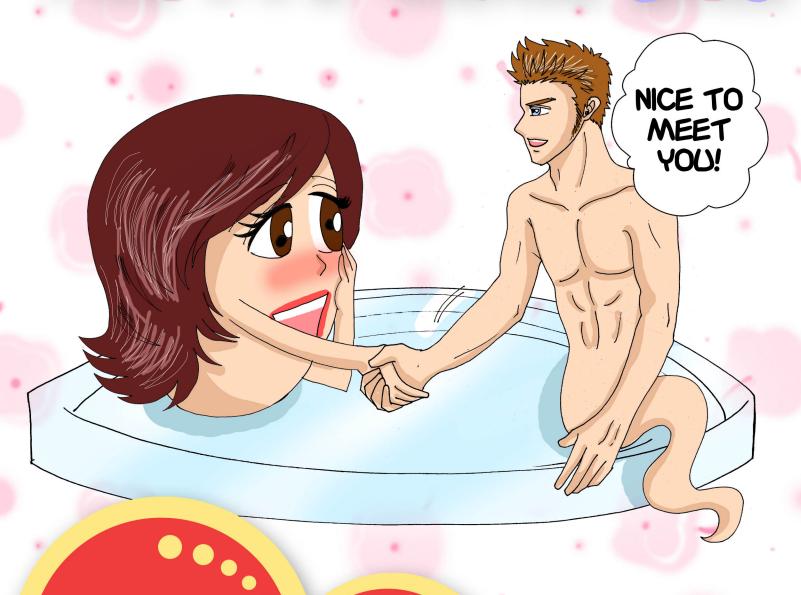
## Malpani Infertility Clinic presents

# THE IVF COMIC BOOK



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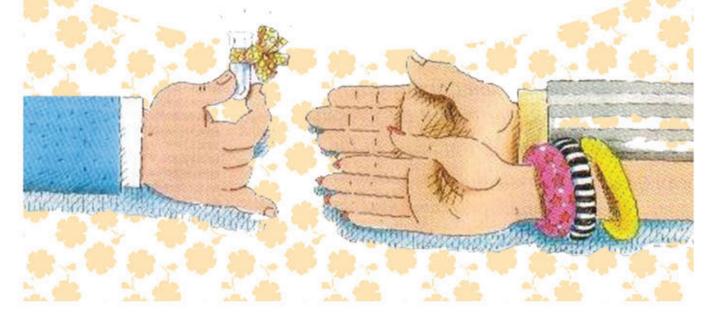
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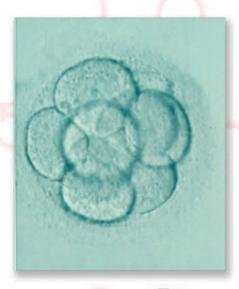


THE BIRTH OF LOUISE BROWN
THROUGH IN VITRO FERTILIZATION
(IVF) IN 1978 WAS A MAJOR
MILESTONE IN INFERTILITY
TREATMENT. IN A FEW DECADES,
IVF HAS BECOME THE
CORNERSTONE OF REPRODUCTIVE
MEDICINE, AND IVF CLINICS TODAY
ROUTINELY PERFORM TECHNIQUES
WHICH WERE THOUGHT TO BELONG
TO THE REALM OF SCIENCE FICTION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

#### WHAT ARE THE ASSISTED REPRODUCTIVE TECHNOLOGIES (ARTS)?

THIS CHAPTER WILL HELP YOU UNDERSTAND ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) SUCH AS IVF AND GAMETE INTRA-FALLOPIAN TRANSFER (GIFT). A FEW YEARS AGO, THESE TECHNIQUES 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.

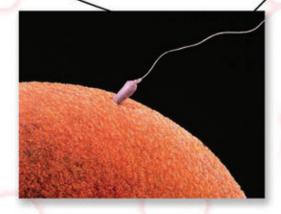




IVF IS THE BASIC ASSISTED REPRODUCTION TECHNIQUE, IN WHICH FERTILIZATION OCCURS IN VITRO (LITERALLY, IN GLASS). THE MAN'S SPERM AND THE WOMAN'S EGG ARE COMBINED IN A LABORATORY DISH, AND AFTER FERTILIZATION, THE RESULTING EMBRYO IS THEN TRANSFERRED TO THE WOMAN'S UTERUS. THE FIVE BASIC STEPS IN AN IVF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

TESTS PRIOR TO IVF
IN ORDER TO PERFORM IVF, ONLY 3
THINGS ARE REQUIRED EGGS, SPERMS
AND A UTERUS, AND BEFORE STARTING
THE IVF CYCLE, THE DOCTOR WILL
CHECK THESE.



FIRST, A SPERM SURVIVAL TEST IS CARRIED OUT. THIS IS A "TRIAL" SPERM WASH, USING EXACTLY THE SAME METHOD AS WILL BE ACTUALLY USED IN IVF, TO ASSESS WHETHER AN ADEQUATE NUMBERS OF SPERMS CAN BE RECOVERED IN ORDER TO DO IVF. THIS TEST WILL ALSO HELP THE LABORATORY TO DECIDE WHICH METHOD OF SPERM PROCESSING SHOULD BE USED DURING IVF. IF THE SPERM ARE POOR, ICSI IS A BETTER OPTION.

A BLOOD FSH LEVEL WILL PROVIDE AN IDEA OF THE "OVARIAN RESERVE", AND PROVIDE INFORMATION ON WHETHER OR NOT THE WOMAN WILL PRODUCE ENOUGH EGGS AFTER SUPEROVULATION, FOR OLDER WOMEN, SOME CLINICS DO A CLOMIPHENE CITRATE CHALLENGE TEST IF THE LEVEL IS VERY HIGH, THIS SUGGESTS EARLY OVARIAN FAILURE, AND IT MAY BE A BETTER IDEA TO CONSIDER DONOR EGGS.

MANY CLINICS MAY DO
A HYSTEROSCOPY, IN
ORDER TO ASSESS
THAT THE UTERINE
CAVITY IS TOTALLY
NORMAL. THEY MAY
ALSO DO A "DUMMY"
EMBRYO TRANSFER TO
MAKE SURE THERE ARE
NO TECHNICAL
PROBLEMS WITH THIS
PROCEPURE.

Chapter 1: What is IVF?

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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.



Chapter 1: What is IVF?

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BLOOD TESTS WHICH MAY BE DONE INCLUDE TESTS FOR IMMUNITY TO RUBELLA: AND TESTS FOR HEPATITIS B, AND AIDS. MOST DOCTORS WILL ALSO ADVISE PATIENTS TO START TAKING FOLIC ACID, AS PART OF PREPREGNANCY CARE, AS THIS HELPS TO REDUCE THE RISK OF CERTAIN BIRTH DEFECTS.





PATIENTS WHO STAND A VERY POOR CHANCE OF SUCCESS WITH IVF INCLUDE THE FOLLOWING: OLDER WOMEN, WHOSE OVARIES ARE FAILING. HOWEVER, THERE IS NO UPPER AGE LIMIT AT WHICH IVF SHOULD NOT BE DONE, AND IN FACT, FOR OLDER WOMEN, IT MIGHT REPRESENT THEIR ONLY CHANCE OF SUCCESS. IT'S NOT REALLY THE AGE OF THE WOMAN WHICH IS THE LIMITING FACTOR - IT'S THE QUALITY OF HER EGGS.

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.





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WOMEN WITH A DAMAGED
UTERUS (FOR EXAMPLE,
BECAUSE OF HEALED
TUBERCULOSIS) BECAUSE THE
CHANCE OF SUCCESSFUL
IMPLANTATION OF THE EMBRYO
IN THE UTERUS BECOMES
VERY POOR.

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 TREATMENTS
ARE USUALLY
RECOMMENDED FIRST.



## WHAT ARE THE 5 BASIC STEPS OF AN IVF TREATMENT CYCLE?

- I. SUPEROVULATION
  - 2. EGG RETRIEVAL
    - 3. FERTILISATION
- 4. EMBRYO CULTURE
  - 5. EMABRYO TRANSFER

Chapter 2A: How is IVF done?

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## 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, MOST OFTEN, THE DRUGS ARE GIVEN OVER A PERIOD OF NINE TO TWELVE DAYS. DRUGS CURRENTLY IN USE INCLUDE: HUMAN MENOPAUSAL GONADOTROPIN (HMG), FOLLICLE STIMULATING HORMONE (FSH) HUMAN CHORIONIC GONAPOTROPIN (HCG) GONODOTROPIN RELEASING HORMONE (GNRH) ANALOGS AND GNRH ANTAGPNISTS.

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 TREATMENTAND THEREBY PREVENTS PREMATURE OVULATION, ALLOWING **POCTORS 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.



Chapter 2A: How is IVF done?



HOW IS SUPEROVULATION MONITORED?

AN ULTRASOUND SCAN IS DONE ON DAY 3, TO CONFIRM THAT THERE ARE NO CYSTS IN THE OVARY, AND THAT DOWNREGULATION HAS BEEN ACHIEVED. A BLOOD TEST FOR ESTRAPIOL 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, 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.

Chapter 2A: How is IVF done?



FOLLICLES USUALLY GROW AT A RATE OF 1-2 MM/DAY, AND A MATURE FOLLICLE HAS A DIAMETER OF ABOUT 16-20 MM IN SIZE . THE ENDOMETRIUM SHOULD ALSO BE EXAMINED CAREFULLY ON THE VAGINAL SCAN, AND THIS SHOULD BE THICK. SOME CLINICS ALSO MEASURE THE BLOOD ESTRADIOL LEVEL, AND EACH MATURE FOLLICLE PRODUCES ABOUT 200-300 PG/ML OF ESTROGEN. WHEN THE FOLLICLES ARE MATURE, AN INJECTION OF HUMAN CHORIONIC GONADOTROPIN (HCG) IS GIVEN TO TRIGGER OVULATION. THIS PRECISE CONTROL ALLOWS THE IVF TEAM TO HARVEST MATURE EGGS 35-38 HOURS AFTER THIS SHOT.

THIS IS WHAT A TYPICAL IVE TREATMENT PROTOCOL IN OUR CLINIC LOOKS LIKE. TREATMENT STARTS FROM DAY I( 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 3 AMPOULES ( 225 IU) OF HMG (MENOGON) DAILY. THE DOSE OF HMG 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.



