Chromosome Studies in Selected Spontaneous Abortions Polyploidy in Man

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Cytogenetics was founded in the cytological and genetical study of plants and insects. The observation of mammalian chromosomes goes back to the 1880s but techniques which make counting accurate have been devised only in the last 15 years. In the dozen years since the first chromosome anomalies in man were described, almost every known type of disorder has been reported either in living subjects or in abortuses.

The reaction of the organism to chromosome disorders varies somewhat between the plant and animal kingdoms as well as among different animal classes. However, there are some general principles which apply to all living organisms:

(1) The presence of one additional autosome, resembling a regular member of the complement, interferes with normal development;

(2) The degree of abnormality varies with the chromosome involved;

(3) The loss of one chromosome has a more serious effect on development than the presence of the same element in excess;

(4) The presence of whole extra sets of chromosomes (polyploidy) has different effects on the plant and animal kingdoms and among the members of the latter;

(5) In general, polyploidy is well tolerated in plants and invertebrate animals. Among the vertebrates, there is considerable difference between classes. In man and other mammals polyploidy appears to be lethal or sublethal.

Thirty abortuses with triploidy or hypertriploidy and 7 with tetraploidy form the subjects of this paper. They have not previously been published in detail but one aspect of their phenotype has been discussed elsewhere (Carr, 1969). The numbers used in this publication are the same as those used for the 9 specimens included in the latter paper.

Material and Methods

The specimens consisted of abortuses which were collected in saline. They formed part of a study of selected spontaneous abortions which fell into one of the following 4 categories:

(1) Abortuses from women who conceived within 6 months of discontinuing oral contraceptives;

(2) Pregnancy termination associated with the use of an intrauterine device;

(3) Abortuses lost within 60 days of the last menstrual period, regardless of contraceptive history;

(4) Specimens with hydatidiform mole or hydatidiform degeneration of the chorionic villi. (The latter term is used to describe specimens in which the chorionic villi are balloon-shaped and this change is visible to the naked eye. These cystic villi measure 3 to 9 mm in diameter.)

The technique for culture has been described in detail elsewhere. (Carr, 1967). It does not involve the use of trypsin or subculture. Most abortuses produce cells suitable for chromosome analysis within 10 days and about 60% of attempted cultures were successful. In addition to culture *in vitro* a direct squash technique was used to study cells in many of the specimens with hydatidiform degeneration or mole. This was similar to the method described by Makino, Sasaki, and Fukuschima (1965). In about half of the specimens in which this was applied a few cells could be analysed and their ploidy defined. We were never sufficiently confident of this method to believe it reliable in detecting aneuploidy.

Interphase nuclei were studied for sex chromatin in most specimens, either in cells grown in culture, whole mounts of amnion or both.

Results

The histories and findings for the 27 triploid, 3 hypertriploid, and 7 tetraploid specimens are listed in Table I.

The commonest sex chromosome complex among the triploid specimens was XXY. Thirteen of the 27 triploid abortuses had this gonosomal complement while 9 were XXX. There were no abortuses with a 69,XXX chromosome complement. The remaining 5 triploid abortuses could not be karyo-

