The aetiology of abortion in a rural community*

P. R. GROB, M.D., M.R.C.G.P., D.Obst.R.C.O.G.
Addlestone, Surrey

THE treatment of a patient with abortion poses a constant problem to general practitioners and obstetricians alike. Often no cause can be found and only general advice, based on probability, can be given for future pregnancies.

The aetiology of an abortion is found afterwards with all the dangers of *post hoc* argument. Care must be taken in extrapolating from experimental studies on foetal wastage in animals, as there are considerable physiological differences between species.

The uncertainty about the cause of abortion is reflected in the widely different treatments offered to patients who abort, Javert (1957), anatomical; Holmes (1956) genetic; Polani; (1966) hormonal; Wood *et al.*, (1961) and infective factors (Dudgeon, 1966). There must however, be many extra and intra-uterine factors which could adversely affect foetal development which are not yet known.

In this study aborting patients admitted to hospital during a 16 month period were classified.

Patients

Patients who aborted at St Peter's Hospital, Chertsey, Surrey between January, 1967 and May, 1968 were studied, 222 in all. Anamestic data were recorded about past and present pregnancies, maternal diseases, and exposure to possible harmful influences, drugs, radiation, trauma and infective agents. The socio-economic group was determined. Patients having therapeutic abortion were excluded from the survey and care was taken to determine if the abortion had been induced criminally. Anamestic data were compared with a control group matched for parity, and age, who conceived at the same time but had a normal pregnancy.

Methods

After the evacuation of the uterus, usually at operation, foetal and placental tissue were examined macroscopically and classified according to the recommendation of the *World Health Bulletin* (1966).

1 *Viral studies on the abortions*

The abortus material was collected in dry sterile containers and kept at 4° Celsius, when possible, tissue, from foetal organs was cultured separately. Foetal tissue was macerated to make a ten per cent suspension in Hanks B.S.S., after centrifugation the supernatant fluid was inoculated into five cell lines, monkey kidney, human embryonic lung fibroblasts (W.I. 38), human amnion cells , the R.K.13 strain and Hela cells. Intra-cerebral inoculation of suckling mice was also undertaken.

Cell cultures were passaged blindly for six weeks before being regarded as negative. Paired sera were used for confirmatory evidence of viral infection.

2 *Viral studies in the community*

During the survey period the incidence of viral diseases was recorded. In some easily recognisable diseases like measles or chickenpox this was based on clinical assessment. In diseases which produced a less definite syndrome, such as the respiratory and entero-

*Based on work submitted to London University for the M.D. degree.

viruses, viral isolation and confirmatory serology were used to identify outbreaks in the community.

RESULTS

The analysis of the anamestic data was as follows:

There was no difference between the aborting group of patients and the control group with regard to socio-economic and ethnic groups, maternal and paternal age, blood groups and disease morbidity.

TABLE I

PREVIOUS PREGNANCY EXPERIENCE OF ABORTION PATIENTS

Outcome of previous pregnancies	*Pregnancy order of index abortion*										
	1	2	3	4	5	6	7	8	9	10	*Total*
Male and female live births	0	54	57	51	19	14	0	11	0	14	220
Stillbirths	0	0	1	1	0	1	0	0	0	0	3
Abortions	0	6	12	14	13	4	0	1	0	4	54
Malformations	0	0	0	0	0	1	0	1	0	0	2
Pairs of twins (included in the above)	0	0	2	0	0	0	0	0	0	0	2
Total past pregnancy experiences (abortions, live and stillbirths, malformations)	0	60	70	66	32	20	0	13	0	18	279
Past abortions expressed as a percentage of total past pregnancy experience	0	*10·0*	*17·3*	*21·1*	*41·2*	*20·0*	0	*7·6*	0	*41·0*	*19·4*
Average age	26·8	28·5	32·5	33·0	33·3	30·5	0	38·0	0	37·0	32·6
Index abortion	64	61	34	22	5	4	0	2	0	2	194

The outcome of previous pregnancies in the aborting group is shown in table I, and shows a high rate of foetal wastage, 19 per cent of previous pregnancies ending in an abortion.

TABLE II

DURATION OF SPONTANEOUS ABORTIONS (IN WEEKS FROM LAST MENSTRUAL CYCLE)

	Weeks of pregnancy																				
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
No. of cases	3	4	6	14	27	42	39	11	8	6	9	3	3	1	4	1	4	4	3	0	1

The duration of the pregnancy as expressed as the interval from the first day of the last normal period to the abortion is shown in table II. The exposure to viral infections did not differ from the control group, but in both groups there was a higher exposure to infection in multiparous women (72 per cent) as compared with primiparous women (54

per cent). No patient was x-rayed while pregnant and none had an occupation which exposed her to irradiation, though one patient was exposed to the toxic effects of selenium dust.