#### THIS IS WHAT THE DAILY SCHEDULE WOULD LOOK LIKE.

DAY I. INJ LUPRIDE, O.2 ML SC. ( DOWNREGULATION STARTS)
DAY 2. INJ LUPRIDE, O.2 ML SC.

DAY 3. INJ LUPRIDE, O.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, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM. SUPEROVULATION STARTS.

DAY 5 INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM DAY 6 INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM DAY 7 INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM DAY 8 INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM DAY 9 INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM DAY 10. INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM DAY 10. INJ LUPRIDE, O.2 ML SC. INJ MENOGON (75 IU), 3 AMP IM.



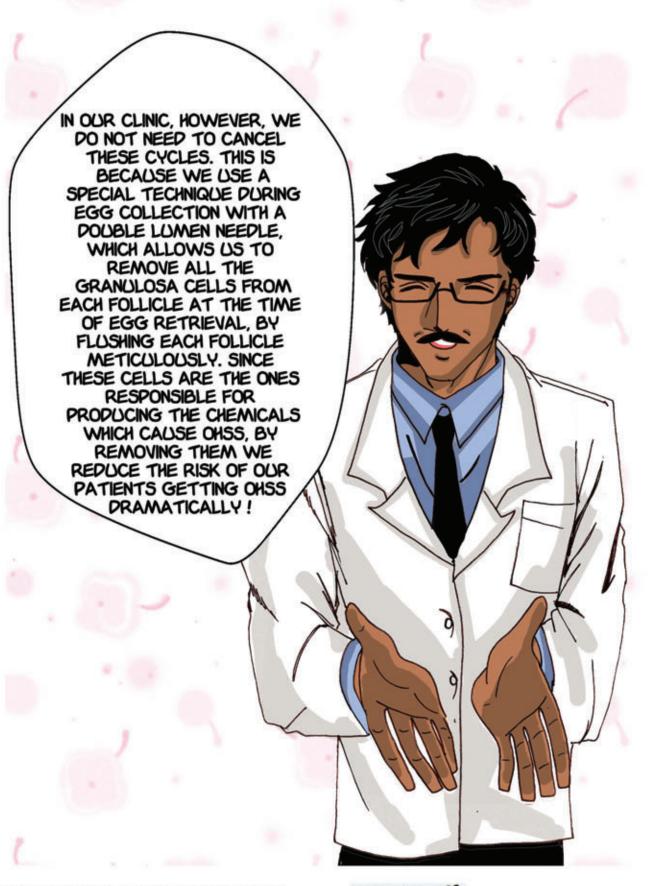
#### WHEN MAY AN IVF CYCLE BE CANCELLED?

THE COMMONEST REASON FOR CANCELING A CYCLE TODAY IS A POOR OVARIAN RESPONSE. IF 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 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.



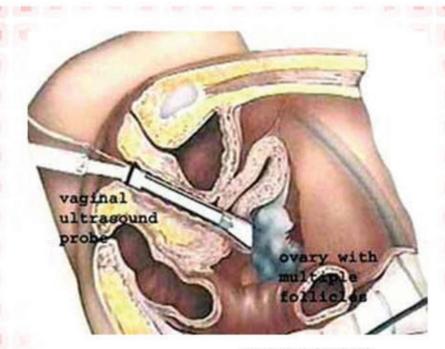


THE OTHER REASON TO CANCEL A CYCLE IS WHEN PATIENTS GROW TOO MANY FOLLICLES! THESE ARE USUALLY PATIENTS WITH PCOD: AND IF THERE ARE MORE THAN 25 FOLLICLES, OR IF THE LEVEL OF THE ESTRADIOL IS MORE THAN 6000 PG/ML, MANY CLINICS WILL CANCEL THE CYCLE, BECAUSE THE RISK OF OVARIAN HYPERSTIMULATION SYNDROME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



Chapter 2B: How is IVF done?





EGG RETRIEVAL

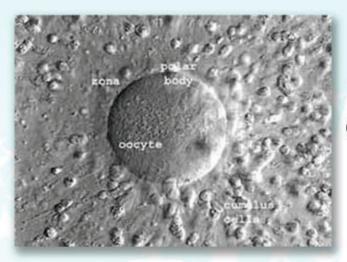
EGG COLLECTION IS ACCOMPLISHED TODAY BY ULTRASOUND-GUIDED ASPIRATION. THIS IS A MINOR SURGICAL PROCEDURE, THAT CAN BE DONE EVEN UNDER INTRAVENOUS SEDATION. IN OUR CLINIC, WE PREFER GENERAL ANESTHESIA, AS THIS IS KINDER. THE DOCTOR GUIDES A NEEDLE THROUGH THE VAGINA INTO EACH MATURE FOLLICLE, UNDER ULTRASOUND 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.

THIS PROCEDURE
REQUIRES CONSIDERABLE
SKILL, AND TAKES ABOUT
10-30 MINUTES TO
PERFORM, DEPENDING UPON
THE NUMBER OF EGGS. ON
AN AVERAGE, WE
RETRIEVE ABOUT 4-16
EGGS FOR EACH PATIENT.
IF THERE ARE FEW EGGS,
WE FLUSH EACH FOLLICLE,
TO ENSURE THAT EACH
EGG
IS RETRIEVED.



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 LABORATORYWHERE 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 MEDIUM, GRADED FOR THEIR MATURITY AND THEN TRANSFERRED INTO THE CO2 INCUBATOR. INSEMINATION CAN BE DONEIMMEDIATELY, BUT 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.

For more information on this chapter, go here: http://www.drmalpani.com/book/chapter25b.html



SOME MEN MAY HAVE
CONSIDERABLE DIFFICULTY
PRODUCING A SEMEN
SAMPLE AT THE
APPROPRIATE TIME,
BECAUSE OF THE "
PRESSURE TO PERFORM".



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 WITH HAS A CONTROLLED TEMPERA-TURE 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"!

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.





### 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.



Chapter 2B: How is IVF done?

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#### 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.





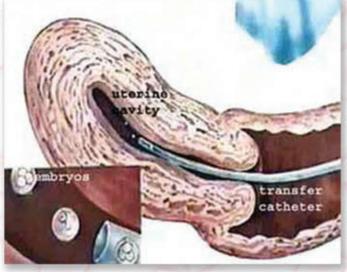
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Chapter 2B: How is IVF done?



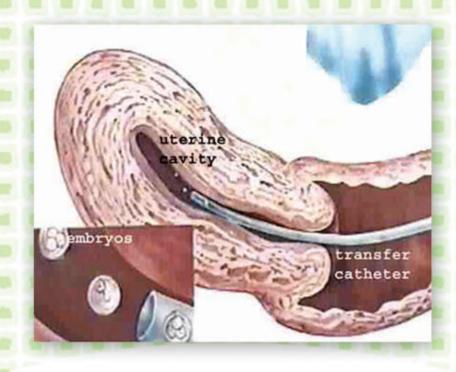
MANY PATIENTS ARE WORRIED THAT THEIR EGGS, SPERMS OR EMBRYOS MAY GET MIXED UP WITH SOMEONE ELSES. WHILE THIS CAN HAPPEN, THE PROBABILITY OF IT HAPPENING IN A WELL-RUN LABORATORY IS VERY LOW, BECAUSE GOOD LABS HAVE QUALITY CONTROL MECHANISMS TO PREVENT SUCH MIXUPS FROM OCCURRING.

AFTER 48 - 72 HOURS, WHEN EMBRYOS USUALLY CONSIST OF TWO TO EIGHT CELLS EACH, THEY ARE READY TO BE PLACED INTO THE WOMAN'S UTERUS. THIS PROCEDURE IS KNOWN AS EMBRYO TRANSFER.



Chapter 2C: How is IVF done?





#### 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 IO AND 20 MINUTES. SOME 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.



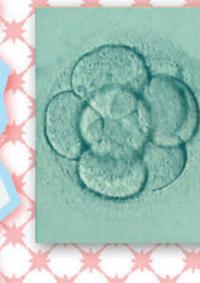


MOST CLINICS TODAY TRANSFER 1-3 GOOD QUALITY EMBRYOS ON DAY 3 OR DAY 5. EMBRYOS ARE GRADED ACCORDING TO THEIR APPEARANCE AND RATE OF CELL-DIVISION AND GOOD QUALITY EMBRYOS ON DAY 2 ARE THOSE WHICH HAVE 6-8 CELLS, OF EQUAL SIZE, WITH CLEAR CYTOPLASM, AND WITH FEW FRAGMENTS. THESE ARE CALLED GRADE A EMBRYOS. EMBRYOS WITH MORE FRAGMENTS ARE ASSIGNED A LOWER GRADE, AND THEY USUALLY HAVE A LOWER CHANCE OF IMPLANTING. HOWEVER, THE BABIES WHICH RESULT FROM THESE 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 AND INDIA, 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.

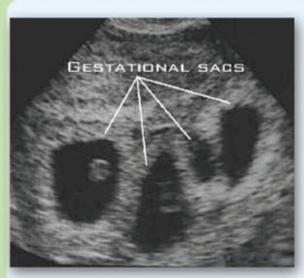




DOCTORS HAVE TRIED TO DEVELOP AN EMBRYO SCORE IN ORDER TO PREDICT THE CHANCES OF A PREGNANCY AFTER EMBRYO TRANSFER.SINCE THE TECHNOLOGY IS STILL NOT PERFECT, AND WE STILL CANNOT PREDICT WHICH EMBRYO WILL BECOME A BABY, THERE IS NO EASY ANSWER AS TO HOW MANY EMBRYOS TO TRANSFER. THIS IS WHY MANY CLINICS 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.

For more information on this chapter, go here: http://www.drmalpani.com/book/chapter25c.html





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! IF EMBRYO FREEZING FACILITIES ARE AVAILABLE. THEN SUPERNUMERARY EMBRYOS CAN BE STORED. AND THIS NEEDS TO BE FACTORED IN AS WELL.

### WHAT HAPPENS AFTER THE EMBRYO TRANSFER?

THE TERRIBLE 2WW - 2 WEEK WAIT- 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 IMPLAN-TATION. HOWEVER. THIS PERIOD IS OFTEN THE HARDEST PART OF AN IVE 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 BLOOD TEST. WHICH MEASURES THE LEVEL OF THE HOR-MONE, BETA HCG , ONLY 10 TO 14 DAYS AFTER THE TRANSFER. FOR MANY PATIENTS, THESE 14 DAYS ARE OFTEN THE LONGEST DAYS OF THEIR LIFE!



