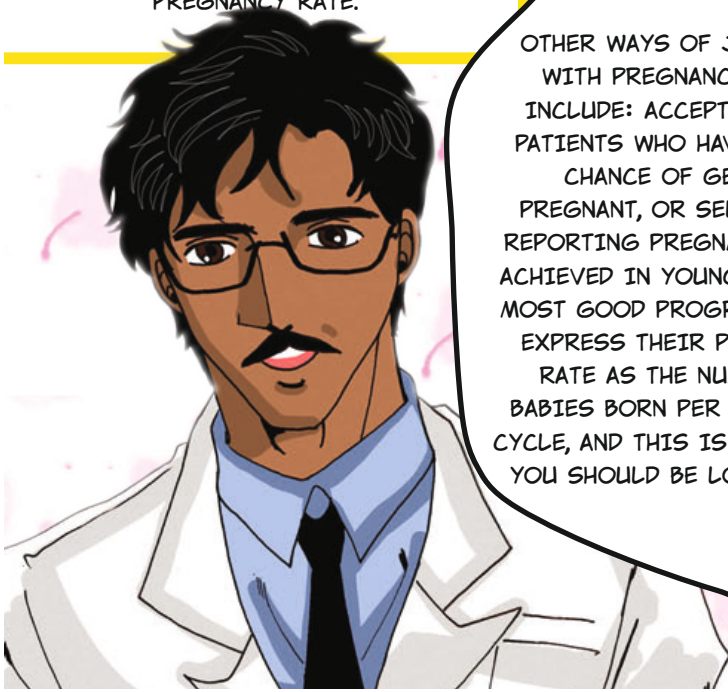
WHAT GAMES DO SOME IVF CLINICS PLAY WITH THEIR PREGNANCY RATES?



DIFFERENT PROGRAMMES DEFINE SUCCESS IN VARIOUS WAYS. TO MOST COUPLES, SUCCESS IS A BABY, NOT A PREGNANCY - SO THAT WHAT NEEDS TO BE DETERMINED IS THE "TAKE HOME BABY RATE". SOME CLINICS QUOTE PREGNANCY RATES WHEN DESCRIBING THEIR SUCCESS RATES - AND THESE CAN BE CONSIDERABLY HIGHER THAN THE LIVE BIRTH RATE, DEPENDING UPON HOW A PREGNANCY IS DEFINED. THUS, SOME PROGRAMS DEFINE PREGNANCY WHEN THE PREGNANCY TEST IS POSITIVE; OTHERS DEFINE PREGNANCY AS A PREGNANCY SAC SEEN ON ULTRASOUND.

CHEMICAL OR BIOCHEMICAL PREGNANCIES ARE ALSO FAIRLY COMMON AFTER IVF. THESE ARE PREGNANCIES CONFIRMED BY A POSITIVE BLOOD TEST FOR BETA HCG, BUT IN WHICH THE EMBRYO DOES NOT DEVELOP BEYOND THE EARLIEST STAGE. NO GESTATIONAL SAC IS SEEN ON ULTRASOUND EXAMINATION. COUNTING BIOCHEMICAL PREGNANCIES WILL, OF COURSE, FALSELY INFLATE THE PREGNANCY RATE.





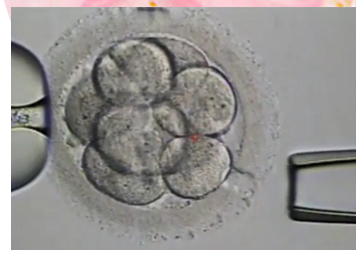
OTHER WAYS OF JUGGLING WITH PREGNANCY RATES INCLUDE: ACCEPTING ONLY PATIENTS WHO HAVE A GOOD CHANCE OF GETTING PREGNANT, OR SELECTIVELY REPORTING PREGNANCY RATES ACHIEVED IN YOUNGER WOMEN. MOST GOOD PROGRAMS TODAY EXPRESS THEIR PREGNANCY RATE AS THE NUMBER OF BABIES BORN PER TREATMENT CYCLE, AND THIS IS THE FIGURE YOU SHOULD BE LOOKING AT.

NEW IVF PROCEDURES

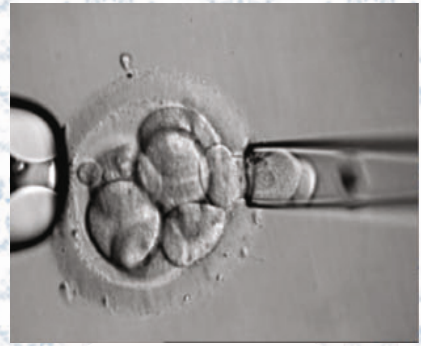
ASSISTED REPRODUCTIVE TECHNOLOGY IS IMPROVING BY LEAPS AND BOUNDS AND MANY EXCITING ADVANCES HAVE TAKEN PLACE RECENTLY.

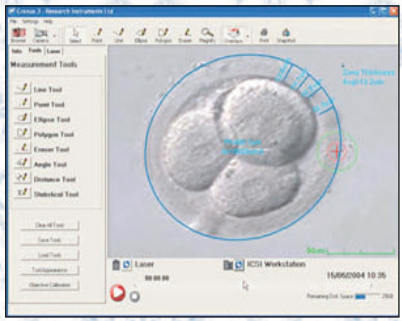
WHAT IS ASSISTED HATCHING?

ONE OF THE MAJOR PROBLEMS WITH IVF TODAY IS THE LOW PREGNANCY RATE AFTER EMBRYO TRANSFER. HE REASON WHY SUCH FEW EMBRYOS IMPLANT SUCCESSFULLY (ONLY 4 OF 10 TOP QUALITY EMBRYOS WILL BECOME A BABY) IS ONE OF THE THINGS WE REALLY DO NOT UNDERSTAND TODAY. DR COHEN BELIEVES THIS IS BECAUSE THE ZONA (THE SURROUNDING SHELL) OF THE EMBRYO HARDENS WHEN CULTURED IN VITRO. WE CAN USE "EMBRYO SURGERY " CALLED ZONA DRILLING OR ASSISTED HATCHING TO "SOFTEN" THE SHELL OF THE EMBRYO , AND THIS MAY INCREASE PREGNANCY RATES SINCE EMBRYO HATCHING IS FACILITATED. THIS CAN BE DONE USING A LASER.



EMBRYO SURGERY HAS ALSO BEEN USED FOR EMBRYO BIOPSY FOR PREIMPLANTATION GENETIC DIAGNOSIS, IN WHICH CELLS ARE REMOVED FROM THE DEVELOPING EMBRYO, TO MAKE SURE THE EMBRYOS ARE HEALTHY AND HAVE NO GENETIC DISEASE.



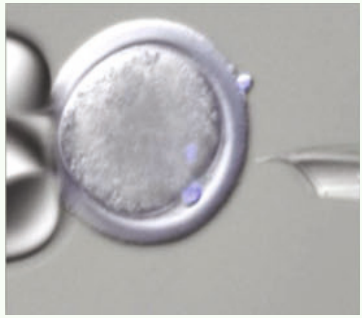


EMBRYO MULTIPLICATION

BY REMOVING THE CELLS FROM THE EMBRYO AND ALLOWING THEM TO DIVIDE INDIVIDUALLY, DOCTORS CAN 'MULTIPLY' THE NUMBER OF EMBRYOS FORMED IN VITRO. THE NEW EMBRYOS CAN THEN BE COATED WITH A NEW SHELL (ZONA) AND THEN TRANSFERRED INTO THE UTERUS. THIS COULD HELP TO INCREASE THE CHANCES OF PREGNANCY IN WOMEN WHO PRODUCE ONLY A SMALL NUMBER OF EMBRYOS

OTHER SCIENTISTS FEEL THAT THE REASON FOR THE POOR IMPLANTATION RATE IS THE POOR QUALITY OF THE CULTURE MEDIUM. THEY HAVE THEREFORE TRIED TO IMPROVE EMBRYO QUALITY IN THE LABORATORY BY TRYING TO PROVIDE IT WITH MORE NATURAL CULTURE CONDITIONS. THIS IS DONE BY A METHOD CALLED CO-CULTURE IN WHICH THE EMBRYO IS CULTURED ALONG WITH 'FEEDER CELLS' IN THE CULTURE DISH.

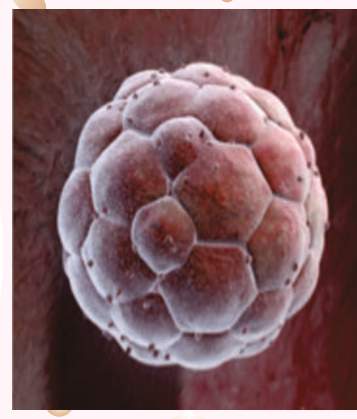
CYTOPLASMIC TRANSFER



SOME PATIENTS GOING THROUGH IVF GROW LOTS OF EGGS, BUT PERSISTENTLY FORM POOR EMBRYOS WHICH FAIL TO IMPLANT. IN SOME OF THEM, THIS MAY BE BECAUSE THEY HAVE A PROBLEM IN THEIR CYTOPLASM, EITHER IN THEIR MITOCHONDRIA OR THE CELL-DIVISION APPARATUS. DR COHEN HYPOTHESISED THAT IT SHOULD BE POSSIBLE TO CORRECT THIS PROBLEM BY REPLACING JUST THE CYTOPLASM OF THE EGG, KEEPING THE MOTHER'S OWN GENETIC CONTRIBUTION (THE DNA CONTAINED IN THE NUCLEUS) TO THE BABY INTACT. THIS HIGH-TECH METHOD IS CALLED CYTOPLASMIC TRANSFER, AND USES CYTOPLASM DONATED FROM THE HEALTHY EGGS OF ANOTHER WOMAN.

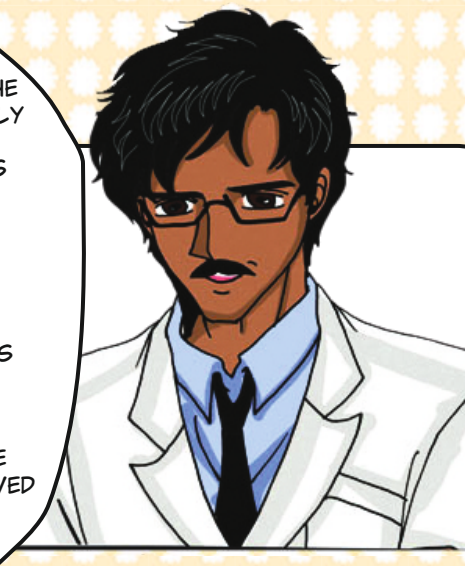
BLASTOCYST TRANSFER

THE FORMULATION OF NEW LABORATORY CULTURE MEDIA - THE LIQUID IN WHICH THE EMBRYO IS GROWN IN VITRO - HAS MADE IT POSSIBLE TO 'GROW" EMBRYOS IN VITRO BEYOND THE TYPICAL 3 DAY STATE OF DEVELOPMENT, TILL THEY BECOME BLASTOCYSTS. A BLASTOCYST IS THE FINAL STAGE OF THE EMBRYO'S DEVELOPMENT BEFORE IT HATCHES OUT OF ITS SHELL (ZONA PELLUCIDA) AND IMPLANTS IN THE UTERINE WALL.



BLASTOCYST TRANSFER HAS HIGHER PREGNANCY RATES THAN A DAY 3 TRANSFER. WAITING TILL THE BLASTOCYST STAGE ALLOWS THE DOCTOR TO SELECT THE "BEST " EMBRYOS, SINCE UNHEALTHY EMBRYOS ARE LIKELY TO DIE (ARREST) BEFORE THEY REACH THIS STAGE. ALSO, THIS MIMICS NATURE MORE CLOSELY, SINCE A DAY 3 EMBRYO BELONGS IN THE FALLOPIAN TUBE AND NOT THE UTERUS !