Patients were classified into the following groups according to aetiology.

Criminal abortions

Twenty-eight (13 per cent) of the total sample of 222 patients were thought to have had criminal abortions as active measures had been taken to terminate the pregnancy.

This classification was based on either direct evidence from the patient herself, or the presence of sepsis, pyrexia or evidence of intra-uterine trauma.

(*a*) *Marital status, age and parity*

Patients with a criminal abortion fell mainly into three groups.

(*i*) *Single women.* These were young women (average age 19—S D 1·3) and comprise 11 (39 per cent) of the 28 cases; of these eight were primigravida.

(*ii*) *Married women.* These were an older age group (average age 38—S D 6·9) and who had three or more children.

(*iii*) *Others.* Six women had conceived extramaritally.

(*b*) *Duration of pregnancy*

Eighteen (64 per cent) had aborted themselves by the end of the first trimester, the remainder induced their abortions in the middle trimester, in effect by the introduction of infection into the uterus.

(*c*) *Clinical condition*

This varied from one patient *in extremis* with generalized septicaemia to good health.

The temperature on admission is given in table III; 17 patients had a temperature of 37·2° Celsius (99°F) or over. Fourteen patients required antibiotic therapy. Four presented with a degree of anaemia inconsistent with the alleged length of bleeding and required transfusion. No viruses were isolated from the abortuses although one patient had an intercurrent gonococcal infection.

TABLE III
TEMPERATURE ON ADMISSION WITH A CRIMINAL ABORTION

Temperature on admission in degrees Celsius	*Number of patients*
36·6 (98°F)	11
37·2 (99°F)	7
37·7 (100°F)	5
over 37·7 (100°F)	5

Spontaneous abortions

The remaining 194 patients were regarded as having had a spontaneous abortion, and were classified as follows:

(*a*) *Defective ova and trophoblast*

The macroscopical appearances of the abortuses are described in table IV. Twelve of the abortuses were abnormal macroscopically, two had multiple abnormalities, one was an

TABLE IV

MACROSCOPIC APPEARANCE OF THE ABORTUSES

Incomplete specimens (obtained by curettage)	111	*58·5*
Ruptured sac.: total number	15	*7·6*
(a) with cord stump	13	
(b) without cord stump	2	
Intact empty sac	6	*3·5*
Embryo present: total number	58	*29·1*
(a) normal embryo	16	
(b) macerated embryo	30	
(c) abnormal embryo	12	
(i) multiple abnormalities	2	
(ii) stunted embryo	8	
(iii) cord abnormalities	2	
Hydatidiform mole	3	*1·3*
TOTAL	194	*100%*

anencephalic with a bifid spine, and the other had a bilateral hare lip, umbilical cysts and leg deformities. They were of the correct size for their gestational ages; this was in contrast to the remaining eight abortuses in which the foetus was markedly stunted, consisting of a nodular mass of tissue with only a vague foetal shape.

Chromosomal analysis showed three abnormalities, trisomies of the A and G groups, and an XO karyotype. Four of the foetuses had a normal karyotype and the remaining five failed to grow.

Abnormalities of the cord were present in two cases: one had numerous vesicular cysts along its length and the foetus was absent; the other was abnormally long, three times the crownrump length, and was wound round the foetal neck and limbs.

Chromosomal anomalies. Eighty-three abortuses (43 per cent) were suitable for chromosomal analysis; of these 33 (40 per cent) grew successfully. There were nine chromosomal abnormalities detected; the relevant data are shown in table V.

(*b*) *Maternal infection*

(*i*) *Bacterial infection.* One abortion was due to bacterial infection; it occurred in a patient who developed acute pyelonephritis. *E. Coli* were isolated from the foetus, liquor and vagina. The foetus was of the correct gestational size and had a normal karyotype (46 XY).

(*ii*) *Viral infection.* Cases were divided into two groups because of the difficulty in the exact significance of viral isolation and serology. First, cases in which a viral infection was the most probable cause of the abortion; this group includes patients in which either the virus was isolated from the abortion or there was a fourfold rise in the antibodies to a known harmful virus (table VI, cases one to six).

The second group consists of either patients who had experienced a viral infection and subsequently aborted or those cases in which a virus was isolated from the abortus, i.e. *Herpes virus hominis*, but in which vaginal contamination must be considered (table VI, cases 7 to 21).

With regard to viral serology, the acute specimen was obtained from the patient at the time of her abortion which in some cases was several weeks after the viral infection.

