Handleiding

Doodsoorzakenclassificatie

bij perinatale audit

WHEN & WHAT

Wigglesworth/Hey, Modified ReCoDe classificatie

WKPLL

Opgesteld door de commissie doodsoorzakenclassificatie van de PAN (nu Perined) in samenwerking met de Werkgroep Kinderpathologie der Lage Landen.

Revisiehistorie

Versie 1	Dec 2009	PAN & WKPLL
Versie 2	Maart 2014	Afschaffing Tulipclassificatie - verwijderd
Versie 3	Maart 2017	met Perined logo
Versie 4	Febr.2018	Morbiditeitsclassificatie verwijderd uitsluitend doodsoorzakenclassificatie

Doodsoorzakenclassificatie t.b.v. registratie van perinatale sterfte bij perinatale audit

Om zorgverleners te ondersteunen in het classificeren van de oorzaak bij perinatale sterfte is een vragenstructuur ontwikkeld, waarbij het gangbare denkpatroon van de zorgverlener wordt gevolgd. Deze gedachtegang sluit aan bij de verschillende doodsoorzakenclassificaties, die zowel nationaal als internationaal gebruikt worden.
De vragen luiden als volgt:

1. Wanneer is de sterfte opgetreden? (WHEN?)

Bij het beantwoorden van deze vraag wordt aangesloten bij de classificatie van Wigglesworth[1] en de Fetal and Neonatal Classification[2], die het tijdstip van overlijden als belangrijk gegeven hanteren.

2. Wat zijn de klinische beelden waaronder de sterfte is opgetreden? (WHAT?)

Bij het beantwoorden van deze vraag wordt grotendeels de classificatie van Gardosi[3] en Chan[4] gevolgd. Alle relevante klinische beelden en maternale risicofactoren kunnen benoemd worden. Daarnaast wordt het meest relevante ziektebeeld aangegeven.

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[1] Wigglesworth JS. Classification of perinatal deaths. Soz Praventivmed 1994; 39(1):11-14.
[2] Hey EN, Lloyd DJ, Wigglesworth JS. Classifying perinatal death: fetal and neonatal factors. BJOG 1986; 93(12):1213-1223.
[3] Gardosi J, Kady SM, McGeown P, Francis A, Tonks A. Classification of stillbirth by relevant condition at death (ReCoDe): population based cohort study. BMJ 2005; 331(7525):1113-1117.
[4] Chan A, King JF, Flenady V, Haslam RH, Tudehope DI. Classification of perinatal deaths: development of the Australian and New Zealand classifications. J Paediatr Child Health 2004; 40(7):340-347.

WHEN?

When did perinatal death occur?

(Wigglesworth, Hey)

Delivery at:

< 24 wks	☐
24-27^{+6} wks	☐
28-31^{+6} wks	☐
32-36^{+6} wks	☐
37-40^{+6} wks	☐
> 41 wks	☐

Intra uterine	☐	
Intrapartum	☐	
Neonatal	☐	
	< 24 hrs	☐
	24 – 1 wk (7 x 24 hrs)	☐
	1 wk – 4 wk (28 days)	☐

WHAT?
What are the clinical conditions?

Guideline for classification

The original ReCoDe classification (Gardosi et al) was designed for stillbirths only. The part on neonatal classification from the Australian-New Zealand classification (PSANZ by Chan et al) has been added to cover the complete perinatal period. Maternal risk factors have been added to complete the outline. No clear guidelines for allocation and definition have been described in the original papers. We propose to use the following rules:

ALL relevant conditions present for a case should be noted. In conclusion, on judgment of the clinician, the MOST important clinical condition must be allocated separately.

