Simplified classification of spontaneous abortions

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SUMMARY A simple classification of products of conception aborted in early pregnancy is described. This classification bears a closer relation to the aetiology of the abortions and the timing of the teratological insult in those conceptuses with morphological abnormalities than have previous classifications. It is hoped it may be of value in counselling patients who abort recurrently and also in the assessment of some environmental hazards purported to cause early pregnancy wastage and congenital malformations.

Products of conception from early human pregnancies are paid scant attention by routine histopathologists. It is not infrequent to find that pathological reports of such specimens do little more than confirm that pregnancy was established. This may be, at least in part, because of the complexity of some current suggested classifications (Mall and Meyer, 1921; Fujikura *et al.*, 1966; Hertig, 1968) together with their apparent lack of relation to the aetiology of abortion. However, recent advances in clinical obstetrics, particularly the development of genetic counselling services and techniques for prenatal diagnosis, have inevitably resulted in increased public awareness of the complications of early pregnancy. This has led to greater pressures on clinicians to explain the significance of spontaneous abortion and the chances of its recurrence in subsequent pregnancies. It is customary to base any advice on purely empirical data with scant regard for the findings of the pathologist, thus implying that examination of these specimens is not worth while. Regrettably some pathologists actively foster this viewpoint in their clinical colleagues. It is illogical and inappropriate to ignore products of conception since these are clearly specific to the patient under investigation. If further abortions occur then accurate knowledge of previous conceptions may be of prognostic value. It is of little value to the obstetrician to know that a patient who has aborted earlier was pregnant. The purpose of this communication is to describe a simplified method of classification which should require neither an increase in workload nor introduction of special histological techniques and which divides the specimens into distinct groups both

pathologically and biologically. It is further suggested that recurrent abortion of a single subgroup of conceptuses is more significant than recurrent abortion of conceptuses from different subgroups.

Materials and methods

The classification is based on the study of 1025 products of conception. These were obtained from several gynaecological units, though over 90% were collected from a single unit of a large general hospital to which the majority of patients admitted to hospital for abortion in the City of Birmingham are referred. The specimens were stored fresh and unfixed in sterile containers at 4°C which were collected daily, except at weekends. All specimens were examined by the author. The material was collected fresh to enable chromosome studies to be performed but this is not an essential requirement for the classification of these conceptuses. Formalin fixed material is equally acceptable. In the majority of cases macroscopical examination of the products permits accurate classification. However, those specimens which do not include an embryo or fetus will frequently require histological examination to enable their assignment to the appropriate group.

In most instances relatively superficial macroscopical examination will reveal the nature of the conceptus, but on occasion, particularly in the presence of large quantities of blood clot, careful teasing out of the specimen may be necessary. In this situation fresh specimens are usually easier to examine and may be dissected in normal saline solution in a large petri dish before fixation. The relevant macroscopical findings are listed in Table 1.

Table 1 *Macroscopical findings in products of conception*

	Proposed grouping
(1) Gestation sac	
(A) Intact containing	
(i) Fluid only	1
(ii) Stunted, amorphous, or cylindrical embryo	1
(iii) Macerated embryo or fetus	2
(iv) Fresh embryo or fetus	3
(B) Ruptured	
(i) No identifiable cord root	1
(ii) Identifiable cord root	
(a) Macerated	1 or 2*
(b) Fresh	3
(c) Equivocal	1, 2, or 3*
(2) Embryo or fetus	
(i) Stunted, amorphous, or cylindrical	1
(ii) Macerated	2
(iii) Fresh	3
(iv) Equivocal	2 or 3*
(3) Placenta	
(i) Absent cord root	1
(ii) Identifiable cord root	
(a) Macerated	2
(b) Fresh	3
(c) Equivocal	1, 2, or 3*
(4) Curettings	
(i) Placental tissue	U*
(ii) Decidua	U
(iii) Blood clot	U
(iv) Other	U

*These specimens may be classifiable after examination of placental histology.

U, unclassifiable.

Identifiable pathological abnormalities other than those listed may be recorded but do not influence the grouping.

Microscopical examination is performed on a single haematoxylin and eosin preparation of placental tissue, the ideal block including amnion, chorion, placental villi, and the basal plate with such decidua as may be attached, i.e. a block taken at right angles to the chorionic plate.

The proposed classification is based primarily on the overall morphology of the conceptus in particular, the presence or absence of an embryo or fetus, their state of preservation, and the morphology of the placenta. It does not require detailed description of malformations or accurate assessment of the stage of embryonic development though such information may be recorded on the pathological report when appropriate.

Classification

GROUP 1: BLIGHTED OVA

- in which the majority of the villi show microscopic hydatidiform change.
- intermediate or mixed pattern (between (a) and (c)).
- in which the majority of the villi shows stromal fibrosis and vascular obliteration:

GROUP 2: MACERATED EMBRYOS OR FETUSES (normal or abnormal)

- with an embryo or fetus.
- without an embryo or fetus.

