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TO: TIME MEDICINE

FROM: LONDON BY: ERIC TRIMMER, MEDICAL STRINGER (BA)

SLUG: TEST TUBE BABY ECH:

WHAT IS THE BASIC PROCEDURE FOR FERTILIZATION AND IMPLANTATION? IN THEORY THIS IS VERY SIMPLE. A SEMEN SAMPLE IS PLACED WITH AN EGG CELL, OR CELLS, IN THE TEST TUBE. THE MIXTURE IS THEN PUT INTO AN INCUBATOR FOR A FEW DAYS AND SUBSEQUENTLY THE FERTILIZED EGG IS INTRODUCED INTO THE WOMB WHERE IT ATTACHES ITSELF AND GROWS INTO A BABY IN THE NORMAL WAY.

HOW DIFFICULT IS THIS PROCEDURE? AN EXPERIENCED LAPOROSCOPIST CAN EASILY LEARN THE TECHNIQUE OF EGG COLLECTION. IN PRACTICE THE EGGS WHICH ARE RIPENING IN FOLLICLES (BAGS) ARE REMOVED TOGETHER WITH THEIR SURROUNDING FLUID AND COLLECTED IN A SMALL JAR. ONE LARGE RIPE FOLLICLE IS USUALLY OBVIOUS IF LAPOROPY IS UNDERTAKEN JUST PRIOR TO NATURAL OVULATION. IT IS POSSIBLE TO ARTIFICIALLY STIMULATE THE OVARIES TO PRODUCE MULTIPLE RIPE FOLLICLES IN WHICH CASE SEVERAL EGG CELLS CAN BE COLLECTED DURING ONE LAPOROSCOPY. THE HUMAN EGG CELL THUS OBTAINED CAN BE AS LARGE AS 0.5CM OR SO AND SO CAN BE EASILY IDENTIFIED. AFTER REMOVAL THE EGG CELL IS ALLOWED TO MATURE FURTHER, INCUBATED IN A SPECIAL NUTRIENT MEDIUM FOR ABOUT 36 HOURS AND SPERM IS THEN INTRODUCED AND FERTILIZATION OCCURS. IN NATURE THE HUMAN EGG IS FERTILIZED IN THE FALLOPIAN TUBE THREE DAYS AFTER IT HAS BEEN RELEASED FROM

THE OVARY. IT IMBEDS ITSELF IN THE WALL OF THE UTERUS AS A BALL OF CELLS CALLED A BLASTOCYST SIX TO SEVEN DAYS AFTER OVULATION OCCURED. EXTRA-UTERINE FERTILIZATION ATTEMPTS TO MIMIC THIS WHOLE NATURAL STORY BUT TECHNICAL DIFFICULTIES ARE MANY. SOME HAVE BEEN SOLVED.

FOR EXAMPLE?

1. THE PROCEDURE OF LAPOROSCOPY INVOLVES INTRODUCING A GAS INTO THE WOMAN'S ABDOMINAL CAVITY. THIS ALLOWS AN ARTIFICIAL SPHERE TO DEVELOP. THE LAPAROSCOPE (A SMALL OPERATING TELESCOPE) CAN THEN BE INTRODUCED AND AS THE VARIOUS ABDOMINAL AND PELVIC ORGANS ARE NOW SEPARATED BY THE INTRODUCED GAS VARIOUS STRUCTURES (THE OVARY, THE FALLOPIAN TUBES AND SO ON) CAN BE DIRECTLY VISUALISED. SMALL INSTRUMENTS CAN THEN ALSO BE INTRODUCED THROUGH THE OPERATING LAPOROSCOPE. IN ORDINARY DIAGNOSTIC LAPOROSCOPY (THE LAPOROSCOPE WAS DEVELOPED SO THAT GYNAECOLOGISTS COULD SCAN OVER THE PELVIC ORGANS WITHOUT MAKING A LARGE ABDOMINAL INCISION) CARBON DIOXIDE GAS SERVED AS A USEFUL AND EASILY AVAILABLE "BLOW UP" SUBSTANCE. STEPTOE HAS FOUND HOWEVER THAT A SPECIFIC GAS MIXTURE IS MANDATORY TO OBTAIN VIABLE EGG CELLS. IT IS COMPOSED OF FIVE PERCENT OXYGEN, FIVE PERCENT CARBON DIOXIDE AND NINETY PERCENT NITROGEN. THIS MAINTAINS A CORRECT TISSUE FLUID ACIDITY/ALKALINITY RATIO (PH) WITHIN THE EGG CELL AND THIS GAS MIXTURE IS MAINTAINED FOR SUBSEQUENT OOCYTE CULTURE AND FERTILIZATION. IT IS "FLUSHED OUT" OF THE WOMAN'S ABDOMINAL CAVITY WITH CARBONDIOXIDE, NITROUS OXIDE AND OXYGEN AT THE END OF THE OPERATION.