Chapter 2C: How is IVF done?

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A POSITIVE BETA HCG LEVEL MEANS YOU ARE PREGNANT, AND THE POCTOR WILL THEN MONITOR YOUR PREGNANCY TO CON-FIRM IT IS HEALTHY; INTRAUTERINE; AND TO CHECK HOW MANY EMBRYOS HAVE IMPLANTED.





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:

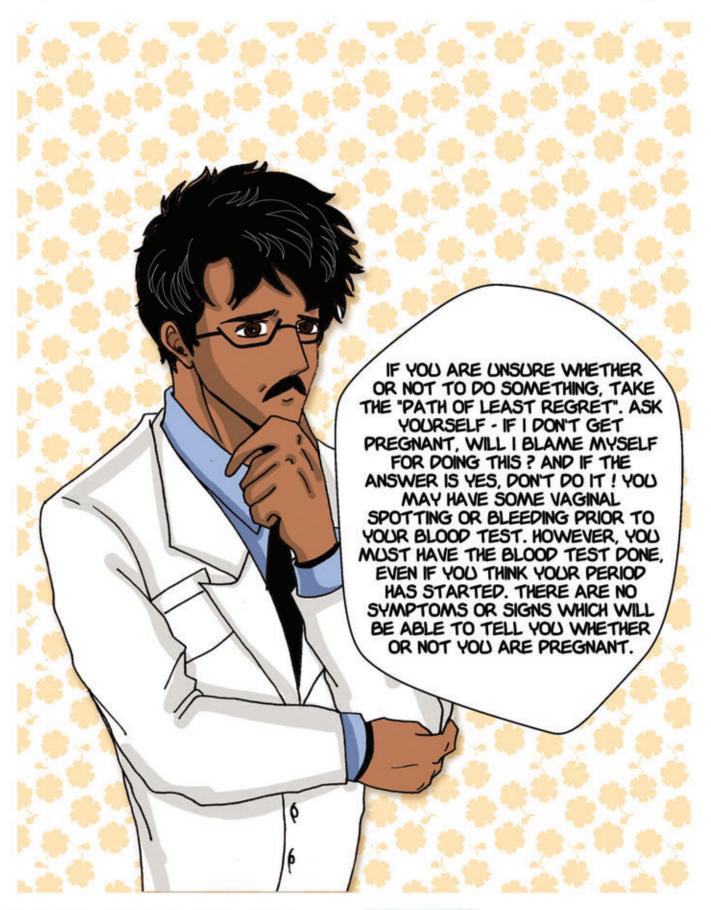


'NO INTERCOURSE OR ORGASMS UNTIL THE FETAL HEARTBEAT IS SEEN ON ULTRASOUND, OR THE PREGNANCY TEST IS NEGATIVE

'DO NOT UNDERTAKE EXCESSIVE PHYSICAL ACTIVITY 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'S SAFE TO TRAVEL 2-3 DAYS AFTER THE TRANSFER.





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 AS NORMAL A 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 LITERINE CAVITY IN THE NORMAL COURSE OF EVENTS, AFTER THE COUPLE HAD SEX, OR AFTER SPENDING 2-3 DAYS IN THE IVF LABORATORY AND THEN BEING TRANSFERRED INTO THE CAVITY WITH A CATHETER?

THUS, THERE ARE NUMBEROUS STAGES TO EVERY IVF
TREATMENT CYCLE, EACH OF WHICH MUST BE REACHED
AND COMPLETED BEFORE MOVING ON TO THE NEXT STAGE:

- MORE THAN ONE SHOULD EGG DEVELOP
  - EGGS SHOULD MATURE
- OVULATION SHOULD NOT OCCUR BEFORE THE EGGS CAN
   BE COLLECTED

- EGGS MUST BE RETRIEVED DURING THE "PICK-UP"
  - "- 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?

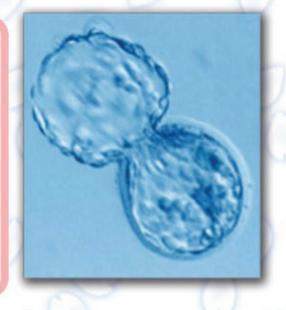
WHILE MODERN
TECHNOLOGY IS VERY
GOOD AT MAKING
EMBRYOS IN THE
LABORATORY, WE STILL
CANNOT CONTROL THE
IMPLANTATION PROCESS.
WE DO NOT KNOW WHICH
EMBRYO WILL BECOME A
BABY AND THIS CAN BE
VERY FRUSTRATING, FOR
BOTH PATIENTS AND
DOCTORS!

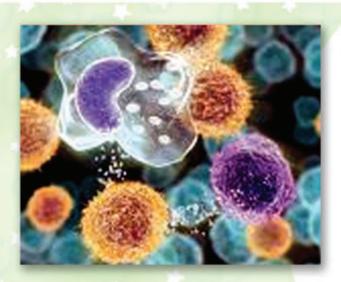




MANY PATIENTS WHO DO NOT GET PREGNANT AFTER AN EMBRYO TRANSFER START BELIEVING THAT THEIR BODIES ARE DEFECTIVE, AND THAT THEY HAVE "REJECTED" THE EMBRYO. THEY FEEL THAT IF THEY FAILED TO BECOME PREGNANT EVEN AFTER THE DOCTOR TRANSFERRED 3-4 GOOD QUALITY EMBRYOS, THAT THEIR UTERUS IS FLAWED . HOWEVER, 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 ENDOMETRIDAM ND INVADE INTO IT.

FIRST, THE EMBRYO HAS TO UNDERGO FURTHER DEVELOPMENT, TILL IT REACHES THE BLASTOCYST STAGE, WHEN 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 10-25%, WHICH MEANS THAT ONLY UPTO 25% OF EMBRYOS 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 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 CHANGE IN DIET OR WEIGHT LOSS OR FAD DIETS DURING 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.

Chapter 2D: How is IVF done?



### WHAT IS EMBRYO FREEZING?

SINCE MOST IVF PROGRAMS SUPEROVULATE PATIENTS TO GROW MANY EGGS. THERE ARE OFTEN 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 STOREDIN 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 30% OF ALL IVE PATIENTS THOSE WHO ARE GOOD OVARIAN RESPONDERS AND GROW LOTS OF EGGS



ABOUT 50-90% OF ALL FROZEN EMBRYOS SURVIVE THE FREEZING -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 BETTER 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 NEWTECHNIQUE CALLED VITRIFICATION ( WHICH USES ULTRA-RAPID COOLING TOGETHER WITH AN INCREASED CONCENTRATION OF CRYOPROTECTANTS ) NOW ALLOWS US TO FREEZE UNFERTILIZED HUMAN OCCYTES AS WELL. THIS ALLOWS THE FACILITY OF EGG STORAGE AND EGG BANKING

### Chapter 2D: How is IVF done?



### WHAT HAPPENS IF THE IVF CYCLE FAILS?

IF YOU DON'T GET PREGNANT AFTER YOUR IVF ATTEMPT, YOU ARE LIKELY TO BE VERY DISAPPOINTED AND DISHEARTENED. HOWEVER, REMEMBER THAT THIS IS NOT THE END OF 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? WHY DIDN'T PREGNANCY OCCUR?

THE MILLION DOLLAR QUESTION. THOUGH THIS IS USUALLY A QUESTION WE STILL CANNOT ANSWER, IS CAN YOU REPEAT THE SAME TREATMENT, OR DO YOU NEED TO MAKE CHANGES BEFORE GOING IN FOR YOUR NEXT ATTEMPT? WHEN CAN YOU START YOUR NEXT IVE CYCLE? AND EVEN IF YOU DO NOT GET PREGNANT, AT LEAST THE FACT THAT YOU ATTEMPTED IVF SHOULD GIVE YOU PEACE OF MIND THAT YOU TRIED YOUR BEST. USING THE LATEST TECHNOLOGY MEDICAL SCIENCE HAS TO OFFER.





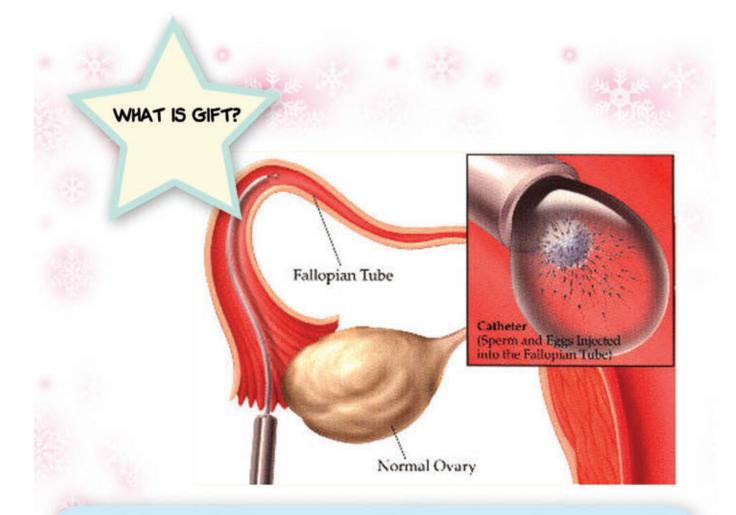
WHAT ABOUT YOUR NEXT IVF CYCLE?

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 MARSHALL 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 IVE SUCCESS IS TIME, PATIENCE, AND ANOTHER ATTEMPT.

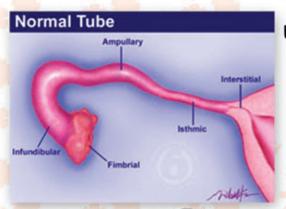
INTERESTINGLY. WE OFTEN FIND THAT COUPLES GOING THROUGH A SECOND IVF CYCLE ARE MUCH MORE RELAXED AND IN CONTROL. THIS MAY BE BECAUSE THEY ARE AWARE OF ALL THE MEDICAL AND PROCEDURAL MINUTIAE, AND ARE BETTER PREPARED FOR THESE: AND ALSO BECAUSE THEY HAVE HAD A CHANCE TO ESTABLISH A PERSONAL RELATIONSHIP 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 TODAYS 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!