GROUP 3: FRESH EMBRYOS OR FETUSES (normal or abnormal)

- with an embryo or fetus.
- without an embryo or fetus.

Groups 2 and 3 are classified whenever possible by examination of the embryo or fetus but in their absence many cases may be placed in the appropriate group after histological examination of the placenta.

Group 1

Blighted ova are characterised by the intact sac containing clear, often slightly mucinous fluid, with no evidence of any embryonic tissue (Fig. 1). Included in this group are conceptuses with amorphous, cylindrical, or stunted embryos (Fig. 2, 3), the latter being grossly growth retarded. The histological subclassification is a further refinement but not critical for assigning cases to group 1 (Fig. 4, 5).

Group 2

Macerated embryos or fetuses are not difficult diagnostically. In many instances specimens may be accurately placed in this group on the basis of histological examination of the placenta in the absence of an embryo or fetus. The major histological features are (Fig. 6, 7): (a) collapse of the villal vasculature which may or may not contain effete red cells.

Fig. 1 *Blighted ovum aborted at 14 weeks. An intact empty sac 3 × 3.5 cm.*

Fig. 2 Amorphous/cylindrical embryo 1.7 cm in diameter aborted at 14 weeks with a sac 6.2×3.4 cm.

Fig. 3 Blighted ovum with stunted embryo 3 mm crown-rump length aborted at 10 weeks in a sac 3.0×4.0 cm (the embryo is arrowed).

(b) obliteration of the arteries of the stem villi and chorionic plate by 'obliterative endarteritis'; (c) sclerosis and fibrosis of the villal stroma; (d) increased syncytial knotting and perivillous and intervillous fibrin deposition; and (e) the deposition of calcium and iron in the villal stroma and on the subtrophoblastic basement membrane.

The entire range of histological changes described may not be seen in every specimen. Certain abnormalities such as iron and calcium deposition appear dependant on the functional maturity of the trophoblast and are, therefore, related to the gestation at which embryonic or fetal death occurs (unpublished data).

These changes are associated with intrauterine death and have been fully described by Wilkin (1965). Since the majority of embryonic or fetal deaths occur at least 1 week and often 5 or 6 weeks before abortion there is usually no difficulty in assigning cases on the basis of histology, but in two circumstances this may be difficult.

- (1) In those cases where the period of intrauterine death has been short, there may be equivocal histological changes but in such circumstances a reticulin preparation will frequently indicate early collapse of the villal stroma.
- (2) There is inevitably some overlap between group 1c and group 2 since the changes found in the former group are essentially identical to the latter though the embryo succumbs at an earlier gestation in group 1c.

Thus it is probable that the peak at approximately 16 weeks' gestation in group 2 will include some cases categorised by placental histology alone in the absence of a conceptus, which would have indicated that the correct category was group 1c.

Group 3

Fresh fetuses provide no difficulty in diagnosis. As in group 2, placental histology may be adequate to assign cases to this group, the placenta being consistent with the clinical gestation and free of secondary degenerative changes associated with intrauterine death.

Unclassifiable

A proportion of specimens will be unclassifiable because of inadequate embryonic, fetal, or placental tissue. This is most frequent when only curettings are available since the majority of these contain only decidua and endometrium.

Fig. 4 Villi from blighted ovum (illustrated in Fig. 1) under dissecting microscope ($\times 100$) showing microscopical hydatidiform change.

Fig. 5 Mixed pattern blighted ovum with villi showing microscopical hydatidiform change (A) and stromal fibrosis (B). (Haematoxylin and eosin. $\times 140$.)

Fig. 6 *Macerated fetus-placenta showing stromal fibrosis, vascular obliteration, and mineralisation of trophoblastic basement membrane (H. and E. $\times 300$.)*

Fig. 7 *Macerated fetus-placenta showing stromal fibrosis, vascular obliteration, and extensive perivillous fibrin deposition. (H. and E. $\times 120$.)*

Table 2 *Percentage distribution of 3 groups at two gynaecological units*

		Unit I	Unit II	Mean gestation (OA)
Group 1	Blighted ova	43	29	9.4
Group 2	Macerated	29	44	14.1
Group 3	Fresh	28	27	18.6

OA = ovulation age, i.e. menstrual age—2 weeks.

Results

Examination was made of 1025 specimens and of these 729 were classified. The 296 unclassified specimens included 170 decidual curettings, 72 specimens from other hospital units, 14 ectopic pregnancies, 15 therapeutic or possibly procured terminations, and 25 cases where the clinical data received with the specimens were inadequate. A further smaller series of 222 cases was classified from the Birmingham Maternity Hospital to assess the effect of differing patient populations on the proportions in each group. The distribution, as percentages, in each group is given in Table 2, together with the mean gestation (ovulation age). Fig. 8–11 illustrate the overall distribution of all cases by gestation and the distribution of the individual groups by gestation.