2. THE CULTURE MEDIUM FOR EGG CELLS AND FERTILIZED EGGS IS ALSO CRITICAL FOR DEVELOPMENT ALTHOUGH THE SOLUTION OF THIS PROBLEM NOW SEEMS TO HAVE BEEN SATISFACTORILY CONCLUDED (SEE

ADDENDUM. IT VARIES FOR DIFFERENT ANIMALS.

3. THE PROBLEM OF "WOMB PRIMING" SO THAT THE UTERUS WILL ACCEPT THE FERTILIZED EGG SEEMS TO HAVE BEEN ONE OF THE MOST DIFFICULT "TEST TUBE" PROBLEMS TO SOLVE. MANY IF NOT ALL OF THE ARTIFICIAL EGG RIPENING DRUGS, AS NOTED PREVIOUSLY, USED TO ALLOW THE LAPOROSCOPIST A CHANCE TO "COLLECT" SEVERAL EGGS FOR SUBSEQUENT FERTILIZATION, SEEM TO ADVERSELY AFFECT THE WOMB'S EMBRYO RECEPTIVITY. IN THIS INSTANCE THE COMPLEX HORMONE CONTROL OF THE HUMAN WOMB SEEMS TO POSE A UNIQUE PROBLEM COMPARED TO OTHER ANIMALS. SUCCESSFUL EMBRYO TRANSFER IN MANY SPECIES WITH OR WITHOUT A PERIOD OF EMBRYO CULTURE OUTSIDE THE BODY HAS BEEN WIDELY SUCCESSFUL OF LATE AND IT IS SAFE TO SAY THAT THOUSANDS OF OFFSPRING HAVE BEEN SO OBTAINED - SOME SINGLE STUDIES INVOLVING 300 SUCH OFFSPRING ARE DOCUMENTED (MOSTLY MOUSE AND RABBIT STUDIES). SEVERAL HUNDRED FARM ANIMALS HAVE NOW BEEN BORN AS A RESULT OF EMBRYO TRANSFER AND NO FETAL ANOMALIES ARE ATTRIBUTED TO THE EXTRA-UTERINE CULTURE OR SUBSEQUENT TRANSFER OF EMBRYOS. THE BIRTH RATES OF IMPLANTATION OF OVA ARE HOWEVER LOWER THAN THOSE BORN AFTER NATURAL MATING. THE REASONS FOR THIS ARE ARE THOUGHT TO BE MECHANICAL (LOSS OF EMBRYOS OR ENDOCRINOLOGICAL (HORMONE) REASONS).

POOR OR ABNORMAL HUMAN "WOMB PRIMING" AND RECEPTIVITY, WITH ITS "HAIRTRIGGER" AND COMPLEX ENDOCRINOLOGICAL BACKGROUND IS PROBABLY A NATURAL PROTECTIVE DEVICE TO PREVENT EITHER PRE OR POST MATURE EMBRYOS BEING NURTURED. ONE OF THE ASSOCIATED PROBLEMS OF EMBRYO TRANSFER IS THAT THE TRANSFERRED EMBRYO WILL "STICK" OR BE NURTURED IN AN EXTRA-UTERINE SITE AS A RESULT OF UTERINE ENDOCRINOLOGICAL DISHARMONY AND THUS THE TRANSFERRED EMBRYO DEVELOPS IN AN ABNORMAL SITE -- THE FALLOPIAN TUBE. CASES

OF THIS OCCURRING ARE ALREADY REPORTED.