Chapter 3: What is GIFT? Page 40



GIFT STANDS FOR GAMETE INTRA FALLOPIAN TRANSFER AND THIS USED TO BE A POPULAR ALTERNATIVE TO IVF IN THE PAST. A GAMETE IS A MALE OR FEMALE SEX CELL: - A SPERM, OR AN EGG. DURING GIFT, SPERM AND EGGS ARE MIXED AND INJECTED INTO ONE OR BOTH FALLOPIAN TUBES. AFTER THE GAMETES HAVE BEEN TRANSFERRED, FERTILIZATION CAN TAKE PLACE IN THE FALLOPIAN TUBE AS IT DOES IN NATURAL, UNASSISTED REPRODUCTION. ONCE FERTILIZED, THE EMBRYO TRAVELS TO THE UTERUS BY NATURAL PROCESSES. AS IN IVF, A GIFT TREATMENT CYCLE BEGINS WITH OVULATION ENHANCEMENT WHICH IS FOLLOWED BY EGG HARVEST, USUALLY BY MEANS OF LAPAROSCOPY. BUT THE SIMILARITY TO IVF ENDS HERE. IN IVF, AN EMBRYO IS TRANSFERRED. IN GIFT, GAMETES ARE TRANSFERRED.

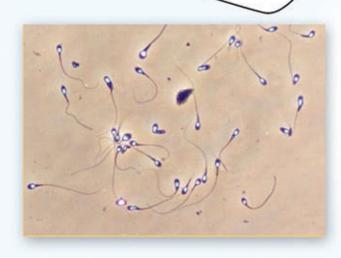


ONLY PATIENTS WITH AT LEAST ONE NORMAL, HEALTHY FALLOPIAN TUBE ARE CANDIDATES FOR GIFT. THESE INCLUDE WOMEN WHO HAVE UNEXPLAINED INFERTILITY OR MILD ENDOMETRIOSIS AND COUPLES WHOSE INFERTILITY RESULTS FROM MALE, CERVICAL, OR IMMUNOLOGICAL FACTORS.

THE BASIC STEPS OF GIFT ARE SUPEROVULATION, EGG HARVEST, INSEMINATION, AND GAMETE TRANSFER. THE EGGS ARE USUALLY HARVESTED DURING LAPAROSCOPY. DURING THIS SAME LAPAROSCOPY PROCEDURE, WHICH TAKES ABOUT AN HOUR, EGGS ARE MIXED WITH SPERM AND THE GAMETES ARE TRANSFERRED.



### INSEMINATION



THE HARVESTED EGGS ARE EXAMINED UNDER THE MICROSCOPE AND GRADED FOR MATURITY. THE SELECTED EGGS ARE PLACED IN INDIVIDUAL DISHES AND COMBINED WITH SPERM (INSEMINATION). THE SPERM ARE PREPARED IN ADVANCE IN THE SAME MANNER AS FOR IVF. MANY PROGRAMS LOAD EGGS AND SPERM INDIVIDUALLY INTO A CATHETER AND INJECT THEM INTO ONE OR BOTH OF THE FALLOPIAN TUBES.



### GAMETE TRANSFER:

THE SPERM EGG MIXTURE IS LOADED INTO A SPECIALLY DESIGNED CATHETER. THIS IS THEN DIRECTED INTO THE FALLOPIAN TUBE(S) THROUGH THEIR FIMBRIAL OPENING WHILE LOOKING THROUGH THE LAPAROSCOPEY. UP TO FOUR EGGS AND SPERM MAY BE INJECTED INTO ONE OR BOTH TUBES. GAMETES WILL BE TRANSFERRED ONLY IF THE FALLOPIAN TUBES APPEAR HEALTHY. IF THE SURGEON DETERMINES THAT THE TUBES ARE UNHEALTHY, IVF SHOULD BE ATTEMPTED INSTEAD. FOR THIS REASON, GIFT SHOULD BE UNDERTAKEN ONLY AT FACILITIES THAT HAVE THE CAPABILITY TO DO IVF.

PREGNANCY RATE SPECIALISTS
GENERALLY AGREE THAT
PREGNANCY RATES ARE HIGHER
FOR GIFT THAN FOR IVF- IN FACT,
GIFT IS ABOUT TWICE AS
SUCCESSFUL AS IVF. IN PART,
THIS MAY BE DUE TO THE TYPE
OF PATIENT ACCEPTED INTO GIFT
PROGRAMS. IT MAY ALSO BE
BECAUSE THE IN VIVO TUBAL
ENVIRONMENT IS MORE
"PHYSIOLOGIC" FOR THE
GAMETES AND EMBRYO THAN
THE IN VITRO ENVIRONMENT.

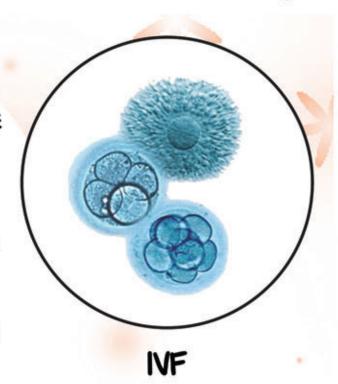


Chapter 3: What is GIFT?

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## HOW DO GIFT AND IVF COMPARE

THERE ARE SEVERAL
DIFFERENCES BETWEEN GIFT
AND IVF. THE MOST
IMPORTANT ONE IS THAT GIFT
REQUIRES AT LEAST ONE
HEALTHY FALLOPIAN TUBE,
WHEREAS IVF IS APPROPRIATE
TREATMENT FOR WOMEN WITH
TUBAL DISEASE OR EVEN NO
FALLOPIAN TUBES AT ALL. AT
PRESENT, GIFT REQUIRES
LAPAROSCOPY FOR TRANSFER,
WHILE AN IVF TREATMENT
CYCLE CAN BE COMPLETED
WITHOUT LAPAROSCOPY.



THIS IS ONE OF THE REASONS MANY IVF CLINICS NO LONGER OFFER GIFT, EVEN THOUGH IT OFFERS A HIGHER PREGNANCY RATE - BECAUSE THEY DO NOT HAVE EASY ACCESS TO AN OPERATION THEATRE. IDEALLY, YOU SHOULD OPT FOR TREATMENT IN A CLINIC WHICH OFFERS ALL THE PROCEDURES, SO THAT THE DOCTOR CAN SELECT THE ONE WHICH IS BEST FOR YOU, DEPENDING UPON YOUR INDIVIDUAL CIRCUMSTANCES.

### THE ADVANTAGES OF THIS TECHNIQUE ARE:

- THE FALLOPIAN TUBE ACTS AS THE LABORATORY
- THE EMBRYO WILL REACH THE UTERUS AT A LATER STAGE IN ITS DEVELOPMENT, AS WITH NORMAL CONCEPTION.
- THE PROCEDURE IS CONSIDERED MORALLY ACCEPTABLE TO SOME RELIGIOUS GROUPS WHICH OBJECT TO IVF, AS CONCEPTION OCCURS WITHIN THE HUMAN BODY.
  - THE ENDOMETRIUM WILL ALSO BE MORE RECEPTIVE TO THE EMBRYO BECAUSE OF THE GREATER TIME THE EMBRYO TAKES TO REACH THE UTERUS.





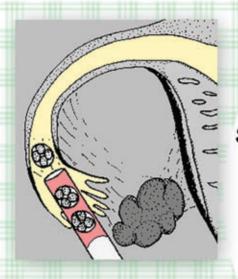
VAGINAL GIFT

A MAJOR DISADVANTAGE WITH CONVENTIONAL GIFT IS THAT A SURGICAL PROCEDURE -LAPAROSCOPY - IS NEEDED TO TRANSFER THE EGGS AND SPERM INTO THE FALLOPIAN TUBE. NON-SURGICAL METHODS HAVE BEEN DEVELOPED IN WHICH THE GAMETES CAN BE TRANSFERRED INTO THE FALLOPIAN TUBES THROUGH THE VAGINA AND CERVIX UNDER ULTRASOUND GUIDANCE. THIS REQUIRES A SPECIAL SET OF CATHETERS WHICH ALLOW THE DOCTOR TO ENTER THE UTERINE ENDS OF THE FALLOPIAN TUBES THROUGH THE CERVIX. ONCE THE CATHETERS HAVE BEEN ACCURATELY POSITIONED - AND ULTRASOUND CAN HELP IN THIS -THE GAMETES ARE INJECTED INTO THE TUBES.

IN THE CASE OF GIFT. FERTILIZATION OCCURS UNOBSERVED INSIDE THE BODY. WITH IVF, FERTILIZATION TAKES PLACE IN A LABORATORY DISH AND CAN BE CONFIRMED VISUALLY WITH A MICROSCOPE. VISUAL CONFIRMATION OF FERTILIZATION IS ESPECIALLY IMPORTANT IN CASES OF MALE FACTOR OR UNEXPLAINED INFERTILITY. TO OBTAIN VISUAL CONFIRMATION AND STILL HAVE THE GREATER CHANCE OF PREGNANCY AFFORDED BY GIFT, ONE OF THE VARIATIONS OF GIFT DESCRIBED LATER MAY BE USED. TO GIVE THE PATIENT THE BENEFIT OF COMBINING THE ADVANTAGES OF BOTH THE PROCEDURES.



UNFORTUNATELY, THE PREGNANCY RATES WITH THIS TECHNIQUE WERE LOW AND THIS IS NO LONGER DONE.