Group A: Fetus Group

1. Congenital anomaly ☐
2. Infection (2.1. Chronic, 2.2. Acute) ☐
3. Non-immune hydrops ☐
4. Iso-immunisation ☐
5. Feto-maternal haemorrhage ☐
6. Twin-twin transfusion ☐
7. Fetal growth restriction * ☐
8. Asphyxia ☐
9. Other ☐

Group B: Neonate

1. Congenital anomaly ☐
2. Asphyxia ☐
3. Prematurity ☐
4. Respiratory Distress Syndrome (RDS) ☐
5. Meconium Aspiration Syndrom (MAS) ☐
6. Persistent Pulmonary Hypertension Neonate (PPHN) ☐
7. Pulmonary hypoplasia ☐
8. Neonatal infection (early)
   a. early ☐
   b. late ☐
9. Necrotising Enterocolitis ☐
10. Hypoxic ischemic encephalopathy ☐
11. Intracranial haemorrhage ☐

Group E: Amniotic fluid

1. Clinical Chorioamnionitis ☐
2. Oligohydramnios # ☐
3. Polyhydramnios # ☐
4. Other ☐

Group F: Uterus

1. Rupture ☐
2. Uterine anomalies ☐
3. Other ☐

Group G: Mother

1. Diabetes ☐
2. Thyroid disease ☐
3. Essential hypertension ☐
4. Hypertensive diseases in pregnancy ☐
5. Lupus or antiphospholipid syndrome ☐
6. Cholestasis ☐
7. Drug misuse ☐
8. Riskfactors:
   a. obesity (BMI ≥25) ☐
   b. thrombophilia ☐
   c. smoking > 10 cig ☐
   d. low educational attainment ☐
   e. previous sga infant * ☐
   f. previous stillbirth ☐

12. Other ☐

Group C: Umbilical cord

1. Prolapse ☐
2. Constricting loop or knot # ☐
3. Velamentous insertion ☐
4. Other ☐

Group D: Placenta

1. Abruptio ☐
2. Praevia ☐
3. Vasa praevia ☐
4. Other 'placental insufficiency' ☐
5. Other ☐

* < 10th weight for gestational age centile

if severe enough to be considered relevant

g. advanced maternal age >35 ☐

9. Other ☐

Group H: Intrapartum

1. Asphyxia ☐
2. Birth trauma ☐
3. Other ☐

Group I: Trauma

1. External ☐
2. Iatrogenic ☐

Group J: Unclassified

1. No relevant condition identified ☐
2. No information available ☐

Group A: FETUS-GROUP

1. Congenital anomaly

Congenital anomaly is defined as any deviation from the expected or average type in structure, form and/or function which is interpreted as abnormal and present at birth. Characterization of anomalies as 'abnormal' distinguishes them from normal variants that are both more frequent and less noxious than anomalies. Chromosomal and structural anomalies are included in this category (for neonatal deaths: group B).

2. Infection

Infections of the fetus and/or placenta as diagnosed by clinical signs and symptoms, placental examination and/or autopsy, supported by results from culture, special diagnostic and/or serologic tests.

Included in this category are:

2.1 Chronic fetal infection is defined as transplacental intra-uterine infection caused by invasion of microorganisms in the bloodstream of the mother leading to placental and/or fetal infection. On placental examination the histologic hallmark of a transplacental intra-uterine infection is (chronic) villitis.

2.2 Acute fetal infection is defined as ascending intra-uterine infection that commences in the vagina and endocervix and then ascends to the uterine cavity resulting in placental and/or fetal infection. On placental examination the histologic hallmarks of an ascending intra-uterine infection are (sub)acute chorioamnionitis and subchorionitis. The fetal response to an ascending intra-uterine infection is characterized by chorionic and umbilical vasculitis.

3. Non-immune hydrops

Fetal non-immune hydrops is defined as a state of profound generalized fetal edema, with a marked accumulation of fluid in two or more compartments (subcutaneous tissue, all body cavities, amniotic fluid compartment, umbilical cord and placenta), without evidence of red-cell antibodies.

4. Iso-immunisation

Iso immunization is defined as hemolytic disease as a result of destruction of fetal erythrocytes by alloantibodies transmitted through the placenta from the maternal blood. It is characterized clinically by anemia, hyperbilirubinemia and erythroblastemia. Intrauterine transfusion may be required. In the most severe form fetal or neonatel death ensues with generalized edema secondary to hemodynamic compensation for severe anemia (fetal hydrops).

5. Feto-maternal haemorrhage (FMH)

FMH is defined as the transplacental passage of fetal cells to the maternal circulation. Inclusion in this category requires substantial (> 10 ml) fetal blood in the maternal circulation, found by kleihauer-betke or other appropriate tests.