BLASTOCYST TRANSFER SIGNIFICANTLY REDUCES THE POSSIBILITY OF POTENTIALLY DANGEROUS HIGH-ORDER MULTIPLE BIRTHS, SUCH AS TRIPLETS. A HIGHER IMPLANTATION RATE ALLOWS DOCTORS TO TRANSFER FEWER BLASTOCYSTS - PERHAPS ONLY ONE - REDUCING OR AVOIDING MULTIPLE BIRTHS AND THEIR ASSOCIATED PROBLEMS. SUPERNUMERARY BLASTOCYSTS CAN ALSO BE SUCCESSFULLY CRYOPRESERVED AND USED IN THE FUTURE AS AND WHEN NEEDED, AFTER THAWING THEM



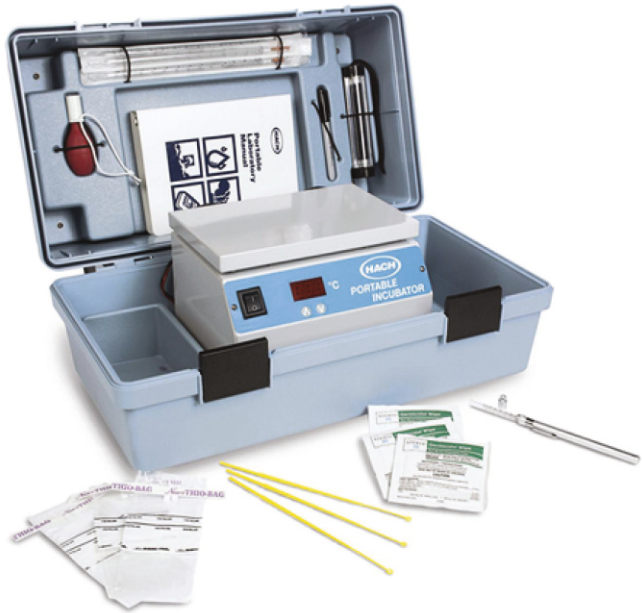

WHILE BLASTOCYST TRANSFER IS A VERY PROMISING ADVANCE FOR PATIENTS WHO GROW LOTS OF EGGS, ITS UTILITY FOR THE DIFFICULT PATIENT - THE POOR OVARIAN RESPONDER - IS STILL DEBATABLE. THIS IS BECAUSE IF THERE ARE FEW EGGS, THERE IS A VERY REAL RISK THAT NONE OF THEM MAY DEVELOP TO THE BLASTOCYST STAGE. ALL OF THEM MAY "ARREST" SO THAT THERE ARE NO EMBRYOS AVAILABLE FOR TRANSFER. EVERY PATIENT NEEDS TO BALANCE THESE RISKS AND BENEFITS, DEPENDING UPON THE CLINIC'S EXPERIENCE AND SUCCESS RATE. WE RECOMMEND DOING ONLY BLASTOCYST TRANSFERS FOR ALL PATIENTS IN OUR CLINIC
HOW CAN WE SIMPLIFY IVF?
SOME PEOPLE MIGHT ASK WHETHER ALL THIS IS RELEVANT TO INDIAN CONDITIONS. WHILE THESE TECHNOLOGIC REFINEMENTS ARE VERY EXCITING, IVF CLINICS IN INDIA SHOULD ALSO FOCUS ON SIMPLIFYING IVF TECHNOLOGY - SO THAT IT CAN BE MADE MORE AFFORDABLE FOR THE AVERAGE INDIAN COUPLE.

IVC (INTRAVAGINAL CULTURE):
IN THIS METHOD, INVENTED BY DR. RANOUX OF FRANCE IN 1984, THE EGGS AND SPERM ARE PLACED IN A STERILE VIAL WHICH IS THEN SEALED AND PLACED IN THE WOMAN'S VAGINA. THUS, THE WOMAN ACTS AS HER OWN INCUBATOR! SINCE EXPENSIVE LABORATORY EQUIPMENT IS NOT NEEDED. THIS IS MUCH CHEAPER - AND IS AS EFFECTIVE AS CONVENTIONAL IVF!

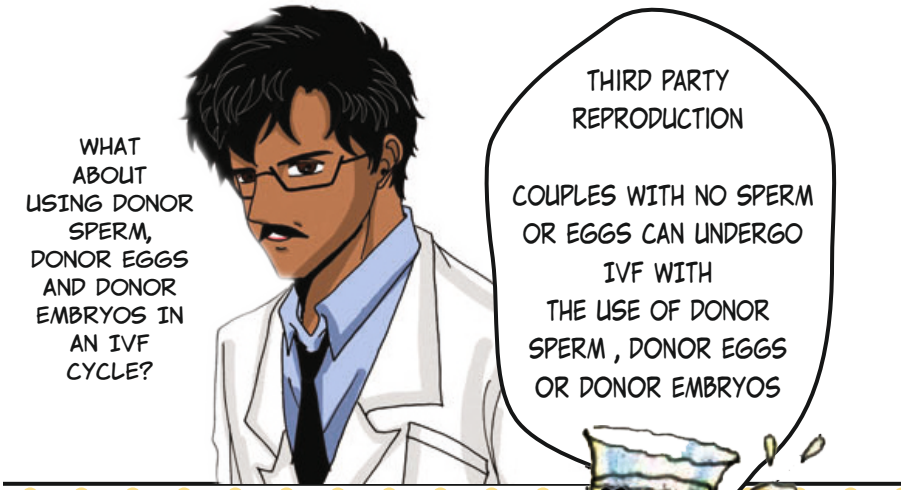
NATURAL CYCLE IVF

IN THIS METHOD, THE SINGLE EGG WHICH THE WOMAN GROWS IN HER UNSTIMULATED OVULATORY CYCLE IS USED FOR IVF. NATURAL CYCLE IVF IS MUCH LESS EXPENSIVE BECAUSE IT DOES AWAY WITH THE HIGH EXPENSE OF GONADOTROPIN INJECTIONS. WHILE THE PREGNANCY RATE IS LOWER, THE EXPENSE IS MUCH LESS!

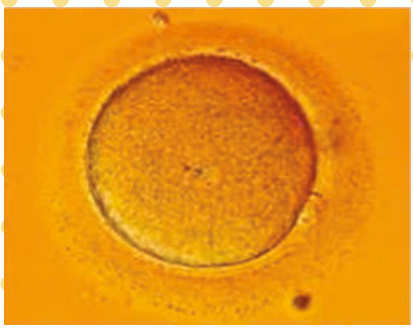
"GENTLE" IVF OR MINI-STIMULATION IVF USING LETROZOLE IS ALSO BECOMING INCREASINGLY POPULAR WORLDWIDE



TRANSPORT IVF: THE EGG RETRIEVAL IS PERFORMED BY THE GYNECOLOGIST IN HIS OWN CLINIC; AND THE EGGS ARE THEN TRANSPORTED TO A CENTRAL IVF LABORATORY BY THE HUSBAND IN A PORTABLE INCUBATOR. INSEMINATION, FERTILIZATION AND EMBRYO TRANSFER TAKE PLACE IN THE CENTRAL LABORATORY. THIS METHOD ENSURES REDUCED COSTS , SINCE ALL LABORATORY PROCEDURES ARE PERFORMED IN A CENTRAL LABORATORY; AND ALSO MINIMIZES PATIENT INCONVENIENCE



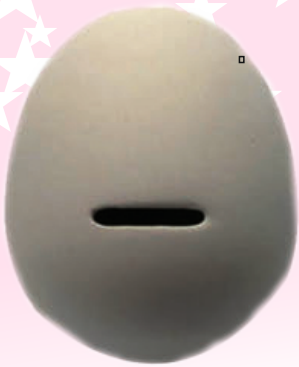
FOR IVF, CRYOPRESERVED DONOR SPERM FROM A SPERM BANK ARE PROCESSED IN THE SAME WAY AS FRESH SPERM.



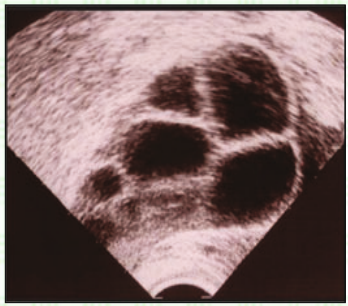
DONOR EGGS CAN BE USED IN IVF FOR WOMEN WHO HAVE NO EGGS (OVARIAN FAILURE) BUT WHO DO HAVE A HEALTHY UTERUS. EMBRYOS RESULTING FROM THE FERTILIZATION OF DONOR EGGS AND THE HUSBAND'S SPERM ARE PLACED INSIDE THE PATIENT'S UTERUS, AFTER PREPARING IT WITH HORMONES SO IT IS RECEPTIVE

The Egg Timer is about to ((((Ring))))

A COUPLE MAY ALSO CHOOSE TO USE DONOR EGGS IF THE WOMAN HAS A GENETIC DISEASE THAT COULD BE PASSED ON TO A CHILD. DONOR EGGS CAN ALSO BE USED IN SOME CASES OF LONG STANDING INFERTILITY WHEN OTHER PROCEDURES HAVE FAILED - FOR EXAMPLE, WOMEN WITH MANY PREVIOUS UNSUCCESSFUL IVF CYCLES. SINCE THE CHANCE OF A PREGNANCY IN THE OLDER WOMAN DEPENDS DIRECTLY UPON THE QUALITY OF HER EGGS, MANY OLDER WOMEN OPT TO USE DONOR EGGS FROM YOUNGER WOMEN- WHICH INCREASES THEIR PREGNANCY RATES DRAMATICALLY. THIS ALSO CREATES HEADLINE NEWS, FOR EXAMPLE, WHEN A MENOPAUSAL WOMAN HAS GIVEN BIRTH WITH DONOR EGGS.



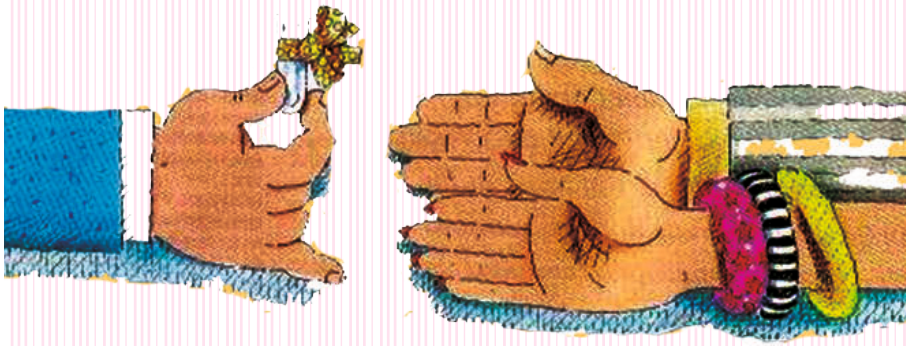
THE GOOD NEWS IS THAT IT'S NOW ALSO POSSIBLE TO FREEZE EGGS, USING THE ADVANCED TECHNIQUE OF FLASH FREEZING CALLED VITRIFICATION. GOOD CLINICS USE ONLY FROZEN EGGS FROM AN EGG BANK, TO ENSURE 24/7 AVAILABILITY , AND TO MATCH PHYSICAL CHARACTERISTICS SUCH AS HEIGHT, COMPLEXION AND BLOOD GROUP



EGG DONATION FOR IVF REQUIRES THE EGG DONOR TO UNDERGO SUPEROVULATION AND OVUM ASPIRATION. THE DONATION OF EGGS CARRIES MORE RISK AND INCONVENIENCE TO THE DONOR THAN DOES THE DONATION OF SPERM..

THE PATIENT NEEDS TO BE TREATED WITH HORMONES, SO THAT HER ENDOMETRIUM IS PRIMED AND IS RECEPTIVE TO THE EMBRYO AT THE TIME OF TRANSFER. FOR AMENORRHEIC WOMEN WITH OVARIAN FAILURE, THIS CAN BE ACHIEVED BY TREATING THEM WITH EXOGENOUS ESTROGENS AND PROGESTERONE. OTHER WOMEN WHO ARE CYCLING NEED TO BE DOWN REGULATED WITH GNRH ANALOGS BEFORE STARTING TREATMENT WITH EXOGENOUS ESTROGENS.

COUPLES WITH BOTH A SPERM AND AN EGG PROBLEM CAN ALSO USE DONOR EMBRYOS. SINCE EMBRYOS CAN BE STORED, SOME INFERTILE COUPLES GOING THROUGH AN IVF CYCLE, WHO HAVE CHOSEN TO FREEZE THEIR SUPERNUMERARY EMBRYOS FOR THEMSELVES, ARE WILLING TO DONATE THEIR SURPLUS FROZEN EMBRYOS TO OTHER INFERTILE COUPLES WHEN THEY GET PREGNANT. YOU CAN THINK OF DONOR EMBRYO TREATMENT AS VERY SIMILAR TO ADOPTING A BABY IN UTERO - WITH THE DIFFERENCE THAT YOU ARE CARRYING THE PREGNANCY AND GIVING BIRTH TO THE BABY!

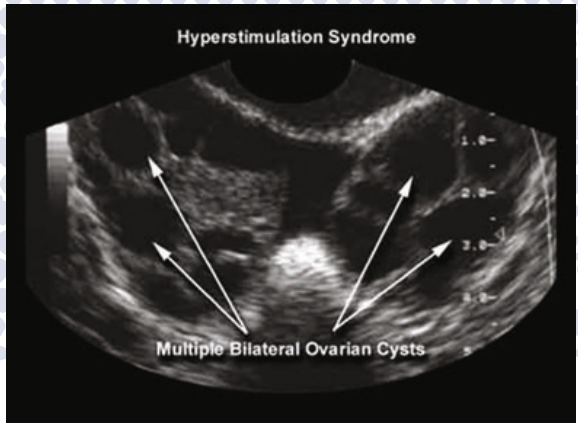


SOME COUPLES ARE WORRIED THAT IF THEY USE DONOR EGGS OR DONOR EMBRYOS, THEIR BODY WILL 'REJECT" THEM, BECAUSE THESE ARE GENETICALLY FOREIGN. HOWEVER, REMEMBER THAT ALL EMBRYOS ARE GENETICALLY FOREIGN TO THE MOTHER, BECAUSE HALF THE GENETIC MATERIAL ALWAYS COMES FROM THE FATHER! THE UTERUS IS AN "IMMUNOLOGICALLY PRIVILEGED" SITE, AND DONOR EMBRYOS HAVE AS GOOD A CHANCE OF IMPLANTING AS NORMAL EMBRYOS. THE UTERUS CANNOT REJECT AN EMBRYO, NO MATTER WHERE IT COMES FROM !

WHAT ARE THE RISKS AND COMPLICATIONS OF IVF?