### WHAT IS ZIFT?

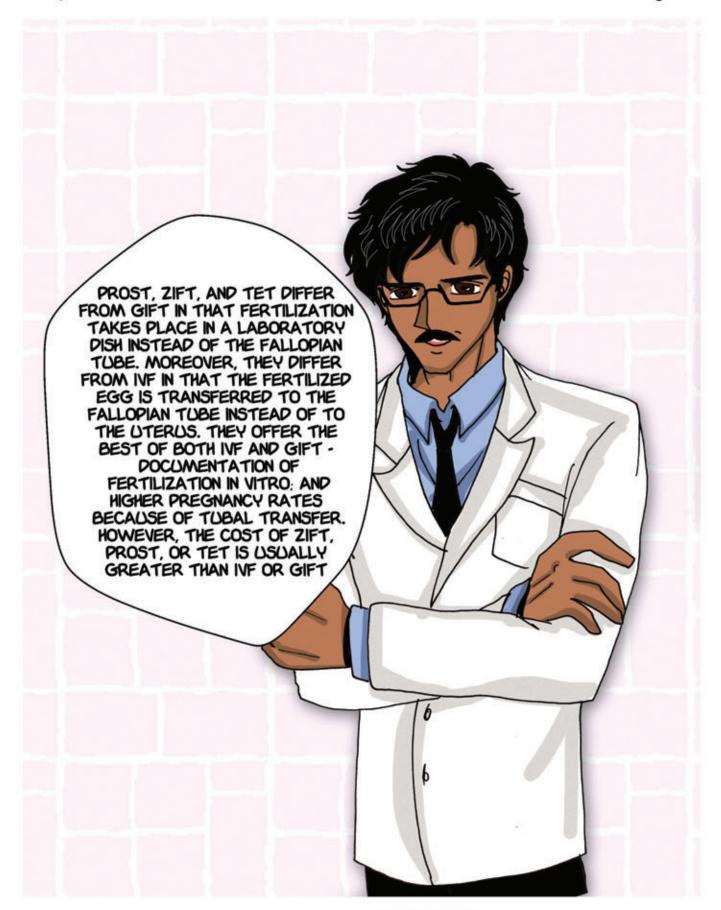
ZIFT, ZYGOTE INTRAFALLOPIAN
TRANSFER, IS ALSO CALLED PROST,
WHICH STANDS FOR PRONUCLEAR
STAGE TRANSFER. A ZYGOTE IS A FERTILIZED EGG BEFORE CELL DIVISION
BEGINS. FOR ZIFT, EGGS ARE
REMOVED BY TRANSVAGINAL
ASPIRATION AND FERTILIZED IN A
LABORATORY DISH. THE NEXT DAY,
WHEN THE FERTILIZED EGGS HAVE
REACHED THE PRONUCLEAR STAGE,
THE EMBRYOS ARE
TRANSFERRED TO THE FALLOPIAN
TUBES DURING LAPAROSCOPY.

APPROXIMATELY 24 HOURS AFTER A FERTILIZED EGG REACHES THE PRONUCLEAR STAGE, IT DIVIDES FOR THE FIRST TIME AND BECOMES A TWO CELL EMBRYO. THIS CELL DIVISION IS CALLED CLEAVAGE. IT IS AT THIS STAGE OR LATER THAT TET, TUBAL EMBRYO TRANSFER, MAY BE ATTEMPTED. THE FERTILIZED AND DIVIDING EGG (EARLY CLEAVAGE STAGE EMBRYO) IS TRANSFERRED TO THE FALLOPIAN TUBE DURING LAPAROSCOPY.



Chapter 3: What is GIFT?

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# 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

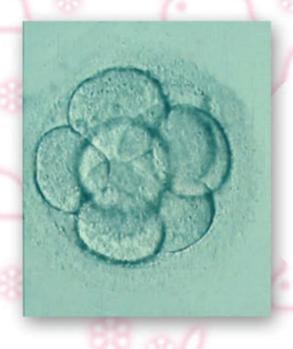






OF COURSE, THERE ARE SOME VARIABLES ABOUT WHICH NOTHING CAN BE DONE - SUCH AS THE WIFE'S AGE. BUT OTHER VARIABLES CAN BE CONTROLLED TO TRY TO MAXIMIZE CHANCES OF A PREGNANCY! THE GOOD NEWS IS THAT WITH IMPROVING IVF TECHNOLOGY, PREGNANCY RATES WITH IVF HAVE INCREASED DRAMATICALLY.



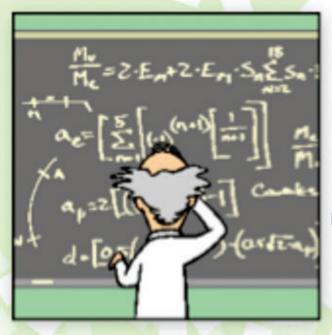


PREGNANCY RATES ARE RELATED DIRECTLY TO HOW MANY EMBRYOS ARE TRANSFERRED. FOR EXAMPLE, WHEN 3 GOOD QUALITY EMBRYOS ARE TRANSFERRED, THE CHANCE OF PREGNANCY IS ABOUT 40% IN THAT CYCLE. THE NUMBER OF EMBRYOS TRANSFERRED NEEDS ALSO TO BE BALANCED AGAINST THE RISK OF MULTIPLE PREGNANCY, WHICH NATURALLY INCREASES WITH MORE EMBRYOS.

Chapter 4: Making sense of success rates



WITH THIS IN MIND, MANY
COUNTRIES NOW RECOMMEND
THAT NO MORE THAN 2
EMBRYOS BE TRANSFERRED
DURING ANY TREATMENT
CYCLE.



### HOW CAN A PATIENT INTERPRET THIS FIGURE ?

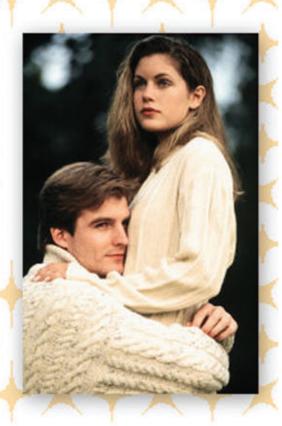
FOR EXAMPLE, LET US CONSIDER A
30 YEAR OLD PATIENT WITH
IRREPARABLE TUBAL DAMAGE WHO
GOES THROUGH ONE IVF CYCLE. SHE
CAN LOOK AT A PREGNANCY RATE
FIGURE OF 30 % IN TWO WAYS. A
SUCCESS RATE OF 30 % MEANS
THERE IS AN 70 % CHANCE SHE WILL
NOT GET PREGNANT. ON THE OTHER
HAND, IF SHE TAKES NO TREATMENT,
HER CHANCE OF GETTING PREGNANT
IS ZERO. THE IVF CYCLE HAS
INCREASED THIS TO 30 % - NO ONE
CAN DO ANY BETTER THAN
THIS TODAY!

Chapter 4: Making sense of success rates



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

IVF AND GIFT 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 4 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 4 CYCLES, THE CHANCES INCREASE TO 80% BECAUSE THE SUCCESS RATE IS CUMULATIVE.



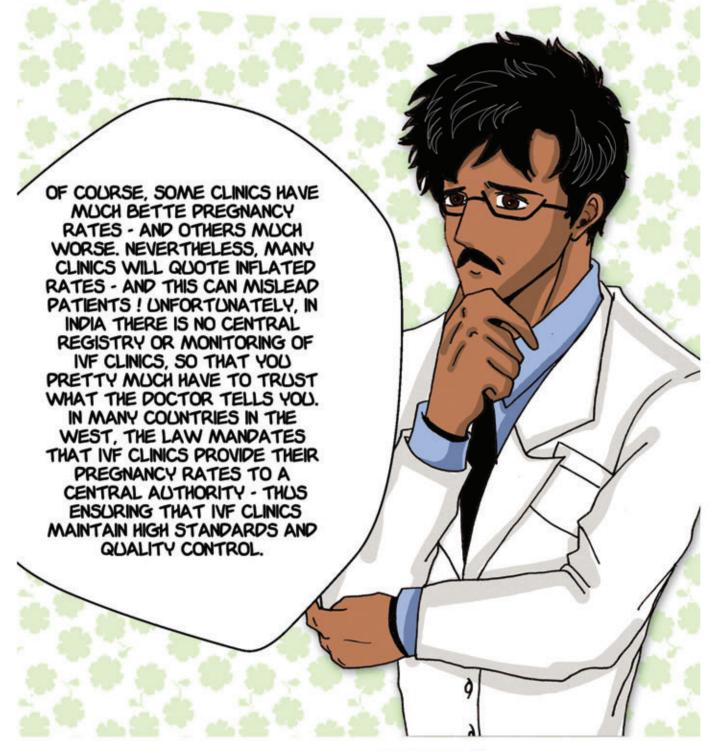


THUS, LET US ASSUME THE PREGNANCY RATE FOR IVF AT A CLINIC IS 30%. IF IO PATIENTS START AN IVF CYCLE, 3 WILL GET PREGNANT, LEAVING 7 PATIENTS. IF THESE 7 DO ANOTHER IVF CYCLE, ANOTHER 30% WILL CONCEIVE. IF THE REMAINING 5 DO ANOTHER CYCLE, I MORE WILL GET PREGNANT: AND AT THE END OF THE 4TH CYCLE, I MORE WILL CONCEIVE: SO THAT OF THE IO PATIENTS WHO STARTED, 7 WILL HAVE GOT PREGNANT IN 4 ATTEMPTS. THIS IS BECAUSE THE CHANCES OF GETTING PREGNANT IN THE NEXT IVE 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.

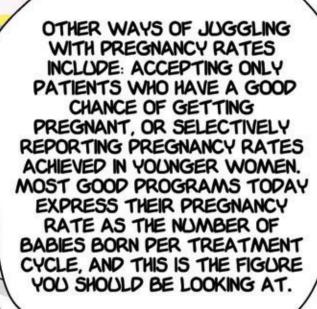
# WHAT GAMES DO SOME IVF CLINICS PLAY WITH THEIR PREGNANCY RATES ?





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 FETUS SEEN ON ULTRASOUND.

SO CALLED BIOCHEMICAL PREGNANCIES ARE ALSO FAIRLY COMMON AFTER IVF. THESE ARE PREGNANCIES CONFIRMED BY BLOOD AND URINE TESTS 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, INFLATE THE PREGNANCY RATE.





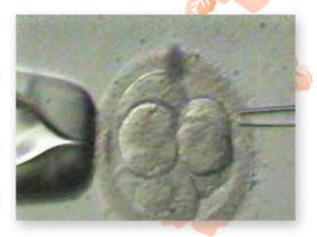




NEWER PROCEDURES IVF
TECHNOLOGY IS
IMPROVING BY LEAPS
AND BOUNDS AND MANY
EXCITING ADVANCES HAVE
TAKEN PLACE
RECENTLY. THESE INCLUDE
THE FOLLOWING.

### WHAT IS ASSISTED HATCHING?

ONE OF THE MAJOR PROBLEMS WITH IVF TODAY IS THE LOW PREGNANCY RATE AFTER SUCCESSFUL EMBRYO TRANSFER. THE REASON WHY SUCH FEW EMBRYOS IMPLANT SUCCESSFULLY (ONLY I OF IO EMBRYOS WILL BECOME A BABY) IS ONE OF THE THINGS WE REALLY DO NOT UNDERSTAND TODAY. DR. COHEN BELIEVES THIS IS BECAUSE 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 AN ACID OR WITH A LASER.