TABLE I
HISTORIES AND FINDINGS IN 37 POLYPLOID ABORTUSES

No.	Maternal Age	Previous Pregnancies		Menstrual Age	Cultures (C) Squash (S)	Sex Chromosomes	Hydropic Villi	Specimen
		Term	Aborted					
<i>Triploidy (69)</i>								
L2	26	1	0	85	C	?	+	18 mm normal embryo; intact sac
L4	27	0	1	61	C	XXX	+	6 mm normal embryo; intact sac
L8	39	1	0	58*	C	XXY	+	Damaged embryo, apparently normal; ruptured sac
PMG11	29	3	0	128	C	XXY	+	Ruptured sac; incomplete specimen
1M	22	1	0	75	C	XXY	+	Ruptured sac; cord present but no embryo
2M	40	1	0	113	C	XXX	+	Intact empty sac
1D	27	2	0	137	C	XXX	+	Grossly malformed embryo; no further details
4M	21	1	0	164	C	XXY	+	24 mm embryo; no further details
UWO	35	3	0	105	C	?	+	Ruptured sac; incomplete specimen
P10	37	1	3	45	C	XXY	—	0.5 mm nodule in small intact sac
P11	32	2	0	78	C	XXY	—	21 mm embryo with meningocele; intact sac
P12	19	0	0	126	C	XXX	+	14 mm macerated normal embryo, ruptured sac
P13	26	2	0	74	C	XXX	—	Broken remains of macerated embryo; intact sac
P14	22	1	0	113	C + S	?	+	Intact empty sac
P15	40	2	1	165	S	?	++	Few vesicles showing 'early molar change'
P16	34	2	1	113	C + S	XXX	+	Ruptured sac; cord present but no embryo
P17	21	1	0	85	C + S	XXX	+	Ruptured sac; incomplete specimen
P18	23	2	0	72	C	XXY	+	Ruptured sac; incomplete specimen
P19	28	1	0	130	C + S	XXX	++	Typical hydatidiform mole; fragments of fetus
P20	30	2	3	105	C	XXY	—	Head of small embryo; incomplete specimen
P21	28	1	0	118	C	XXY	+	17 mm macerated normal embryo
P22	21	2	0	?	C + S	XXX	+	Incomplete specimen
P23	22	0	0	90	C	XXY	+	Intact empty sac
P24	25	1	0	129	C	XXY	+	42 mm macerated normal fetus
P25	29	1	0	138	C	XXY	+	11 mm macerated embryo with meningocele; intact sac
P26	21	0	0	94	S	?	+	Ruptured sac. Cord present but no embryo
P27	18	0	0	138	C	XXY	+	Intact empty sac
<i>Hypertriploid (70)</i>								
P28	41	5	0	100	C	70,XXX,D +	+	Grossly deformed 3 mm embryo; ruptured sac
P29	37	2	3	55	C	70,XXY,16 +	—	Intact empty sac
P30	44	2	0	94	C	70,XXX,16 +	+	Ruptured sac; incomplete specimen
<i>Tetraploid (92)</i>								
6M	20	1	0	86	C	XXXX	+	Intact empty sac
P32	38	2	0	67	C	XXYY	—	Intact empty sac
P33	33	1	0	58	C	XXYY	—	Ruptured sac; incomplete specimen
P34	27	0	3	86	C	XXXX	—	Ruptured sac; incomplete specimen
P35	22	1	0	64	C	XXYY	—	Intact empty sac
P36	24	1	2	83	C	?	—	Intact empty sac
P37	24	0	0	81	C	XXYY	+	Intact empty sac

* Therapeutic termination.

typed and the sex chromosome complement was therefore unknown. The diagnosis of triploidy was, however, definitely confirmed by chromosome counts which were consistently in the 69 range.

The mean menstrual age for 12 of the 69,XXY specimens was 106.7 days. One other specimen was not included because it came from a therapeutic abortion. The mean menstrual age of 8 triploid specimens with XXX gonosomes was 104.9 days. There does not appear to be any significant difference in gestational age at the time of abortion,

between the two types of triploidy, 69,XXY and 69,XXX.

The mean maternal ages for the XXY and XXX triploids were 27.3 and 27.0 years respectively. They did not differ significantly from one another, nor from the mean maternal age of 151 women who aborted chromosomally normal abortuses. This mean age was 27.1 years (Carr, 1965).

Some of the specimens were unsuitable for sex chromatin analysis for various reasons. In those specimens which were suitable, the number of Barr

bodies found was variable. They were not always the same in cultured cells and in whole mounts of amnion. The results of sex chromatin analysis in the suitable specimens are summarized in Table II. Two of 6 abortuses with a 69,XXX chromosome complement had double Barr bodies. Six out of the twelve 69,XXY specimens had chromatin posi-

mole for which chromosome analysis was possible. Six were diploid and one was diploid/tetraploid mosaic of doubtful significance. Although the numbers of diploid and tetraploid cells was equal, the total number of cells counted was small (16). In view of the possibility that the tetraploid cells arose in a rather poor culture, no great importance

