Women with fetal abnormality or obstetric indication for immediate delivery were excluded.

Interventions Participants were randomly allocated to either serial weekly trans-abdominal amniotomies when the deepest pool of amniotic fluid was less <2 cms or expectant management.

Results 58 pregnancies recruited: 28 in the amniotomy group (AI); 28 in the expectant management group (exp); two post-randomisation exclusions. Overall perinatal survival in both groups was 17/56.

Mean gestational age for AI group was 28.4 weeks vs. 29.8 weeks for exp (mean SD-1.4, 95% CI -0.2-1.5). One case of severe maternal sepsis requiring admission to HDU in the expectant management arm.

Overall chance of surviving without long-term respiratory or neurodevelopmental disability is 7.1%; 4/28 (14%) in the AI group and 0/28 in the exp group (RR 9.0; 95% CI 0.51, 159.70).

Conclusions The pilot findings do not suggest that clinicians should alter the current practise of expectantly managing rupture of membranes between 16 + 0 and 24 + 0 weeks of pregnancy. A larger definitive study to evaluate whether amniotomy has a cost-effective and acceptable role in improving healthy survival in very early rupture of membranes indicated.

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4.2 VARIATION IN BETA DEFENSIN 1 GENOTYPE IS ASSOCIATED WITH PRETERM BIRTH

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¹CP James, ²M Bajaj-Elliott, ³A Syngelaki, ²N Klein, ³K Nicolaides, ¹D Peebles. ¹UCL Institute for Women's Health, London, UK; ²UCL Institute of Child Health, London, UK; ³Fetal Medicine Unit, King's College Hospital, London, UK

Introduction Human beta defensin 1 (HBD1) is an antimicrobial and immunomodulatory peptide present in cervical mucus. Variation in cervical antimicrobial expression is associated with preterm labour. We hypothesised that SNPs in the HBD1 gene may be associated with preterm birth.

Methods This is a retrospective case control study using blood collected at 11–13 weeks from women attending King's College Hospital March 2006–September 2010. 50 women with PPRM and 50 with spontaneous preterm labour were matched with 300 who delivered >37/40. SNPs rs1799946 (5'UTR) and rs1047031 (3'UTR) were genotyped by KASP assay (Kompetitive Allele Specific PCR, KBioscience). Data were analysed using multiplicative (rs1047031) and recessive (rs1799946) models and Chi Square Test.

Results There was no difference in BMI, smoking status or ethnicity between groups. Genotyping was successful in 98% (n = 390) and 97% (n = 386) samples for rs1047031 and rs1799946 respectively. Allele distribution demonstrated Hardy-Weinberg equilibrium. AA-homozygotes (rs1799946) had increased risk of PPRM; OR 2.24 (95%CI 1.11–4.49), p = 0.0257. 117 women had at least one prior delivery <37/40, 36 had a history of delivery <28/40. AA-homozygotes (rs1799946) had increased risk of delivery <37/40; OR 2.14 (95%CI 1.24–3.68), p = 0.005 and <28/40; OR 4.08 (95%CI 1.93–8.63), p < 0.0001. A allele carriers (rs1047031) were less likely to deliver <28/40; OR 0.288 (95%CI 0.121–0.683), p = 0.003.

Conclusion rs1799946 is associated with PPRM, a doubled risk of delivery <37/40 and a four-fold increase in the risk of delivery <28/40. rs1047031 may be protective. Variation in immune genotype may contribute to the clinical phenotype of women who deliver preterm.

4.3 THE RELATIONSHIP BETWEEN CAUSE AND TIMING OF PREVIOUS STILLBIRTH AND THE RISK OF STILLBIRTH IN SECOND PREGNANCIES

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AA Moraitis, GC Smith. University of Cambridge, Cambridge, UK

Background Women with a previous stillbirth are at increased risk of stillbirth in their second pregnancy. However, there is little information on the relationship between the cause and timing of stillbirth in the first pregnancy and the risk in the second.

Methods and Results We identified 244,122 records in nationally collected Scottish data with complete information on their first and second births. The risk of stillbirth in the second pregnancy was 2.7 per 1,000 among 242,800 women with previous live birth and 15.9 per 1,000 among 1,323 women with previous stillbirth (odds ratio [OR] = 5.95 [95% CI 3.84–9.22] p < 0.001). Adjustment for maternal characteristics had no material effect. The risk was similarly elevated for different causes of stillbirth in the first pregnancy. It was also similarly elevated whether the previous stillbirth was extreme preterm (24–32 weeks) or late preterm/term (33–43 weeks). However, the association in the second pregnancy significantly varied across the range 24–43 weeks (test of proportional hazards assumption p = 0.01). Previous stillbirth was strongly associated with the risk at 24–28 weeks (15.66 [8.44–29.05], P < 0.001), at 29–32 weeks (5.16 [1.64–6.27], P = 0.005) and 33–36 weeks (6.03 [2.47–14.72], P < 0.001) but there was no significant association at term (1.7 [0.42–6.82]), probably due to routine elective delivery at 37–38 weeks.