#### Chapter 5: Newer advances

EMBRYO SURGERY HAS ALSO BEEN USED FOR EMBRYO BIOPSY, FOR PREIMPLANTATION GENETIC DIAGNOSIS, IN WHICH SINGLE CELLS ARE REMOVED FROM THE DEVELOPING EMBRYO, TO MAKE SURE THE EMBRYOS ARE HEALTHY AND HAVE NO GENETIC DISEASE. THIS IS DESCRIBED IN MORE DETAIL IN CHAPTER 26.





EMBRYO MULTIPLICATION, BY REMOVING SOME OF THE CELLS FROM THE EMBRYO AND ALLOWING THEM TO DIVIDE, CAN ALLOW DOCTORS TO "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 IS THE POOR QUALITY OF THE EMBRYO CULTURED IN VITRO. 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.



### Chapter 5: Newer advances



### 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 CEL L-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 2 TO 3 DAY STATE OF DEVELOPMENT, TILL THEY BECOME BLASTOCYSTS. A BLASTOCYST IS THE FINAL STAGE OF THE EMBRYOS DEVELOPMENT BEFORE IT HATCHES OUT OF ITS SHELL (ZONA PELLUCIDA) AND IMPLANTS IN THE UTERINE WALL.



Chapter 5: Newer advances



SOME DOCTORS BELIEVE THAT
BLASTOCYST TRANSFER MAY YIELD
HIGHER PREGNANCY RATES. THERE
MAY BE TWO POSSIBLE REASONS FOR
THIS. 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.

BLASTOCYST TRANSFER SIGNIFICANTLY REDUCES THE POSSIBILITY OF POTENTIALLY DANGEROUS HIGH-ORDER MULTIPLE BIRTHS, SUCH AS TRIPLETS. HIGHER IMPLANTATION RATES 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 WITH RESULTING PREGNANCIES AFTER THAWING.

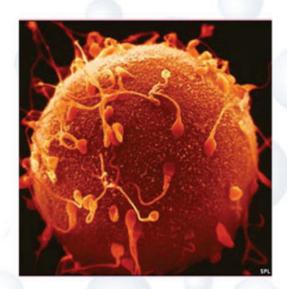




WHILE BLASTOCYST TRANSFER IS A VERY PROMISING ADVANCE FOR PATIENTS WHO GROW LOTS OF EGGS. ITS UTILITY FOR THE DIFFICULT PATIENT - THE POOR OVARIAN RESPONDER - IS STILL DEBATABLE. THIS IS BECAUSE IF THERE ARE FEW EGGS, THERE IS A VERY REAL RISK THAT NONE OF THEM MAY DEVELOP TO THE BLASTOCYST STAGE. ALL 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 CLINICS EXPERIENCE AND SUCCESS RATE.

### 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.



### Chapter 5: Newer advances



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 ACTS AS HER OWN INCUBATOR! SINCE EXPENSIVE LABORATORY EQUIPMENT IS NOT NEEDED, THIS IS MUCH CHEAPER - AND 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 USED FOR SUPEROVULATION. WHILE THE PREGNANCY RATE IS LOWER, THE EXPENSE) IS MUCH LESS! INTERESTINGLY "GENTLER" IVF IS BECOMING INCREASINGLY POPULAR IN THE WEST AS WELL.





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 HIGH QUALITY, SINCE ALL
LABORATORY PROCEDURES ARE PERFORMED IN A
CENTRAL LABORATORY; AND ALSO
MINIMIZES PATIENT INCONVENIENCE

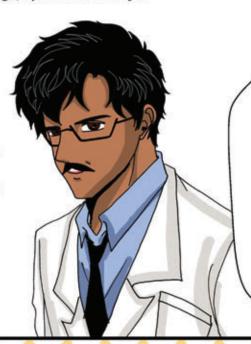
Chapter 6: Donor eggs, sperm and embryos

WHAT
ABOUT
USING PONOR
SPERM,
PONOR EGGS
AND PONOR
EMBRYOS IN
AN IVF
CYCLE?

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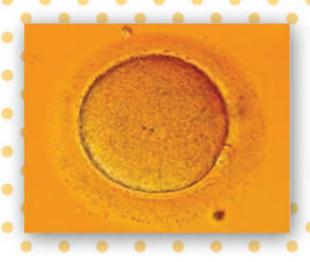
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DONOR SPERMS,
DONOR EGGS AND
DONOR
EMBRYOS. COUPLES
WITH NO SPERM OR
EGGS CAN UNDERGO
IVF AND GIFT WITH
THE USE OF DONOR
SPERM OR EGGS.

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



DONOR EGGS CAN BE USED IN GIFT OR IVF FOR WOMEN WHO HAVE NO EGGS (OVARIAN FAILURE) BUT WHO DO HAVE A HEALTHY UTERUS.

AEMBRYOS 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



Chapter 6: Donor eggs, sperm and embryos



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

At age 41, I'm almost out of good eggs...

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 VIT-RIFICATION. HOWEVER, THIS IS STILL EXPERIMENTAL, WHICH IS WHY MOST CLINICS WILL USE FRESH DONOR EGGS FOR DONOR EGG TREATMENTS. THESE MAY COME EITHER FROM ANOTH-ER INFERTILE PATIENT: OR A VOLUNTEER EGG DONOR: OR A FRIEND OR RELATIVE, WHO OFFERS TO DONATE EGGS.

Chapter 6: Donor eggs, sperm and embryos

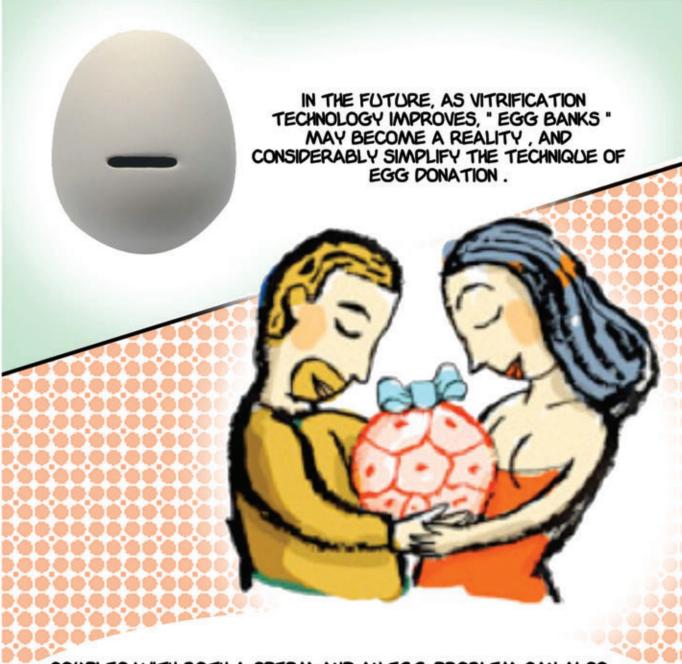


EGG DONATION FOR IVF
REQUIRES THE EGG DONOR TO
UNDERGO SUPEROVULATION
AND OVUM ASPIRATION. THE
DONATION OF EGGS CARRIES
MORE RISK AND INCONVENIENCE
TO THE DONOR THAN DOES THE
DONATION OF SPERM.

THE USE OF DONOR EGGS REQUIRES THAT THE CYCLES OF THE DONOR AND THE RECIPIENT BE CLOSELY SYNCHRONIZED. THIS REQUIRES TREATMENT OF THE RECIPIENT, SO THAT HER ENDOMETRIUM IS PRIMED AND IS RECEPTIVE TO THE EMBRYOS 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 DOWNREGULATED WITH GNRH ANALOGS BEFORE STARTING TREATMENT WITH EXOGENOUS ESTROGENS.

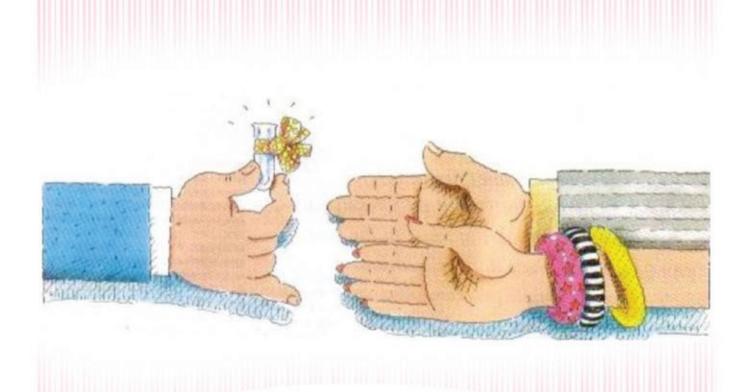


Chapter 6: Donor eggs, sperm and embryos



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 - WITH THE DIFFERENCE THAT YOU ARE CARRYING THE PREGNANCY AND GIVING BIRTH TO THE BABY!

Chapter 6: Donor eggs, sperm and embryos



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 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 IVE?



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 ARENT 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!

OVER A MILLION
BABIES HAVE BEEN
BORN AFTER IVF
TREATMENT, AND THE
RISK FOR BIRTH
DEFECTS IS NOT
INCREASED AFTER IVF
TREATMENT.



### Chapter 7: Risks and complications of IVF



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

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Chapter 7: Risks and complications of IVF



WHAT IS OHSS (OVARIAN HYPER STIMULATION SYNDROME)?

THE MOST WORRISOMECOMPLICATION 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 READJUST. 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

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.

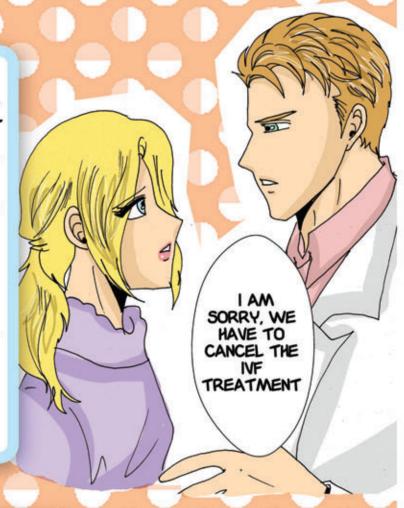
THIS IS BECAUSE HER PLACENTA IS MAKING HCG AND STIMULATING THE OVARIES TO CONTINUE TO POUR OUT LARGE AMOUNTS OF ESTROGEN-RICH FLUID. SO ALTHOUGH IT IS A VERY UNPLEASANT SIDE EFFECT TO ENDURE, HYPERSTIMULATION SYNDROME

OFTEN MEANS GOOD NEWS.