Rubella—Only two of the 11 cases ascribed to rubella showed the clinical syndrome;

TABLE V
CHROMOSOMAL ABNORMALITIES

Case number	*Age*	*Blood group*	*Previous obstetric history*	*Duration of pregnancy*	*Macroscopic appearance of abortus*	*Chromosomal abnormality*
1	38	AB−	Gravida 3	10 weeks	curettings only	XO
2	27	O+	Primi-gravida	11 weeks	curettings only	Model No. 92, XXYY, Tetraploid
3	27	A+	Gravida 1	8 weeks	curettings only	XO
4	24	O+	Gravida 1	15 weeks	normal foetus	Mosaic-90% cells were normal female; 10% of cells were monosomy E (probably 16)
5	23	O+	Gravida 1	20 weeks	placental tissue only	Model No. 69, XXX Triploid
6	35	A+	Gravida 2	10 weeks	abnormal stunted embryo	Trisomy G; XY
7	24	B+	Gravida 1	10 weeks	curettings only	Trisomy D; XX
8	22	A+	Gravida 1	14 weeks	abnormal embryo	Trisomy A_2; XX
9	36	A+	Gravida 1	12 weeks	curettings only	Trisomy E; XY (trisomy of 16)

the course of the disease may have been modified in the remaining nine cases as all but one of the patients were given gamma globulin 750 mg immediately after exposure to the infection. Three of these 11 patients were primigravidae and six patients had been infected by their own children.

In one patient (case 2) the possibility of pre-conceptual rubella was considered. When six weeks pregnant she was exposed to rubella; gamma globulin 750 mg was given eight days after exposure. She remained asymptomatic but aborted five weeks later; the rubella virus was isolated from the abortus, and her serum showed a rising titre of rubella antibodies. Inadvisedly she conceived again when she next ovulated some two to three weeks later. She had an apparently normal pregnancy but the foetus died early in the first stages of labour, and she was delivered of a fresh stillborn female infant, with a birth weight 3210 grams. A necropsy showed a heart lesion, and atrial septal defect of the secundum type one cm in diameter was present. No other abnormality was detected, and extensive viral investigation failed to isolate the rubella virus from any of the foetal organs. In view of this and the birth weight it was concluded that rubella was probably not the cause of the stillbirth.

Herpes simplex. Herpes virus hominis was isolated from the abortus in two cases; neither patient had any clinical evidence of herpetic infection. Further investigation eight weeks after the abortion failed to isolate *Herpes virus hominis* from the vaginal flora and cervical smears were normal.

Influenza. A small outbreak of *Influenza A2 virus* occurred in January 1968 and caused five abortions, probably more by the fever and toxaemia of the infection than by direct viral invasion of the foetus.

Mumps. One patient contracted mumps whilst 18 weeks pregnant. Foetal movements were not felt and the uterus did not increase in size. Seven weeks later she aborted, passing a small macerated foetus. The mumps virus could not be isolated from the abortus, but maternal antibody tests confirmed a recent mumps infection.

TABLE VI

ABORTIONS DUE TO VIRAL INFECTIONS

Case number	Virus	Clinical syndrome	Time interval between viral exposure and abortion	Viral isolation		Serology*	
				(i) *from foetus*	(ii) *from mother*	*Acute*	*Convalescent*
1	Rubella	absent (g)	3 weeks	†	—	32	32
2	Rubella	absent (g)	5 weeks	†	—	neg	32
3	Rubella	absent (g)	20 weeks	†	—	512	512
4	Rubella	present (g)	1 week	—	†	64	3840
5	Rubella	present	2 days	—	†	64	512
6	Rubella	absent (g)	1½ weeks	—	—	64	512
7	Rubella	absent (g)	2 weeks	—	—	256	512
8	Rubella	absent (g)	5 weeks	—	—	256	64
9	Rubella	absent (g)	2 weeks	—	—	128	512
10	Rubella	absent	5 weeks	—	—	512	512
11	Rubella	absent (g)	3 weeks	—	—	125	512
12	Mumps	present	7 weeks	—	—	v=320	s-160
13	Herpes Simplex	absent	not known	†	—	10	10
14	Herpes Simplex	absent	not known	†	—	20	10
15	Influenza A2	present	12 hours	—	†	both sera anticomplementary	
16	Influenza A2	present	2 days	—	†	neg	160
17	Influenza A2	present	3 days	—	—	neg	20
18	Influenza A2	present	7 days	—	—	20	80
19	Influenza A2	present	5 days	—	†	not done	
20	Para-influenza III	present	4 days	—	†	neg	160
21	Infective Hepatitis	present	10 weeks	—	—	not done	

† indicates virus isolation
(g) indicates administration of gamma globulin
* expressed as the reciprocal of the titre.
Antibody tests used: Rubella—Haemagglutination inhibition antibodies.
Influenza—Complement fixation antibodies.
Herpes virus hominis—Complement fixation antibodies
Parainfluenza—Complement fixation antibodies
Mumps—Complement fixation antibodies.