TABLE II
SEX CHROMATIN FINDINGS IN CELLS OF POLYPLOID SPECIMENS

Specimen No.	Chromosome Complement	Cells Examined	Sex Chromatin			
			Negative	Single Positive	Double Positive	Total
L2	?	Culture	24	175	1	200
L4	69,XXX	Culture	66	34	0	100
		Amnion	99	1	0	100
2M	69,XXX	Amnion	83	100	17	200
P12	69,XXX	Culture	85	15	0	100
P14	?	Amnion	32	68	0	100
P16	69,XXX	Amnion	57	43	0	100
P17	69,XXX	Culture	75	25	0	100
P28	70,XXX,D +	Culture	62	38	0	100
		Amnion	63	107	30	200
L8	69,XXY	Amnion	100	0	0	100
PMG11	69,XXY	Amnion	79	120	1	200
1M	69,XXY	Amnion	100	0	0	100
P10	69,XXY	Amnion	41	9	0	50
P11	69,XXY	Amnion	165	35	0	200
P18	69,XXY	Culture	100	0	0	100
P20	69,XXY	Amnion	99	1	0	100
P21	69,XXY	Amnion	78	22	0	100
P24	69,XXY	Amnion	41	59	0	100
P25	69,XXY	Amnion	92	8	0	100
P27	69,XXY	Amnion	200	0	0	200
P29	70,XXY,16 +	Culture	100	0	0	100
6M	92,XXXX	Amnion	53	29	18	100
P34	92,XXXX	Amnion	34	44	22	100
P32	92,XXYY	Amnion	100	0	0	100
P33	92,XXYY	Culture	100	0	0	100

tive cells and the percentage of Barr bodies varied from 8 to 60%. On the two occasions when satisfactory preparations were obtained in cultured cells and in whole mounts of amnion, the findings were different.

The relationship between vesicular chorionic villi (either hydatidiform degeneration or mole) and chromosome findings is noted in Table III. Among 35 specimens which showed swelling of the chorionic villi, clearly visible to the naked eye, 70% were triploid or hypertriploid. No more than 20% had normal chromosome complements and the number may have been less. This is because about half of the 'diploid' specimens failed in culture or grew poorly and were diagnosed on cells from direct squash preparations of the chorion. As already noted we were unable to eliminate aneuploidy using this technique because variations in counts of one or two chromosomes were not detectable.

There were only 9 specimens of hydatidiform

TABLE III
HYDATIDIFORM DEGENERATION OF CHORIONIC VILLI AND HYDATIDIFORM MOLE IN RELATION TO CHROMOSOME FINDINGS

	Hydatidiform Degeneration	Hydatidiform Mole
Diploid	7	6
Triploid	22	2
Hypertriploid	2	0
Other abnormal	4	1
Total	35	9

is attached to this finding. Two of the hydatidiform moles were triploid and one of them was typical on gross and microscopic examination. The other specimen included only a few large vesicles measuring up to 1 cm in diameter. The pathological report was 'early molar change'. It is presumed that most of the tissue was passed at home

and the few vesicles recovered did indeed represent the remains of a typical mole.

Of the 27 triploid specimens, 85% had hydatidiform degeneration of the chorionic villi or true mole. This was the most characteristic phenotypic finding but the embryos themselves presented some features of interest. There were 11 embryos or fetuses, partial or complete, for which some information is available. Three were not available for detailed study but one of these was photographed. Including the latter, there were 9 embryos or fetuses available to us. Of these, 5 were normal on external examination, two had meningomyeloceles and two were damaged and incomplete.

The 5 apparently normal embryos ranged in developmental age from 31 to 58 days. Four of the 5 specimens were examined internally and no abnormalities were found. The largest of these specimens (P24) is shown in Figure 1. The fingers and toes should be separated at this time but maceration caused the digits to stick together but it would be wrong to consider this an anomaly.

The striking feature about the two abnormal specimens was the low level of the sacral meningo-myeloceles. The position was identical in the two embryos (Figs. 2 and 3).

One of the incomplete specimens was damaged during therapeutic abortion. In contrast to the appearance of most spontaneous abortions, the organs were well preserved. The other incomplete specimen was very fragmentary but of great interest. This fetus was found among the tissue from the typical hydatidiform mole (P19). A trunk, head, and one limb of a severely macerated fetus were found. The trunk was almost eviscerated but close dating was possible from the head. The eyelids of the left eye were closed and those of the right eye, almost so. This finding along with the presence of a simple, formed external ear suggests that the fetus was at the end of the ninth week of development (about 63 days).

The 9 embryos and fetuses were dated according to established criteria (Patten, 1946; Hamilton, Boyd, and Mossman, 1962; Davies, 1963). The

FIG. 1. Fetus of about 9 weeks developmental age, 69,XXY. Swelling over the posterior neck region is an artefact due to maceration (mm scale).