Three observations can be made on these results.

- (1) The reversal of the proportions of groups 1 and 2 at the two units.
- (2) The equal incidence of group 3 cases at both units.
- (3) The discrimination of the groups by gestational age.

Groups 1 and 2 would be included in Hertig and Sheldon's (1943) pathological ova group and the overall incidence of 72 to 73% is comparable with Hertig's incidence of 61.7%. The differences in the incidences of blighted ova and macerated embryos or fetuses in the two units is almost certainly the result of the differing populations served and different admission policies. Unit I only admits booked patients who are encouraged to contact the hospital via their general practitioner if any complications arise during early pregnancy. Unit II will admit any patient who is aborting but because of pressure of beds there will be a bias to the more seriously incapacitated patient and abortions occurring in later pregnancy. Furthermore delays in admission are more likely to occur in the latter group thus increasing the likelihood of passage of the products before admission. It is, therefore, important that any unit adopting the proposed classification should determine its own distribution pattern.

Fig. 8 *Macerated fetus-placenta with stem villus showing vascular collapse and stromal fibrosis. (Elastic van Gieson $\times 120$.)*

Fig. 9 Overall distribution of 1025 spontaneous abortions (menstrual age).

Fig. 10 Group 1 blighted ova, distribution (ovulation age).

COMPARISON WITH OTHER CLASSIFICATIONS
The original classification of Mall and Meyer (1921) contained 7 groups (Table 3) and excluded fresh conceptuses. This has generally been considered as over-complicated for routine pathological use. Hertig (1968) produced slight modifications to this classification but retained 7 groups. These classifications are primarily descriptive and do not relate to the gestation at which abortion occurs or to the aetiology and mechanism of abortion. Thus the first three groups show a wide gestational spread since they will include examples from each of the three

Fig. 11 Group 2 macerated fetuses, distribution (ovulation age).

Fig. 12 Group 3 fresh fetuses, distribution (ovulation age).

groups of the proposed classification. Equally the groups consisting of chorionic vesicles, with nodular stunted or cylindrical embryos all fall into group 1.

Fujikura *et al.* (1966) introduced a further simplified anatomical classification, with 4 major categories but this is open to the same criticisms as above.

BIOLOGICAL SIGNIFICANCE OF CLASSIFICATION

The earlier classifications emphasised the quality of the embryo or fetus, and the pathology of the placenta was largely ignored. This undoubtedly stems from the widely accepted notion that abortion occurs because the embryo or fetus is abnormal. The mechanisms concerned in the elimination of abnormal conceptuses

Table 3 *Classification of spontaneous abortions*

<i>Mall and Meyer (1921)</i>	<i>Hertig (1968)</i>	<i>Fujikura et al. (1966)</i>	<i>Present study</i>
1 Villi only	1 Villi only	1 Incomplete specimens	1, 2, or 3 (may be U)
2 Chorion without amnion or cyema	2 Chorion only (empty)	2 Ruptured empty sacs with or without a cord stump	1, 2, or 3
3 Chorion with amnion	3 Chorion containing amnion only	3 Intact empty sacs	1
4 Chorionic vesicles with nodular cyemata	4 Chorion, amnion, and nodular embryo	4 Embryo or fetus with or without a chorionic sac	1, 2, or 3
5 Cylindrical cyemata	5 Chorion, amnion, and cylindrical embryo	(a) Normal embryo or fetus (macrated or stunted)	1 or 2
6 Stunted cyemata	6 Chorion, amnion and stunted embryo	(b) Deformed embryo-nodular amorphous, cylindrical	1 or 2
7 Fetus compressus	7 Chorion, amnion, and macerated fetus	(c) Malformed embryo	1 or 2
		(d) indeterminate	1 or 2

are ill understood but it is logical to expect that the placenta will play a major role, in that it is the source of the hormones that are concerned in maintaining an intrauterine environment suitable for the continuation of pregnancy. It is common knowledge that intra-uterine death of the embryo or fetus does not result in immediate expulsion of the conceptus. The proposed classification indicates that there are three basic patterns of abortion with relatively specific distribution curves. These are gestation related and it is, therefore, likely that they reflect the timing and severity of the insult to the conceptus. Data will be presented elsewhere to show that groups 1 and 2 are the result of failure of establishment of a normal maternal circulation in the placenta, together with an absent or hypoplastic villal circulation in the former, and to the effects of cessation of the villal circulation after intra-uterine death in the latter group. In both instances this presupposes that the primary defect in these pregnancies is in the conceptus and not the uterine environment. In group 3 the pathological evidence suggests that development proceeds normally until the time of abortion and in these cases the underlying aetiological factors are considered to be environmental.

