### Serious Hazards of Pregnancy, 2018

# **Abnormally Invasive Placenta**

# S Robson

Professor of Fetal Medicine Newcastle University



- Epidemiology
  - Pathophysiology
  - Screening / diagnosis
  - Management
    - Haemorrhage



# Abnormally invasive placenta Histological Classification

- Accreta Direct attachment of EVT to myometrium
- Increta EVT invasion into myometrium
- Percreta EVT invasion to serosa and/or adjacent structures



# Abnormally invasive placenta Degree of invasion



# **Abnormally invasive placenta**







# Abnormally Invasive Placenta Incidence & rate of prenatal diagnosis

|                                     | <b>UK (UKOSS)</b><br>(Fitzpatrick et al. 2013) | US (MFMU)<br>(Bailit et al. 2015)           | Canada<br>(Mehrabadi et al. 2015)            | Nordic (NOSS)<br>(Thurn et al. 2015) |
|-------------------------------------|--|---|--|--------------------------------------|
| Setting                             | <sup>2010-11</sup><br>221 hospitals<br>n=134   | <sup>2008-11</sup><br>25 hospitals<br>n=158 | <sup>2009-10</sup><br>All hospitals<br>n=819 | 2009-12<br>All hospitals<br>n=205    |
| Diagnosis                           | Clinical & Path                                | Clinical & Path                             | ICD (Canada)                                 | Clinical                             |
| Incidence<br>(per 10,000 mat)       | 1.7  | 13.7  | 14.4   | 3.4                                  |
| Prenatal dx                         | 50%  | 53%   | 53%  | 29%                                  |
| <u>No</u> risk factors<br>(PP + CS) | 5%   | PP 68%<br>CS 37%                            | 69%  | 31%                                  |
| Accreta                             | 65%  | 71%   |  |                                      |
| In/Per-creta                        | 5/29%  | 15/11%                                      |  |                                      |
| Hysterectomy                        | 59%  | 70%   | 17%  | 47%                                  |

# AIP Risk Factors

Caesarean sectionPlacenta praevia

Uterine curettage (repeated/post delivery) Uterine surgery Endometrial ablation

| Silver et al. 2006 | Placenta | No placenta |
|--------------------|----------|-------------|
| Caesarean Delivery | praevia* | praevia     |
| First              | 3.3      | 0.03        |
| Second             | 11       | 0.2         |
| Third              | 40       | 0.1         |
| Fourth             | 61       | 0.8         |
| Fifth              | 67       | 0.8         |
| ≥ Sixth            | 67       | 4.7         |

# Uterine pathologies associated with AIP

| Classification       | Type of uterine pathologies       |
|----------------------|-----------------------------------|
| Direct surgical scar | Cesarean delivery                 |
|                      | Surgical termination of pregnancy |
|                      | Dilatation and curettage          |
|                      | Myomectomy                        |
|                      | Endometrial resection             |
|                      | Asherman's syndrome               |
| Nonsurgical scar     | IVF procedures                    |
|                      | Uterine artery embolization       |
|                      | Chemotherapy and radiation        |
|                      | Endometritis                      |
|                      | Intra-uterine device              |
|                      | Manual removal of placenta        |
|                      | Previous accreta                  |
| Uterine anomalies    | Bicornuate uterus                 |
|                      | Adenomyosis                       |
|                      | Submucous fibroids                |
|                      | Myotonic dystrophy                |
|                      |                                   |

<sup>a</sup>Source: Irving and Hertig,<sup>1</sup> Jauniaux and Jurkovic,<sup>2</sup> Jauniaux et al.,<sup>3</sup> Parra-Herran and Djordjevic,<sup>4</sup> Jauniaux E, et al.,<sup>14</sup> Wu et al.<sup>15</sup> Number of uterine proceduresAdj RR AIP in primiparous women11.5 (1.1-1.9)22.7 (1.7-4.4)≥35.1 (2.7-9.6)Laparoscopy, hysteroscopy, currettage Incl.<br/>TOP), endomtrial ablation<br/>Baldwin et al. 2018

Assisted reproductive technology Nordic OSS aOR 3.1 (1.1-9.0) UK OSS aOR 32.1 (2.0-509) but No increase in RR in meta-analysis cohort studies (Qin et al. 2016)

