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H. J. Huisjes

SPONTANEOUS ABORTION

Churchill Livingstone



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Spontaneous Abortion

Series Editor

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Spontaneous Abortion

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Foreword

No aspect of pregnancy has received as little attention as the first trimester; indeed in many areas it is the practice to admit patients threatening to abort to a gynaecological unit rather than a maternity hospital with the implied suggestion that such women have not yet become 'obstetric' problems. This attitude has been reinforced by the fact that a minority of women are referred to an antenatal booking clinic before 10 weeks gestation and many not until the first trimester has passed. These attitudes are changing and it is becoming accepted that the first trimester is a time of considerable importance. Not only is organogenesis completed within this phase but about 30% of all human conceptions are lost during these early weeks. It is the practice to express perinatal mortality per thousand births so in equivalent terms loss from spontaneous abortion is 300 per thousand — a figure which makes all other causes of pregnancy loss pale into insignificance.

The first trimester is a difficult time to investigate both from an ethical viewpoint and because many women miscarry at or shortly after the time they appreciated conception had occurred; nevertheless it is difficult to excuse the lack of knowledge about this phase of human development. Much is made of the role of 'fetal abnormality' or 'uterine abnormality' as a cause of spontaneous abortion — but how good are the data supporting such suggestions? What is the obstetric prognosis for a woman who had had one or more previous spontaneous abortions; do environmental and other influences induce abortion — and so on.

Prof. Huisjes is professor of obstetrics and gynaecology at Groningen University, Holland, and has had a considerable interest in these and other questions for many years. He has compiled data from a huge reference base and presents the evidence in a concise

Foreword

and balanced way making the various chapters easy to read and assimilate; I do not think the subject has been so thoroughly dealt with in any previously published work. This book should not only be of immediate benefit to those working towards higher qualifications in obstetrics and gynaecology but should be an invaluable reference work to those practising in this speciality.

Newcastle upon Tyne
1984

Tom Lind

Preface

'I have chosen this topic for the reason that, as I look back over my experience in the medical profession . . . I recall nothing which in times past has caused me more anxiety and doubt, or in regard to which I have found it more difficult to get any satisfactory rules from books, than the treatment of abortion.'

T. Gaillard Thomas, 1894

The number of books on spontaneous abortion is small. The most recent one that more or less covers the subject is *Embryonic and fetal death* (1980), a compilation of contributions edited by I H Porter and E B Hook. Earlier monographs are C T Javert's well-known *Spontaneous and habitual abortion* (1957) and the comprehensive and scholarly volume by F J Taussig, *Abortion, spontaneous and induced. Medical and social aspects* (1936). A detailed and up-to-date discussion of the aetiology of miscarriage is not to be found in any of these books or in textbooks of obstetrics. The present book attempts to pay ample attention to aetiology, and is written by an obstetrician for obstetricians.

It might be argued that the aetiology of abortion relates to so many medical disciplines, including epidemiology, genetics, pathology, reproductive endocrinology and immunology, that it would be better treated by several specialists. In a sense this is undoubtedly true: the knowledgeable reader will certainly find deficiencies which arise from the author's lack of in-depth knowledge. On the other hand, a holistic approach means that the subjects covered are not determined by the number of existing disciplines, which would leave the coverage incomplete. Another possible advantage is that the questions asked are not primarily those of the scientist, but of the clinician, and the answers are

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formulated accordingly. I hope that I have made the most of these advantages.

This book would not have been written without the opportunity given to me by the University of Michigan, USA, and the Dutch Government, to spend the better part of a year in Ann Arbor, Michigan. The hospitality of the Department of Obstetrics and Gynecology and its Chairman, Dr Alan E. Beer and, certainly not less important, of the marvellously well-supplied libraries of the University of Michigan, in particular the Taubman Medical Library, are gratefully acknowledged. I thank also Drs Iain Chalmers, Richard E. Lappöhn, Tom Lind, Zena A. Stein and Patricia Yudkin, who read the penultimate version of the manuscript or portions of it and provided their comments. Obviously, any remaining inaccuracies or omissions are my responsibility.

Groningen, 1984

H.J.H.

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Introduction

In daily obstetric practice, spontaneous abortion is usually considered a minor problem. It is hardly life-threatening, and diagnosis and therapy are straightforward. Serious complications are rare: only septic abortion and recurrent or 'habitual' abortion pose major problems for the obstetrician's skills, but septic abortion has virtually ceased to be seen in countries where induced abortion has been legalised. Nevertheless even solitary, early and uncomplicated abortion is an important aspect of reproductive failure in its wider sense, for several reasons.