Others. In two further cases a viral aetiology was considered; one patient aborted during a respiratory illness caused by parainfluenza III infection and another woman contracted infective hepatitis and aborted shortly afterwards.

Community infection. The abortions caused by rubella and influenza corresponded with outbreaks of the infection occurring simultaneously in the surrounding area.

(c) *Uterine abnormalities*

(i) Congenital uterine abnormalities were detected twice; one patient had an incomplete uterus septus and aborted at ten weeks. The conceptus was lodged in the left side of the

uterus and she had bled intermittently throughout her pregnancy; the other patient had a subseptate uterus.

(ii) Cervical incompetence caused seven abortions (four per cent); one patient aborted twice during the survey. These abortions with one exception occurred in the middle trimester of pregnancy, with an average duration of pregnancy of 17 weeks; the foetuses were fresh and of the correct gestational size, with a normal chromosomal complement.

Five of these patients had experienced a previous gynaecological operation, usually dilatation and curettage for dysmenorrhoea.

(c) Fibroids were present in four women, but in only one case was it thought that they caused the abortion.

(d) Uterine retroversion was present in 18 women (nine per cent) but in only four cases (two per cent) was retroversion the probable cause of the abortion. In two patients the uterus had become incarcerated and in two the patient aborted shortly after her retroversion had been corrected.

(d) Generalized maternal disease

No patient suffered from any systemic disease severe enough to cause her abortion. It was thought two abortions were caused by severe rhesus factor immunization; both cases had a history of a rising titre of rhesus antibodies causing progressive harm to each pregnancy.

(e) Maternal trauma

A vague history of trauma preceding the abortion was not uncommon (nine per cent) but the length of the time relationship, or the minimal nature of the trauma made it unlikely that it could have had any harmful effect on the pregnancy.

Four more cases had a more definite history of trauma, but in only one patient, a woman who fractured her pelvis and aborted an hour after the accident, was it thought that the trauma was the cause of the abortion.

(f) Miscellaneous

(i) Some abortions were associated with a retained intra-uterine contraceptive device (IUD).

The exact mechanism by which an IUD prevents conception is not fully understood; it must interfere with implantation or induce an early rejection of the ova. It would follow that an IUD which has failed to prevent conception may dispose toward that patient aborting at a later date.

Three patients had an IUD *in situ* at the time of the abortion; two had a Lippes loop which remained *in situ* at the time of the abortion, and the third had a Marguilles spiral which was expelled with the abortus.

(ii) Selenium poisoning. The toxic effect of selenium powder was carefully investigated in one patient. She worked in a laboratory using large quantities of sodium selenite powder in the preparation of selenite broth. She was exposed to the selenium powder for the first eight weeks of her pregnancy and aborted spontaneously at 16 weeks. The obstetric history of her fellow workers was bad. During the preceding five years, five pregnancies had occurred; one woman had conceived twice. One pregnancy ended in an infant with bilateral club feet; the remaining four pregnancies all ended in abortion.

At necropsy no macroscopical abnormalities were detected in the foetus or placenta. Chromosomal analysis revealed two abnormalities: (a) In one cell there were only 45 chromosomes, the missing chromosome coming from the G group. There was also an acentric fragment. (b) In two cells in the E group the chromosomal structure was abnor-

mal. Unfortunately, despite neutron activation analyses, atomic absorption spectroscopy, fluorimetric and colorimetric methods, it was not possible to obtain any reliable results in the tissue levels of selenium in the aborted foetus.

Discussion

An aetiological factor was found in 101 (46 per cent) of the total sample of 222 cases of abortions under investigation. This work was undertaken before the Abortion Act became effective, and the morbidity caused by the criminal abortions was a matter for concern.

It is suggested that the 13 per cent of criminal abortions is an accurate measure in the sample studied but it must be an underestimate in the general community; when the sample was stratified for socio-economic classes, there was a deficiency in the social classes I and II suggesting that these groups were more efficient at avoiding the complications of induced abortion.

An abnormal embryo or trophoblast has been found in a large number of early abortions, the exact percentage varies according to the classification of individual authors (Javert, 1957). This classification, which has essentially an anatomical basis, may now be expanded by chromosomal analysis.

