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Abruptio placentae
A "classic" dedicated to Elizabeth Ramsey

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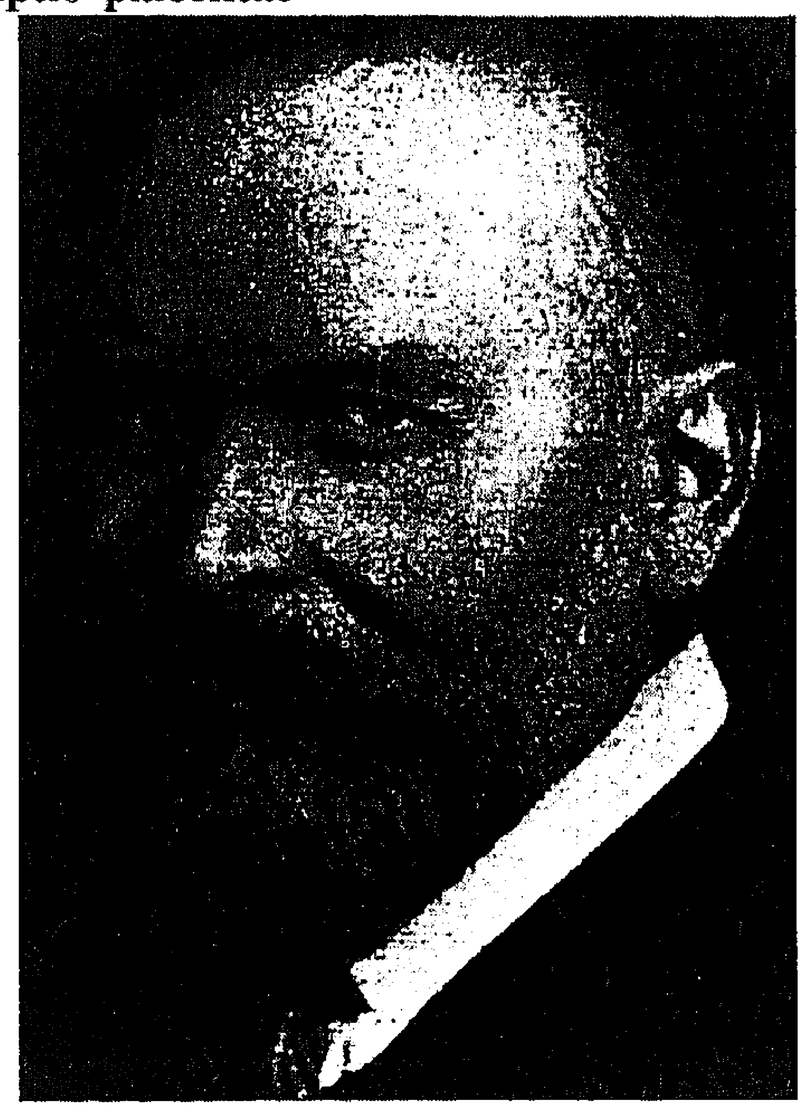
Abstract

The syndrome of abruptio placentae was originally described in 1997. Total hysterectomy was advocated by Couvelaire in 1991. The placenta is fixed to the uterine wall by anchoring villi. When spiral arteries lack the physiologic trophoblast invasion, like in case of maternal hypertension placental infarcts/abruption might occur. Infusion of thromboplastic material induces disseminated intravascular coagulation. The uterus "en bois" representing hypertonicity and polysystolia probably safe-guard the entrance of further thromboplastic material into the maternal circulation. Prompt restoration of the intravascular volume with full blood avoids hysterectomy. Preventive measures are avoidance of the supine position, cocaine and smoking. Treatment of hyperhomocysteinemia probably can prevent vascular damage. © 1997 Elsevier Science Ireland Ltd.

Keywords: Abruptio placentae history; Placental architecture; Placental circulation; Uterine contractility; DIC; Hypertension; Haemorrhage

1. Abruptio placentae



In 1911, Couvelaire [1] reported the surgical treatment of uteroplacental bleeding with separation of the normally implanted placenta by performing hysterectomy. The patient was a 26-year-old primigravida who had abdominal pain, a tender hard uterus, symptoms of shock and proteinuria. Because the clinical situation worsened despite artificial rupture of the membranes and failure of cervical dilatation, Couvelaire undertook cesarean section to empty the uterus despite the absence of fetal heart sounds. The placenta was found to be completely separated and the uterine cavity was full of blood. The surface of the uterus was covered with subserosal haemorrhages and the myometrium, the broad ligaments and the adnexa were infiltrated with blood.

After hysterectomy and bilateral adnexectomy the patient recovered. The 'uteroplacental apoplexy' was described by Couvelaire, including all the clinical entities that we now know as total placental abruption: tender uterus, shock, retroplacental clots, dead fetus and coagulation problems.