FIG. 2. Macerated embryo of about 33 days developmental age showing meningocele in sacral region (mm scale).

menstrual and developmental ages are listed in Table IV. Unfortunately, death of the embryo and subsequent degeneration (maceration) produce distortion. However, the developmental dating should be accurate to within a few days.

TABLE IV
MENSTRUAL AND DEVELOPMENTAL AGES OF
EMBRYOS AND FETUSES

Specimen No.	Menstrual Age (Days)	Developmental Age (Days)	Difference (Days)
L2	85	37	48
L4	61	31	30
L8	58	35	23
P11	78	42	36
P12	126	33	93
P19	130	63	67
P21	118	37	81
P24	129	58	71
P25	138	33	105

There were 6 specimens with 'embryonic remnants'. Three of these consisted of a cord with no embryo, 2 had fragments of macerated embryonic remains and one consisted of a 0.5 mm nodule. The latter type of specimen represents the most severe degree of growth disorder. In accordance with past experience section of the nodule showed that it had 'cavitated', an apparently fundamental tendency of developing embryonic tissue.

Four of the abortuses were intact empty sacs with no evidence of embryonic tissue within the chorionic cavity and 6 specimens were incomplete,

FIG. 3. Embryo of about 42 days developmental age showing meningocele in sacral region. The pigmented retina appears incomplete but microscopic section shows the choroid fissure of the optic cup is closed (mm scale).

FIG. 4. Partial karyotypes showing D and E groups of hypertriploid cells from abortions P23 and P28.

consisting of varying remnants of ruptured chorionic sacs.

There were 3 specimens with hypertriploidy and the mean maternal age was 40.7 years. The mean menstrual age at abortion was 83 days. In each instance, the modal number of chromosomes was 70. Each member of the complement was represented 3 times (as in triploidy) plus one extra element which was consistent for the particular specimen. In abortus P28, there were 70 chromosomes 69,XXX plus an additional member in group D (Fig. 4).

The ruptured sac contained a 3 mm, grossly abnormal and stunted embryo (Fig. 5). The most striking feature of this embryo was its numerous protuberances. In spite of marked maceration, microscopic section showed that there had been an attempt to form a nervous system, notochord, probably optic vesicles, and limb buds. The prominent vesicular bulge at the cephalic end was not related to any known normal structure.

The other 2 hypertriploid abortuses had an additional chromosome 16 consistently present. One was an intact empty sac with the chromosome complement 70,XXY,16+ and the other was a ruptured sac (70,XXX,16+).

There were 7 tetraploid specimens collected during the same period. Four were 92,XXYY and 2 were 92,XXXX. Karyotyping of the other specimen was not possible so the sex chromosome complement is unknown. The mean menstrual age of the 7 tetraploid specimens was 75 days. This is strikingly shorter than for the triploid specimens.

In no instance was an embryo or embryonic remnant found. Five of the tetraploid conceptuses were intact empty sacs, the other two being incomplete, ruptured sacs. The mean maternal ages of women aborting tetraploid specimens was 26.9 years.

Discussion

Triploidy is a relatively common event in man. If we assume that 15% of all pregnancies end in abortion it is likely that one third of these have a chromosome anomaly. This includes a correction for early abortions which are frequently lost at home and which contribute heavily to the load of chromosomally abnormal specimens (Carr, 1970a). It may not be correct, but let us assume for the moment that triploidy is no more common in the early abortions than it is in those recovered from patients admitted to the hospital. Then it appears that almost one fifth of the chromosomally abnormal abortuses are triploid (Boué and Boué, 1970; Carr, 1970b). In that case, at least 1% of all conceptuses in man are triploid. Almost all of these are aborted by the end of the third month of gestation. However, it is possible for an infant who is apparently triploid in all cells in the body, to reach term. Five such cases have been reported and others are known (Bernard *et al*, 1967; Edwards *et al*, 1967; Papiernik-Berkhauer, 1968; Butler *et al*, 1969; Walker and Gregson, 1969; Conen, 1970; Schindler and Mikamo, 1970). Two infants died shortly before birth

Fig. 5. Abnormal and stunted hypertriploid embryo (P28) 3 mm long. Body stalk (which forms umbilical cord) seen in lower third of the photograph (mm scale).

but the others lived for hours or days. This means that triploidy is compatible with live birth in man. The 5 triploid infants for which details are published exhibited a constellation of anomalies but there was no clear syndrome. The findings have been reviewed by Butler *et al* (1969). Anomalies mentioned in at least 4 of the 5 cases include low set, malformed ears, large posterior fontanelle, hypertelorism of the eyes, syndactyly, and abnormal external genitalia. Coloboma of the iris and single palmer creases were noted in 3 of the 5 infants. Also in 3 of the infants, the placenta was twice the normal size for the stage of pregnancy and 2 of these showed hydatidiform change.