4. ONE DIFFICULTY THAT WAS A PROBLEM TO EARLY EMBRYO WORKERS INVOLVED SPERM TRANSPORT AND CHANGE THAT OCCUR NATURALLY IN SPERMATOZOA IN THE FEMALE GENITAL TRACT. IN WOMEN SPERM CAN REACH THE FERTILIZATION AREA IN THE FALLOPIAN TUBE BETWEEN A FEW MINUTES AND THREE HOURS OF COITUS. DURING THIS TIME AND DURING THE TIME (PERHAPS SEVERAL DAYS) THAT THEY CAN REMAIN VIABLE AT THE FERTILIZATION SITE IN THE FALLOPIAN TUBE SPERM CELLS UNDERGO VARIOUS CHANGES SOME OF WHICH MAY BE MATURATION AND SOME OF WHICH MAY BE BROUGHT ABOUT BY THE FEMALE REPRODUCTIVE TRACT AND ITS SECRETIONS. THESE CHANGES ARE DESCRIBED AS CAPOCITATIONAL AND ACROSOMAL. THERE IS NO ACCEPTED THEORY THAT EXPLAINS THESE PHENOMENA AND THE MANNER IN WHICH THESE CHANGES ARE BROUGHT ABOUT IS NOT UNDERSTOOD, BUT BROADLY SPEAKING THEY INVOLVE THE REMOVAL OF THE SURFACE COATS OF THE SPERM CELL HEAD WHICH RESULTS IN A "SHARPENING" OF THE ACROSOME (EXTREME END) OF THE SPERM CELL AFTER WHICH IT CAN PENETRATE AND FERTILIZE THE OVUM. MANY FAILURES IN EARLY EMBRYO TRANSFER INVOLVED COPOCIRATIONAL AND OEROSOMAL PROBLEMS UNTIL IT WAS FOUND THAT A SIMPLE AND YET CAREFULLY DEFINED MEDIUM CONTAINING SERUM, A PARTICULAR RATIO OF SODIUM AND POTASSIUM, A CRITICAL PH AND THE PRESENCE OF CALCIUM WAS ESSENTIAL FOR FRESHLY SHED SPERM TO BE EFFECTIVE FOR EXTERNAL FERTILIZATION IN THE TEST TUBE.

5. FINALLY, IN A RELATIVELY UNRECEPTIVE UTERUS THE EMBRYO MAY BE IMPLANTED IN THE FALLOPIAN TUBE (SEE LANCET 24 APRIL 1976).

ARE OTHER WORKERS INVOLVED IN EXTRA-UTERINE EMBRYO FERTILIZATION AND REIMPLANTATION? CLEARLY THERE ARE MANY CENTERS INVOLVED BUT IN VIEW OF PUBLICITY WORRIES HAVE REMAINED SILENT. FEW TEAMS LIKE THE EDWARDS/STEEPTOE ORGANISATION IN WHICH A

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RESEARCH PHYSIOLOGIST HAS JOINED FORCES WITH A PIONEER LAPAROSCOPIST GYNAECOLOGIST EXIST. A SHORT BIBLIOGRAPHIC LIST WOULD INVOLVE 750 SCIENTIFIC PAPERS. C E ADAMS, G R AUSTIN, B D BAYISTER, A E BEER, H H BEIER, R J BLANDAU, R L BRINSTER, R G EDWARDS, R L GARDNER, K P MCNATTY, P C STEPTOE, R YANAGIMACHI, ARE ALL PROMINENT IN THE RESEARCH AND/OR PRACTICAL FIELD.

DO RESEARCHERS SEE OTHER IMPLICATIONS OTHER THAN IN FERTILITY AND SEX? NOT LIKELY, ALTHOUGH SUCH SUBJECTS AS THE CONTROL OR FACILITATION OF MULTIPLE BIRTHS IS POSSIBLE, ALSO THE POSSIBILITIES OF "OVUMBANKS" LIKE SPERM BANKS EXIST. NEW KNOWLEDGE OF OVUM REJECTION MECHANISMS MAY LEAD TO NEW FAMILIES OF CONTRACEPTIVES BEING DISCOVERED. FINALLY, THE VEXED QUESTION OF THE "DONOR" WOMAN AND THE "SURROGATE MOTHER" BEING IMPLANTED WITH AN EMBRYO MUST BE CONSIDERED.

THE HUXLIAN CREDO: THERE SEEMS LITTLE LIKELIHOOD OF "SUPER-PEOPLE" EVOLVING IN ANY WAY AS A RESULT OF HUMAN EMBRYO TRANSPLANTATION BUT IN ANIMAL HUSBANDRY SEVERAL POSSIBILITIES EXIST THAT COULD HAVE INTERESTING COMMERCIAL POSSIBILITIES. I.E. QUICK BREEDING OF CERTAIN STRAINS. SEX SELECTION MIGHT BE A FUTURE POSSIBILITY.

HOW CAN WE BE SURE THAT A TEST TUBE BABY WAS REALLY FERTILIZED OUTSIDE THE BODY? TO BE ABSOLUTELY SURE THE WOMAN MUST HAVE SUCH SEVERELY DISEASED FALLOPIAN TUBES THAT POTENCY IS IMPOSSIBLE, OR PREFERABLY ABSENT OR COMPLETELY DIVIDED AND TIED FALLOPIAN TUBES.

WHAT ARE THE RISKS OF MALFORMED BABIES?