It is certain that Couvelaire's radical approach occupied a prominent place in obstetric practice and that this approach saved maternal lives. It is equally certain that

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they have been responsible for the needless removal of many uteri in recent times.

2. The syndrome 'abruptio placentae'

The syndrome of abruptio placentae was originally described by Edward Rigby in 1775 [2].

Placental abruption is evoked by haemorrhage behind the placenta in the decidua basalis. A decidual haematoma leads to separation and compression of the adjacent parts. The retroplacental haematoma is most probably caused by a rupture of a decidual spiral artery.

When one inspects the delivered placenta a circumscribed depression covered by dark clotted blood can be seen, the so-called 'delle'. A totally abrupted placenta may not differ on the maternal surface from a normal placenta at delivery. Haemorrhage can even be concealed in utero and not be brought to notice by vaginal bleeding [3].

Placental abruption is one of the leading causes of perinatal deaths, accounting for 15%–25% of placental mortality [4]. This was found in the large collaborative project of the Perinatal Research Branch of the National Institute of Neurological Diseases and Blindness involving a prospective study of 54 000 women and their children [5]. Placental abruption increases the risk of neonatal morbidity mainly due to hypoxia, prematurity and growth retardation [6].

Maternal hypertension seems to be most consistently identified factor predisposing to placental abruption [7]. External maternal trauma or rapid decompression of the overdistended uterus are less common causes of placental abruption.

Usually the diagnosis of abruption is based on the clinical judgement of the physician: abdominal pain, tender or wooden uterus, vaginal bleeding and/or coagulapathy. Inspection of the placenta can reveal a retroplacental clot and 'delle', coagula coming first at caesarean section, or rapid delivery of the placenta and coagula after the birth of the child.

3. How is the placenta fixed to the uterine wall anyway?

If one observes the ease with which the placenta separates from the uterine wall postpartum, in most cases, one wonders how the placenta is fixed to the uterine wall during pregnancy.

The anchoring villi of the human hemochorial trophoblast can easily be seen about the 12th day. Proliferation of cellular trophoblasts at the tips of the villi form cytotrophoblast columns 'anchoring' to the decidua at the basal plate.

While at the 3rd and 4th month the greater part of the chorion loses its villi becoming the chorion laeve, the villi on the side of the chorion toward the decidua basalis branch elaborately to form the chorion frondosum. The cytotrophoblast penetrates no further than the deepest layer of the decidua, except into the spiral arteries.

Whenever the trophoblast comes into contact with extraplacental extracellular matrix, oncofetal fibronectin can be found. Fibronectin molecules bear a unique glycopeptide domain and seem to connect extravillous trophoblast and trophoblastic cell columns to the uterine decidua at human implantation sites [8]. They function as 'a trophoblast glue' (Fig. 1) [9].

Fetal cotyledons are separated by septa, which run from the basal decidual plate of the placenta toward the