#### Jauniaux et al.2018

# Abnormally invasive placenta Diagnosis

# Screening

- History (e.g. number CS)
- First trimester US scar + trophoblast]

### - Second trimester US

(a) Praevia(b) Lacunae / Anomalies uterus-bladder interface

# Diagnosis

- US (first, second trimester)
  - (a) Individual features (6 gray scale, 4 CD)
  - (b) Risk scores (Multiple US features ± history)
    - Accreta Index, Two Criteria System

# MRI (second, third trimester) (a) Individual features (5 T2W features)

Pro forma for ultrasound reporting in suspected abnormally invasive placenta (AIP): an international consensus

Z. ALFIREVIC<sup>\*</sup>, A.-W. TANG<sup>\*</sup>, S. L. COLLINS<sup>†</sup>, S. C. ROBSON<sup>‡</sup> and J. PALACIOS-JARAQUEMADA<sup>§</sup>, on behalf of the Ad-hoc International AIP Expert Group

| Cervical length (without funnel or placental tissue)   |     |    | mm        |
|--|-----|----|-----------|
| Greyscale ultrasound parameters and definition   | Yes | No | Unsure    |
| Loss of 'clear zone'   |     |    |           |
| - Loss, or irregularity, of the hypoechoic plane in the myometrium underneath the placental bed                |     |    |           |
| (the 'clear zone')   |     | -  |           |
| Myometrial thinning  |     |    |           |
| <ul> <li>Thinning of the myometrium overlying the placenta to &lt;1mm or undetectable</li> </ul>               | -   | -  |           |
| Abnormal placenta lacunae  |     |    |           |
| - Presence of numerous lacunae including some that are large and irregular, often containing                   |     | 1  |           |
| turbulent flow visible in greyscale imaging  | -   | -  |           |
| Bladder wall interruption  |     |    |           |
| - Loss or interruption of the bright bladder wall (the hyperechoic band or 'line' between the                  |     |    |           |
| uterine serosa and the bladder lumen)  |     |    |           |
| Placental bulge  |     |    |           |
| - Deviation of the uterine serosa away from the expected plane, caused by an abnormal bulge of                 |     |    |           |
| placental tissue into a neighbouring organ, typically the bladder. The uterine serosa appears                  |     |    |           |
| intact but the outline shape is distorted  |     |    |           |
| Focal exophytic mass   |     |    |           |
| - Placental tissue seen breaking through the uterine serosa and extending beyond it. Most often                |     |    |           |
| seen inside a filled urinary bladder   |     |    |           |
| Colour Doppler ultrasound parameters and definition  | Yes | No | Unsure    |
| Utero-vesical hypervascularity   |     |    |           |
| - Striking amount of colour Doppler signal seen between the myometrium and the posterior wall                  |     |    |           |
| of the bladder. This sign probably indicates numerous, closely packed, tortuous vessels in that                |     |    |           |
| region (demonstrating multi-directional flow and aliasing artefact)  |     | -  |           |
| Sub-placental hypervascularity   |     |    |           |
| - Striking amount of colour Doppler signal seen in the placental bed. This sign probably indicates             |     |    |           |
| numerous, closely packed, tortuous vessels in that region (demonstrating multi-directional flow                |     |    | 1         |
| and aliasing artefact)   | -   | -  |           |
| Bridging vessels   |     |    |           |
| <ul> <li>Vessels appearing to extend from the placenta, across the myometrium and beyond the serosa</li> </ul> |     | 1  | · · · · · |
| into the bladder or other organs. Often running perpendicular to the myometrium                                |     |    |           |
| Placental lacunae feeder vessels   |     |    |           |
| - Vessels with high velocity blood flow leading from the myometrium into the placental lacunae,                |     |    |           |
| causing turbulence upon entry  |     | -  |           |
| Parametrial involvement  | Yes | No | Unsure    |
| - Suspicion of invasion into parametrium   |     |    |           |

#### **Clinical Significance of Ultrasound Findings**

| Probability of clinically significant AIP<br>Extent of AIP | High<br>Focal | Intermediate Diffuse | Low |
|--|---------------|----------------------|-----|
|--|---------------|----------------------|-----|