UNTIL SEVERAL ARE BORN NOBODY CAN KNOW WITH CERTAINTY BUT IF EVIDENCE FROM WIDE EXPERIENCE FROM EXPERIMENTS ON ANIMALS IS ACCEPTABLE THEN THE RISK SEEMS REMOTE.

HOW CAN DOCTORS TELL IF A PRE IMPLANTATION EMBRYO IS NORMAL? IT IS POSSIBLE TO TEST FOR CERTAIN GENETIC MALFUNCTIONS IN EMBRYOS PRIOR TO IMPLANTATION. A VERY FEW CELLS CAN BE REMOVED WITHOUT JEOPARDIZING THE FUTURE GROWTH OF THE FOETUS AND MICROANALYTICAL METHODS OF TESTING ARE FEASIBLE. ABNORMAL CLEAVAGE OF CERTAIN TYPES OF EMBRYO (IN WHICH A SERIES OF MITOTIC CELL DIVISIONS AND INCOMPLETE CELL CYCLES PREDOMINATE THE PICTURE) CAN BE SELECTED AGAINST BY USING SPECIFIC NUTRIENT MEDIA. ROUTINE PEDIATRIC TESTING AT BIRTH CAN PREDICT WITH A HIGH DEGREE OF CERTAINTY THAT A BABY IS NORMAL.

IF A TEST TUBE BABY IS FOUND ABNORMAL WHAT IS THE MALPRACTISE SITUATION? NOBODY KNOWS BUT WE WOULD EXPECT THAT THE PARENTS OF SUCH A CHILD WOULD SIGN A WAIVER AGAINST SUCH A CLAIM BEING MADE PRIOR TO IMPLANTATION.

ARE THERE ANY CHILD ADJUSTMENT PROBLEMS ANTICIPATED IN THE TEST TUBE BABY? NONE AT ALL UNLESS THE PUBLICITY AND OR FINANCIAL ADVANTAGE ARISING FROM SUCH A BIRTH DISTRACTS THE PARENTS HANDLING THE CHILD'S UPBRINGING.

RELEVANT BACKGROUND INFORMATION: THE HISTORY OF OVUM MANIPULATION HAS NOT BEEN WRITTEN. IT MAY HAVE STARTED WHEN PINCUS AND ENZMANN IN 1935 PUBLISHED A PAPER IN THE JOURNAL OF EXPERIMENTAL MEDICINE 62,665 ENTITLED "THE COMPARITIVE BEHAVIOUR OF MAMMALIAN EGGS IN VITRO AND IN VIVO."

HOW EXTENSIVE IN BRITAIN IS HUMAN EMBRYO REIMPLANTATION NOT KNOWN. RUMOUR HAS IT THAT STEPTOE AND OTHERS HAVE IMPLANTED FERTILIZED OVA MANY TIMES INTO FIRST OF ALL WOMBS DUE FOR HYSTERECTOMY SAY 3 MONTHS LATER. NO EVIDENCE TO MY KNOWLEDGE. PLENTY OF ANIMAL WORK IS PUBLISHED HOWEVER.

HOW LONG IS THE BODY OUTSIDE THE WOMB? THE EGG IS ALIVE ALL

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BUT THE FERTILIZED OVUM, THE EMBRYO, IS IDEALLY IMPLANTED IT IS BELIEVED SIX TO SEVEN DAYS AFTER FERTILIZATION AT BLASTOCYST (32 CELL?) STAGE. THERE IS PROBABLY AN OPTIMAL STAGE FOR REIMPLANTATION IN MAN BUT BECAUSE OF "HUMAN FACTORS" THIS CANNOT BE REALIZED FROM THE PRACTICAL POINT OF VIEW. IN ANIMALS IT IS POSSIBLE TO IMPLANT EMBRYOS INTO FEMALES AT AN ENDOCRINOLOGICALLY PEAK RECEPTIVITY PERIOD. IN COWS IF REIMPLANTATION IS SYNCHRONISED WITH PEAK ENDOCRINOLOGICAL ACCEPTABILITY THE MEAN CONCEPTION RATE IS SIXTY FOUR PERCENT. IMPLANTATION ONE DAY EARLY REDUCES THIS TO FIFTY FIVE PERCENT -- ONE DAY LATER TO FIFTY PERCENT. SO CLEARLY THERE IS NO "FIXED" LIFE OUTSIDE THE WOMB FOR AN EMBRYO. BUT ITS CHANCE OF GROWING INTO A MATURE ARRIVAL IS RELATED TO AN OPTIMAL BUT AS YET UNKNOWN TIME.