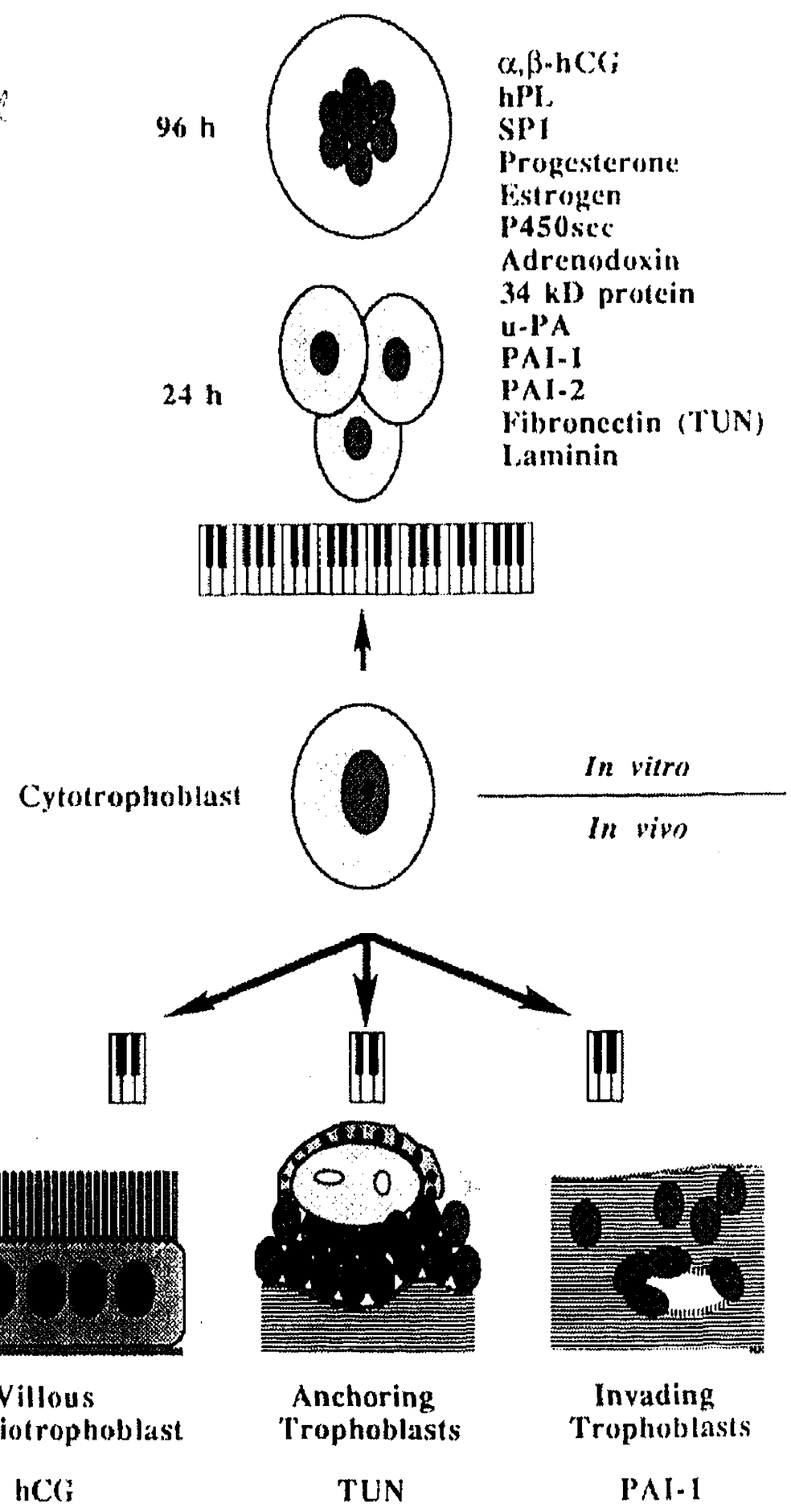

Fig. 1. Kliman HJ and Feinberg HJ (1992) [9]. Differentiation of the trophoblast. In: Barnea ER, Hustin J, Jauniaux E, editors. The first twelve weeks of pregnancy. Springer Verlag, Berlin page 19, (with permission of authors and publisher).

chorionic plate. These septa probably are also designed to prevent shifting of the placenta during pregnancy.

Measurements of intra-uterine pressure in the relaxed state [10] demonstrate a somewhat higher pressure than in the peritoneal cavity and the outside environment. This could mean that the placenta is constantly pressed against the uterine wall.

4. Placental architecture: the spiral artery

Placental architecture had already drawn much attention in the seventeenth and eighteenth centuries.

In 1774, the Hunters [11] injected molten wax into the uterine arteries and found that it lodged in the placenta. The wax was not found in the umbilical cord, thus identifying two separate circulations. "The arteries of the uterus ... passed through the decidua ... making two or three close spiral turns upon themselves, they open at once into its spongy substance without any diminution in size .... The intention of the spiral turns would appear to be that of diminishing the force of the circulation as it approaches the spongy substance of the placenta ... for quick motion of the blood is not wanted".

The branches of the uterine artery penetrate the lateral margins of the uterine wall obliquely. Penetrating the endometrium, a branch supplies the stratum basale—the so-called basal artery. Spiral arteries supply the stratum functionalis.

The first histological studies on spiral arteries in late pregnancy appear to have been carried out by Friedländer (1870) quoted by Brosens et al. [12]. He described large basophilic cells with prominent nuclei in the wall of the arteries and suggested that they were trophoblastic cells with power to invade.

From the work of Boyd and Hamilton [13] a clear picture of the changes affecting the spiral arteries in normal pregnancy emerged.

The pathologist–anatomist Elizabeth Ramsey published her meticulous studies of the morphology and the physiology of placental circulation in a classic book [14]. Beautiful drawings of human uteroplacental arteries at various stages of pregnancy, based on three-dimensional models constructed from serial sections, gave insight into the correct anatomy (Fig. 2) [14].

Arts [15] used plastic solution injected into the uterine arteries in extirpated uteri. With the placenta in situ he demonstrated a larger diameter of the ascending branch of the uterine artery in the placental implantation region than in the corresponding vessel in the remainder of the uterus. The uteroplacental arteries opened into the intervillous space beneath the entire basal plate of the placenta, showing no definite position relative to the cotyledons. This is in contrast with the one-to-one assignment in the rhesus monkey [16].

Placentation in the human is interstitial. The entire blastocyst becomes embedded in the endometrium. This is in contrast with the implantation in the monkey, which is superficial, leading to two placentas: the main one and a second 'cake' on the opposite wall connected by intermembrane fetal vessels.