6. Twin-twin transfusion

Twin-twin transfusion is defined as unbalanced blood flow from one twin (the donor) to its co-twin (the recipient) through superficial chorionic large vessel anastomoses or arterio-venous anastomoses deep within shared placental lobules. The donor eventually develops severe anemia and the recipient suffers from cardiac failure due to polycythemia and develops hydrops.

Twin-twin transfusion can be acute or chonic, or acute superimposed on chronic.

Diagnosis is made by disparities in amniotic volume, bladder, content, bodyweight, bloodflow patterns and haemoglobin concentrations between twins.

7. Fetal growth restriction

Fetal growth restriction is defined as failure of the fetus to reach its genetic growth potential**.**

Fetal growth restriction is diagnosed when birth weight is < 10^{th} weight for gestational age centile (SGA) or slowing of the growth curve at successive ultrasound biometry measurements, with decreasing amniotic fluid and/or pathological umbilical blood flow doppler measurements.

8. Asphyxia

Ashyxia is defined as pathological changes caused by lack of oxygen, resulting in hypoxia and hypercapnia.

Severe CTG abnormalities are indicative for fetal hypoxia as well as increased number of nucleated red blood cells on autopsy (cave parvo infection or low Hb), small internal hemorrhages in thymus, pleura, pericard or cerebrum.

9. Other

Other clinically and/or pathologically defined fetal conditions, not listed above.

Group B: NEONATE

1. Congenital anomaly

Congenital anomaly is defined as any deviation from the expected or average type in structure, form and/or function which is interpreted as abnormal and present at birth. Characterization of anomalies as 'abnormal' distinguishes them from normal variants that are both more frequent and less noxious than anomalies. Chromosomal and structural anomalies are included in this category.

2. Asphyxia

Ashyxia is defined as pathological changes caused by lack of oxygen, resulting in hypoxia and hypercapnia.

Asphyxia in the newborn is diagnosed in case of (according the definition of the AAP and ACOG):

1) Profound metabolic or mixed acidemia, (pH < 7.00), on an umbilical cord arterial blood sample,
2) Persistance of an Apgar score of 0 to 3 for > 5 min,
3) Clinical neurologic sequelae in the immediate neonatal period to include seizures, hypotonia, coma, or hypoxic ischemic encephalopathy.

3. Prematurity

Prematurity is defined as delivery before 37 weeks of gestation.

4. Respiratory distress syndrome (RDS)

Respiratory distress syndrome is defined as an acute illness, usually of preterm infants, characterized clinically by a respiratory rate ≥ 60, dyspnoea with a predominantly diaphragmatic breathing pattern and a characteristic expiratory grunt or moan, all presenting within 4-6 hours of delivery, usually because of insufficiency of surfactant production and structural immaturity in the lungs. Oxygen administration is required to prevent cyanosis, and there is a reticulogranular chest X-ray appearance as a result of widespread atelectasis.

5. Meconium aspiration syndrome (MAS)

Meconium aspiration syndrome is defined as an illness following the aspiration of meconium before, during or immediately after delivery. The baby will fulfil the standard criteria for respiratory distress, with tachypneu ≥ 60 and dyspnoea, although grunting is rare. The meconium fluid is irritating and possibly leading to chemical pneumonia. Sustained additional oxygen is required. Inhaled meconium can cause persistent pulmonary hypertension of the neonate.

6. Persistent Pulmonary Hypertension Neonate (PPHN)

PPHN describes neonates with a structurally normal heart but a large right-left shunt at the level of the atria or ductus arteriosus secondary to pulmonary hypertension. By definition PPHN must be diagnosed when a neonate has: severe hypoxaemia, without severe lung disease, evidence of a right-to-left ductal shunt, or a large shunt at the foramen ovale in the absence of a ductal shunt.

7. Pulmonary hypoplasia

Pulmonary hypoplasia is defined as the incomplete development of the lung, with a reduction in the number of airway branches, alveoli, arteries and veins. The diagnosis should be considered in any infant in whom high infiltrating pressures are necessary at resuscitation and during subsequent ventilation, particularly if this is associated with clinical signs as oligohydramnios.