First, it is of paramount importance to realise that every phase of the reproductive process is part of a continuum. We are inclined to divide and subdivide pregnancy and delivery into many separate entities for the sake of scientific analysis and classification. This may be necessary, but it distracts our attention from the fact that complications in late pregnancy may have their foundations in the early weeks. Pre-eclampsia, for instance, used to be seen as a gestosis characteristic for the third trimester. The work of Brosens et al (1972) has shown that it probably has its roots in the very early stages, when sections of the spiral arteries fail to become invaded by cells migrating from the trophoblast into the deeper layers of the endometrium. Indeed, for a time abortion 'belonged' to gynaecology and preterm birth to obstetrics, but women who have earlier miscarried are predisposed to preterm birth, and somewhere there must be a pathophysiological connection between the two. Spontaneous abortion is a manifestation of early pregnancy pathology and it should be studied not only for the sake of its clinical problems, but even more because of the possibility that it expresses fundamental disorders of the reproductive process.

Second, there is hardly an aspect of reproductive medicine in

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which so many methodological mistakes have been made so persistently. Conceptual misunderstandings and heuristic fallacies have resulted in large scale-clinical maltreatment, not only in the past, but up to the present day. This may be understandable to a certain extent when one realises that it was a chore for the obstetrician almost completely lacking any insight in the causes of abortion to be confronted with the despair of women suffering miscarriage after miscarriage. But it did lead to calamities such as DES-treatment and to the perhaps lesser evil of scores of unwarranted 'therapies' for 'habitual' abortion. There is every reason to try to understand the aetiology of abortion, because that is the only sound basis for treatment. Fortunately, an important improvement has been achieved in the past decade with the discovery of chromosomal errors as a frequent feature in early abortion. This has at least brought home the limitations of treatment.

Third, it has been suggested (Oakley, 1975; Kline et al, 1977; Warkany, 1978) that analysis of aborted material may be useful in detecting teratogenic agents. The thalidomide tragedy has demonstrated that it may take months or even years to trace the origin of severe and conspicuous congenital malformations. If such anomalies can be found in abortuses, it should be possible to reduce the delay by several months. This presupposes systematic and large-scale monitoring of abortions, which is even more difficult than monitoring of congenital anomalies. In addition, however, it might have associated uses for the study of the aetiology of abortion.

Lack of time and space have made it necessary to restrict the treatment of the subject. Most attention is paid to the causes of abortion. Structural and genetic abnormalities are not causes in the strict sense: they may occasion the death of the embryo or fetus* but are themselves the result of other, for the most part yet undisclosed, failures of the genetic and developmental processes. These will be discussed in a separate chapter. Treatment and diagnosis are dealt with in relation to specific causes, and in a more general fashion in the chapter on clinical management. Routine treatment has not been extensively discussed; surgical procedures,

* The semantic difference between 'embryo' and 'fetus' will not be consistently observed in the following chapters to avoid endless repetition. The term 'embryo' will be used whenever the embryo proper is specifically meant, i.e. not including the trophoblast, and during the first three months; 'fetus' will at times stand for both embryo and fetus.

for instance, have not been illustrated. On the other hand, controversial issues have been given ample space.

Epidemiology

Spontaneous abortion is a nosological entity only in so far as it means the expulsion of a product of conception before it has acquired viability. It can have many causes, different pathological substrates and varying clinical manifestations. One might stress its importance by putting it on a par with arthritis, cancer and even disease and death, rather than with more circumscribed conditions such as lobar pneumonia or duodenal ulcer. Obvious as this may seem, this notion seems to have escaped completely all those who have littered obstetric literature with reports on the therapeutic effects on abortion in general of certain measures or drugs, especially sex steroids. Clearly, treatment will be of no avail in those cases, for instance, where the embryo is absent in the first place. Any trial concerning treatment should take into consideration the cause of abortion, that is, it should be restricted to one of the many types of abortion.