A marked decidual reaction with swelling of stromal cells occurs in the endometrium during the implantation process. The trophoblast grows around and finally through maternal capillaries. This establishes communication between the trophoblastic interstitial spaces and the endometrial capillaries. These spaces, called lacunae and lined by syncytiotrophoblast represent the earliest 'intervillous space'.

The radioangiographic studies of the maternal circulation in primate and human placenta [17–19], all reported that maternal blood enters the intervillous space of the

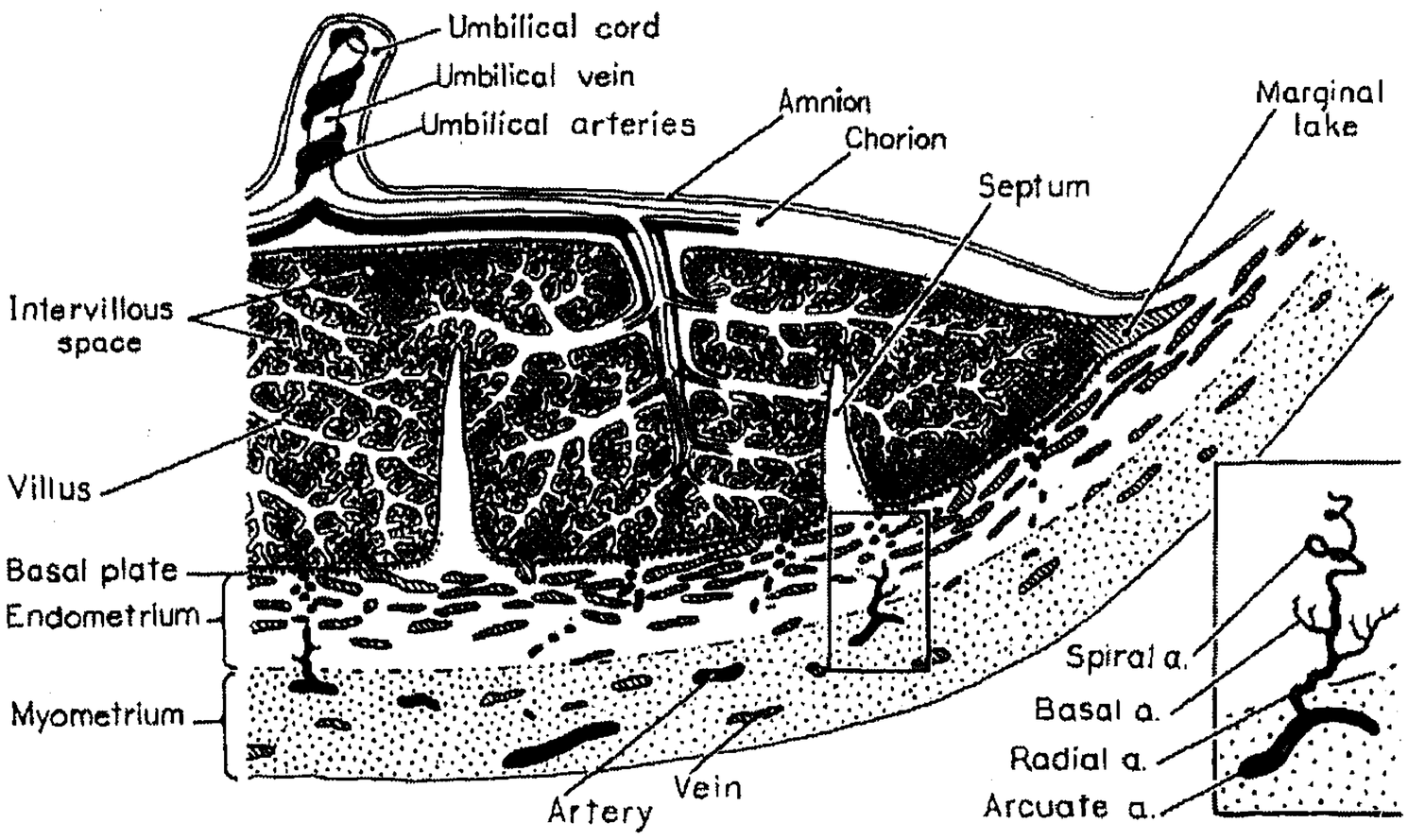

Fig. 2. After Ramsey EM and Donner MW (1980) [14]. Placental vasculature and circulation. Stuttgart, Thieme Verlag (with permission of publisher).

villous hemochorial placenta in the form of discrete 'spurts' or 'jets'. The terminology of 'spurts' or 'jets' suggests an entry of arterial blood under arterial pressure.