For more information on this chapter, go here: http://www.drmalpani.com/book/chapter25h.html



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. SINCE 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 HARVEST 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.

#### Chapter 7: Risks and complications of IVF



# WHAT ABOUT THE RISK OF A MULTIPLE PREGNANCY AFTER IVE?

IN ALL TECHNIQUES OF ASSISTED REPRODUCTIVE TECHNOLOGY, THE CHANCE OF MULTIPLE PREGNANCY IS INCREASED WHEN MORE THAN ONE EMBRYO OR EGG 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 ( AS A RESULT OF INADVERTENT TRAUMA DURING THE PROCEDURE ) ISABOUT 10% IN EXPERIENCED HANDS.



Chapter 7: Risks and complications of IVF



THERE IS LESS THAN THREE PERCENT CHANCE OF AN ECTOPIC PREGNANCY WITH IVF AND GIFT. 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 AND FATIGUE,
AND THIS MAYBE
COMPOUNDED BY THE
SOMETIMES EXTENSIVE
TRAVELLING REQUIRED
EACH DAY. SOME PEOPLE
FIND TREATMENT
CONFLICTS WITH THEIR
EMPLOYMENT 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 ONE OR MORE IVF CLINICS TODAY. THIS IS ALL FOR THE BEST, BECAUSE INFERTILE COUPLES NO LONGER NEED TO TRAVEL LONG DISTANCES FOR IVF TREATMENT. HOWEVERMANY 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. MOST 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!



Chapter 7: Risks and complications of IVF



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.

HOW CAN YOU SUPPORT EACH OTHER DURING YOUR IVE CYCLE?

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 HELPFULYOU MAY ALSO SEEK THE SPECIALIZED ASSISTANCE OF A COUNSELOR, WHO IS EITHER ATTACHED TO THE CLINIC OR BASED IN THE COMMUNITY







#### Chapter 8: Selecting the right IVF clinic



HOW CAN YOU SELECT THE BEST IVF CLINIC FOR YOURSELF?

THERE ARE NOW OVER 300 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 PERSONNEL,
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 TUBAL TRANSFER, ZIFT, 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 CAN BE USED.







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

- I. HOW MANY DOCTORS WILL BE INVOLVED IN MY TREATMENT?
  - 2. TO WHAT DEGREE CAN MY OWN DOCTOR PARTICIPATE IN MY TREATMENT?
- 3. WHAT TYPES OF COUNSELLING AND SUPPORT SERVICES AREAVAILABLE?
  - 4. WHOM DO I CALL IF I HAVE A PROBLEM?
- 5. IS DONOR SPERM AVAILABLE IN YOUR PROGRAM? DONOR EGGS?

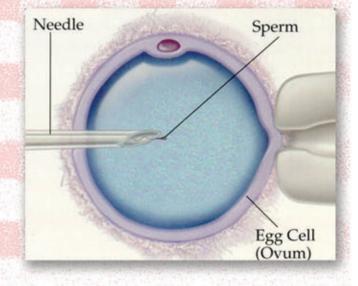
6. DO YOU HAVE AN AGE LIMIT?





THE INTRODUCTION OF MICROINJECTION TECHNOLOGY INTO THE IN VITRO FERTILIZATION LABORATORY HAS REVOLUTIONIZED OUR TREATMENT OF THE INFERTILE MAN. INTRACYTOPLASMIC SPERM INJECTION, OR ICSI, USES MICROMANIPULATION TECHNOLOGY FOR TREATING MALE INFERTILITY. WHAT ICSI PROMISES IS THE POSSIBILITY FOR EVERY MAN TO FATHER HIS OWN BABY - NO MATTER WHAT HIS MEDICAL PROBLEM!

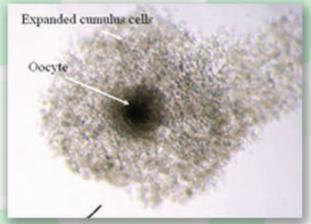
AS THE NAME SUGGESTS, ICSI IS A TECHNIQUE IN WHICH A SINGLE SPERM IS INJECTED INTO THE CENTRE OF THE CYTOPLASM OF THE EGG. IN ORDER TO ACHIEVE FERTILIZATION. THE BEAUTY OF THE TECHNIQUE IS THAT SINCE THE SPERM IS BEING INJECTED DIRECTLY INTO THE EGG, ALL THAT IS NEEDED TO ACHIEVE FERTILIZATION ARE LIVE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



#### THE PROCEDURE FOR ICSI

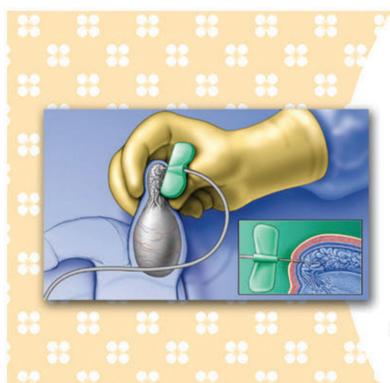
ICSI IS DONE IN A
SUPEROVULATED CYCLE DURING
WHICH FERTILITY DRUGS (HUMAN
MENOPAUSAL GONADOTROPIN HMG-INJECTIONS) ARE
ADMINISTERED TO THE WIFE TO
AID IN THE PRODUCTION OF
MULTIPLE EGGS, WHICH ARE
THEN REMOVED UNDER VAGINAL
ULTRASOUND GUIDANCE AS IS
DONE FOR IVE.





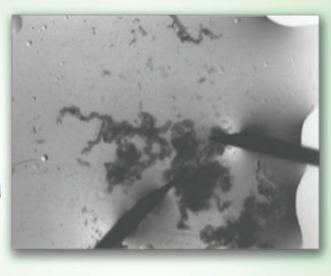
IN NORMAL CIRCUMSTANCES. THE EGG IS SURROUNDED BY A CLUSTER OF CELLS KNOWN AS THE CUMULUS CORONA CELLS. THIS IS CALLED THE OOCYTE CUMULUS CORONA COMPLEX. THESE CUMULUS CELLS ARE REMOVED BY REPEATED PASSAGE OF THE COMPLEX THROUGH FINE PIPETTES. AND BY TREATING THEM WITH A CHEMICAL CALLED HYALURONIDASE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

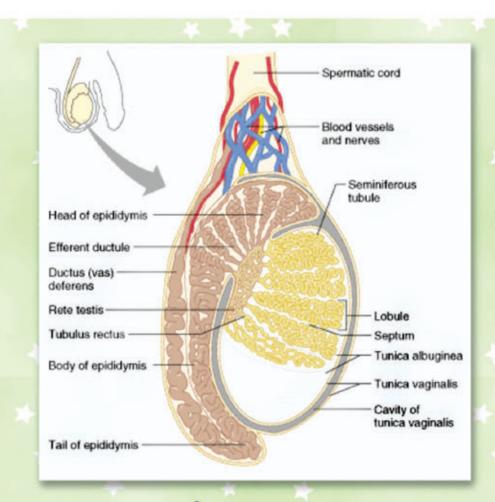




FOR MEN WITH VARIABLE SPERM COUNTS, WHICH VARY FROM ZERO TO A FEW THOUSAND, IT MAY BE HELPFUL TO FREEZE A SAMPLE IN ADVANCE, FOR PATIENTS WITH AZOOSPERMIA, SPERM HARVESTING TECHNIQUES NEED TO BE USED TO RETRIEVE THE SPERM. FOR MEN WITH OBSTRUCTIVE AZOOSPERMIA. THE SIMPLEST TECHNIQUE IS CALLED PESA IN 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.





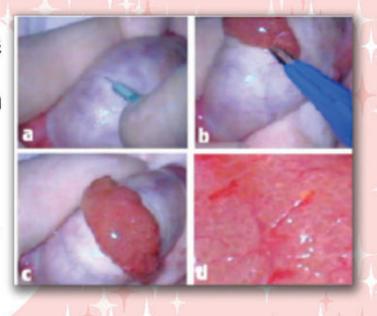
USING SPERM FROM THE EPIDIDYMIS AND TESTIS FOR ICSI IN ORDER TO TREAT PATIENTS WITH OBSTRUCTIVE AZOOSPERMIA IS LOGICAL, AND THUS CONCEPTUALLY EASY TO UNDERSTAND. HOWEVER, SURPRISINGLY, IT IS POSSIBLE TO FIND SPERM EVEN IN PATIENTS WHO HAVE TESTICULAR FAILURE (NONOBSTRUCTIVE AZOOSPERMIA) - EVEN IN MEN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



THIS MEANS THAT EVEN IF SPERM PRODUCTION IS ABSENT IN A CERTAIN AREA, THERE MAY BE OTHER AREAS IN THE TESTIS WHERE SPERM PRODUCTION WOULD BE NORMAL SINCE SUCH FEW SPERM ARE NEEDED FOR ICSI, WE CAN FIND ENOUGH SPERM IN OVER 30 PER CENT OF PATIENTS WITH TESTICULAR FAILURE, EVEN IF THEIR TESTES ARE AS SMALL AS A PEANUT!

### 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.





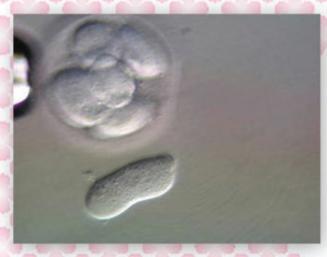
FINDING SPERM IN THE TESTICULAR TISSUE CAN BE A LABORIOUS PROCESS DEPENDING ON THE DEGREE OF SPERM PRODUCTION, AND FOR SOME MEN WITH PARTIAL TESTICULAR FAILURE, IT CAN TAKE UPTO 2-3 HOURS TO FIND THE SPERM. ALSO. TESTICULAR SPERM ARE TECHNICALLY HARD TO WORK WITH IN THE LABORATORY AND ONLY SOME IVF CLINICS HAVE THE REQUISITE EXPERTISE. FOR MEN WITH NON OBSTRUCTIVE AZOOPSERMIA. SOME CLINICS PERFORM THE TESE THE DAY PRIOR TO EGG RETRIEVAL. THEY CULTURE THE TESTICULAR TISSUE IN THE INCUBATOR FOR 24 HOURS AND THIS CAN HELP THE SPERM TO ACQUIRE MOTILITY.