MANY COUPLES ARE STILL WORRIED THAT BABIES BORN AFTER IVF ARE ABNORMAL OR WEAK. YOU NEED TO REMEMBER THAT IN ONE SENSE THERE IS NOTHING "ARTIFICIAL' ABOUT THESE BABIES - THEY AREN'T SYNTHETIC BABIES WHICH ARE BEING MANUFACTURED IN THE LABORATORY! IVF IS SIMPLY A FORM OF ASSISTED REPRODUCTIVE TECHNOLOGY, WHERE TECHNOLOGY IS BEING USED TO ASSIST NATURE TO ACCOMPLISH WHAT IT HAS FAILED TO DO FOR THE INFERTILE COUPLE!

MILLIONS OF BABIES HAVE BEEN BORN AFTER IVF TREATMENT, AND THE RISK FOR BIRTH DEFECTS IS NOT INCREASED AFTER IVF TREATMENT.

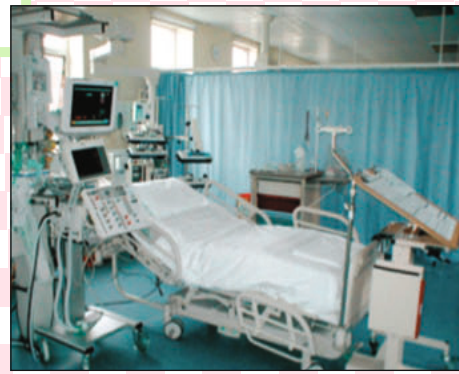


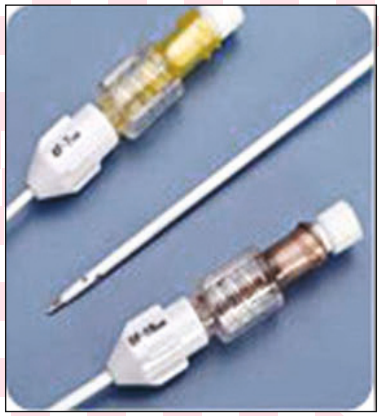
WHAT IS OHSS (OVARIAN HYPER STIMULATION SYNDROME)?

THE MOST WORRISOME COMPLICATION OF IVF IS THAT OF OVARIAN HYPERSTIMULATION SYNDROME (OHSS). SUPEROVULATED OVARIES CONTAIN MANY FOLLICLES WHICH ARE LOADED WITH ESTROGEN. AFTER OVULATION, A HUGE AMOUNT OF ESTROGEN-RICH FLUID IS POURED DIRECTLY OUT OF THE ENLARGED OVARIES INTO THE ABDOMINAL CAVITY. THIS FLUID ALSO CONTAINS CHEMICALS LIKE KALLIKREIN-KININ AND VEGF (VASCULAR ENDOTHELIAL GROWTH FACTOR), WHICH COAT THE LINING OF THE ABDOMINAL CAVITY AND CAUSE IT TO BECOME VERY PERMEABLE (LEAKY).

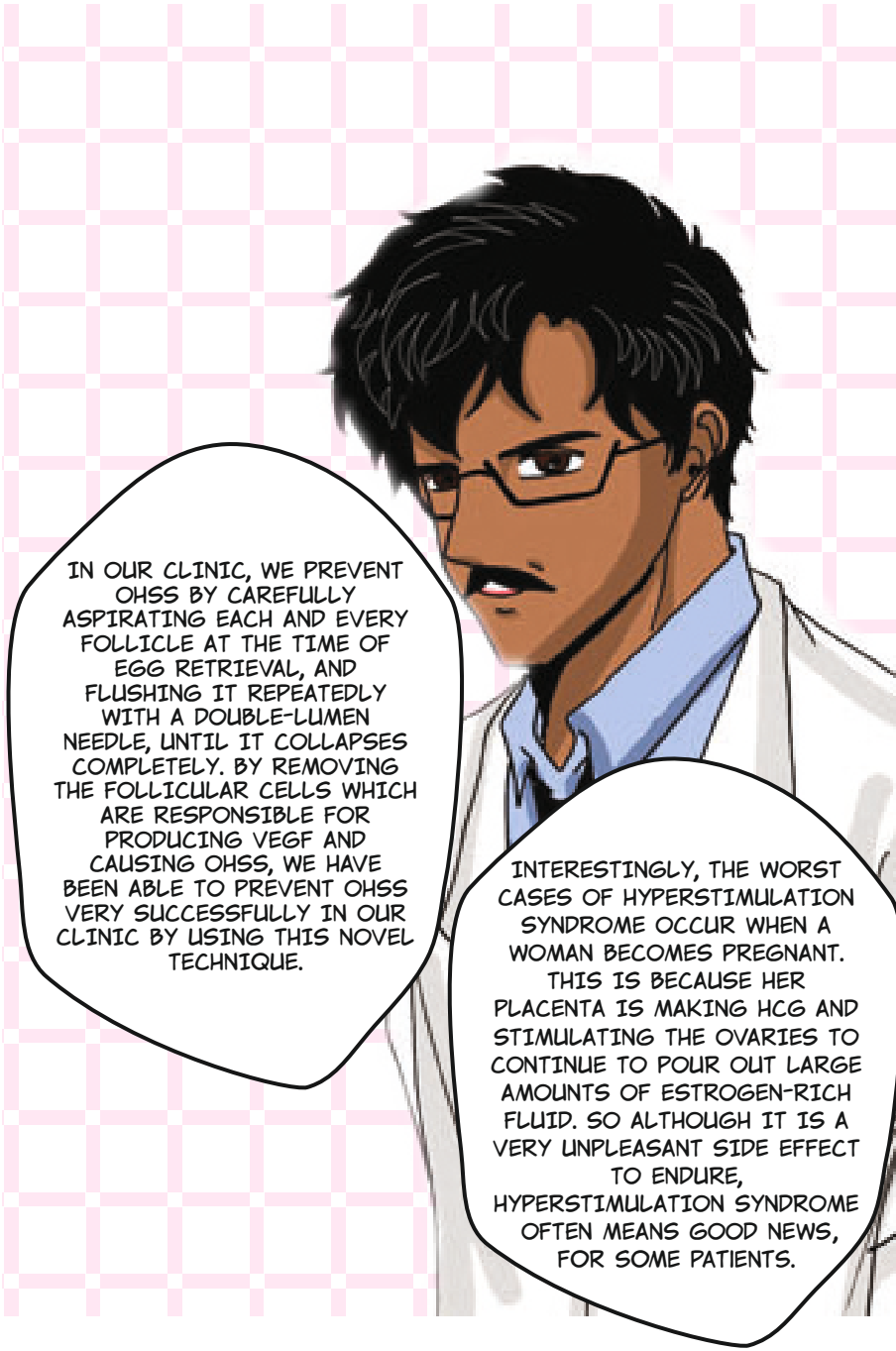
FLUID (SERUM) LITERALLY POURS OUT OF YOUR BLOODSTREAM INTO THE PERITONEAL CAVITY BECAUSE OF THE 'LEAKINESS " OF THE ABDOMINAL CAVITY'S LINING. THE OVARIES BALLOON IN SIZE, YOUR ABDOMEN SWELLS, AND YOU MAY GET DIZZY BECAUSE OF THE DECREASED BLOOD VOLUME. MANY WOMEN WILL HAVE MILD DEGREES OF OHSS. THIS DOES NOT REQUIRE HOSPITALIZATION, JUST BED REST AT HOME. IT IS ONLY THE RARE, SEVERE CASES THAT REQUIRE HOSPITALIZATION

THE OCCASIONAL PATIENT WHO DEVELOPS SEVERE HYPERSTIMULATION MUST GO INTO THE HOSPITAL, HAVE INTRAVENOUS FLUIDS FOR SEVERAL DAYS, AND WAIT FOR HER OVARIES TO REDUCE IN SIZE AND FOR HER BODY TO GO BACK TO NORMAL. SOME PATIENTS MAY EVEN NEED TO BE ADMITTED INTO AN INTENSIVE CARE UNIT FOR MONITORING AND OBSERVATION, SINCE THIS CAN BE LIFE-THREATENING.

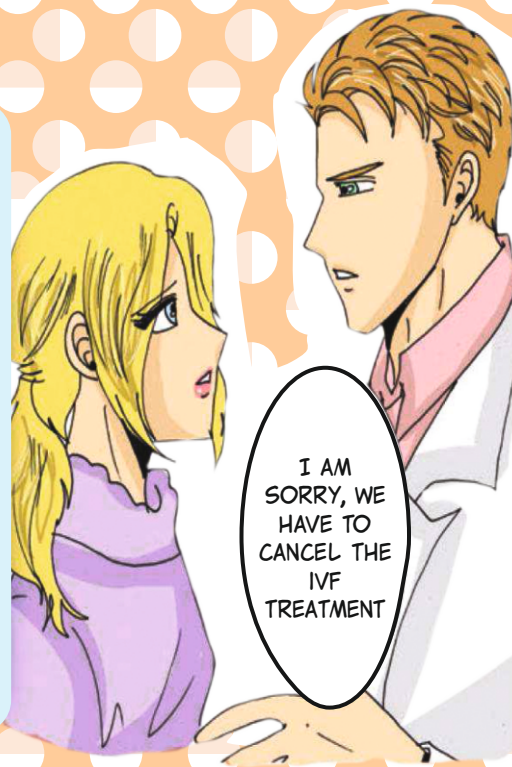


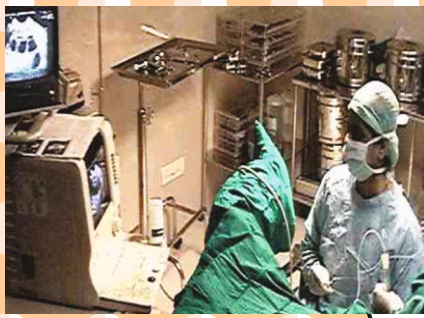


AT ONE TIME THIS WAS A VERY DANGEROUS CONDITION ONLY BECAUSE IT WAS NOT FULLY UNDERSTOOD. WE NOW KNOW THAT BY PUTTING A SMALL "PARACENTESIS" CATHETER INTO THE ABDOMEN AND DRAINING THIS FLUID, THE PATIENT IS MADE MUCH MORE COMFORTABLE, AND FLUID LEAKAGE INTO THE ABDOMEN SLOWS DOWN DRAMATICALLY. THUS, EVEN IN THE RARE CASES OF SEVERE HYPERSTIMULATION SYNDROME, KNOWLEDGEABLE TREATMENT MAKES THE LIKELIHOOD OF ANY DANGEROUS COMPLICATION VERY RARE

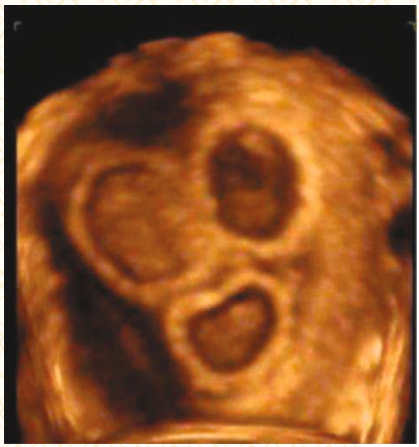

IN OUR CLINIC, WE PREVENT OHSS BY CAREFULLY ASPIRATING EACH AND EVERY FOLLICLE AT THE TIME OF EGG RETRIEVAL, AND FLUSHING IT REPEATEDLY WITH A DOUBLE-LUMEN NEEDLE, UNTIL IT COLLAPSES COMPLETELY. BY REMOVING THE FOLLICULAR CELLS WHICH ARE RESPONSIBLE FOR PRODUCING VEGF AND CAUSING OHSS, WE HAVE BEEN ABLE TO PREVENT OHSS VERY SUCCESSFULLY IN OUR CLINIC BY USING THIS NOVEL TECHNIQUE.
INTERESTINGLY, THE WORST CASES OF HYPERSTIMULATION SYNDROME OCCUR WHEN A WOMAN BECOMES PREGNANT. THIS IS BECAUSE HER PLACENTA IS MAKING HCG AND STIMULATING THE OVARIES TO CONTINUE TO POUR OUT LARGE AMOUNTS OF ESTROGEN-RICH FLUID. SO ALTHOUGH IT IS A VERY UNPLEASANT SIDE EFFECT TO ENDURE, HYPERSTIMULATION SYNDROME OFTEN MEANS GOOD NEWS, FOR SOME PATIENTS.

IF YOU GROW TOO MANY FOLLICLES (MORE THAN 25). OR IF YOUR ESTRADIOL LEVEL IS VERY HIGH, THE DOCTOR MAY BE FORCED TO CANCEL THE IVF CYCLE, BECAUSE OF THE RISK YOU RUN OF DEVELOPING OHSS. IN SOME CLINICS, DOCTORS CAN SALVAGE THIS CYCLE BY COLLECTING ALL THE EGGS AND FREEZING ALL THE EMBRYOS. BECAUSE THE EMBRYOS ARE NOT TRANSFERRED, THE RISK OF HYPERSTIMULATION IS REDUCED AND THE FROZEN EMBRYOS CAN THEN BE TRANSFERRED IN A FUTURE CYCLE.