Triploid/diploid mosaicism is relatively rare among abortuses (Schlegel *et al*, 1966; Boué and Boué, 1970; Carr, 1970c). There have, however, been 6 reported cases of triploid/diploid mosaicism in living infants. The findings in these cases have also been reviewed by Butler *et al* (1969). The defects mentioned above occurred irregularly in the mosaic patients but the findings were even less consistent than in the pure triploid infants. In view of the finding of asymmetry in certain triploid/diploid mosaic infants, Johnston and Penrose (1966)

studied 9 patients with congenital asymmetry. One patient exhibited a few hypertriploid cells in a culture from the hypertrophied side. Another example of local hypertriploidy was reported by Gropp, Jussen, and Odunju (1964). They found cells with 72 chromosomes in cell cultures of the palatal mucosa from a case of cleft palate. However, later studies from cleft palate patients failed to show further examples of this anomaly (Jackson, 1966; Soukup and Warkany, 1966).

The sex chromatin studies which were possible for the triploid specimens strengthened the previous evidence that X inactivation in triploidy is irregular (Mittwoch, Atkin, and Ellis, 1963; Carr, 1965). Triploid abortuses with XXX gonosomes sometimes had 2 Barr bodies, as a maximum, and in other instances, only single bodies were found. Likewise 69,XXY specimens were either chromatin-positive or negative. Harnden (1961) proposed a formula for calculating the relationship between the number of Barr bodies (S), the number of X chromosomes (X) and the number of sets of autosomes (A). If one applies the triploid situation to his formula $S = X - A/2$ the answer is $\frac{1}{2}$ for 69,XXY and $1\frac{1}{2}$ for 69,XXX. The existence of 'halves' is not a biological function but one could broadly interpret it to mean an unstable effect of the autosome complement. In this sense, the number of Barr bodies with a 69,XXY complement would be 0 or 1 and with 69,XXX, S would equal 1 or 2. This is precisely what is found in practice.

When the formula is applied to the tetraploid specimens no problem arises. Tetraploids with XXYY gonosomes are chromatin-negative and 92,XXXX produces a maximum of two Barr bodies per cell.

In considering the abortuses with triploidy some important points must be borne in mind. Most embryos from spontaneous abortions, abnormal or normal in morphology, are dead for some time before being aborted. This retention in the uterus leads to breakdown of tissue to a varying degree known as maceration. In the presence of severe maceration only the grossest anomalies are detectable. It is easy to confuse some of the deforming effects of maceration with defects of development. Defective development in spontaneous abortions tends to be over diagnosed for this reason. Even considering these facts, it is clear that many triploid embryos are abnormal, the commonest defects in development affecting the neural tube. The findings in 87 triploid abortuses, including the 30 described in this paper, are summarized in Table V.

The described cases of Boué *et al* (1967) are included in Table V. However, these investiga-

TABLE V

PHENOTYPIC AND GENOTYPIC FINDINGS IN TRIPLOIDY AND HYPERTRIPLOIDY

Type of Triploid	Incomplete Specimen	Intact Empty Sac	Disorganized Embryo	Embryo with Focal Anomaly	Normal Embryo	Insufficient Detail	Total
69,XXY	14	6	10	4	8	2	44
69,XXX	6	2	4	6	7	1	26
69,XXY	1	0	0	0	2	1	4
69, Sex chromosomes unknown	4	1	0	1	1	2	9
70, Assorted	1	1	2	0	0	0	4
Total	26	10	16	11	18	6	87

References: Penrose and Delhanty, 1961; Delhanty, Ellis, and Rowley, 1961; Szulman, 1965; Singh and Carr, 1967; Thiede and Metcalfe, 1966; Inhorn, 1967; Waxman, Arakaki, and Smith, 1967; Schlegel *et al*, 1966; Bowen and Lee, 1969; Rashad and Kerr, 1966; Stenchever, Hempel, and Macintyre, 1967; Makino, *et al*, 1964; Makino *et al*, 1967; Atkin and Klinger, 1962; Beischer and Fortune, 1968; Boué, Boué, and Lazar, 1967; Edwards *et al*, 1967; Larson, 1969; Shephard *et al*, 1968; Stonova and Selezniowa, 1968; Wieczorek, 1968; Smith, McNab, and Ferguson-Smith, 1969; Mikamo, 1970.

tors have now selected specimens for study and have collected 267 chromosomally abnormal abortuses. Of these, 51 (19.1%) were triploid but they have not yet been described in detail (Boué and Boué, 1970).