Indeed Alvarez and Caldeyro [20] thought this pressure to be 70–80 mmHg and Elizabeth Ramsey [21] came to the 'physiological concept' on uteroplacental circulation:

"Arterial blood enters the placenta from the endometrial arteries under a head of pressure sufficiently higher than prevailing in the vast, amorphous lake of the intervillous space that the incoming stream is driven high up toward the chorion. Gradually this force is spent and lateral dispersion occurs, aided by the villi which, acting as baffles, promote mixing and slowing and by their own pulsation effect a mild stirring. Eventually the blood in the intervillous space falls back upon the orifices in the basal plate which connect with maternal veins, and since there is an additional fall in pressure between the intervillous space and the endometrial veins, drainage is accomplished. This circulatory progress is enhanced by intermittent myometrial contractions throughout pregnancy" [21]. This description suggests to the reader a rather high pressure input force.

Moll and colleagues [22,23], however using glass capillaries in the spiral artery of the Rhesus monkey reported a much smaller pressure head of around 20 Torr in contrast to the 70–80 Torr previously suggested. Also, intervillous space pressures were identical with amniotic fluid pressure [24].

The spiral arteries seem to be 'end-arteries'. At least in the rhesus monkey, all stages of infarcts could be produced by ligating the spiral arteries [25].

Only the spiral arteries react to hormonal stimuli during the menstrual cycle. Markee [26] transplanted endometrium into the anterior eye chamber of the Rhesus monkey and observed intermittent vasoconstriction of the radial arteries.

Hustin and Schaaps [27] reconsidered classic theories about maternoplacental circulation in early pregnancy. They studied hysterectomy specimens with an early pregnancy in situ.The so-called physiological changes at the spiral artery level were impressive. Most of the spiral arteries were occluded by trophoblastic plugs. By also using angiographic and ultrasound techniques they hypothesized that there is a delayed blood flow in the intervillous space and that only some watery plasma-like fluid eventually wells out of the inner openings of the trophoblastic shell and fills the intervillous space. Such an arrangement seems to favour a low oxygen content milieu for proper embryonic and early fetal development.

5. The placental bed

Dixon and Robertson [28] introduced a new technique which they called 'the placental bed biopsy'. The word 'bed' was chosen deliberately, instead of site, emphasizing the necessity to include not only decidua but also underlying myometrium containing the uteroplacental spiral arteries.

The comprehensive studies of Brosens, Robertson and Dixon have brought clarity into the vascular changes in uterine arteries during normal and abnormal pregnancies [29].

Brosens et al. [12] studying placental bed biopsies could describe the physiological changes in the conversion of the decidual parts of the spiral arteries by a wave of endovascular trophoblast migration in the first trimester, replacing the normal musculo-elastic wall with a mixture of fibrinoid material. A subsequent wave occurred in the second trimester, proximally into the myometrial portions of the spiral arteries, even involving the terminal segments of the radial arteries.

The purpose of these vessel changes is thought to be to allow a great volume of blood to be delivered to and carried from the intervillous space and possibly also to reduce the head of arterial pressure inflow. The changes in these vessels also seem to make them incapable of responding to vasomotor influences: a low-resistance utero-placental system to be the end result.

Hertig [30] first described a distinctive necrotizing lesion of the uterine spiral arteries in hypertensive pregnancy which he called 'acute atherosis'. Since that time several studies have confirmed the presence of this arterial lesion and this is now recognized as virtually pathognomonic of albuminuric hypertension in pregnancy [29].

In pregnancies complicated by long-standing hypertension, hyperplastic changes are seen in the uteroplacental arteries. When (pre-)eclampsia is superimposed on pre-existing essential hypertension hyperplastic arteriosclerotic lesions may be found.

This spectrum of vasculopathies, seen as an endothelial cell disorder [31], may lead to vascular thrombosis, placental infarcts and vessel rupture leading to retroplacental haemorrhage.

In placental bed biopsies in cases of placental abruption, the majority demonstrated absence of the physiological transformation of the utero-placental arteries. Also, abnormal vascular structures deep in the myometrium or intramyometrial haemorrhage could be observed [32].

In pre-eclampsia and small-for-gestational-age infants, the physiological changes are restricted to the decidual segments of the spiral arteries alone. Frequently complete absence of physiological changes occurred throughout the entire length of some spiral arteries [33].

The observations of absence of physiological changes in a proportion of spiral arteries implies that the maternal vascular response to placentation in abnormal pregnancies is qualitatively and quantitatively inadequate to form a proper haemochorial placenta.

A case report described abnormal flow velocity waveforms in both uterine arteries showing a pronounced

notch some hours before placental abruption at 29 weeks gestation [34].

Morrow and Knotch Ritchie [35] also reported pathologic flow velocity waveforms in the uterine arteries shortly after placental abruption.