STEPTOE AND EDWARDS STORY:

DATES BACK TO THE LATE SIXTIES WHEN THEIR ACTIVITIES FIRST REACHED THE MEDICAL PRESS. AN EARLY SYMPOSIUM ORGANISED BY SCHERING PHARMACEUTICALS IN BERLIN IN 1969 WAS FOLLOWED IN "WORLD MEDICINE" BY HINTS OF ETHICAL CRITICISM WITH THE THEN ARCHBISHOP OF WESTMINSTER (CARDINAL HEENAN) REFERRING TO THE REPORTS AS TEST TUBE MURDER, WHEN THE RESULTS OF EARLY EXTRA CORPORAL FERTILIZATION AND TESTING WAS DISCUSSED. THE ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS OF BRITAIN WAS ASKED TO DEFINE THE CRITERIA THAT NEEDED TO BE ESTABLISHED BEFORE "BIOLOGICAL EXPERIMENTS" WERE "ALLOWED" TO BECOME CLINICAL REALITY. AT ABOUT THE SAME TIME DOUGLAS BEVIS AND ERLE WILSON AT SHEFFIELD REPORTED THEIR WORK. IN VITRO FERTILIZATION OF HUMAN OVA WAS ACHIEVED IN 1964 IN THE U.S. BY JOHN ROCKOND, AGAIN IN 1965 BY LANDRUM B SHETTLES.

THE CLINICAL MARRIAGE OF EDWARDS THE PIONEER LAPAROSCOPIST FROM OLDHAM PATRICK STEPTOE HOWEVER CAPTURED THE IMAGINATION OF

THE WORLD AND THEIR VARIOUS HINTS, DISCLOSURES AND SOMETIMES RETRACTIONS INTERESTED THE NEWS MEDIA IN THE FOLLOWING 18 YEARS. BOTH WERE OFFERED AND RESISTED VAST SUMS OF MONEY FOR STORIES OF THE "FIRST TEST TUBE BABY".

"BLUE SKY" SPECULATION:

1. PERHAPS A FORGOTTEN ASPECT OF THIS STORY IS THE POSSIBILITY OF HELPING IN CERTAIN MALE INFERTILITY PROBLEMS WHEN VERY LOW SPERM COUNTS PRECLUDE FERTILIZATION. ONLY COMPARITIVELY FEW SPERM ARE NEEDED FOR TEST TUBE FERTILIZATION.

2. ANOTHER POSSIBILITY IS AN ANSWER TO ECTOPIC PREGNANCY. ONE ECTOPIC PREGNANCY IS FREQUENTLY FOLLOWED BY ANOTHER LEAVING SUCH A WOMAN STERILE IF BOTH FALLOPIAN TUBES ARE SACRIFICED. OVUM IMPLANTATION AFTER SUCH MULTIPLE ECTOPIC PREGNANCY COULD MAKE SURE THAT UTERINE IMPLANTATION OCCURS.

3. EMBRYO STORAGE, BY FREEZING, IS A DISTINCT POSSIBILITY IN HUMANS. IT IS ALREADY PROVED TO BE POSSIBLE IN THE MOUSE, RAT, RABBIT, COW AND SHEEP. THIS PROCESS COULD ALLOW FAR MORE EFFICIENT REIMPLANTATION TECHNIQUES IN THE FUTURE. FOR INSTANCE A WOMAN'S (MULTIPLE) OVA CAN BE COLLECTED AFTER HORMONAL STIMULATION, FROZEN, AND THEN REIMPLANTED WHEN HER WOMB HAS SETTLED DOWN A MONTH OR SO LATER.

4. THE GREATEST BOON THAT WILL ACCRUE TO TEST TUBE FERTILIZATION AND EMBRYO IMPLANTATION IS NOT "PIE IN THE SKY" HOWEVER BUT A BABY IN THE BED. INFERTILITY DUE TO BLOCKED TUBES ACCOUNTS FOR 18 TO 33 PERCENT OF ALL FEMALE INFERTILITY AND PRESENT METHODS OF TREATMENT, PLASTIC REPAIR AND TUBAL REIMPLANTATION SURGERY IS OFTEN VERY DISAPPOINTING.

ADDENDUM: THE FORMULA FOR THE MEDIA USED FOR FERTILIZATION IN VITRO, AS WELL AS DIAGRAMS FOR TIME MAPS, IS IN TIME PIX PACKET



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LEAVING TONIGHT AND DUE IN NEWYORK EARLY THURSDAY YOUR TIME.  
PLEASE CHECK WITH TIME PIX AND TIME MAPS.

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