Conclusion Previous stillbirth is a strong risk factor for stillbirth in second pregnancies irrespective of the cause of the first stillbirth. The recurrence risk is much higher at extreme preterm gestational ages, but is still present at 33–36 weeks.

Fetal Medicine Posters

PF.01 PRENATAL CHROMOSOMAL MICROARRAY USE: A PROSPECTIVE COHORT OF FETUSES AND A SYSTEMATIC REVIEW AND META-ANALYSIS

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¹SC Hillman, ²DJ McMullan, ²G Hall, ²FS Togneri, ³N James, ³EJ Maher, ⁴CH Meller, ²D Williams, ⁶RJ Wapner, ¹ER Maher, ¹MD Kilby. ¹School of Clinical and Experimental Medicine, College of Medicine and Dentistry, University of Birmingham, Birmingham, UK; ²West Midlands Regional Genetics Laboratories and the Department of Clinical Genetics, Birmingham Women's Foundation Trust, Birmingham, UK; ³South East UK Cytogenetics Service, Western General Hospital, Edinburgh, UK; ⁴Fetal Medicine Centre, Birmingham Women's Foundation Trust, Birmingham, UK; ⁵Obstetric Division, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; ⁶Department of Obstetrics and Gynecology, Columbia University Medical Center, New York, United States of America

Background Chromosomal microarray testing (CMA) is utilised in prenatal diagnosis to detect chromosomal abnormalities not visible by full, conventional karyotyping. We present our prospective cohort of women undergoing fetal microarray and karyotyping for an abnormal prenatal ultrasound scan (USS). This cohort is presented in the context of a systematic review and meta-analysis of the literature (until December 2012) which defines overall detection rates by microarray over karyotyping.

Systematic review methods: MEDLINE (1970–June 2012), EMBASE (1980–June 2012), Cinhal (1982–June 2012) were searched electronically. Selected studies had >5 cases and microarray testing was performed prenatally in addition to karyotyping. The search yielded 559 citations. Full manuscripts were retrieved for 85 and 24 primary studies were included in the systematic review.

Cohort Methods A prospective cohort study of 243 women undergoing microarray testing alongside karyotyping when a structural abnormality was detected on prenatal USS.

Results When clinical indication for testing was abnormal fetal USS our cohort study noted a 4.1% increase in detection rate; lower than the rate of 10.1% (95% CI 8.0–12.7%) by meta-analysis. When any clinical indication for prenatal microarray was meta-analysed the detection rate over karyotyping was 5.6% (95%CI 3.0–10.6%) and the variant of unknown significance (VOUS) rate was 1.4% (95%CI 0.5–3.7%).

Conclusion Chromosomal microarray is useful prenatally particularly for an abnormal fetal USS. Prospective counselling should include the approximate VOUS rate (1.4% rising to 2.1% for abnormal USS). It is likely that microarray testing will replace karyotyping in high risk pregnancies (such as abnormal USS).

PF.02 THE ROLE OF QUANTITATIVE FETAL FIBRONECTIN AND CERVICAL LENGTH IN PREDICTING SPONTANEOUS PRETERM BIRTH IN MULTIPLE PREGNANCIES

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R Mapara, DS Abbott, NL Hezelgrave, AH Shennan. *Division of Women's Health, KCL, Women's Health Academic Centre, KHP, London, UK*

Background Multiple pregnancies are associated with a higher risk of spontaneous preterm birth (sPTB). Whilst fetal fibronectin (fFN) and cervical length (CL) measurement can predict sPTB in singleton pregnancies (Kurtzman *et al*, 2009), their value for twin pregnancies is unknown.

Methods Prospective blinded secondary analysis of longitudinal samples of cervicovaginal fluid fFN concentration (nanograms per milliliter) using a bedside 10 qfFN analyzer (HOLOGIC, USA), and transvaginal ultrasound CL of 93 consecutive women with multiple pregnancies attending a Preterm Surveillance Clinic at St. Thomas Hospital from 18 weeks gestation (Oct 2010–Jan 2012). qfFN was assigned 4 ranges; <10, 10–50, 50–200, >200 (ng/ml) to detect spontaneous delivery before 30, 34 and 37 weeks. qfFN was blinded to clinicians using an embedded code in the analyzer.

Results The rate of sPTB (<37 weeks) rose increased with increasing qfFN from 17.5% (<10 ng/ml) to 61.5% (>200 ng/ml) and the negative prediction value for sPTB <30 weeks at <10 ng/ml was 98%. 4/13 (30%) of women with qfFN > 200 ng/ml delivered <30 weeks gestation. Using combined CL/qfFN testing, the positive prediction value of a qfFN value >200 ng/ml and CL < 25 mm was 87.5% for SPTB <37 weeks.