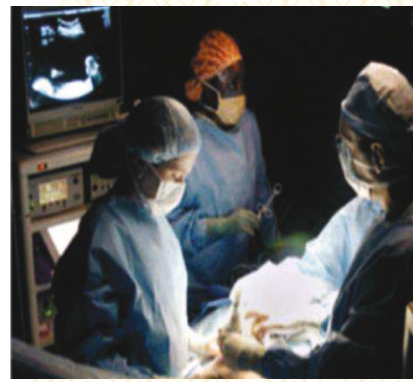
COMPLICATIONS CAN ALSO OCCUR DURING THE EGG RETRIEVAL PROCEDURE. THE REMOVAL OF EGGS THROUGH AN ASPIRATING NEEDLE ENTAILS A SLIGHT RISK OF BLEEDING, INFECTION, AND DAMAGE TO THE BOWEL, BLADDER, OR A BLOOD VESSEL. THIS IS VERY RARE IN A GOOD CLINIC

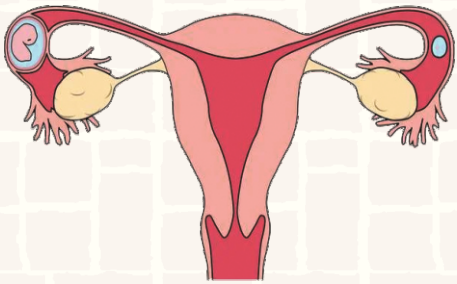


WHAT ABOUT THE RISK OF A MULTIPLE PREGNANCY AFTER IVF ?

IN ALL TECHNIQUES OF ASSISTED REPRODUCTIVE TECHNOLOGY, THE CHANCE OF MULTIPLE PREGNANCY IS INCREASED WHEN MORE THAN ONE EMBRYO IS TRANSFERRED. ALTHOUGH SOME WOULD CONSIDER HAVING TWINS TO BE A HAPPY RESULT, THERE ARE MANY PROBLEMS ASSOCIATED WITH HIGH ORDER MULTIPLE PREGNANCY. WOMEN CARRYING A MULTIPLE PREGNANCY MAY NEED TO SPEND WEEKS IN BED OR IN THE HOSPITAL. THERE IS ALSO A GREATER RISK OF LATE MISCARRIAGES OR PREMATURE DELIVERY IN MULTIPLE PREGNANCIES. THERE MAY BE ENORMOUS BILLS FOR THE PROLONGED AND INTENSIVE CARE FOR PREMATURE BABIES.

A RECENT TREATMENT OPTION FOR WOMEN WITH MULTIPLE PREGNANCIES IS THAT OF SELECTIVE FETAL REDUCTION, IN WHICH ONE OR MORE OF THE FETUSES IS SELECTIVELY DESTROYED (USUALLY BY INJECTING THE TOXIC CHEMICAL, POTASSIUM CHLORIDE INTO ITS HEART UNDER ULTRASOUND GUIDANCE). IN MOST CASES, THE KILLED FETUS IS THEN REABSORBED BY THE BODY - AND THE OTHER FETUSES CONTINUE TO GROW. THE RISK OF A MISCARRIAGE AFTER THIS IS ABOUT
10 - 20 % IN EXPERIENCED HANDS.





THERE IS LESS THAN THREE PERCENT CHANCE OF AN ECTOPIC PREGNANCY WITH IVF. THIS IS NOT BECAUSE OF THE PROCEDURE, BUT RATHER BECAUSE WOMEN GOING THROUGH IVF ALREADY HAVE DAMAGED TUBES, WHICH PREDISPOSES THEM TO HAVING AN ECTOPIC.

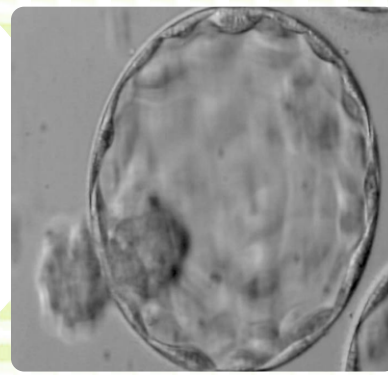
IVF IS PHYSICALLY DEMANDING - AND STRESSFUL! HORMONE STIMULATION CAUSES LETHARGY, FATIGUE, MOOD SWINGS AND FLUID RETENTION. THOUGH THIS IS TEMPORARY, SOME PEOPLE FIND TREATMENT CONFLICTS WITH THEIR JOB OR OTHER COMMITMENTS.

IN REAL LIFE, THE MAJOR RISKS OF IVF ARE FINANCIAL AND PSYCHOLOGICAL.
EVEN AFTER SPENDING ALL THE TIME, MONEY AND ENERGY REQUIRED FOR A TREATMENT CYCLE, ALL PATIENTS WILL NOT GET PREGNANT. THESE PROCEDURES CREATE HIGH EXPECTATIONS BUT ARE MORE LIKELY TO FAIL THAN TO SUCCEED IN A GIVEN CYCLE. UNSUCCESSFUL COUPLES WILL FEEL FRUSTRATED AND IT IS COMMON TO FEEL ANGRY, ISOLATED, AND RESENTFUL TOWARD BOTH THE SPOUSE AND THE MEDICAL TEAM. THE SUPPORT OF FRIENDS AND FAMILY MEMBERS IS VERY IMPORTANT AT THIS TIME.

THE DANGER OF OVERTREATMENT AND UNDERTREATMENT

IVF TECHNIQUES HAVE NOW BECOME WELL ESTABLISHED, AND MOST TOWNS IN INDIA HAVE MANY IVF CLINICS TODAY. THIS IS GOOD , BECAUSE INFERTILE COUPLES NO LONGER NEED TO TRAVEL LONG DISTANCES FOR IVF TREATMENT. HOWEVER MANY CLINICS ARE POORLY EQUIPPED, AND THE STAFF INADEQUATELY TRAINED, WITH THE RESULTS THAT PREGNANCY RATES ARE POOR MANY CLINICS HAVE STARTED. AND THEN CLOSED DOWN IN A FEW MONTHS, WITHOUT BEING ABLE TO ACHIEVE EVEN A SINGLE PREGNANCY !

UNFORTUNATELY, THIS OFTEN MEANS THAT ALL IVF CLINICS START GETTING A BAD REPUTATION. IN ORDER TO PROTECT YOURSELF, IT'S A GOOD IDEA TO ASK THE CLINIC STAFF TO ACTUALLY SHOW YOU YOUR EMBRYOS UNDER THE MICROSCOPE. GOOD CLINICS DO THIS ROUTINELY, AND SOME EVEN OFFER VIDEO RECORDS. NOT ONLY IS THIS REASSURING FOR THE PATIENT, IT ALSO HELPS THEM TO "BOND" WITH THE EMBRYOS!



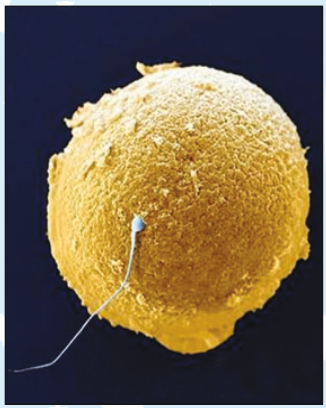
ANOTHER DANGER OF TOO MANY IVF CLINICS IS THE RISK OF OVERTREATMENT. IN ORDER TO REMAIN PROFITABLE, MANY CLINICS NOW OFFER IVF TO INFERTILE COUPLES AS A TREATMENT OF FIRST CHOICE. PARADOXICALLY, WHILE RICH PATIENTS END UP GETTING IVF EVEN WHEN THEY DON'T NEED IT, POOR PATIENTS ARE OFTEN DEPRIVED OF THIS TREATMENT EVEN THOUGH THEY NEED IT, BECAUSE OF THE EXPENSE INVOLVED. UNFORTUNATELY, THE GOVERNMENT STILL DOES NOT CONSIDER THAT PROVIDING INFERTILITY TREATMENT SHOULD BE A PART OF ITS FAMILY PLANNING PROGRAM.

SUPPORTING EACH OTHER

IF YOU DON'T HAVE A FAMILY OR A FRIEND WHO CAN PROVIDE SUPPORT, THEN THE SENSITIVE ASSISTANCE OFFERED BY A SUPPORT GROUP MAY BE VERY HELPFUL. YOU MAY ALSO SEEK THE SPECIALIZED ASSISTANCE OF A COUNSELOR, WHO IS EITHER ATTACHED TO THE CLINIC OR BASED IN THE COMMUNITY

GOING THROUGH AN IVF CYCLE CAN BE VERY STRESSFUL, AND YOU NEED TO BE PREPARED FOR THE UPS AND DOWNS. MANY CLINICS HAVE FOUND THAT OPTIMISTIC AND WELL-PREPARED PATIENTS HAVE BETTER PREGNANCY RATES, AND COUNSELLING AND EMOTIONAL SUPPORT CAN BE VERY HELPFUL IN IMPROVING YOUR CHANCES OF GETTING PREGNANT!

EVERY TIME YOU START A CYCLE, YOU HAVE TO HOPE FOR THE BEST AND BE PREPARED FOR THE WORST. IT LITERALLY IS LIKE GAMBLING - AND HOPING THAT YOU HIT THE JACKPOT! MANY PATIENTS FIND THE FIRST CYCLE THE MOST STRESSFUL - AND FIND IT MUCH EASIER TO DO A SECOND CYCLE, BECAUSE THEY ARE MORE IN CONTROL AND UNDERSTAND MUCH BETTER WHAT THEY ARE GOING THROUGH.



IF YOU JUDGE THE OUTCOME OF AN IVF CYCLE ONLY ON THE BASIS OF WHETHER OR NOT YOU GET PREGNANT, THEN WITH THE LIMITATIONS OF TODAY'S TECHNOLOGY, YOU ARE MORE LIKELY TO BE DISAPPOINTED THAN OTHERWISE. HOWEVER, DO REMEMBER THAT EACH CYCLE ALSO PROVIDES YOU WITH VALUABLE DIAGNOSTIC AND PROGNOSTIC INFORMATION, SUCH AS WHETHER THE SPERM FERTILISE THE EGG OR NOT, SO THAT YOU CAN PLAN YOUR FUTURE COURSE OF TREATMENT. GOING THROUGH AN IVF CYCLE CAN ALSO GIVE YOU PEACE OF MIND THAT YOU TRIED YOUR BEST!

HOW CAN YOU SELECT THE BEST IVF CLINIC FOR YOURSELF?

THERE ARE NOW OVER 3000 IVF CLINICS IN INDIA, SO HOW DO YOU GO ABOUT SELECTING THE BEST? THIS CAN BE DIFFICULT AND CONFUSING, BUT REMEMBER THAT WHEN SELECTING AN IVF PROGRAM, INFORMATION IS CRUCIAL. IMPORTANT POINTS FOR CONSIDERATION INCLUDE THE QUALIFICATIONS AND EXPERIENCE OF THE STAFF, TYPES OF PATIENTS BEING TREATED, SUPPORT SERVICES AVAILABLE, COST, CONVENIENCE, AND SUCCESS RATES.

THE RANGE OF SERVICES OFFERED BY AN IVF PROGRAM SHOULD BE CAREFULLY CONSIDERED. NOT ALL PROGRAMS ARE EQUIPPED TO PROVIDE ALL SERVICES, SUCH AS SPERM DONORS, ICSI AND CRYOPRESERVATION OF EMBRYOS. IT IS BEST TO SELECT A FULL-SERVICE CLINIC, WHICH OFFERS ALL THE POSSIBLE TREATMENT OPTIONS, SO THAT THE ONE WHICH IS BEST FOR YOU CANBE USED. PLEASE MAKE SURE YOUR CLINIC IS REGISTERED UNDER "THE ASSISTED REPRODUCTIVE TECHNOLOGY (REGULATION) ACT"

WHAT QUESTIONS SHOULD YOU ASK WHEN SELECTING AN IVF CLINIC ?

COST AND CONVENIENCE

1. HOW MUCH DOES THE ENTIRE PROCEDURE COST, INCLUDING DRUGS PER TREATMENT CYCLE?

2. DO WE PAY IN ADVANCE? HOW MUCH?

3. WHAT ARE THE MODES OF PAYMENT?

4. HOW MUCH DO WE PAY IF MY TREATMENT CYCLE IS CANCELLED BEFORE EGG RECOVERY? BEFORE EMBRYO TRANSFER?

5. WHAT ARE THE COSTS FOR EMBRYO FREEZING, STORAGE, AND TRANSFER?

6. HOW WILL THE TREATMENT SCHEDULE AFFECT OUR COMMITMENTS AT WORK?

7. IF I MUST HAVE LODGING, IS THERE A LOW COST PLACE FOR ME TO STAY? DO YOU HELP ARRANGE THIS?

8. IF I DO NOT GET PREGNANT, WHEN DO I MAKE MY NEXT APPOINTMENT FOR FURTHER EVALUATION AND COUNSELING?

DETAILS ABOUT THE PROGRAM

1. HOW MANY DOCTORS WILL BE INVOLVED IN MY TREATMENT?

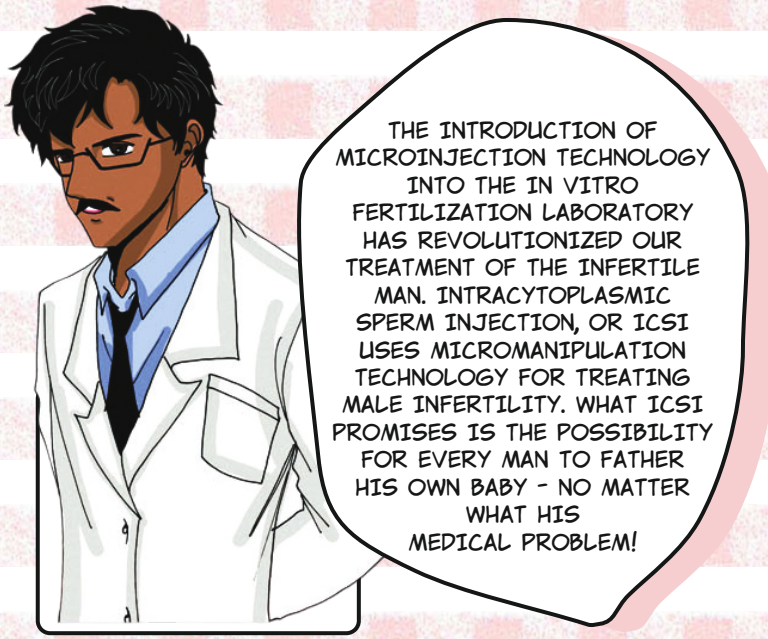
2. TO WHAT DEGREE CAN MY OWN FAMILY DOCTOR OR A GYNECOLOGIST PARTICIPATE IN MY TREATMENT?