The relation between chromosomal abnormalities, anatomical malformations, and metabolic disorders of the conceptus and abortion is yet to be clarified. It is evident that there is a high degree of selectivity in the elimination of individual abnormalities and malformations (Nishimura *et al.*, 1968; Rushton, 1968) but the variation in the survival rates of differing abnormalities and the determinants of survival or abortion are ill understood. While it is not difficult to accept that a blighted ovum with no embryo will be aborted, it is extremely difficult if not impossible to sustain a logical argument to explain why some relatively minor malformations such as hare-lip or polydactyly should be aborted. Hare-lip is 8.3 times as frequent in the second month of pregnancy than at term and polydactyly 9.3 times as frequent (Nishimura *et al.*, 1968). It is apparent that the proposed classification does not identify the underlying cause of abnormal development or fetal death, though it is to be expected that

there will be a high proportion of chromosomal abnormalities in group 1 (Mikamo, 1970).

However, this does not necessarily imply that classification will be without prognostic value since with a few exceptions it is unusual for recurrent abortions to show identical defects (Wilson, 1969; Lucas *et al.*, 1972; Kohn *et al.*, 1975; Tsenghi *et al.*, 1976). Only group 3 cases show any consistent pattern, e.g. recurrent abortion associated with cervical incompetence. Since the factors concerned in the production of abnormalities in the conceptus are complex and their effects vary with the timing of the teratological insult, similar circumstances may produce differing abnormalities. However, if there are final common pathways of abortion, as this classification implies, and they are related to the gestation at which abortion occurs and thus to the timing of the insult then it seems logical to expect a patient showing a consistent pattern of recurrent abortion of one group of the classification to have a different prognosis from a patient who aborts successive pregnancies in different groups. Furthermore, recurrent abortion of groups 3 conceptuses must be a clear indication to investigate the genital tract in an effort to identify local environmental factors responsible for abortion.

The pathological features that indicate the classification of aborted conceptuses are not a complete catalogue of lesions found in products of conception. However, other lesions such as microscopical, partial, or macroscopical molar degeneration, maternal floor infarction (Benirschke and Driscoll, 1967), and subchorionic haematoma (Shanklin and Scott, 1975), chorioamnionitis, villitis, decidual lesions, and specific malformations of the embryo or fetus do not affect the classification, though they may, on occasion, give an indication of the aetiology of the abortion.

It is, as yet, too early to estimate the overall effectiveness of this classification in counselling patients who abort recurrently since it will take several years to accumulate adequate data. The incidence of habitual aborters in the current series was only 1.3% of patients. It does, however, provide a possible

method by which account of the nature of aborted products of conception can be taken in the assessment of the reproductive outcome of the few unfortunate patients who are classified as habitual aborters.

It is also hoped that this classification may be of value in the assessment of other hazards arising in early pregnancy which may influence the abortion rate or the nature of the conceptus. The total clinical abortion rate must be considered a very crude indicator of disturbances occurring in early pregnancy since aborted products of conception are clearly a very heterogeneous population. Furthermore, clinically apparent abortions are a highly selected group (Rushton, 1975). Thus, changes in the distribution between different groups may be of far greater significance than changes in the overall abortion rate. Thus a consistent increase in the relative proportions in groups 1 or 2 may be the result of the effectiveness of a therapeutic regimen in preventing some group 3 losses or alternatively it might be the initial indication that a new teratogenetic hazard has arisen.

Recent controversy over the role of anaesthetic pollution and abortion rates in exposed theatre staff is based entirely on statistical evidence obtained from relatively small numbers of patients. There is no information as to the nature of conceptuses aborted in these patients (Cohen *et al.*, 1974; Knill-Jones *et al.*, 1975).

Roberts and Lloyd (1973) have suggested that the wide variations in the incidence of anencephaly may at least in part, result from alterations in the selectivity of the process of elimination. In order to assess such a hypothesis proper knowledge of the local incidence of malformations in abortions is required.

Finally it has become very important to assess the relative risks and advantages of diagnostic amniocentesis. A significant proportion of patients (compared with those in which an abnormality is diagnosed) having an amniocentesis will subsequently abort (Medical Research Council of Canada, 1977), yet it is often difficult if not impossible to obtain any information about such conceptuses. It seems essential that these should be adequately examined to decide whether the abortion is related to the procedure or might have occurred in any event. Equally a significant number of therapeutic terminations performed for non-genetic social indications will show evidence of pathology which suggests abortion was inevitable (unpublished data).

The author wishes to thank all those obstetricians and gynaecologists who co-operated in the collection of these specimens and those pathologists who allowed him to examine them. Part of this study was financed by a grant from the United Birmingham Hospitals

Endowment Fund. I also wish to thank Mrs O. Brooke for her help in the preparation of this manuscript.

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