Unfortunately, many specimens are incomplete when received by the investigator. Intact sacs, without evidence of an embryo, are relatively uncommon in association with triploidy. It is recommended that embryos which are grossly abnormal in development be listed in a special category (Geneva Conference, 1966). In some cases it is impossible to tell whether an embryo is grossly malformed or deformed by maceration and many of the latter are probably wrongly classified as 'disorganized embryo'. The apparently normal embryos ranged in age from about 30 to 63 days of developmental age. There were 11 triploid embryos with a focal, external anomaly. Six of them had meningo-myelocele, one had an encephalocele, and 4 had facial anomalies including cleft lip and palate.

The most consistent phenotypic feature in triploidy involves the placenta and not the embryo. Makino *et al* (1964) reported the presence of cystic chorionic villi in 3 triploid abortuses. The association of hydatidiform degeneration and triploidy has been repeatedly confirmed and recently reviewed (Schlegel *et al*, 1966; Carr, 1969). As mentioned already, hydatidiform degeneration or frank mole was noted in 85% of our triploid specimens. Conversely, 70% of the specimens with hydatidiform degeneration (not mole) were triploid.

The mean gestational age of chromosomally abnormal specimens is significantly shorter than that of conceptuses with normal chromosomes (Carr, 1965). However, the gestational ages of the 30 triploid specimens described in this paper is almost identical to that found in 144 specimens with normal chromosomes, which was 106.7 (± 8.97 days).

It has been suggested that triploid specimens tend to manifest as 'missed abortions' (Szulman, 1965). Unfortunately, this term is used loosely in gynaecology and there is no strict definition of missed abortion. The term is generally restricted to pregnancy loss in the second trimester in which the developmental age of the fetus is 2 months less than the menstrual age. All 5 of the triploid abortuses which were lost in the second trimester of amenorrhea were missed abortions by this definition. Specimen 24 which was obtained at therapeutic abortion had a menstrual age of 58 days. If one assumes that conception occurred about 14 days after the first day of the last menstrual period, the embryo showed very little retardation in development at this stage.

Judging by the literature, as well as our own experience, tetraploidy is one fifth to one quarter as common as triploidy (Boué and Boué, 1970; Carr, 1970b). There were 7 tetraploid specimens among the selected abortuses reported here. Five were intact empty sacs and the other two were incomplete specimens. So far, there has not been a formed embryo in a purely tetraploid abortus (Carr, 1965; Boué *et al*, 1967; Gropp, 1967; Waxman *et al*, 1967; Stonova and Selezniowa, 1968; Thiede and Metcalfe, 1966; Mikamo, 1970). This does not mean that formation of an embryo is impossible in tetraploidy. However, it does suggest that tetraploidy has a more serious effect on development than triploidy. This is further supported by the mean gestational age of the tetraploid abortuses which was about one month less than that of the triploid specimens.

In spite of the severe effects of polyploidy on human development, living triploid infants have been born. Knowing the variation in all biological phenomena, it is reasonable to suppose that pure tetraploid embryos, perhaps even a living individual,

will eventually be described. A mosaic tetraploid/diploid infant has already been reported (Kohn *et al.*, 1967) and there have been several such examples of mosaic tetraploid abortuses, some with fetuses (Inhorn, 1967; Suzumori, 1968; Valenti, 1968; Citoler, Pera, and Schwarzscher, 1969).

Man seems similar to other mammals in his reaction to polyploidy. In the mouse, triploid blastocysts were about 10 times as frequent as tetraploid ones in $3\frac{1}{2}$ -day-blastocysts. It also appears that tetraploid embryos failed to progress to later stages while triploid embryos were found at 9½ days (almost mid-term). Furthermore, these embryos, though small, were developing normally (Beatty, 1957). Bomsel-Helmreich (1965) found triploid rabbit embryos at mid-term (15 days). On the other hand, Ekins and Shaver (1969) also working with rabbits, found a significant reduction in triploid conceptuses by day 10. The difference in their results may be due to the fact that the triploid embryos were in competition with diploid ones, whereas, in the studies of Bomsel-Helmreich (1965) almost 100% of the conceptuses were triploid.