# Abnormally invasive placenta Ultrasound features

• Lacunae (Gray scale + CD



| AIP<br>Yang et al.<br>2006 | Grade 0<br>None | <b>Grade 1</b><br>1-3 small | <b>Grade 2</b><br>4-6 larger,<br>more irregular | <b>Grade 3*</b><br>> 6 large,<br>irregular |
|----------------------------|-----------------|-----------------------------|---|--|
| None                       | 22              | 6                           | -   | -  |
| Accreta                    | 3               | 4                           | 1   | -  |
| Increta                    | -               | -                           | 5   | 4  |
| Percreta                   | -               | -                           | 5   | 1  |
| Total                      | 25              | 10                          | 11  | 5  |

Abnormally invasive placenta Ultrasound features

- Lacunae (Gray scale + CD
- Loss of retroplacental hypoechoic zone
   (Gray scale)
   (Gray scale)

- Abnormalities of uterus-bladder interface (Gray scale + Colour Doppler)
- Abnormal placental vascularization
   (3D Power Doppler)





# Abnormally invasive placenta Ultrasound features

- Lacunae
- Loss of retroplacental hypo-echoic zone
- Abnormalities of uterus-bladder interface
- Abnormal placental vascularization



# Abnormally Invasive Placenta US diagnosis

 More US features present – greater risk of: (a) AIP
 (b) Percreta



| Number of features  | No Al                                    | Accreta          | In/per-creta         |
|---|--|------------------|----------------------|
| 0   | 412                                      | 5                | 0                    |
| 1 or 2  | 8  | 12               | 6                    |
| >2  | 0  | 10               | 32                   |
| Lacunae<br>Loss R/P hypo-echoic zone,<br>Abn. U-B interface<br>Abn. placental vascularization | SPR = 14%<br>FPR 1.7%<br>Dehiscence, Vas | scular malformat | tion (prior surgery) |

# Abnormally invasive placenta Placental MRI features

### Heterogeneous signal intensity

- Large, tortuous placental vessels
- High signal on FISP (=vascular flow )

### Interruption of myometrium

- Thinning & disruption myometrium

### • Dark intraplacental bands (T2)

- Low signal on FISP ? 2° to fibrin deposition
- Number /size of bands  $\propto$  degree of AIP.
- Uterine bulging
- Extra-uterine invasion







# Abnormally invasive placenta Purpose of prenatal diagnosis

### **Avoid False Negative**

Undiagnosed major invasion at CS



Risk of major morbidity/mortality from haemorrhage

### **Avoid False Positive**



#### Unnecessary caesrean hysterectomy



Risk of major surgical morbidity/mortality

### NE & NC AIP Service Screening/diagnosis pathway



All women with Uterine scar Placenta implanted over scar

Newcastle Fetal Medicine Centre by 28 w

#### Appendix 1: Ultrasound features of abnormally invasive placenta (from\*)

 Lacunae (large [>1 cm] Irregular echoluscent areas usually with visible turbulent flow the more/larger the lacunae the more likely there is AIP and the more likely this is placenta increta/percreta (sensitivity 78%, specificity 95%)



Absormal placental lacunae (a,b) and normal placenta (c) on grayscale ultrasound

 Loss of retoplacental hypoechoic space (loss of decidua and subplacental vascular space (sensitivity 66%, specificity 96%)



Loss of clear core (a) and normal placents (b) on grayscale ultrasound

 Abnormalities of uterus-bladder interface – bulge or focal exophytic mass (typically extending beyond serosa and seen inside filled bladder (sensitivity 50%, specificity 99.8%)



Bladder wall interruption / exophytic mass (a,b) and normal placents (c) on grayscale ultrasound

 Colour Doppler abnormalities – subplacental and/or uterovesical hypervascularity (sensitivity 91%, specificity 88%)



Uterovesical hypervascularity (a) and a normal vascularity on colour Doppler Imaging.