3. WHAT TYPES OF COUNSELLING AND SUPPORT SERVICES ARE AVAILABLE?

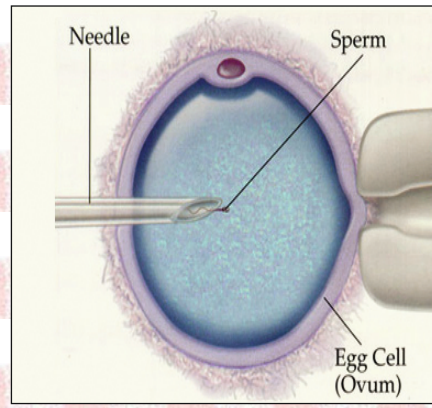
4. WHOM DO I CALL IF I HAVE A PROBLEM?

5. IS DONOR SPERM AVAILABLE IN YOUR PROGRAM? DONOR EGGS?

6. DO YOU HAVE AN AGE LIMIT?

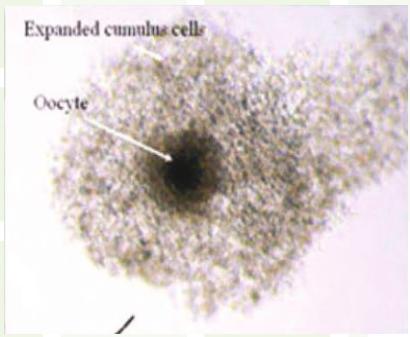


AS THE NAME SUGGESTS, ICSI IS A TECHNIQUE IN WHICH A SINGLE SPERM IS INJECTED INTO THE CENTRE OF THE CYTOPLASM OF THE EGG IN ORDER TO ACHIEVE FERTILIZATION. THE BEAUTY OF THE TECHNIQUE IS THAT SINCE THE SPERM IS BEING INJECTED DIRECTLY INTO THE EGG, ALL THAT IS NEEDED TO ACHIEVE FERTILIZATION ARE LIVE SPERM - NO MATTER HOW ABNORMAL THESE MAY APPEAR TO BE. WITH ICSI THE EQUATION "1 EGG PLUS 1 SPERM = 1 EMBRYO" BECOMES POSSIBLE!

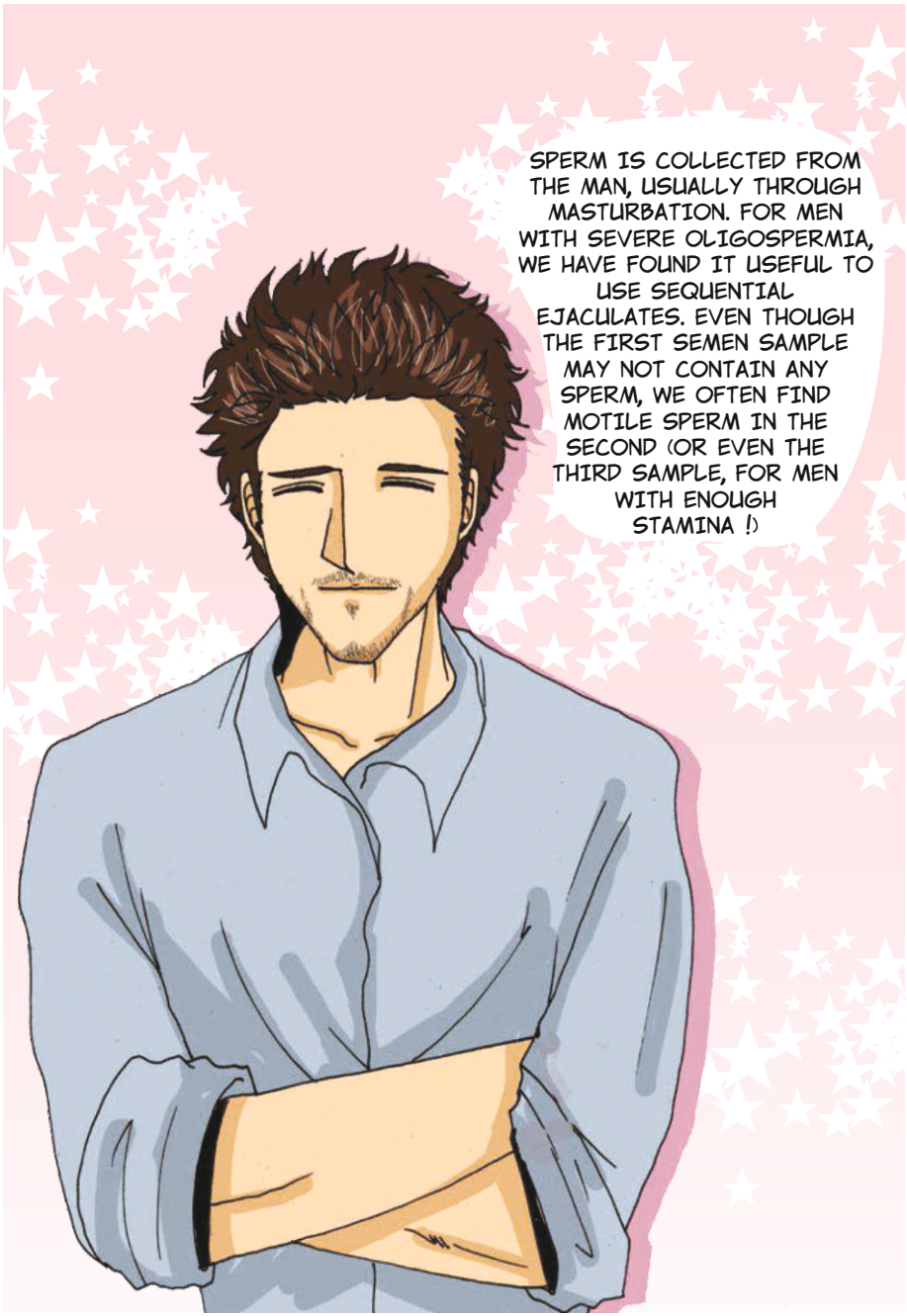


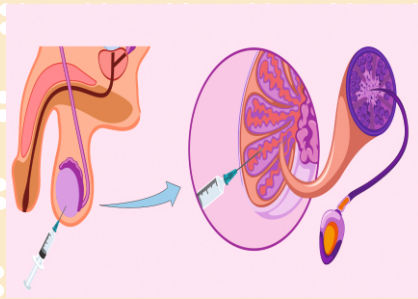
THE PROCEDURE FOR ICSI

ICSI IS DONE IN AN IVF CYCLE, DURING WHICH FERTILITY DRUGS ARE ADMINISTERED TO THE WIFE TO AID IN THE PRODUCTION OF MULTIPLE EGGS, WHICH ARE THEN REMOVED UNDER VAGINAL ULTRASOUND GUIDANCE, AS IS DONE FOR IVF.



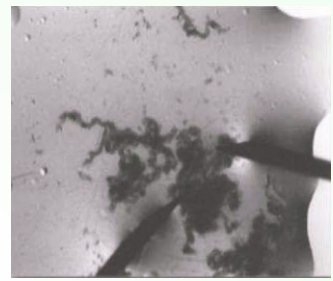
IN NORMAL CIRCUMSTANCES, THE EGG IS SURROUNDED BY A CLUSTER OF CELLS KNOWN AS THE CUMULUS CORONA CELLS. THIS IS CALLED THE OOCYTE CUMULUS CORONA COMPLEX. THESE CUMULUS CELLS ARE REMOVED BY REPEATED PASSAGE OF THE COMPLEX THROUGH FINE PIPETTES, AND BY TREATING THEM WITH A CHEMICAL CALLED HYALURONIDASE SO THAT THESE CELLS ARE STRIPPED OFF. THE DENUDED EGGS ARE EXAMINED, AND ONLY MATURE EGGS IN METAPHASE-II STAGE ARE USED FOR ICSI.

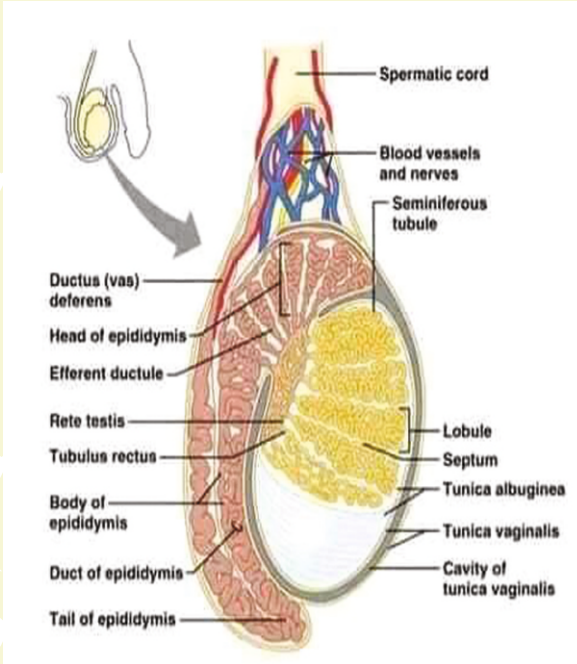

SPERM IS COLLECTED FROM THE MAN, USUALLY THROUGH MASTURBATION. FOR MEN WITH SEVERE OLIGOSPERMIA, WE HAVE FOUND IT USEFUL TO USE SEQUENTIAL EJACULATES. EVEN THOUGH THE FIRST SEMEN SAMPLE MAY NOT CONTAIN ANY SPERM, WE OFTEN FIND MOTILE SPERM IN THE SECOND (OR EVEN THE THIRD SAMPLE, FOR MEN WITH ENOUGH STAMINA !)



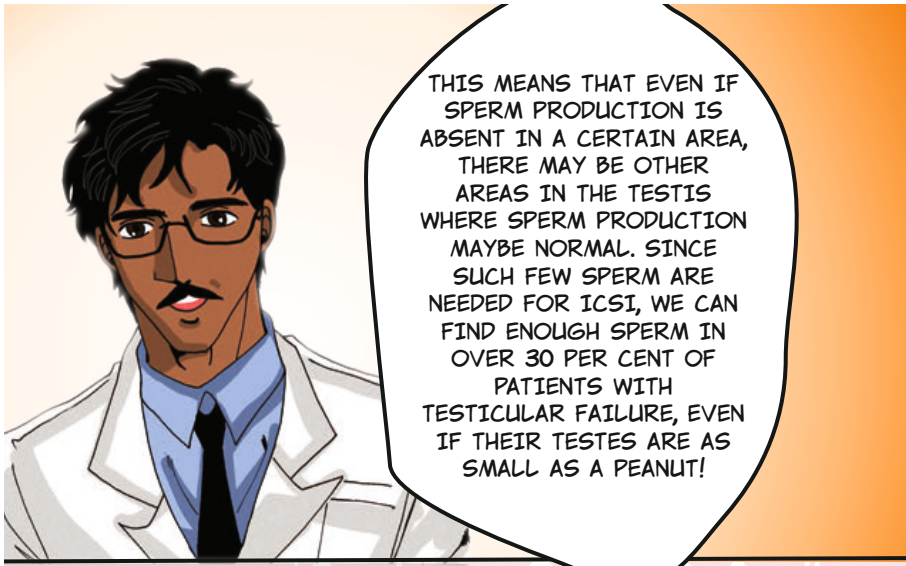
FOR MEN WITH VARIABLE SPERM COUNTS, WHICH VARY FROM ZERO TO A FEW THOUSAND, IT MAY BE HELPFUL TO FREEZE A SAMPLE IN ADVANCE. FOR PATIENTS WITH AZOOSPERMIA, SPERM HARVESTING TECHNIQUES NEED TO BE USED TO RETRIEVE THE SPERM. FOR MEN WITH OBSTRUCTIVE AZOOSPERMIA, THE SIMPLEST TECHNIQUE IS CALLED PESA OR PERCUTANEOUS EPIDIDYMAL SPERM ASPIRATION IN WHICH THE SPERM IS SUCKED OUT FROM THE EPIDIDYMIS BY PUNCTURING IT WITH A FINE NEEDLE.