On autopsy lung hypoplasia is best defined as the ratio of lung weight to body weight. This ratio is 0.012 for infants of 28 weeks gestation or more and 0.015 or more for those of lower gestation. Age-related standards have been established (Wigglesworth, Perinatal Pathology. 1996; second edition: page 166; De Paepe et al. Postmortem lung weight/bodyweight standards for term and preterm infants. Pediatr Pulmonol. 2005;40:445-8).

Radial alveolar counting to quantify the degree of acinar development may also be used to assess lung development (Askenazi SS, Perlman M. Pulmonary hypoplasia: lung weight and radial alveolar count as criteria of diagnosis. Arch Dis Child. 1979;54:614-8).

8. Neonatal infection

Neonatal infection is defined as an infection in a live born infant acquired in utero, during passage of the birth canal or at the maternity/neonatal ward or at home in the first 28 days of life.

Included in this category are:

1) Early neonatal infection is defined as symptomatic neonatal infection presenting within the first 72 hours of life.
2) Late neonatal infection is defined as symptomatic neonatal infection presenting after 72 hours of life.

9. Necrotizing enterocolitis

Necrotizing enterocolitis represents a type of ischemic injury to the small bowel and colon. Early signs and symptoms of NEC may be subtle and nonspecific, such as apnea, bradycardia, and lethargy. More specific gastrointestinal signs include abdominal distension, absent bowel sounds, vomiting, blood in stool and diarrhea. Disease stage has been classified according to Bell's modified criteria:

– stage I, suspected NEC: characterized mainly by intestinal dilatation;

- stage II, definite NEC: mild to moderate illness, with intestinal dilatation, ileus, and pneumatosis;
- stage III, advanced NEC: severe illness, with or without bowel perforation.

10. Hypoxic ischemic encephalopathy

Hypoxic ischemic encephalopathy (HIE) is defined as brain damage from a shortage of oxygen or blood flow to the tissues, leading to abnormalities in tone, convulsions, feeding difficulties, altered consciousness and ventilatory disturbance.

Included in this category are:
1) Neuronal necrosis in the asphyxiated full-term newborn,
2) Periventricular leukomalcia,
3) Cerebral infarction.

11. Intracranial hemorrhage

Included in this category are:
1) Subgaleal hemorrhage.
2) Subdural hemorrhage.
3) Primary subarachnoid hemorrhage.
4) Germinal matrix-intraventricular hemorrhage.
5) Thalamic hemorrhage.
6) Intracerebellar hemorrhage.
7) Other intracranial hemorrhage.

12. Other

Other clinically and/or pathologically defined conditions, not listed above, including chronic lung disease of the neonate, pulmonary hemorrhage, pneumothorax, multiorgan failure, treatment complications, hemolytic disease of the newborn and trauma.

Group C: UMBILICAL-CORD

Umbilical cord complication is defined as obstruction or disruption of the umbilical cord flow.

1. Prolapse

Cord prolapse is defined as prolapse of the umbilical cord through a dilated cervix when the membranes are ruptured. The prolapse is of clinical importance if the fetal circulation is compromised due to the prolapse, as indicated by cardiotocography or ultrasound or with histopathological evidence of congestion and stasis of the circulation.

2. Constricting loop/knot

A constricting loop or knot of clinical importance compromises the fetal circulation which is clinically identified by fetal heart rate abnormalities on cardiotocography or ultrasound. The umbilical cord shows evidence of congestion and stasis of the circulation.

3. Velamentous insertion

A velamentous insertion is defined as an umbilical cord that does not insert into the placental mass but, instead, traverses the fetal membranes before it inserts into the umbilical cord.

A velamentous insertion can result in fetal bleeding due to disruption of the vessels or to compromise of the fetal circulation due to compression by fetal parts, usually during delivery. Clinically this is identified by fetal heart rate abnormalities on cardiotocography or ultrasound or vaginal bleeding. The umbilical cord shows either evidence of congestion and stasis of the circulation or disruption of the vessels.

4. Other

Other clinically and/or pathologically defined umbilical cord conditions, not listed above, like furnicate cord insertion, tethered cord insertion (amniotic web), umbilical cord stricture and umbilical cord torsion.

Group D: PLACENTA

1. Placental abruptio

Placental abruptio refers to the clinically symptomatic state, in the mother, of premature separation of a normally implanted placenta before the birth of the fetus.

