



February 2015 Literature Alert

1.

Prenat Diagn. 2015 Jan;35(1):81-9. doi: 10.1002/pd.4487. Epub 2014 Sep 30.
Consanguinity and pregnancy outcomes in a multi-ethnic, metropolitan European population. Becker R1, Keller T, Wegner RD, Neitzel H, Stumm M, Knoll U, Stärk M, Fangerau H, Bittles A.

Abstract

Objective

The aim of the present study was to assess the risk of major anomalies in the offspring of consanguineous couples, including data on the prenatal situation.

Methods

Over 20 years (1993–2012), 35 391 fetuses were examined by prenatal sonography. In 675 cases (1.9%), parents were consanguineous, with 307 couples (45.5%) related as first cousins, 368 couples (54.5%) beyond first cousins. Detailed information was retrieved on 31 710 (89.6%) fetuses, (consanguineous 568: 1.8%).

Results

Overall prevalence of major anomalies among fetuses with non-consanguineous parents was 2.9% (consanguineous, 10.9%; first cousins, 12.4%; beyond first cousins, 6.5%). Adjusting the overall numbers for cases having been referred because of a previous index case, the prevalences were 2.8% (non-consanguineous) and 6.1% (consanguineous) (first cousin, 8.5%; beyond first cousin, 3.9%). Further adjustment for differential rates of trisomic pregnancies indicated 2.0%/5.9% congenital anomalies (non-consanguineous/consanguineous groups), that is, a consanguinity-associated excess of 3.9%, 6.1% in first cousin progeny and 1.9% beyond first cousin.

Conclusions

The prevalence of major fetal anomalies associated with consanguinity is higher than in evaluations based only on postnatal life. It is important that this information is made available in genetic counseling programs, especially in multi-ethnic and multi-religious communities, to enable couples to make informed decisions.

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2.

J Ultrasound Med. 2015 Jan;34(1):137-42. doi: 10.7863/ultra.34.1.137.

Chorionic bump on first-trimester sonography: not necessarily a poor prognostic indicator for pregnancy. Arleo EK, Troiano RN.

Abstract

OBJECTIVES:

The purpose of this study was to determine the live birth rate of pregnancies with a diagnosis of a chorionic bump, a convex bulge from the choriodecidual surface into the first-trimester gestational sac.

METHODS:

Pregnant patients at least 18 years old with the finding of a chorionic bump on first-trimester sonography were included in this prospective observational study. The independent variables were chorionic bump size and number and presence or absence of a history of infertility or coagulation disorder. The primary end point was pregnancy outcome.

RESULTS:

During the 4-year study period, 52 pregnancies had a diagnosis of a chorionic bump. Overall, 34 resulted in live births, corresponding to an absolute live birth rate of 65%, and 18 were nonviable. Forty-one chorionic bump pregnancies were otherwise normal (ie, pregnancies in which a gestational sac, yolk sac, and embryo with heartbeat were seen at some point), and in this subset, the live birth rate was 83% (34 of 41). All pregnancies with more than 1 chorionic bump (4) ended in demise (100%). The average maximum dimension of the chorionic bump was 1.3 cm (range, 0.5-3.8 cm); however there was not a statistically significant correlation between chorionic bump size and pregnancy outcome (P = .5866; odds ratio, 0.54; 95% confidence interval, 0.06-5.01). Nine patients (17%) had a history of infertility treatment, and 4 (8%) had a history of coagulation disorder. Only 1 chorionic bump pregnancy was associated with a birth defect.

CONCLUSIONS:

The live birth rate in our chorionic bump cohort was 65% overall and even higher (83%) if the pregnancy was otherwise normal. The clinical implication is that a chorionic bump on first-trimester sonography is not necessarily associated with a guarded prognosis.

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PMID: 25542949 [PubMed - in process]

3.

Pediatrics. 2015 Jan;135(1):e92-8. doi: 10.1542/peds.2014-0596. Epub 2014 Dec 1.