FOR PATIENTS WITH OBSTRUCTIVE AZOOPSERMIA IN WHOM SPERM CANNOT BE FOUND IN THE EPIDIDYMIS, IT IS ALWAYS POSSIBLE TO FIND SPERM IN THE TESTIS. THE EASIEST WAY TO RETRIEVE THIS IS THROUGH TESA OR TESTICULAR SPERM ASPIRATION IN WHICH THE TESTICULAR TISSUE IS SUCKED OUT THROUGH A FINE NEEDLE, UNDER LOCAL ANAESTHESIA. THE TESTICULAR TISSUE IS PLACED IN CULTURE MEDIA AND SENT TO THE LAB, WHERE IT IS PROCESSED. THE SEMINIFEROUS TUBULES ARE DISSECTED, THUS LIBERATING THE SPERM WHICH ARE THEN USED FOR ICSI.



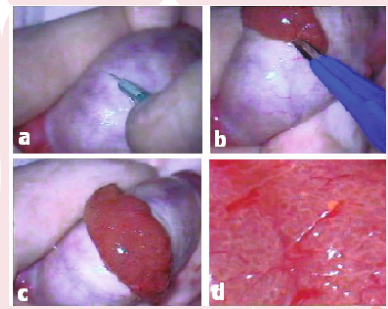


USING SPERM FROM THE EPIDIDYMIS AND TESTIS FOR ICSI IN ORDER TO TREAT PATIENTS WITH OBSTRUCTIVE AZOOSPERMIA IS LOGICAL, AND THUS CONCEPTUALLY EASY TO UNDERSTAND. HOWEVER, SURPRISINGLY, IT IS POSSIBLE TO FIND SPERM IN SOME PATIENTS WHO HAVE TESTICULAR FAILURE (NON-OBSTRUCTIVE AZOOSPERMIA) - EVEN IN MEN WITH VERY SMALL TESTES. THE REASON FOR THIS IS THAT DEFECTS IN SPERM PRODUCTION ARE "PATCHY"- THEY DO NOT AFFECT THE ENTIRE TESTIS UNIFORMLY.



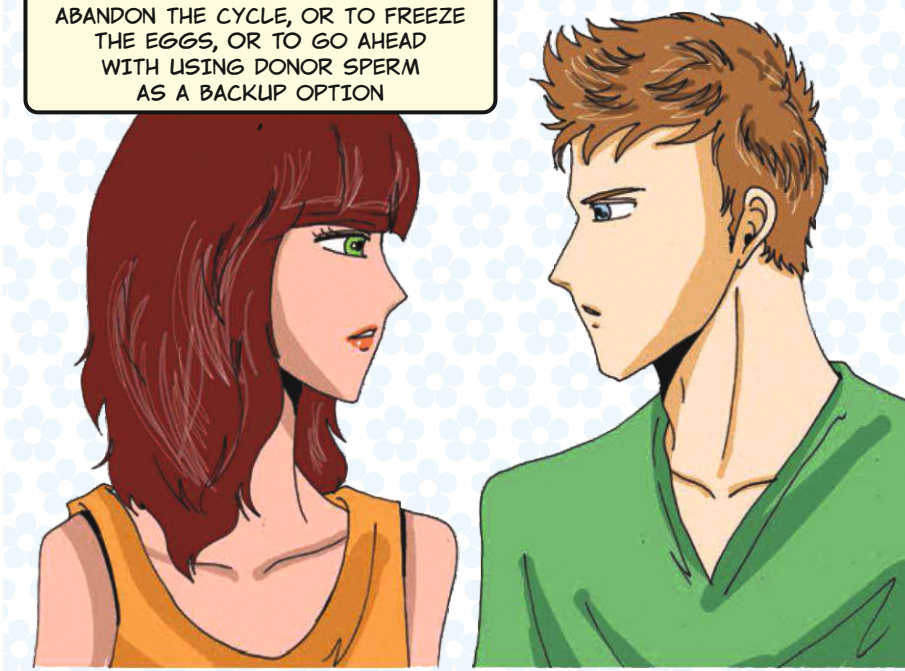
WHAT IS TESE (TESTICULAR SPERM EXTRACTION) ICSI ?

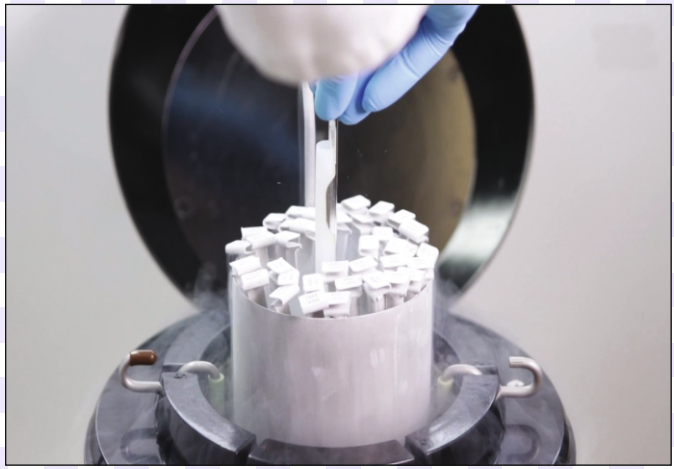
WHILE FINDING SPERM IS QUITE EASY IN MEN WITH OBSTRUCTIVE AZOOSPERMIA (SINCE THEIR TESTES ARE FUNCTIONING NORMALLY), PATIENTS WITH NON OBSTRUCTIVE AZOOSPERMIA (TESTICULAR FAILURE) CAN BE VERY CHALLENGING. OFTEN, SPERM PRODUCTION IN THESE MEN IS SPARSE, AND MULTIPLE SITES IN THE TESTIS MAY NEED TO BE SAMPLED BEFORE BEING ABLE TO FIND SPERM. THIS CAN BE DONE BY PERFORMING MUTIPLE TINY MICROBIOPSIES. AND THIS IS CALLED TESE OR TESTICULAR SPERM EXTRACTION.



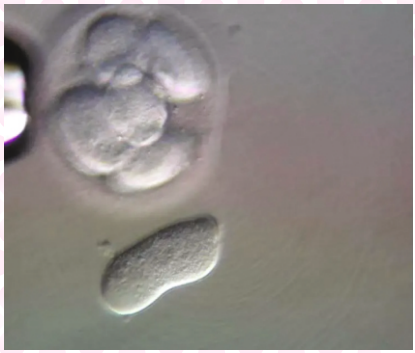
FINDING SPERM IN THE TESTICULAR TISSUE CAN BE A LABORIOUS PROCESS, DEPENDING ON THE DEGREE OF SPERM PRODUCTION, AND FOR SOME MEN WITH PARTIAL TESTICULAR FAILURE, IT CAN TAKE UPTO 2-3 HOURS TO FIND THE SPERM. ALSO, TESTICULAR SPERM ARE TECHNICALLY HARD TO WORK WITH IN THE LABORATORY AND ONLY SOME IVF CLINICS HAVE THE REQUISITE EXPERTISE. FOR MEN WITH NON OBSTRUCTIVE AZOOPSERMIA, SOME CLINICS PERFORM THE TESE A FEW HOURS PRIOR TO EGG RETRIEVAL. THEY CULTURE THIS TESTICULAR TISSUE IN THE INCUBATOR AND THIS CAN HELP THE SPERM TO ACQUIRE MOTILITY.

IN CASE NO SPERM ARE FOUND, EITHER THE COUPLE DECIDES TO CANCEL THE EGG RETRIEVAL AND ABANDON THE CYCLE, OR TO FREEZE THE EGGS, OR TO GO AHEAD WITH USING DONOR SPERM AS A BACKUP OPTION





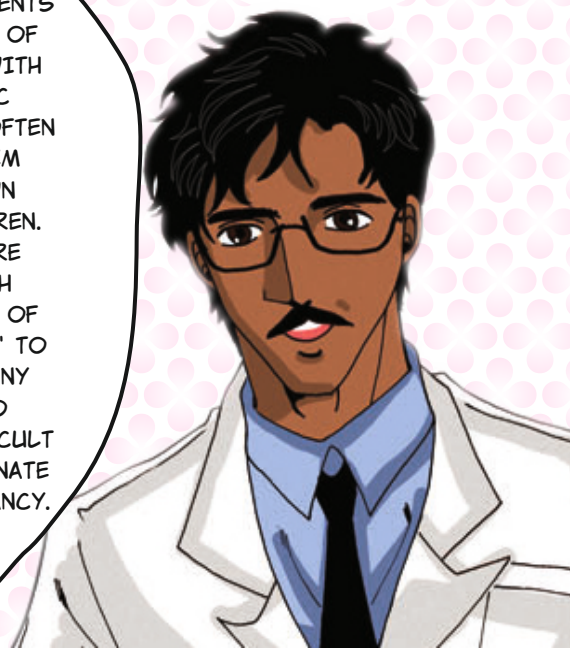
IN PATIENTS IN WHOM SURGERY NEEDS TO BE PERFORMED IN ORDER TO RECOVER TESTICULAR OR EPIDIDYMAL SPERM, IT IS NOW POSSIBLE TO FREEZE THE EXCESS SPERM. THESE SPERM CAN THEN BE THAWED AND USED IN FUTURE CYCLES AS NEEDED, THUS SPARING THE PATIENT THE NEED FOR REPEATED SURGERY FOR SPERM RETRIEVAL. HOWEVER, THE PREGNANCY RATES WITH FRESH TESTICULAR SPERM IS MUCH HIGHER THAN WITH FROZEN TESTICULAR SPERM



WHAT IS PGD (PREIMPLANTATION GENETIC DIAGNOSIS) ?

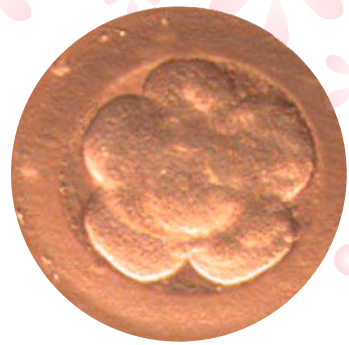
PGD, OR PREIMPLANTATION GENETIC DIAGNOSIS, IS A NEW TECHNIQUE, WHICH MARRIES THE RECENT ADVANCES IN MOLECULAR GENETICS AND ASSISTED REPRODUCTIVE TECHNOLOGY. PREIMPLANTATION GENETIC DIAGNOSIS ENABLES PHYSICIANS TO IDENTIFY GENETIC DISEASES IN THE EMBRYO, PRIOR TO IMPLANTATION, BEFORE THE PREGNANCY IS ESTABLISHED.

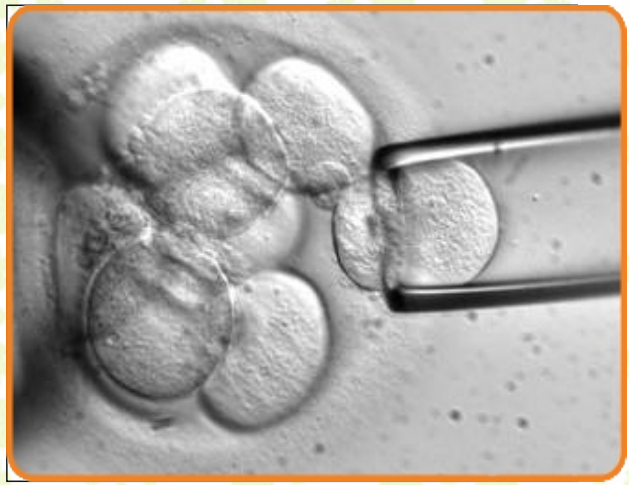
PGD WAS FIRST DEVELOPED FOR PATIENTS WHO WERE AT RISK OF HAVING CHILDREN WITH SERIOUS GENETIC DISORDERS, WHICH OFTEN DISCOURAGED THEM HAVING THEIR OWN BIOLOGICAL CHILDREN. THESE COUPLES ARE OFTEN FACED WITH ATTEMPTING A TYPE OF "RUSSIAN ROULETTE" TO HAVE CHILDREN, MANY TIMES HAVING TO CONFRONT THE DIFFICULT DECISION TO TERMINATE AN AFFECTED PREGNANCY.

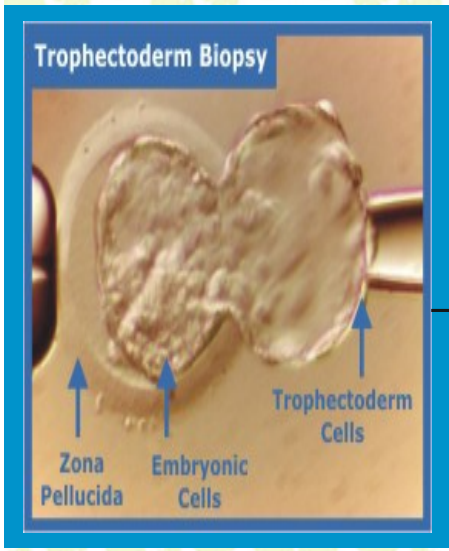


CONSIDER A WOMAN KNOWN TO BE CARRYING AN X-LINKED DISEASE WITH A 50% RISK OF AN AFFECTED MALE IN EACH PREGNANCY, SUCH AS DUCHENNE MASCULAR DYSTROPHY. SHE MAY NOT WISH TO BECOME PREGNANT IF SHE HAS TO MAKE DECISIONS ABOUT AN AFFECTED CHILD IN A VIABLE PREGNANCY. HOWEVER, SHE WOULD BECOME PREGNANT IF SHE KNEW SHE HAD CONCEIVED A DAUGHTER, AND WITH PREIMPLANTATION DIAGNOSIS THIS POSSIBILITY BECOMES A REALITY. PGD THUS ELIMINATES THE NEED FOR POSSIBLE PREGNANCY TERMINATION AFTER PRENATAL DIAGNOSIS OF A GENETICALLY-AFFECTED FETUS.