Introduced in 2015



1.5 T (T1 W (sagittal), T2 W (axial, coronal, sagittal) Balanced GE (axial, sagittal)

### NE & NC AIP Service Referrals to Newcastle for AIP diagnosis

### Newcastle Fetal Medicine Centre

**MDT** 

#### Degree (in/percreta vs accreta)

GA at delivery Anaesthetic: regional/general IR: IIA/CIA/ Aortic Ureteric stenting Incision (skin/uterus) Placental removal Hysterectomy Myometrial resection

Cell salvage / blood products

Surgical plan / Consent (by 30 wk)

FM specialist (2) (Uro)gynaecologist (3) Radiologist (IR) (3) Obstetric Anaesthetist (2) Midwife (1)



75%

# Abnormally Invasive Placenta Surgical Management – Options

# Resective primary surgery

Hysterectomy (total vs subtotal)
Uterine conservation (complete vs. partial [3P]) *Iliac vs aortic endovascular occlusion Ureteric stenting*

# Placental conservation

- Await spontaneous expulsion / resorption
- Secondary hysterectomy

# AIP – Surgical Management 'Conservative' surgery

### One-stop (complete) resection Palacios Jaraquemada 2004, 2012

- 1. Disconnection of vesico- & colpouterine anastomotic systems
- 2. T/V hysterotomy
- 3. Ligation of uterine arteries
- 4. Resection of invaded tissue and entire placenta in one piece





1° Failure (PPH)  $\rightarrow$  CH - S1 (n=46) 4% - S2 (n=22) **72%** UT damage 5% 2° PPH (CH) – 0% Infection/Sepsis – 3% DIC/VTE – 3% Recurrent AIP – 2%

# Case series of 'Conserving' CS in AIP



<sup>1</sup>Review of 48 (case) reports <sup>2</sup>Review of experience from 25 French centres

 $1^{\circ} \text{ PPH} \rightarrow \text{CH} (15\text{-}20\%)$   $2^{\circ} \text{ PPH} \rightarrow \text{CH} (10\text{-}20\%)$ Infection / sepsis – 30% / 10% DIC/VTE - 10%Recurrent AIP 30%



### NE & NC AIP Service Referrals to Newcastle for AIP diagnosis



### Management of AIP

### Strategies to minimise the risk of major haemorrhage

- Accurate prenatal diagnosis & surgical planning (MDT)
- Optimisation pre-delivery Hb (aim > 110 g/L) parenteral Fe
- Elective delivery by experienced surgical team
- Availability blood and blood products on site (MOH protocol)
- 24 h Haematology advice (protocols for rapid access to platelets and clotting factors)
- Interventional radiology (iliac / aortic occlusion)
- Intraoperative cell salvage
- Tranexamic acid
- Haemostatic agents & sealants
- 'Advanced' compression or respective surgery

# Placenta percreta / accreta Haematological support

90% women with in-/per-creta will need transfusion Average blood loss is 3-5 L

- Inform consultant haematologist in advance
   Massive Obstetric Haemorrhage protocol
- IV access Large bore peripheral lines - Arterial line
- Intraoperative cell salvage (leucodepletion filter)
   Two suction probes
- Monitor loss and haemostatic competence
  - POC HemoCue
    - Thromboelastography (TEG) / Thromboelastometry (ROTEM)
  - Lab Fibrinogen (aim > 1 g/L)
    - PT (aim < 1.5 x normal)
    - Platelets (aim > 50 x 109/L)
    - Lactate

# Management of AIP Intraoperative cell salvage

### Advantages

No risk allogenic transfusion reactions or blood borne infections Avoid immune-modulating effects allogenic transfusion (nocosomial infection) Immediate availability blood Accepted by some Jehovah's Witnesses More physiological than stored blood

|                    | ICS Collected Blood                   | Packed Red Blood Cells      |
|--------------------|---------------------------------------|-----------------------------|
| Temperature        | Room temperature                      | 1-10°C                      |
| Levels of 2,3-DPG  | Physiological                         | Decreased by up to 90%      |
| Potassium          | Physiological or slightly decreased   | Increased                   |
| Haematocrit        | 50-80%                                | 60%                         |
| Removed Components | Plasma, platelets, activated clotting | Plasma, platelets, clotting |
|                    | Idelois                               | lacions                     |
| Additive           | None*                                 | Citrate                     |

### Disadvantages

Capital costs Set-up time Insufficient volume salvaged blood

### FMH (with alloimmunisation) Hypotension

(with leucocyte depletion filter) Bacterial contamination

Key challenge in AIP: Rate of haemorrhage vs Rate salvage/allogenic transfusion

Close liaison with the hospital transfusion laboratory is essential for women presenting with placenta praevia or a low-lying placenta. [*New 2018*]



Rapid infusion and fluid warming devices should be immediately available. [New 2018]

Cell salvage is recommended for women where the anticipated blood loss is great enough to induce anaemia, in particular, in women who would decline blood products.