The classic symptoms and signs are maternal circulatory collaps, vaginal bleeding, abdominal pain, uterine contractions, and uterine tenderness combined with fetal demise. Not all of these are always present and the absence of one or more does not exclude the diagnosis or necessarily suggest a mild form.

Sudden, complete, or substantial placental separation with a recently formed soft retroplacental hematoma is identifiable with certainty by direct observation of the detached placenta within the uterine cavity at the time of caesarean section.

Ultrasound is not sufficiently sensitive to reliably either diagnose or exclude placental abruption. Likewise, the clinical diagnosis of placental abruption may not be confirmed by gross examination of the placenta.

2. Placenta praevia

Placenta praevia is defined as placental implantation in the lower uterine segment with some placental parenchyma near or overlying the internal uterine cervical os.

The hallmark of placental praevia is the sudden onset of painless bleeding in the second or third trimester of pregnancy. Absence of bleeding before term does not exclude placenta praevia. In approximately 10% of cases, bleeding begins only with the onset of labour.

Diagnosis is made by transabdominal, transperineal or transvaginal ultrasound examination.

3. Vasa praevia

Vasa praevia is defined when fetal bloodvessels between the placenta and the fetus are not in the umbilical cord, but incorporated into the fetal membranes. In addition, these vessels are located between the presenting part of the fetus and the cervix.

It is rare for this diagnosis to be made before delivery. Vasa praevia may be detected by colour-flow Doppler techniques. In most cases, however, emergency caesarean delivery takes place on the bases of severe variable decelerations on CTG. Yet, due to rapid fetal exsanguination, fetal death or neonatal asphyxia often ensues.

4. Placental insufficiency

The concept of placental insufficiency appears to offer a plausible explanation for fetal or neonatal disease. In reality, however, placental insufficiency is most difficult to define precisely.

Clinically, placental insufficiency is characterized by intra-uterine growth restriction (IUGR) and/or fetal hypoxia/asphyxia and as such the mode of death in case of placental insufficiency can be chronic, acute or acute and chronic.

Imaging of placental function in vivo is possible by Doppler ultrasound.measurement of the fetal and placental circulation.

Fetal placental perfusion can be evaluated by measuring umbilical venous volume flow.

Umbilical artery blood flow velocity is related to placental vascular impedance and serves to predict outcome in high-risk pregnancies. A decrease in diastolic blood velocity is frequently related to IUGR and adverse pregnancy outcome. Absent or reversel of diastolic (AERD) umbilical artery blood velocity is the most severe sign of vascular impedance and is associated with IUGR and distal villous hypoplasia on placental examination.

Uterine artery Doppler provides information on vascular impedance of the uteroplacental vascular bed. Increased uteroplacental impedance after 24 weeks of gestation is strongly associated with the development of preeclampsia and/or IUGR later in pregnancy.

The cause of placental insufficiency is varied and can be separated into conditions associated with decreased placental growth (e.g. placental hypoplasia due to utero-placental vascular insufficiency), parenchymal destruction (e.g. infarction, vilitis of unknown aetiology or fetal thrombotic vasculopathy) or an increased diffusion distance between maternal and fetal blood (e.g. placental maturation defect, massive perivillous fibrin deposition/maternal floor infarction).

If not supported by clinical signs or symptoms, placental insufficiency can be diagnosed by placental pathology known to cause placental dysfunction with on autopsy and/or placental examination evidence of chronic and/or acute fetal distress.

5. Other

Other clinically and/or pathologically defined placental conditions, not listed above.

Group E: ANNIOTIC-FLUID

1. Clinical Chorioamnionitis

Clinical chorioamnionitis can be diagnosed when at least two out of four signs are present:
1) Uterine tenderness.
2) Foul smelling vaginal discharge.
3) Maternal fever > 38°C (most sensitive sign).
4) Fetal tachycardia > 160 bpm.

Note: not all women with an ascending infection present with fever, leukocytosis, uterine tenderness, or maternal or fetal tachycardia, and many have no symptoms at all. Reversely, only some women with clinical chorioamnionitis have signs of ascending infection on placental examination. I.e. clinical chorioamnionitis is not sufficient to allocate a cause of death to this category.