RESEARCH HAS SHOWN THAT IT IS POSSIBLE AT THREE DAYS AFTER FERTILISATION TO REMOVE ONE OR TWO CELLS FROM AN 8-10 CELLED EMBRYO WITHOUT DETRIMENT TO ITS FURTHER DEVELOPMENT. EMBRYOS WERE SEXED ON THE BASIS OF THE PRESENCE OR ABSENCE OF A DNA FRAGMENT SPECIFIC FOR THE Y CHROMOSOME; IN 1990 TWO SETS OF TWIN GIRLS WERE BORN TO FIVE COUPLES AT RISK OF PASSING ON AN X LINKED DISORDER. SUBSEQUENTLY, A NUMBER OF BABIES HAVE BEEN BORN AFTER PREIMPLANTATION GENETIC TESTING HAS RULED OUT THE DIAGNOSIS OF CYSTIC FIBROSIS, TAY SACHS DISEASE, LESCH NYHAN SYNDROME AND DUCHENNE MUSCULAR DYSTROPHY

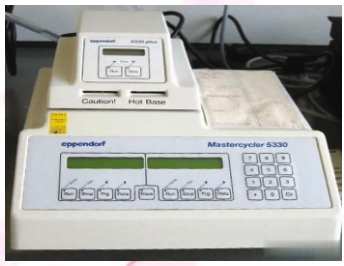


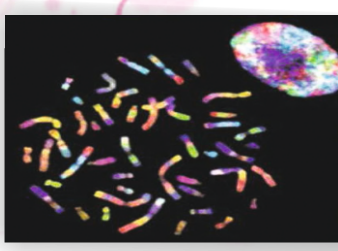




HOW IS PGD DONE?

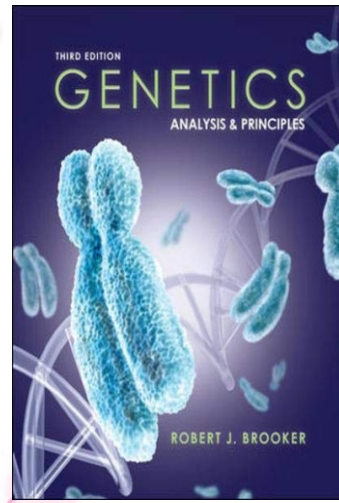
AFTER IVF, ON THE 3RD DAY, THE 8-CELL EMBRYO IS BIOPSED TO OBTAIN BLASTOMERES (SINGLE CELLS) FOR MOLECULAR DIAGNOSIS. AN EMBRYO BIOPSY IS DONE USING MICROMANIPULATORS. UNDER VISUAL CONTROL, A SINGLE CELL IS REMOVED BY GENTLE SUCTION. THIS CELL IS THEN AVAILABLE FOR GENETIC DIAGNOSIS. A NEWER OPTION ALLOWS EMBRYO BIOPSY TO BE DONE ON BLASTOCYSTS (ON DAY 5). THIS IS FAR BETTER , AS WE CAN SAMPLE MORE CELLS , TO MAKE A MORE RELIABLE DIAGNOSIS

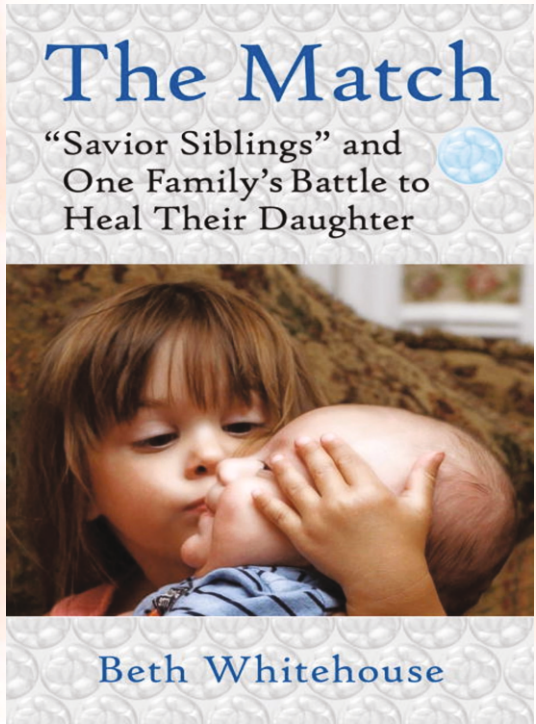




ANALYSIS OF GENETIC MATERIAL (DNA) FROM A SINGLE CELL IS PERFORMED EITHER USING A TECHNIQUE CALLED FISH (FLUORESCENT IN SITU HYBRIDISATION) OR PCR (POLYMERASE CHAIN REACTION) . FISH UTILISES FLUORESCENT PROBES, WHICH ARE SPECIFIC FOR A GIVEN CHROMOSOME, AND ALLOWS DOCTORS TO SCREEN EMBRYOS FOR CHROMOSOMAL NORMALITY. PCR ALLOWS ONE TO AMPLIFY (MUTIPLY) A SELECTED DNA SEQUENCE OF INTEREST, SO THAT IT CAN BE ANALYSED. WHILE AWAITING THE GENETIC RESULTS, THE EMBRYOS CAN BE FROZEN. ONCE THE APPROPRIATE MOLECULAR DIAGNOSIS IS MADE, THE NORMAL EMBRYOS CAN BE TRANSFERRED BACK INTO THE UTERUS IN THE NEXT CYCLE.

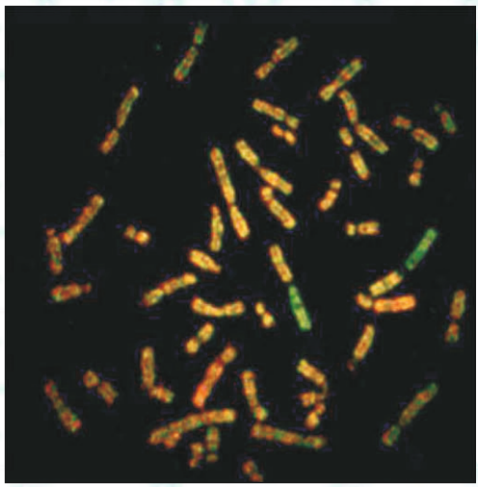
NEWER GENETIC TECHNIQUES INCLUDE MICROARRAY , CGH (COMPARATIVE GENOMIC HYBRIDISATION) AND NGS (NEXT GENERATION SEQUENCING) . PGD CAN BE USED TO PREVENT THOSE GENETIC DISEASES FOR WHICH WE HAVE SPECIFIC GENETIC MARKERS. AS THE SCIENCE OF MOLECULAR GENETICS ADVANCES RAPIDLY, THIS LIST ALSO KEEPS ON INCREASING DAILY. SOME OF THESE DISEASES INCLUDE: CYSTIC FIBROSIS, BETA-THALASSEMIA, SICKLE CELL DISEASE, HUNTINGTON'S DISEASE. DUCHENNE MUSCULAR DYSTROPHY AND CHROMOSOMAL TRANSLOCATIONS.



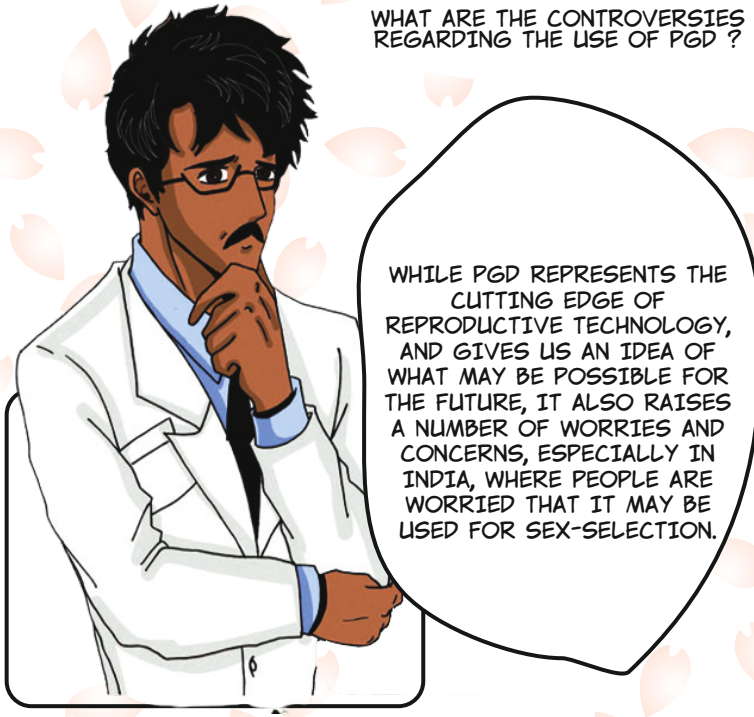


PGD CAN ALSO BE USED FOR CREATING SAVIOR SIBLINGS. THE EMBRYOS CAN BE HUMAN LEUKOCYTE ANTIGEN (HLA) TYPED, SO THAT THE NEWBORN'S HLA MATCHES A SICK SIBLING'S. THE BABY'S CORD BLOOD CAN BE USED FOR STEM CELL DONATION, TO TREAT MONOGENIC DISEASES SUCH AS FANCONI ANAEMIA OR BETA-THALASSEMIA.

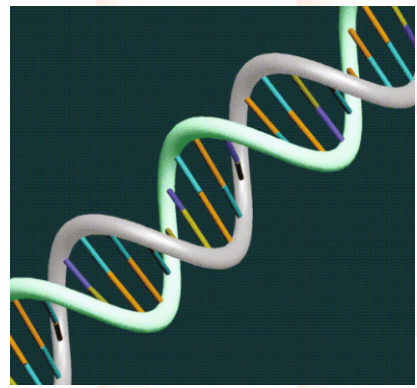
THE COMMONEST REASON FOR PGD TODAY IS PGS (PREIMPLANTATION GENETIC SCREENING) FOR ANEUPLOIDY SCREENING, TO TRY TO INCREASE PREGNANCY RATES FOR OLDER INFERTILE WOMEN. ONE OF THE REASONS OLDER WOMEN HAVE A POORER PREGNANCY RATE IS BECAUSE THEIR EMBRYOS ARE OFTEN CHROMOSOMALLY ABNORMAL, BECAUSE THEY HAVE OLDER EGGS WHICH MAY HAVE GENETIC DEFECTS. PGS ALLOWS THE DOCTOR TO SELECT ONLY THE CHROMOSOMALLY NORMAL EMBRYOS, SO THAT ONLY THESE CAN BE TRANSFERRED BACK INTO THE UTERUS. HOWEVER, THIS REDUCES PREGNANCY RATES.



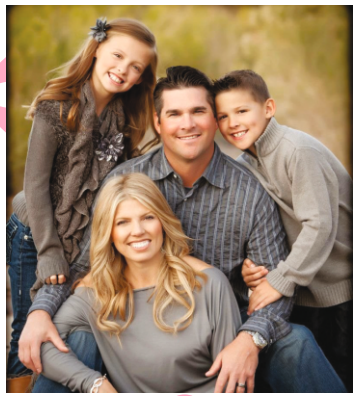
PGD TECHNOLOGY IS EVOLVING RAPIDLY. IN THE PAST WE COULD TEST THE EMBRYO ONLY FOR A FEW CHROMOSOMES. NEW APPROACHES SUCH AS WHOLE GENOME AMPLIFICATION, COMPARATIVE GENOMIC HYBRIDIZATION, AND PREIMPLANTATION GENETIC HAPLOTYPING ALLOW US TO TEST FOR ALL THE CHROMOSOMES, THUS IMPROVING ACCURACY AND SENSITIVITY.



PGD IS EMOTIONALLY A VERY TOUCHY AREA, BECAUSE NOT ONLY ARE WE DEALING WITH HUMAN EMBRYOS - THE VERY START OF NEW LIFE, BUT WE ARE STUDYING THEIR BASIC BLUEPRINT - THEIR GENES - THE STUFF OF WHICH HUMANITY IS MADE. MANY PEOPLE CONFUSE PGD WITH GENETIC ENGINEERING.

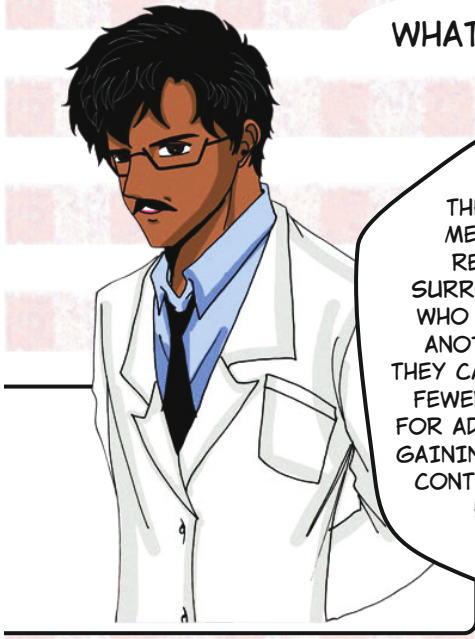


THE OTHER VIEW POINT IS - WHY NOT ? IF MAN CAN IMPROVE ON NATURE , THEN WHY SHOULD HE NOT TRY? AFTER ALL , BUILDING A HOUSE IS SIMPLY MAN'S WAY OF IMPROVING ON NATURE - AND IF WE CAN IMPROVE MAN HIMSELF , THEN STUDYING THE MOLECULAR GENETICS OF THE HUMAN EMBRYO WOULD BE THE ULTIMATE GOAL OF ALL MEDICINE . IN THE PAST, DOCTORS USED TO TREAT ADULTS . IN THE BEGINNING OF THE 20TH CENTURY, WE STARTED TREATING CHILDREN, AND THE FIELD OF PEDIATRICS WAS BORN. WE CAN NOW TREAT THE FETUS- AND THE FUTURE PATIENT OF THE 21ST CENTURY WILL BE THE EMBRYO - THIS IS A LOGICAL PROGRESSION !