Conclusion This is the first report of 10 qfFN in twins, demonstrating that it adds predictive value to the qualitative results (negative cut-off at 50 ng/ml). High levels, even in early pregnancy, are associated with preterm delivery. Using cervical length and qfFN, management can be targeted to this group; e.g. antenatal maternal steroids. Further research should evaluate interventions to prolong pregnancy in this highest risk group, while lower risk women can be reassured.

PF.03 CRITERIA FOR A LEGITIMATE LIFE: TERMINATION OF PREGNANCY FOR NON-LETHAL FETAL ANOMALY AS AN ACCEPTABLE OUTCOME FOR AN AFFECTED PREGNANCY

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L Crowe, RH Graham, SC Robson, J Rankin. *Newcastle University, Newcastle Upon Tyne, UK*

Introduction Advances in diagnosis and treatment, coupled with increased social status of people with disabilities, make society's responses to termination of pregnancy for fetal anomaly (TOPFA) more contentious. This study aims to understand medical and social care professionals' perspectives on the meanings and implications of non-lethal disability from birth, and to evaluate the relationship with perceptions of TOPFA.

Methodology Qualitative, in-depth interviews were conducted with 14 medical professionals and 9 social care professionals. The data were analysed using a generative thematic approach.

Results For social care professionals, abnormal experience of life had become the norm; their narratives of the consequences of fetal anomaly for family life were more nuanced, containing more detailed discussion of the complexities of living with a disabled person. In contrast, medical professionals' accounts of family life with an affected person were dominated by the consequences for the

affected individual. The impact of predicted long term outcome in relation to decisions about TOPFA varied across both professional groups; at one end of the spectrum, some professional felt perceived risk was enough to support TOPFA; at the other extreme, individuals who had seen positive outcomes with a specific condition felt TOPFA was not acceptable.

Conclusion The professional groups discuss similar issues, but interpret them differently. Social care professionals focused on their professional insight into life with an affected person; this was used as a rationale for both accepting and not accepting TOPFA. Medical professionals focused on the perceived seriousness of the condition and the wording of the legislation.

PF.04 ABNORMAL PLATELET REACTIVITY IN PREGNANCIES COMPLICATED BY INTRAUTERINE GROWTH RESTRICTION

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¹S Mullers, ¹N Burke, ¹K Flood, ¹H O'Connor, ¹M Dempsey, ²B Cotter, ¹E Tully, ²P Dicker, ¹M Geary, ²D Kenny, ¹FD Malone. ¹RCSI, Rotunda Hospital, Dublin, Ireland; ²Royal College of Surgeons Ireland (RCSI), Dublin, Ireland

Platelet function in pregnancies complicated by intra-uterine growth restriction (IUGR) is not well understood. We sought to evaluate platelet function in response to multiple concentrations of multiple agonists in pregnancies complicated by IUGR using a novel platelet function assay.

Cases of intrauterine growth restricted singleton pregnancies were recruited following ultrasound diagnosis between 24–40 weeks gestation (estimated fetal weight <10th centile for gestational age) in a tertiary referral centre. A modification of standard light transmission aggregometry was used to assess platelet reactivity. Several agonists were assessed at incremental concentrations to characterise the response to multiple receptors. The findings were compared to healthy controls matched for gestational age with normal fetal weight.

A total of 24 pregnancies complicated with IUGR and 36 healthy controls were recruited. Platelet reactivity in response to the agonists Arachidonic acid, Adenosine-diphosphate, Epinephrine and Thrombin-receptor activating protein was significantly reduced in the IUGR cohort. There was a nonsignificant trend to decreased reactivity in response to collagen (Table 1).

Abstract PF.04 Table 1 Concentration of EC₅₀ for each agonist

Agonist	EC50		P value
	Normal pregnancy	IUGR	
Arachidonic acid	0.064	0.283	<0.0001
Adenosine-diphosphate	21	54	0.0007
Collagen	0.052	0.427	0.0973
Epinephrine	231.4	3839	0.0015
Thrombin-receptor activating protein	10.27	71.54	<0.0001

In pregnancies complicated by IUGR there is a significant decrease in platelet function compared to healthy pregnant controls. This may reveal valuable insights into the patho-physiology of the disease, and may represent an inadequate growth factor response in IUGR. Further evaluation of the role of platelets may aid in the development of future interventions for IUGR.

PF.05 ADVANCES IN TRISOMY 21 SCREENING IN THE WEST MIDLANDS, 1995–2011

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¹AM Tonks, ¹AS Gornall, ²SA Larkins, ²S Hamilton, ¹JO Gardosi. ¹Perinatal Institute, Birmingham, UK; ²West Midlands Regional Genetics Laboratory, Birmingham, UK