Aetiology. There are various mechanisms by which triploidy can arise but they are based on one of three events: (1) The female contributes 2 haploid gametes and the male, one; (2) the male contributes 2 haploid gametes and the female, one; (3) either the male or female gamete is diploid, the other being haploid.

Tetraploidy most likely arises by failure of cytokinesis when karyokinesis occurs at the first division of the zygote. There are other possible mechanisms, however, such as fertilization of a normal ovum by three sperms. All tetraploid abortuses so far known have an XXXX or XXYY gonosomal complex so there is no reason to suspect any mechanism other than the first mentioned.

There is a known relationship in man between trisomy and increased maternal age (Penrose, 1961). However, the mean maternal age of the XXY and XXX triploids in Table V is 27.1 and 27.5 years, respectively. The mean maternal age for 18 women aborting tetraploid embryos, already referred to, was 25.7 years. Thus, there is no evidence of any maternal age effect in polyploidy. This agrees with the assessment of others (Boué, Boué, and Lazar, 1969; Arakaki and Waxman, 1970). We had 3 hypertriploid embryos and the mean maternal age was 40.7 years. This seems to reflect an ageing effect associated with the presence of one extra chromosome in addition to the triploid complement. However, the numbers are very small and the only other reported example of a hypertriploid abortus came from a woman of 25 years (Mikamo, 1970).

There appears to be a definite relationship between the post-oral contraceptive state and the tendency to triploid conceptions in man. This may also apply to tetraploidy but there were too few specimens to be significant. Possible mechanisms have been discussed elsewhere (Carr, 1970c).

There is a known increase in triploid conceptuses from rabbits and mice if fertilization is delayed for some hours (Shaver and Carr, 1969; Vickers, 1969). The importance of this factor in man would be difficult to substantiate. There is suggestive evidence that the fertilization of ageing ova greatly increases the risk of anomalous development in man (Hertig, 1967) but the possible relationship between this and polyploidy cannot be assessed with certainty.

Summary

In a selected study of spontaneous abortions, 27 triploid, 3 hypertriploid and 7 tetraploid specimens were collected. Among the triploid abortuses, 13 were 69,XXY, 9 were 69,XXX; and the gonosome complements of the other 5 were unknown. Nine embryos or fetuses, which were available for study, had a developmental age ranging from 31 to 63 days. Five of these embryos were apparently normal, two had meningocele and the other two were incomplete. Their mean gestational age was similar to that found among abortuses with normal chromosomes.

The three hypertriploid abortuses had chromosome complements 70,XXX,D+; 70,XXY,16+; and 70,XXX,16+. Only the first mentioned contained an embryo and it was grossly abnormal. The sex chromatin pattern in triploidy is irregular. The XXY triploid cells may be chromatin-positive or negative and the XXX ones may have a maximum of one or two Barr bodies.

Eighty-five per cent of the triploid and hypertriploid embryos showed hydatidiform degeneration or mole. Conversely, 70% of specimens with hydatidiform degeneration (not mole) were triploid.

None of the 7 tetraploid specimens contained an embryo and the mean gestational age was 4 weeks less than that for the triploid specimens. The increased lethality of tetraploidy over triploidy in man is similar to that found in the mouse but the reason is not clear.

The mean maternal age in polyploid abortions is not increased but the post-oral contraceptive state in man does appear to predispose to triploidy.

The findings in our 37 cases of polyploidy are comparable to those in other published examples of polyploid abortuses in man. The literature has been reviewed.

The author wishes to thank the physicians and nurses at St Joseph's and Hamilton General Hospitals, Hamilton; their cooperation made this study possible. Details of specimens, UWO were kindly supplied by Dr R. P. Singh, University of Western Ontario, London and 1D by Drs L. Weiss and M. A. Ayers of Henry Ford Hospital, Detroit. The assistance of Mrs D. Lyons, Mrs G. Feleki, and Miss E. Law is gratefully acknowledged. The manuscript was typed by Mrs S. Herman with her usual efficiency.

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