WE SHOULD ALLOW PATIENTS THE FREEDOM TO CHOOSE FOR THEMSELVES - MEDICAL TECHNOLOGY SHOULD EMPOWER THEM WITH CHOICES THEY CAN MAKE FOR THEMSELVES! PGD IS PERHAPS THE ULTIMATE FORM OF FAMILY PLANNING THERE IS!

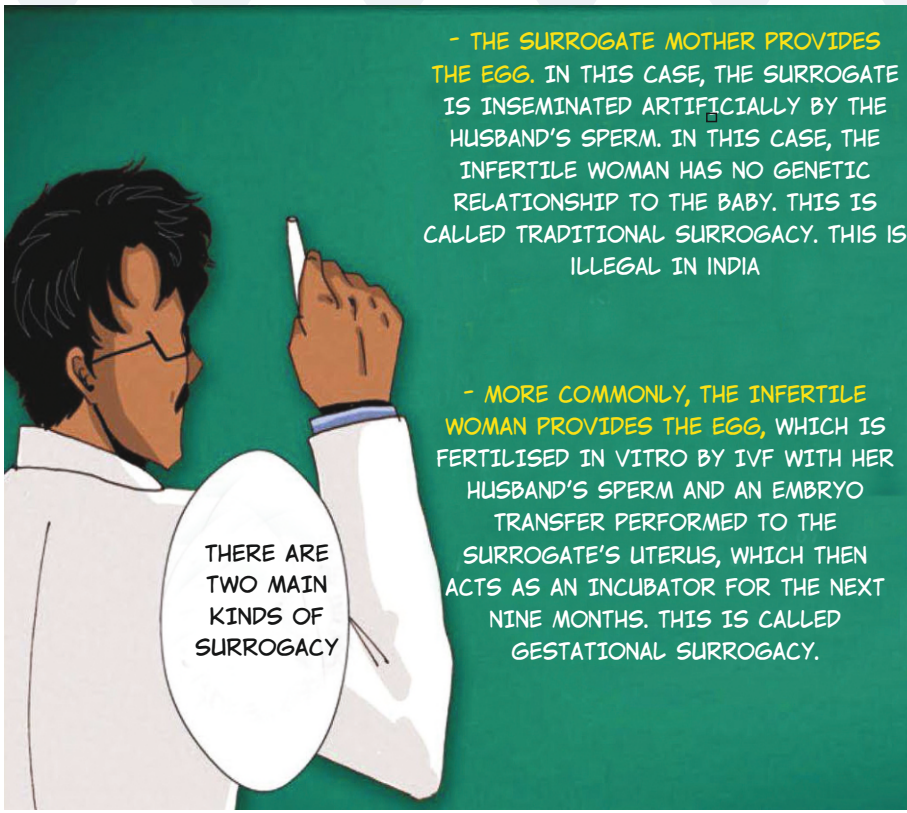
WHAT IS SURROGACY?



WHO NEEDS SURROGACY TREATMENT?

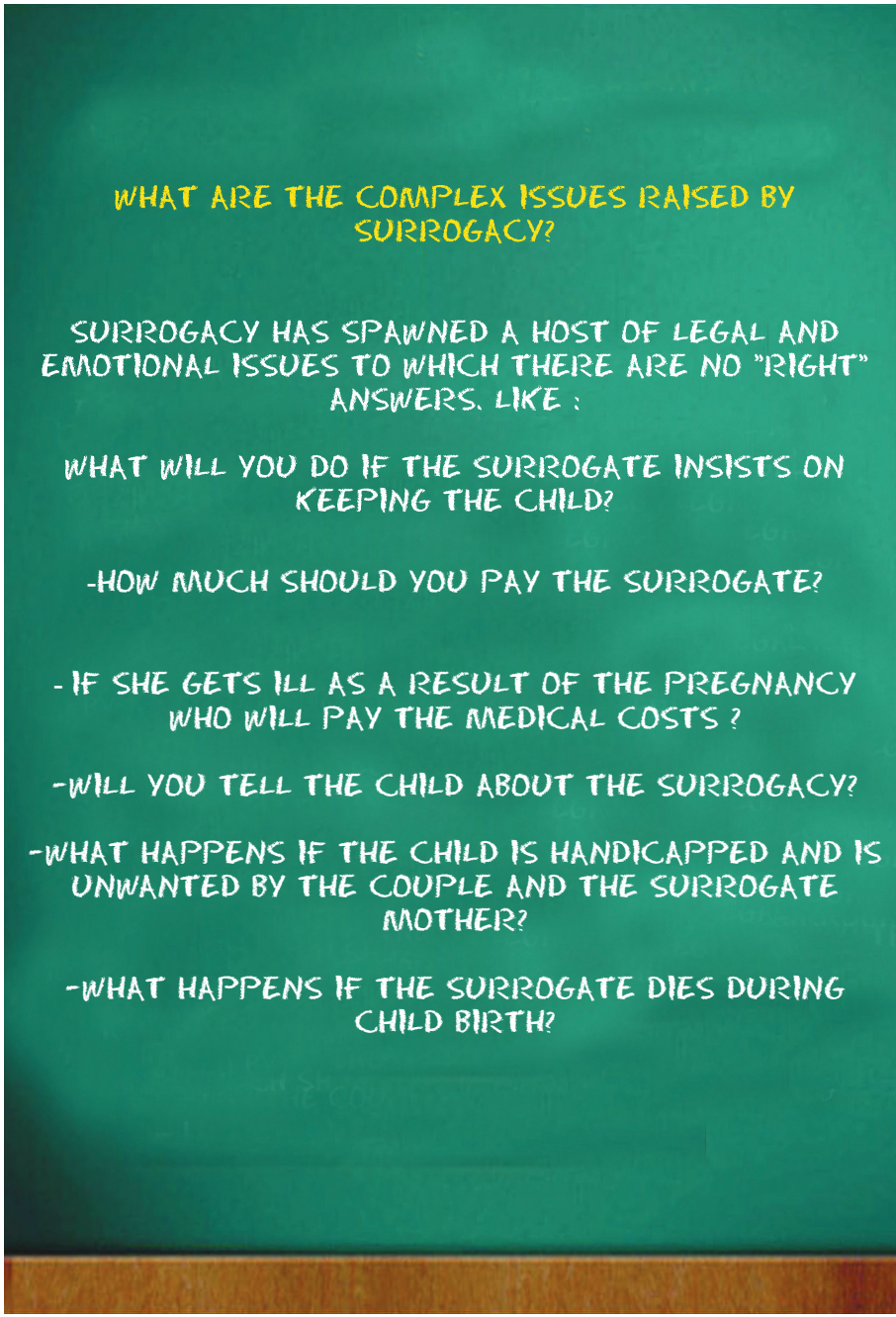
THE COMMONEST REASON IS A WOMAN WHO HAS NO UTERUS OR WHOSE UTERUS HAS BEEN DAMAGED. THE UTERUS MAY BE ABSENT FROM BIRTH (MULLERIAN AGENESIS); OR MAY HAVE BEEN REMOVED SURGICALLY (HYSTERECTOMY FOR LIFE-SAVING REASONS, SUCH AS EXCESSIVE BLEEDING DURING A CAESAREAN). OTHER WOMEN WHO MAY WISH TO EXPLORE SURROGACY INCLUDE THOSE WHO HAVE HAD MULTIPLE MISCARRIAGES: OR WHO HAVE FAILED REPEATED IVF ATTEMPTS FOR UNEXPLAINED REASONS.

WOMEN WHO AGREE TO BECOME SURROGATES MAY DO SO FOR COMPASSIONATE REASONS. THESE INCLUDE A SISTER, MOTHER OR CLOSE FRIEND OF THE COUPLE. THEY MAY ALSO DO SO FOR FINANCIAL REMUNERATION - AND THIS COULD BE A WOMAN, WITH OR WITHOUT CHILDREN, KNOWN OR UNKNOWN TO THE COUPLE, WHO RENTS HER WOMB FOR A FEE.



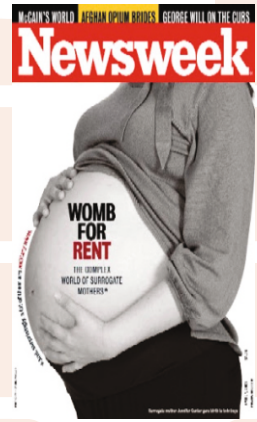
CERTAIN GUIDELINES HAVE BEEN LAID DOWN TO TRY TO MINIMISE MISUSE OF THE SURROGACY TECHNIQUE; AND A SURROGATE MOTHERHOOD CONTRACT NEEDS TO BE DRAWN UP, WHICH SHOULD SPECIFY THAT THE CHILD WILL BECOME THE LEGITIMATE CHILD OF THE INFERTILE COUPLE, THE INTENDED PARENTS. THIS NEEDS TO BE SIGNED BY THE COUPLE, THE SURROGATE, AND HER HUSBAND. THE LEGAL WATERS OF SURROGATE MOTHERHOOD CONTINUE TO BE MURKY. THE NEW SURROGACY (REGULATION) ACT SHOULD HELP TO CLARIFY THESE ISSUES

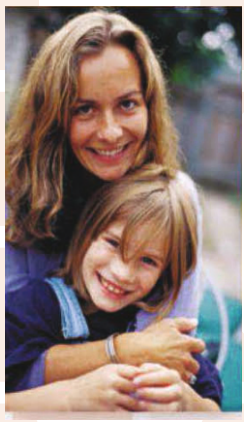
IT IS VITAL THAT THE SURROGATE AND THE COUPLE CONSIDER THE FUTURE OF THE CHILD. THE RECEIVING MOTHER SHOULD IDEALLY BE PRESENT AT THE BIRTH AND CARE FOR THE BABY IN HOSPITAL. SHE CAN EVEN BE PREPARED FOR BREAST FEEDING (INDUCED LACTATION) BY HORMONE TREATMENT.


WHAT ARE THE COMPLEX ISSUES RAISED BY SURROGACY?
SURROGACY HAS SPAWNED A HOST OF LEGAL AND EMOTIONAL ISSUES TO WHICH THERE ARE NO "RIGHT" ANSWERS. LIKE :
WHAT WILL YOU DO IF THE SURROGATE INSISTS ON KEEPING THE CHILD?
-HOW MUCH SHOULD YOU PAY THE SURROGATE?
- IF SHE GETS ILL AS A RESULT OF THE PREGNANCY WHO WILL PAY THE MEDICAL COSTS ?
-WILL YOU TELL THE CHILD ABOUT THE SURROGACY?
-WHAT HAPPENS IF THE CHILD IS HANDICAPPED AND IS UNWANTED BY THE COUPLE AND THE SURROGATE MOTHER?
-WHAT HAPPENS IF THE SURROGATE DIES DURING CHILD BIRTH?

MANY PEOPLE ARE WORRIED ABOUT THE POSSIBILITY OF THE SURROGACY TECHNIQUE BEING MISUSED. THEY FEEL IT MAY ALLOW THE EXPLOITATION OF POOR WOMEN WHO MAY BE USED AS "MOTHER MACHINES" TO BEAR BABIES - MUCH LIKE THE WET NURSES OF YESTERYEAR.

SURROGACY HAS RECEIVED QUITE A LOT OF BAD PRESS RECENTLY - ESPECIALLY WHEN THE CONTRACT GOES SOUR AND THERE IS A DISPUTE OVER THE BABY BETWEEN THE COMMISSIONING PARENTS AND THE SURROGATE MOTHER - THIS MAKE HEADLINE NEWS. THE COURTS THEN NEED TO HAVE THE WISDOM OF SOLOMON TO ASSIGN THE RIGHTS OF THE "GENETIC" MOTHER, THE "BIRTH" MOTHER: AND THE "SOCIAL OR REARING MOTHER.





NEVERTHELESS, WE MUST REMEMBER THAT SURROGACY DOES OFFER ONE METHOD OF ACHIEVING PARENTHOOD TO A FEW COUPLES WHO COULD NEVER HAVE A BABY BY ANY OTHER MEANS. THE ROAD TO SURROGACY IS A ROCKY ONE AND REQUIRES MUCH THOUGHT. IT IS PERHAPS THE MOST COMPLEX AND DIFFICULT WAY TO ACHIEVE PARENTHOOD

Dr. Aniruddha Malpani, MD and Dr.Anjali Malpani, MD are leading IVF specialists practicing in Mumbai. They have more than 60 years of experience together in treating infertile couples. Malpani Infertiltiy Clinic attracts patients from all over the world and thousands of babies have been born as a result of their treatment. They have pioneered a number of firsts in India, including sperm banking, TESA - ICSI and PGD (pre-implantation genetic diagnosis).

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