D

### Management of AIP Cell salvage during CS where 'at risk' of PPH (SALVO trial)

| Analysis   | Number (%)                     |                                     | Crude analysis                            |  |                 | Adjusted analysis <sup>1</sup>            |  |                 |
|--|--------------------------------|-------------------------------------|---|--|-----------------|---|--|-----------------|
|  | Control<br>( <i>n</i> = 1,492) | Cell salvage<br>( <i>n</i> = 1,498) | Risk<br>difference<br>percent<br>(95% CI) | Intervention<br>odds ratio<br>(95% CI) | <i>p</i> -Value | Risk<br>difference<br>percent<br>(95% CI) | Intervention<br>odds ratio<br>(95% CI) | <i>p</i> -Value |
| Primary analysis                                 |                                |                                     |   |  |                 |   |  |                 |
| Received donor blood<br>transfusion              | 52 (3.5%)                      | 37 (2.5%)                           | -1.02 (-2.23, 0.20)                       | 0.70 (0.46, 1.08)                      | 0.10            | -1.03 (-2.13,<br>0.06)                    | 0.65 (0.42, 1.01)                      | 0.056           |
| Sub-group analysis by<br>indication for cesarean |                                |                                     |   |  |                 |   |  |                 |
| Emergency cesarean (n = 1,641)                   | 37 (4.6%)                      | 25 (3.0%)                           |   |  |                 |   | 0.58 (0.34, 0.99)                      |                 |
| Elective cesarean ( $n = 1,349$ )                | 15 (2.2%)                      | 12 (1.8%)                           |   |  |                 |   | 0.83 (0.38, 1.83)                      |                 |
| Sub-group analysis by placentation <sup>2</sup>  |                                |                                     |   |  |                 |   |  |                 |
| Normal placentation $(n = 2,720)$                | 40 (2.9%)                      | 24 (1.8%)                           |   |  |                 |   | 0.56 (0.34, 0.94)                      |                 |
| Abnormal placentation (n = 270)                  | 12 (8.9%)                      | 13 (9.6%)                           |   |  |                 |   | 0.98 (0.42, 2.32)                      |                 |

Sensitivity analysis: assuming return salvaged blood in control group in emergency situation avoided transfusions – aOR 0.56 (0.36, 0.86)

Secondary outcomes: No differences in maternal outcomes (e.g. stay, Hb, fatigue) **FMH** increased in salvage group: 10.5% vs 25.6% (aOR 5.53 [1.43, 22.1])

#### Khan et al. BMJ 2018

## Management of AIP Intraoperative cell salvage

Retrospective analysis pre & post routine IOCS in AIP

|                        | Controls<br>(n=115) | IOCS<br>(n=108)  | OR (95% CI)      |
|------------------------|---------------------|------------------|------------------|
| EBL (ml)               | 1600 (200, 6500)    | 1575 (300, 5500) |                  |
| Allogenic RBC Tx (ABT) | 66 (57%)            | 21 (19%)         | 0.17 (0.10-0.33) |
| FFP                    | 33 (29%)            | 8 (7%)           |                  |
| Volume colloids        | 500 (0,1500)        | 9 (0, 1500)      |                  |



Relationship between EBL and blood volume recovered

Zeng et al. 2018



Control: BL >2L nearly all required ABT IOCS; ABT avoided in 80% (BL 2.1-3L) 29% (BL 3.1-4L & > 4L)

# Placenta percreta / accreta Haematological support

90% women with in-/per-creta will need transfusion Average blood loss is 3-5 L

- Blood products
  - Packed RBC (4u available)
  - Fresh frozen plasma
  - Platelets
  - Cryoprecipitate