6. Two types of uterine contractility

Total placental abruption is diagnosed by severe abdominal pain and the palpation of the 'wooden uterus' or 'uterus en bois'.

Using an intra-uterine open-tip fluid filled catheter system and pressure recording equipment Cobo et al. [36] described two patterns of uterine contractility: the low versus high activity type, the latter demonstrating hypertonicity and high frequency of uterine contractions (Fig. 3) [36].

Eskes et al. [37] could confirm this finding and added that amniotomy did not have a constant effect on contractility and that hypertonicity was due to polysystolia.

One can understand that this hypercontractility is provoked by intra-uterine haemorrhage. Would it also protect the mother from invasion of hypercoagulable intra-uterine material?

Borell et al. [38] studied the influence of uterine contractions on the uteroplacental blood flow at term by radioangiography and found a marked retardation of blood flow during contraction judged by the number of dye-spots on the X-ray films. Such a retardation of flow was nicely demonstrated in monkeys using the microsphere-flow-determination technique [39].

Such a retardation of blood flow in the placenta can be due to compression of the effluent veins, local compression of the arterial wall by the myometrium either by intra-uterine pressure or by a slinglike arrangement of the myometrial bundles.

Caldeyro-Barcia [40] reported the intramyometrial pressure recorded with microballoons to be two or three times higher than the amniotic pressure. Hendricks et al. [41], however, who determined the myometrial pressure by open-end catheters with a miniature fluid pool at the tip of the catheter, did not find a substantial difference between the intramyometrial pressure and the amniotic pressure except for a gradient from inwards to outwards over the myometrial layer itself.

If uterine veins are compressed during the hypercontractile state of placental abruption, this then seems to prevent the entrance of further thromboplastic material into the systemic circulation, preventing further enhancement of the coagulation cycle.

7. Coagulation and Disseminated Intravascular Coagulation (DIC)

Blood obtained in a test tube will readily clot. In some patients with placental abruption, weak or absent clotting

