10 Biological Risks of In Vitro Fertilization and Embryo Transfer

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There are numerous possible complications associated with the procedure of IVF and ET. Many of these have been discussed elsewhere as they may follow treatment prior to oocyte collection, laparoscopy, embryo transfer or pregnancy. As well as these problems, the procedure carries a large number of potential biological complications which will form the basis of the present discussion. The “risks” are those which are faced by the ovum, the sperm and the zygote both while residing in the in vitro culture system and when returned to the uterine lumen for the pregnancy. Some of these risks occur as an intrinsic quality of the particular sperm and ovum used for IVF, such as chromosomal aberrations and genetically inherited diseases which are also found in a small proportion of normal pregnancies. Others may occur because of suboptimal control of the artificial environment used in the laboratory during fertilization and early development. Even when the embryo returned to the genital tract continues to grow, implants and a pregnancy commences, further complications may arise which place the quality of the pregnancy in jeopardy.

Much of the following discussion will be concerned with theoretical dangers. Although a number of groups have now been able to achieve successful pregnancies in their IVF programmes (Edwards et al. 1980; Lopata et al. 1980; Wood et al. 1981), data within the scientific and medical literature remain sparse. Furthermore, most of the data report successes rather than failures and as the overall success rate generally remains low, there have been few recorded instances of biological abnormalities.

10.1 Congenital Abnormalities and Malformations

The ultimate quality of an embryo depends largely upon the quality of the gametes used in a particular fertilization. Thus a most fundamental risk of IVF relates to the normality of the genetic constitution of the ovum and sperm which are used for IVF.

An intrinsic abnormality will lead to the production of an abnormal embryo, which will be returned to the patient if normal cleavage occurs. The likelihood of
these anomalies occurring is similar to that expected in all other pregnancies, and discussion of congenital defects is usually achieved by reviewing the known causes of embryonic and fetal wastage (Schlesselman 1979).

10.1.1 Chromosome Aberrations

The most severe forms of abnormality result from gross problems of chromosome additions and deletions. The most common forms are the monosomies and trisomies which are a result of incorrect separation of chromosomes during the reduction division of meiosis. During gametogenesis, one member of each of the 23 pairs of chromosomes migrates into each new ovum or sperm. In some pairs, separation fails (non-disjunction) such that one new gamete will contain both members of the pair while the other new gamete will contain neither of the pair. If, at fertilization, fusion occurs between a normal spermatozoon and an ovum which has resulted from non-disjunction, the resulting embryo grows with each cell either containing only one of a particular chromosome pair instead of two or having three sets of a particular chromosome. Similarly, an embryo may result from fertilization of a normal ovum with an abnormal sperm. The embryo with only one of a chromosome pair is a monosome while the alternative with three chromosomes is a trisome. A typical example of monosomy is seen in Turner's syndrome where either of the sex-determining chromosomes X or Y is missing. Down's syndrome in which chromosome 21 is present as a triplet is the major example of trisomy. Other examples of mono- and trisomies have been described in adult humans (Austin 1972). Furthermore, there have been a number of other similar disturbances to chromosome structure as a result of non-disjunction described in embryos which are not compatible with life, and development ceases presumably due to derangement of the control of genetic information.

The second major type of chromosomal defect is found when the embryo contains multiples greater than two of the 23 haploid chromosomes, a condition referred to as polyploidy. The presence of three sets of chromosomes (triploid) is the most common form and is estimated to occur in a surprisingly large proportion (2%) of clinically identified conceptions (Jacobs et al. 1978). Polyploidy may arise in two ways. Fertilization of a haploid oocyte can occur after entry of more than one haploid spermatozoon into the ooplasm and is classified as polyspermy. Alternatively, triploidy may result from complete non-disjunction of the second meiotic division during gametogenesis so that the ovum retains 23 pairs of chromosomes (i.e. remains diploid). The triploid arises when a diploid ovum or sperm is fertilized by or fertilizes a haploid sperm or ovum respectively. The embryo in this case has undergone polygyny.

The formation of embryos after polyspermic fertilization is fairly easily recognized during IVF if the embryo is carefully examined following gentle removal of the surrounding cumulus oophorus and corona radiata complex 12–20 h after insemination. At this time, pronuclei are clearly visible and the presence of more than two is highly suggestive of polyspermic fertilization.

An embryo resulting from polygyny in vitro is not easily identified. If the oocyte was diploid, only one polar body will be present after fertilization, but the constitution of polar bodies is difficult to visualize in the living state using a dissecting microscope. Embryos often contain small cytoplasmic fragments in the