Pre-implantation loss and occult abortion

To place both the definition and the incidence of abortion in a proper light, it is necessary to discuss briefly what may happen to a human ovum after fertilisation. In the first place, most ova are not fertilised. Fecundability, that is the probability of pregnancy per menstrual cycle given optimal conditions, is about 25%. This is based on several epidemiological studies in communities where no contraception was practised (Short, 1976). Hertig (1967), in his well-known analysis of 34 fertilised ova recovered from 211 hysterectomy preparations, gives a higher estimate: the probability of conception is 85%. However, 10 to 15% of fertilised ova

degenerate before implantation, and 30% after implantation but before menstruation is missed, resulting in a fecundability of about 42%. The incidence of 30% post-implantation degeneration has recently been confirmed in a prospective study with the use of a radioimmunoassay of beta-HCG in urine during the luteal phase (Miller et al, 1980). Philippe (1980) found as many as 30 abnormal ova among 42 removed by chance during an endometrial biopsy. Admittedly this was not a normal population, and in general the incidence is probably lower. Nevertheless, the estimated loss after conception is extremely high; including clinically obvious spontaneous abortions it has been calculated at 78% (Roberts & Lowe, 1975), but this hypothesis rests on a number of assumptions and again the percentage is probably lower.

In the case of the degeneration of an implanted blastocyst, menstruation may be delayed for a few days, the woman may only notice a more than average blood loss, or the menstruation may be perceived as perfectly normal. This has been called occult abortion (Bloch, 1976). Occult abortion may be an important cause of apparent infertility (Chartier et al, 1979; Onoue et al, 1981).

Definition of spontaneous abortion

A difficulty in defining abortion is that the term is meant to imply the period during which the fetus was not viable, and viability is not constant. Until recently most infants born before week 30 of gestation, and virtually every infant born before week 28, would die. Since the beginning of the past decade, however, an increasing number of infants are being kept alive and well, even when delivered before week 28 of pregnancy.

In 1977, the World Health Organisation defined abortion as '... the expulsion or extraction from its mother of a fetus or an embryo weighing 500 grams or less (approximately equal to 20-22 completed weeks of gestation), or an otherwise product of gestation of any weight and specifically designated (e.g. hydatiform mole) irrespective of gestational age and whether or not there is evidence of life . . .'. This is clumsily formulated, but the essence of it is that the vast majority of abortions are defined by birthweight. Viability comes into it only in so far as it is tacitly assumed that no infant of 500 g or less can survive. (In point of fact, this is probably still true for immature infants with a birthweight appropriate for their gestational age, but there is at

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least one documented case of an infant who survived for at least one year after its birth, which was 'about two months early', weighing 397 g (14 oz) one day after birth (Monro, 1939).

In most of the literature the above definition is not strictly adhered to, although many authors consider an expulsion before 20 weeks as abortion. I shall therefore for the rest of this book use this definition or the gestational age of 20 weeks. Wherever possible, occult abortion and ectopic gestation will be considered as a separate entity and not included under the heading of spontaneous abortion. Since the incidence of abortion reaches its lowest level between 20 and 27 weeks (Fig. 2.1), most epidemiological data will correspond reasonably well to the definition of abortion as given by the World Health Organisation.

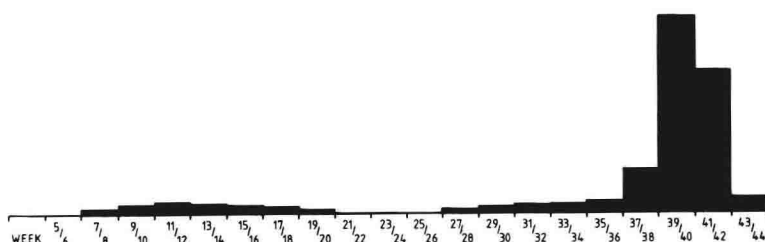


Fig. 2.1 Distribution of gestational ages at time of termination of 11 357 pregnancies. Department of Obstetrics, University Hospital, Groningen, the Netherlands.

Incidence of abortion

While it is generally agreed that the incidence of spontaneous abortion must be somewhere around 15%, a flawless epidemiological study has not yet been reported. Investigations are wont to be marred by one or more variables. For example, in studies involving hospital populations, early abortions are likely to be under-represented, because symptoms are light and women are unlikely to seek medical or specialist advice. Many reported incidences based on such hospital data are therefore low (Roth, 1963). When induced abortion was still synonymous with criminal abortion, there was a high probability that it would be reported as spontaneous, but the magnitude of this effect is very difficult to assess. It depends on the country, the period, the design of the investigation and on the social structure of the population studied. Even now, however, rates of spontaneous abortion should be