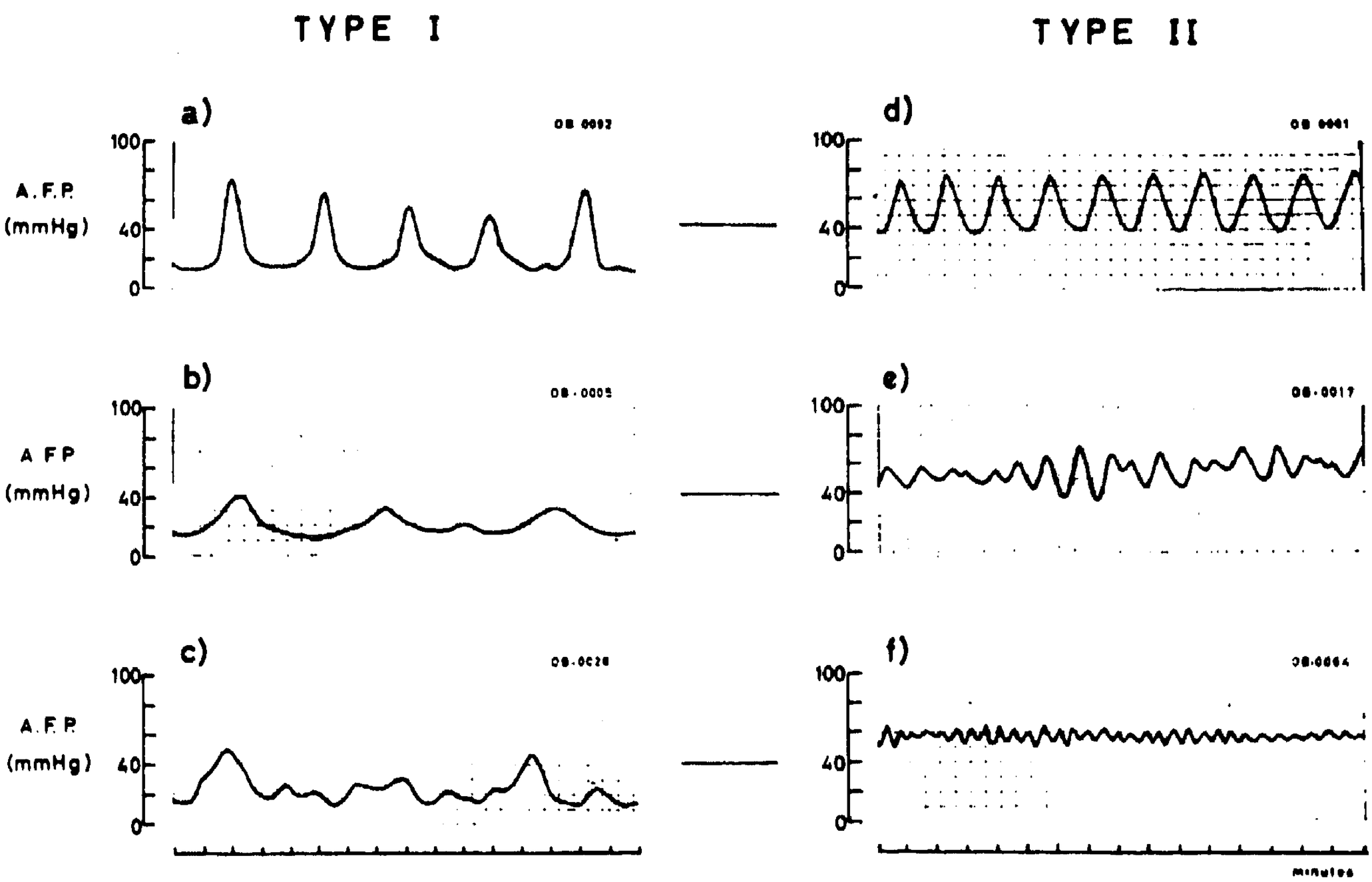

Fig. 3. After Cobo et al. (1965) [35]. Am J Obstet Gynecol 93, 1151–1156, (with permission of authors and publisher).

can be observed. Coagulation studies will then be grossly abnormal including low fibrinogen levels, low platelets and fibrin degradation products.

The coagulation cascade can easily be activated by the presence of large amounts of tissue phospholipids. These contribute to the utilisation of large amounts of clotting factors and lead to a consumptive coagulopathy. When coagulation of blood is widespread, lytic processes are called into action. Large amounts of fibrin produces fibrin split products.

Dieckmann [42] suggested that the pathogenesis of hypofibrinogenemia was to be found in the consumption of fibrinogen in the retroplacental blood cells. Another theory holds that thromboplastin of placental origin invades the maternal circulation [43].

Pritchard et al. [44], however, found that intravascular coagulation accounted best for the coagulation defects. So the adequacy of the circulation and the prompt and accurate treatment of hypovolemia is still advocated in cases of placental abruption and shock. Continuous monitoring of urine flow serves, then, as an excellent indicator of the adequacy of the circulation.

Instead of the administration of fibrinogen or even antifibrinolytics, the administration of whole blood only can rapidly restore a severe maternal obstetrical disaster.

Disseminated Intravascular Coagulation (DIC) occurs as a secondary event in several illnesses. The condition is characterized by an excess production of activated Factor X and thrombin in the circulation.

Activation of the clotting mechanism in vivo may occur as the result of:

1. endothelial cell injury (activating the Hageman Factor XII and the **intrinsic** clotting system as well as the fibrinolytic system like in sepsis.
2. liberation of tissue thromboplastin from injured or necrotic tissue (activating the **extrinsic** clotting system like in abruptio placentae) and
3. release of phospholipid from red cell or platelet injury (affecting both clotting systems like in haemolytic transfusion reaction or microangiopathic hemolyticaemia)

Pritchard's 'poem' nicely illustrates the multifactorial situations in which DIC can occur:

"DIC (Disseminated Intravascular Coagulation)
See DIC
See DIC run and play in the blood vessels
See Jane
See Jane run and play
See Jane not run but play and get pregnant
Jane will now get DIC since
DIC occurs in abruptio placentae
DIC occurs with most obstetric complications
If Jane's baby Dick is asphyxiated Dick may get DIC
Jane should not have gotten pregnant
But the pill, while preventing Dick, may cause DIC
But so can malaria, virus-infections, a bad bump on the head, even infectious mononucleosis
More and more it appears most things in life can cause DIC
Probably no one ever dies alone
There is always DIC."

8. Prevention

8.1. The supine hypotensive syndrome

In contrast to the more popular belief that arterial ischemia, decidual necrosis and arterial rupture are the underlying defects of placental abruption, Mengert et al. [45] drew attention to the possibility that compression of the inferior caval vein could separate the placenta from the uterine wall. By manual compression of the inferior caval vein during caesarean section in two patients before delivery of the child, the placenta was found to be separated and large amounts of dark blood were present.