In this series nine out of 33 (28 per cent) of the abortuses had an abnormal chromosomal complement, and this is in keeping with other findings (Dhadial *et al.*, 1970).

An additional number of abortions must fall into this category, had it been possible to grow tissue from them for chromosomal analysis. Recent work (Boué and Boué, 1970) has suggested that as many as 51 per cent of early abortions have chromosomal anomalies.

These abortions are usually non-recurrent and the patient may therefore be reassured about future pregnancies. Active treatment to save the foetus is not indicated in this group; this is in contrast to abortions occurring in the middle trimester of pregnancy when the anatomical causes, especially the incompetent cervical os, occur. In this group the foetus appears fresh, and is of the correct gestational size with a normal chromosomal complement. Anatomical causes of abortion are recurrent and active operative treatment is indicated.

Infective causes account for about ten per cent of spontaneous abortions and it is suggested that the commonest outcome of a viral infection in early pregnancy is an abortion. Rubella and influenza both cause abortions, as probably do other common viral infections.

The administration of gamma globulin to women exposed to rubella does not seem to protect the foetus, and may well convert a clinical infection to an asymptomatic one. Stoller and Collmann (1965) demonstrated an association between the viral infection, infective hepatitis and the occurrence of Down's syndrome. There was no evidence to suggest that the group of abortuses with a chromosomal anomaly had experienced a preceding viral infection, nor were the foetuses from the abortion due to viral infections, chromosomally abnormal.

A patient will often attribute her abortion to some preceding injury, but critical review of this data suggests that trauma is a rare cause of an abortion.

The toxic effect of selenium powder on the foetus rests on circumstantial evidence, but it is obvious that pregnant women should avoid such potential hazards. The investigation of the cause of abortion is difficult, as an aetiological factor is often based on circumstantial evidence, but it is suggested that the family doctor, because of his knowledge of the ethnic and social background of his patient, the course of her early pregnancy, and

the prevalence of infections in the community, is in the best position to undertake such an investigation.

Summary

The cause of 222 abortions occurring in a rural district was investigated. An aetiological factor was found in 46 per cent and the practical significance of this is discussed.

Acknowledgements

I am deeply indebted to Mr P. R. Norris and the gynaecological staff of St Peter's Hospital for their continuous help. My sincere thanks are extended to Dr G. T. Cook, Director of the Public Health Laboratory, Guildford, and his technical staff who gave generously of their time and skills, and to Professor P. E. Polani, Mrs A. M. Machin and Dr R. K. Dhadial of the Paediatric Research Unit, Guy's Hospital, for their valuable assistance in the chromosomal studies. I would like to record my gratitude to Professor W. J. H. Butterfield, Professor of Medicine, Guy's Hospital, without whose continuous help and encouragement this project would not have been undertaken.

References

Boué, J. G. & Boué, A. (1970). *Presse Médicale*, **78**, 635–641.
Dhadial, R. K., Machin, A. M. & Tait, S. M. (1970). *Lancet*, **2**, 20–21.
Dudgeon, J. A. (1966). *Proceedings of the Royal Society of Medicine*, **59**, 1084–1087.
Holmes, J. A. (1956). *British Medical Journal*, **1**, 1144–1147.
Javert, C. T. (1957). *Spontaneous and Habitual Abortion*. New York: McGraw-Hill Book Co. Inc.
Polani, P. E. (1966). *Developmental Medicine and Child Neurology*. **8**, 67–70.
Stoller, A. & Collmann, R. D. (1965). *Lancet*, **2**, 1221–1223.
Standardization of Procedures for Chromosome Studies in Abortion (1966). *Bulletin of the World Health Organization*, **34**, 765–782.

Requests for reprints should be addressed to:
P. R. Grob, M.D.,
Devonshire House,
Addlestone,
Surrey.

ABORTION IN GENERAL PRACTICE

As part of a national study of birth control services in 52 areas of England and Wales, 900 randomly selected general practitioners in the areas were sent postal questionnaires in late 1970. Twelve per cent of the respondents expressed a conscientious objection to abortion.

A substantial minority of the general practitioners (35 per cent) were in favour of abortion on request. One third of National Health Service referrals were, by their estimates, turned down. Half of the doctors faced with this situation did nothing further towards arranging an abortion, almost one third referred these patients privately, and one in ten referred them again within the National Health Service.

Waite, Marjorie & Cartwright, Ann (1971).

General practitioners and birth control advice in 1970/71. Paper read at XV Annual Meeting Society for Social Medicine.

BIRTH RATE IN THE UNITED STATES

The birth rate in the United States fell from 18·2 per thousand people in 1970 to 17·2 per thousand in 1971. This is the lowest level for more than 150 years.