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 IN
NEEDED, THUS SPARING THE
PATIENT THE NEED FOR
REPEATED SURGERY FOR
SPERM RETRIEVAL

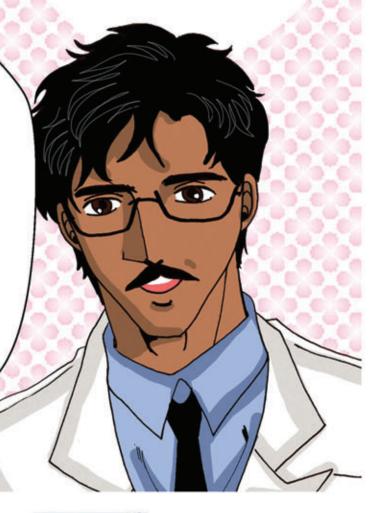
Chapter 10: What is PGD?



## 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. 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.



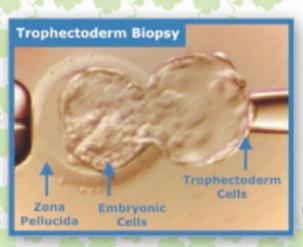
RESEARCH HAS SHOWN THAT IT IS POSSIBLE AT THREE DAYS AFTER FERTILISATION TO REMOVE ONE OR TWO CELLS FROM AN 8-10 CELLED EMBRYO WITHOUT DETRIMENT TO ITS FURTHER DEVELOPMENT. EMBRYOS WERE SEXED ON THE BASIS OF THE PRESENCE OR ABSENCE OF A DNA FRAGMENT SPECIFIC FOR THE Y CHROMOSOME: IN 1990 TWO SETS OF 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 THE PREIMPLANTATION GENETICS HAS RULED OUT DIAGNOSIS OF CYSTIC FIBROSIS, TAY SACHS DISEASE, LESCH NYHAN SYNDROME, DUCHENNE MUSCULAR DYSTROPHY AND FOR DISEASES CARRIED ON THE X CHROMOSOME.

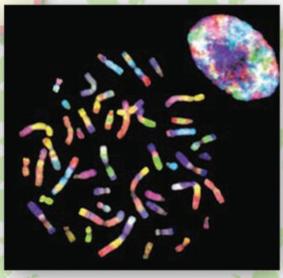


Chapter 10: What is PGD?

SEXING THE EMBRYO TO AVOID X
LINKED DISEASE REMAINS THE
COMMONEST REASON FOR
PREIMPLANTATION DIAGNOSIS,
NOW OPTIMALLY CARRIED OUT BY
THE MOLECULAR CYTO GENETIC
TECHNIQUE OF FISH (FLUORESCENT
IN SITU HYBRIDISATION) WITH DNA
PROBES DERIVED FROM THE X AND
Y CHROMOSOMES







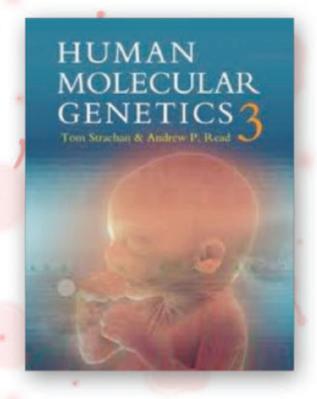
HOW IS PGD DONE?

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. THE CELL IS THEN AVAILABLE FOR GENETIC DIAGNOSIS. A NEWER OPTION ALLOWS EMBRYO BIOPSY TO BE DONE ON BLASTOCYSTS (ON DAY 5).



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. AFTER THE ANALYSIS ON THE SINGLE CELL, THE EMBRYOS ARE KEPT IN CULTURE AND ALLOWED TO FURTHER DIVIDE. ONCE THE APPROPRIATE MOLECULAR DIAGNOSIS IS MADE. THE NORMAL EMBRYOS CAN BE TRANSFERRED BACK INTO THE UTERUS IN THE IVF CYCLE.

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, SPINAL MUSCULAR ATROPHY TYPE I. MYOTONIC DYSTROPHY, HUN-TINGTON'S DISEASE CHARCOT-MARIE-TOOTH DISEASE: FRAGILE X SYNDROME, HAEMOPHILIA A. DUCHENNE MUSCULAR DYSTROPHY AND CHROMOSOMAL TRANSLOCATIONS.



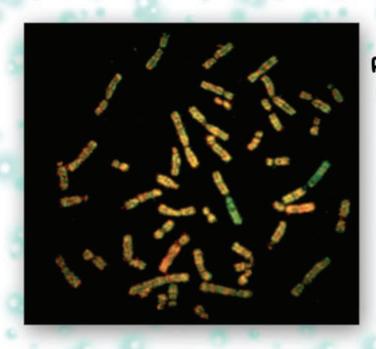


PGD CAN ALSO BE USED FOR CREATING SAVIOR SIBLINGS. THE EMBRYOS CAN BE HUMAN LEUKOCYTE ANTIGEN (HLA) TYPED, SO THAT THE NEWBORNS HLA MATCHES A SICK SIBLING. THE BABYS CORD BLOOD CAN BE USED FOR STEM CELL DONATION, TO TREAT MONOGENIC DISEASES SUCH AS FANCONI ANAEMIA OR BETA-THALASSEMIA

Chapter 10: What is PGD?

THE COMMONEST REASON FOR PGD TODAY IS PGS (PREIMPLANTATION GENETIC SCREENING) FOR ANEUPLOIDY SCREENING, TO TRY TOINCREASE PREGNANCY RATES FOR OLDER INFERTILE WOMEN. ONE OF THE REA-SONS 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, RESULTING IN A HIGHER PREGNANCY RATE.





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.



WHAT ARE THE CONTROVERSIES REGARDING THE USE OF PGD?

WHILE PGD REPRESENTS THE CUTTING EDGE OF REPRODUCTIVE TECHNOLOGY, AND GIVES US AN IDEA OF WHAT MAY BE POSSIBLE FOR THE FUTURE, IT ALSO RAISES A NUMBER OF WORRIES AND CONCERNS, ESPECIALLY IN INDIA, WHERE PEOPLE ARE WORRIED THAT IT MAY BE USED FOR SEX-SELECTION.

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.



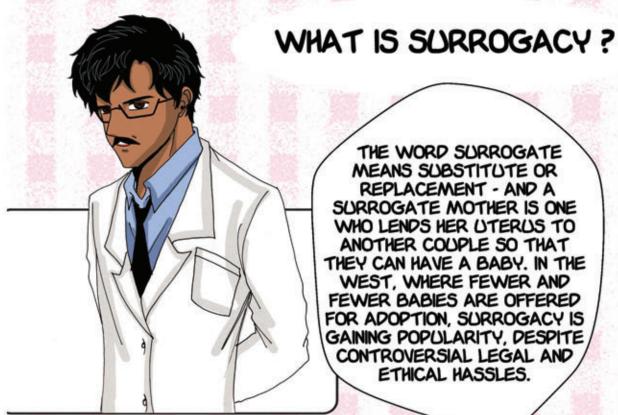


THE OTHER VIEW POINT IS - WHY NOT? IF MAN CAN IMPROVE ON NATURE, THEN WHY SHOULD HE NOT TRY? AFTER ALL, BUILDING A HOUSE IS SIMPLY MAN'S WAY OF IMPROVING ON NATURE - AND IF WE CAN IMPROVE MAN HIMSELF, THEN WHY NOT? SEEN IN THIS LIGHT, THEN STUDYING THE MOLECULAR GENETICS OF THE HUMAN EMBRYO WOULD BE 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 2IST CENTURY WILL BE THE EMBRYO - THIS IS A LOGICAL PROGRESSION!





WE SHOULD ALLOW
PATIENTS 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!



THE WORD SURROGATE MEANS SUBSTITUTE OR REPLACEMENT - AND A SURROGATE MOTHER IS ONE WHO LENDS HER LITERUS TO ANOTHER COUPLE SO THAT THEY CAN HAVE A BABY. IN THE WEST, WHERE FEWER AND FEWER BABIES ARE OFFERED FOR ADOPTION, SURROGACY IS GAINING POPULARITY, DESPITE CONTROVERSIAL LEGAL AND ETHICAL HASSLES.

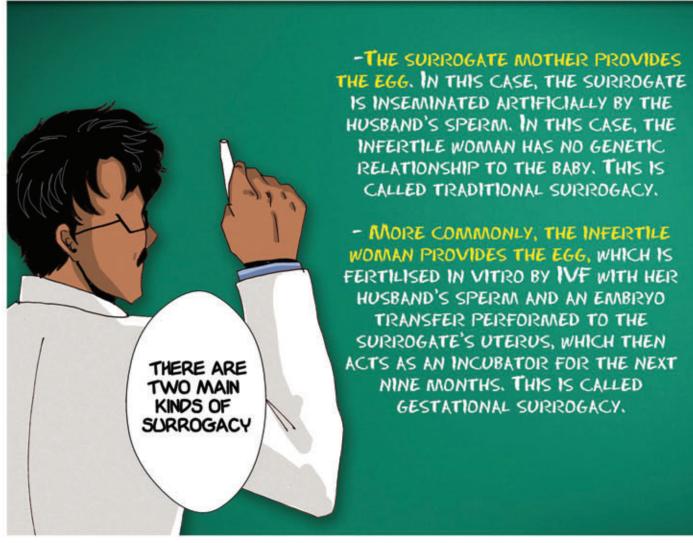
#### WHO NEEDS SURROGACY TREATMENT?

THE COMMONEST REASON IS A WOMAN WHO HAS NO LITERUS OR WHOSE LITERUS 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 BLEED-ING DURING A CAESAREAN). OTHER WOMEN WHO MAY WISH TO EXPLORE SURROGACY INCLUDE THOSE WHO HAVE HAD MULTIPLE MISCARRIAGES: OR WHO HAVE FAILED REPEATED IVE 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.





For more information on this chapter, go here: http://www.drmalpani.com/book/chapter28.html





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 ADOPTED 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.

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?

Chapter 11: What is surrogacy?



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