Multiple placental abruptions could also be produced in dogs by ligation of the vena cava below the level of the renal veins [46]. It is well known that the large pregnant uterus can compress the inferior vena cava and can increase the venous pressure up to 35 mmHg (Fig. 4) [47]. It is not unlikely that such pressures can increase intervillous space pressure producing rupture of the 'trophoblast box.' Therefore it seems wise to avoid the 'supine hypotensive syndrome' [48] especially in artificial conditions

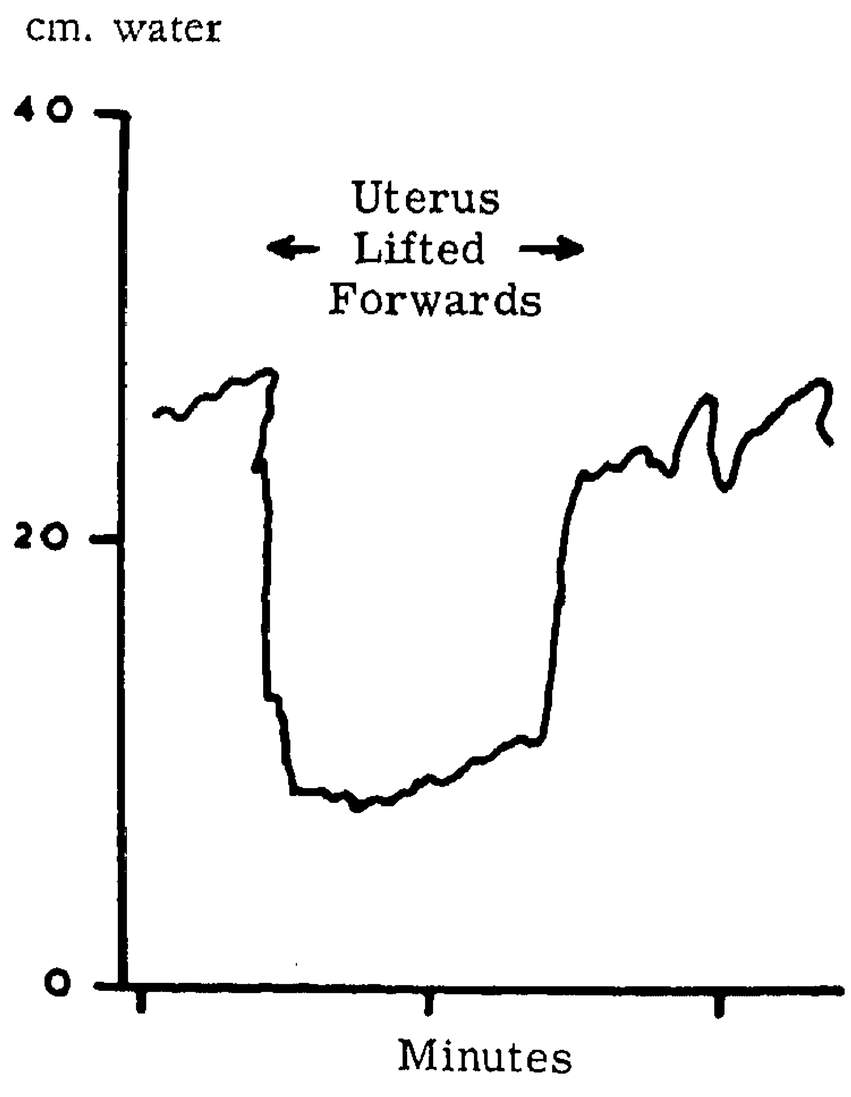

Fig. 4. After Kerr MG (1965) [47]. J Obstet Gynaecol Br Commonw 72, 513, (with permission of authors and publisher).

like measuring bloodpressure during prenatal care, supine position for caesarean section and ultrasound investigations.

8.2. Cocaine

Dombrowski et al. [49] demonstrated in a retrospective study that abuse of cocaine nearly doubled the risk of placental abruption. Although uterine blood vessels seem to be rather resistant to vasoconstrictors, cocaine might overcome this 'blockade', as does cigarette smoking.

8.3. Nutrition: the role of folic acid

Nutrition has long been considered to be of importance in the development of placental abruption, due to the association with small-for-dates babies and poor socio-economic conditions.

Hibbard and Hibbard [50] reported that folic acid deficiency could be associated with placental abruption.

This possibility is now under investigation because of the reported incidence of 31% of hyperhomocystinaemia in these women [51,52].

Recent studies attribute a vascular damaging effect towards homocysteine [53]. It remains to be seen whether folates and other vitamins of the B-series are able to overcome the vascular endothelial damage and so prevent the disaster of placental abruption.

9. Epilogue

The syndrome of placental abruption has a written history from 1775 onwards including surgical treatment by hysterectomy [1].

Anatomical studies yielded some information on nidation, early trophoblastic invasion and the final placental architecture. The spiral artery is considered central to the pathogenesis of the disease, lacking the physiologic trophoblast invasion especially in cases of chronic hypertension. Retroplacental bleeding and/or placental infarcts count for most of the high perinatal mortality and-morbidity. Maternal death may be imminent, especially when disseminated intravascular coagulation is present requiring prompt restoration of intravascular volume by fluid and full blood. Preventive measures are scarce. These include measures like supine position, avoidance of cocaïne and smoking. Folic acid deficiency and dependency as nutritional factors are under investigation.

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