Move to military trauma transfusion protocols **5:2:2:1** / 4.5:2:1:1 / 4.5:1:1

- Tranexamic Acid (1g IV) 2<sup>nd</sup> dose after 30 min if haemorrhage continues or recurs within 24h
- [rFVIIa risk of arterial thrombosis]

#### Fibrinogen content

1 u FFP 1 10 u cryoppt

#### 1 PRBC

1 6 pack platelets

#### 400 mg/250 mL 2500 mg/150 mL < 100 mg 480 mg

# Endovascular occlusion in AIP Internal iliac arteries

- Widely practiced
- Complications 6-16% (*Dilauro et al.* 2012) Haematoma, aneurysms, dissection, TE (2-3%)
- One RCT (n=27) no effect on blood loss or RBC transfusion (Salim et al. 2015)
- Meta-analysis of effect 'IR' (D'Ontonio et al 2018)
  - Heterogeneity of technique (embolization) & effect
  - Reduced blood loss but no effect on transfusion & major morbidity
- 'Failure' rates' high (35-58%)
- (Clark 1985, Chattopahyay et al. 1990)
- Limited haemodynamic effects
  - Pulse pressure  $\downarrow$  85% (Burchall 1964)
  - Uterine artery Doppler PI no change (Chitrit et al. 2000)





### Management of AIP

### Role of interventional radiology: SR and meta-analysis

| 15 studies (995 women)<br>Only 1 study at low risk of bias | N. Studies<br>(sample) | Mean difference (95% CI) or<br>Rates (Pooled OR [95% CI]) | р      |
|--|------------------------|---|--------|
| All women  |                        |   |        |
| Blood loss (L)   | 13 (821)               | -1.01 (-1.59, -0.43)                                      | <0.001 |
| PRBC transfused (u)  | 9 (254)                | -2.20 (-5.52, 1.13)                                       | 0.2    |
| FFP transfused (u)   | 3 (106)                | -2.59 (-7.09, 1.92)                                       | 0.3    |
| $BL \ge 2.5L$  | 4 (126)                | 29% vs 65% (OR 0.18 (0.04-0.78))                          |        |
| PRBC transfused $\geq$ 5u                                  | 5 (112)                | 33% vs 52% (OR 0.45 (0.17-1.24))                          |        |
| PND AIP undergoing hysterector                             | ny                     |   |        |
| Blood loss (L)   | 6 (258)                | -0.68 (-1.24, -0.12)                                      | 0.02   |
| PRBC transfused (u)  | 5 (160)                | -2.92 (-9.34, 3.50)                                       | 0.4    |
| FFP transfused (u)   | 3 (205)                | -1.66 (-2.71, -0.61)                                      | 0.02   |
| BL ≥ 2.5L  | 4 (155)                | 23% vs 63% (OR 0.10 (0.02-0.47))                          |        |
| PRBC transfused $\geq$ 5u                                  | 4 (150)                | 32% vs 54% (OR 0.57 (0.07-4.67))                          |        |

No differences in: PLT or Cryoppt transfused, operative time, length of stay Surgical complications, bladder-ureteral injuries, re-laparotomy, infection, DIC

D'Antonio et al. 2018

## Management of AIP Multidisciplinary specialised team (MST)

- Retrospective series suggest MST approach reduces maternal morbidity (Walker et al. 2012, Shamshirsaz et al. 2014)
- 'Benefits' mainly related to:
  - blood loss (BL), transfusion vs. organ damage/uterine conservation
  - prenatally diagnosed cases with major invasion
  - Management of placenta at laparotomy
- Morbidity higher in planned vs. urgent deliveries (Shamshirsaz et al. 2018)
- BL /transfusion requirements improve with experience (Shamshirsaz et al. 2017)

In UK care for women with AIP (diagnosis & management) to be a specialised (nationally) commissioned service in small number of regional centres (NHSE 2018)

Abnormally invasive placenta Conclusions

- Care pathways need to focus on minimising morbidity by

   (a) accurate prenatal diagnosis and (b) appropriately conducted surgical delivery by an experienced (multidisciplinary) team.

   All obstetricians need to know how to manage unexpected AIP
- Conservative (resective) surgery feasible in a minority of carefully selected cases but with definitive diagnosis of in/percreta primary CH remains current treatment of choice
- Strong case for all suspected cases to be managed by a regional specialised team