2. Oligohydramnios

Oligohydramnios is defined as an amniotic fluid index (as measured on ultrasound, sum of pockets in 4 quadrants, in cm) < p5 or < 5 cm.

3. Polyhydramnios

Polyhydramnios is defined as an amniotic fluid index of > p95 or > 25 cm.

4. Other

Meconium stained amniotic fluid.

Group F: UTERUS

1. Rupture

Uterus rupture is defined as dehiscence of a previous uterine scar, or spontaneous rupture of the myometrium with or without expulsion of parts of the conceptus into the abdomen. Clinical signs may be abdominal pain in the area of the scar, fetal distress on cardiotocgraphy or bloody urine. Definite diagnosis is made at laparotomy. From studies performing routine vaginal examination of the continuity of a previous caesarean section scar, many asymptomatic windows in the old scare have been found. These should not be classified here.

2. Uterine anomalies

The clear presence of known congenital uterine anomalies like bicornuate uterus, unicornuate uterus, septate uterus, uterine didelphys etc. These diagnoses are usually proven earlier by laparoscopy/tomy or hysteroscopy/ultrasound. In most cases fertility is unaffected, but obstetric outcome is poor due to recurrent miscarriage, second trimester loss, preterm delivery, malpresentation and stillbirth.

3. Other

Other clinically and/or pathologically defined conditions of the uterus, not listed above.

Group G: MOTHER

1. Diabetes

Chronic syndrome of impaired carbohydrate, protein, and fat metabolism due to insufficient secretion of insulin or to target tissue insulin resistance.

Included in this category are:

1) Type 1 diabetes defined as a chronic autoimmune disease that results from a complex interaction of genetic and environmental factors.
2) Type 2 diabetes defined as a disease arising from progressive tissue insulin resistance, hyperglycemia, and hyperlipidemia, mediated by obesity and sedentary lifestyle.
3) Gestational diabetes defined as glucose intolerance that begins or is first recognized during pregnancy. In many instances gestational diabetes is simply preclinical type 2 diabetes unmasked by the hormonal stress imposed by the pregnancy.

2. Thyroid disease

Thyroid disease is defined as abnormal function of the thyroid gland, resulting in deranged thyroid hormone homeostasis. Frequently abnormal function is due to the presence of auto antibodies to various cell components of the thyroid gland and these may stimulate or block function, or induce thyroid inflammation leading to destruction of the thyroid gland.

Abnormal function of the thyroid gland can be separated in:

1) Hyperthyroidism: a condition caused by excessive production of iodinated thyroid hormones. Diagnosis is made by measuring excess of circulating free thyroid hormones: thyroxine (T_4) (> 20 pmol/l), triiodothyronine (T_3), or both and a decrease in thyroid stimulating hormone (TSH) (< 0.3mlU/l). There are several causes of hyperthyroidism such as autoimmune disease (M Graves) or a toxic nodule or thyroiditis.
2) Hypothyroidism: a condition caused by deficiency of thyroid hormone activity. Diagnosis is made by measuring an increase of thyroid stimulating hormone and insufficient levels of free thyroid hormones: thyroxine (T_4), triiodothyronine (T_3), or both.

3. Essential hypertension

Hypertension that is present before pregnancy or diagnosed before the 20th week of gestation without discoverable organic cause.

4. Hypertensive diseases in pregnancy

Included in this catergory are:

1) Pregnancy induced hypertension: newly diagnosed hypertension initiated after 20 weeks of gestation. Diagnosis is made in women with a systolic blood pressure of ≥ 140 mmHg and/or diastolic blood pressure of ≥ 90 mmHg (Korotkoff V), measured twice on separate occasions and in whom proteinuria is not identified.
2) Preeclampsia: pregnancy induced hypertension or pre-existent hypertension associated with proteinuria (≥ 300mg/24hrs).
3) Eclampsia: onset of convulsions in a woman with preeclampsia that cannot be attributed to other causes.
4) HELLP: Hemolysis, Elevated Liver enzymes, Low Platelets, usually in combination with the criteria for preeclampsia.

Note: HELLP is also possible with a normal blood pressure.

5. Lupus or antiphospholipid syndrome

Antiphospholipid antibody syndrome (APS) is an autoimmune syndrome in which clinical manifestations are associated with high titers of circulating antibodies directed against proteins with affinity for anionic phospholipids. In vivo these antibodies induce a hypercoagulable state. Many patients have a well-defined autoimmune disease, such as systemic lupus erythematosus and have secondary APS. The remainder show no evidence of other autoimmune disorder and exhibit only the manifesations of the hypercoagulable state (primary APS). Pregnancy-related complications are frequent and include miscarriage, stillbirth, preterm delivery, or severe preeclampsia. In 2006, revised criteria for the diagnosis of APS were published in an international consensus statement. At least one clinical criterion and one laboratory criterion must be present for a patient to be classified as having APS (Miyakis S et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006;4:295-306).

6. Cholestasis

Intrahepatic cholestasis of pregnancy is a multifactorial condition of pregnancy characterised by intense pruritus in the absence of a skin rash. The disorder presents typically in the third trimester. The symptoms usually resolve within days of delivery. In clinical practice, abnormalities in transaminases,gamma glutamyl transferase, bilirubin and/or bile salts are considered sufficient to support the diagnosis of obstetric cholestasis. Of these serum bile acids are elevated in most cases and have been reported to be the most sensitive laboratory abnormality. Although a wide variety of cut-off points have been used for defining abnormal liver function tests and bile salts, pregnancy-specific ranges should be applied. Other causes of abnormal liver function tests should be excluded. The outcome for the mother is excellent, though the sequelae for the fetus may be grave and risk for preterm birth and stillbirth is increased.

7. Drug misuse

Drug misuse represents the excessive use of legal and illegal drugs. Examples include alcohol, prescription/over-the-counter drugs, cocaine or heroine. Constant use of any drug increases tolerance which requires larger doses to achieve the same effects. This in turn can lead to psychological dependence which may have a significant effect on the person's life-style; often the drug becomes central to their existence.

Alcohol misuse is defined as more than one standard drink per day any time during pregnancy from the moment the pregnancy was confirmed.

Note: smoking is considered as a risk factor.

8. Risk factors

a. obesity is defined as a BMI ≥ 25 kg/m^2.
b. thrombophilia: an inherited derangement of haemostasis:protein S,C or factor V Leiden, prothrombin mutation or comparable entity.
c. smoking: any smoking of cigarettes during pregnancy.
d. low education attainment: no further secondary education.
e. previous small for gestation infant (< 10^{th} weight for gestational age centile).
f. previous stillbirth from 22 weeks onwards.
g. advanced maternal age is defined as maternal age > 35 (at booking, from 6 weeks onwards).

9. Other

Maternal conditions that had the potential to influence the pregnancy, not listed above, e.g. previous cardiac surgery, surgery during this pregnancy.

Group H: INTRAPARTUM

1. Asphyxia

Intrapartum asphyxia is defined as: evidence of severe hypoxemia after the onset of labour, in the presence of contractions. Either Apgarscore below 4 at 5 minutes or arterial umbilical cord blood pH < 7.0. Neonatal neurological signs or multi-organ failure due to severe hypoxia are also included. CTG abnormalities during labour without evidence of hypoxemia are not coded here.

2. Birth Trauma

Neonatal trauma sustained during labor and delivery. Predisposing factors are large size of the infant, cephalopelvic disproportion, dystocia, prolonged labor, breech presentation, and assisted delivery. Sings of traumatic birth are amongst others: subgaleal hemorrhage, laceration of tentorium cerebelli, massive subdural hemorrhage, occipital osteodiastasis, and fractures.

3. Other

Other clinically and/or pathologically defined intrapartum conditions, not listed above.

Group I: TRAUMA

1. External

External trauma is defined as any external force to the pregnant mother or neonate (severe enough to be considered relevant). Examples are: (traffic) accidents and physical abuse.

2. Iatrogenic

Iatrogenic trauma is defined as any external force to the pregnant mother or neonate that happened during medical treatment (severe enough to be considered relevant). If occurring during delivery, group H2 should be classified.

Group J: UNCLASSIFIED

1. No relevant condition identified

Written reports are available and no conditions are identified although investigations (such as blood pressure and blood tests) have been performed.

2. No information available

Lack of written reports or lack of investigation