Cesarean section and chronic immune disorders. Sevelsted A, Stokholm J, Bønnelykke K, Bisgaard H.

Abstract

OBJECTIVES:

Immune diseases such as asthma, allergy, inflammatory bowel disease, and type 1 diabetes have shown a parallel increase in prevalence during recent decades in westernized countries. The rate of cesarean delivery has also increased in this period and has been associated with the development of some of these diseases.

METHODS:

Mature children born by cesarean delivery were analyzed for risk of hospital contact for chronic immune diseases recorded in the Danish national registries in the 35-year period 1977-2012. Two million term children participated in the primary analysis. We studied childhood diseases with a suspected relation to a deviant immune-maturation and a debut at young age. The effect of cesarean delivery on childhood disease incidences were estimated by means of confounder-adjusted incidence rate ratios with 95% confidence intervals obtained in Poisson regression analyses.

RESULTS:

Children delivered by cesarean delivery had significantly increased risk of asthma, systemic connective tissue disorders, juvenile arthritis, inflammatory bowel disease, immune deficiencies, and leukemia. No associations were found between cesarean delivery and type 1 diabetes, psoriasis, or celiac disease.

CONCLUSIONS:

Cesarean delivery exemplifies a shared environmental risk factor in early life associating with several chronic immune diseases. Understanding commonalities in the underlying mechanisms behind chronic diseases may give novel insight into their origin and allow prevention.

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PMID: 25452656 [PubMed - in process]

4.

Fetal Diagn Ther. 2015;37(1):1-5. doi: 10.1159/000358301. Epub 2014 Dec 16.

Amniotic band syndrome: a single-institutional experience. Iqbal CW, Derderian SC, Cheng Y, Lee H, Hirose S.

Abstract

INTRODUCTION:

Amniotic band syndrome (ABS) is uncommon. We review our single-institutional experience to define its natural history and outcomes.

MATERIALS AND METHODS:

We conducted a retrospective analysis from a single, tertiary referral center of patients evaluated for and confirmed to have ABS from 1997 to 2012.

RESULTS:

Twenty-eight patients had confirmed ABS. The mean \pm SD maternal age was 27.9 \pm 5.9 years, and the mean gestational age at diagnosis was 20.7 \pm 3.8 months.

Oligohydramnios was reported in 4 patients. Eleven patients had membrane disruption, of whom 4 had undergone a prior percutaneous intervention.

Extremities were the most common site affected (n = 20), followed by the umbilical cord (n = 7), abdomen (n = 5), limb-body wall complex (n = 5), head (n = 1), and

chest (n = 1). Nine patients were felt to be candidates for fetal intervention; 5 underwent fetoscopic amniotic band lysis with 4 survivors. Overall survival, excluding 3 terminations, was 74%. There were 5 fetal demises and one neonatal death. Cord involvement was higher in nonsurvivors (67%) compared to survivors (19%, p = 0.05).

DISCUSSION:

ABS most commonly involves the extremities. Membrane disruption is not always present. Fetoscopic lysis is appropriate for select patients, and special consideration should be given for cord involvement, which is associated with a worse outcome. ©

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PMID: 25531236 [PubMed - in process]

5.

Ann Intern Med. 2015 Jan 6;162(1):35-45. doi: 10.7326/M14-1456.

Screening and treatment of thyroid dysfunction: an evidence review for the U.S. Preventive services task force. Rugge JB, Bougatsos C, Chou R.

Abstract

BACKGROUND:

In 2004, the U.S. Preventive Services Task Force found insufficient evidence to recommend thyroid screening.

PURPOSE:

To update the 2004 U.S. Preventive Services Task Force review on the benefits and harms of screening and treatment of subclinical and undiagnosed overt hypothyroidism and hyperthyroidism in adults without goiter or thyroid nodules.

DATA SOURCES:

MEDLINE and Cochrane databases through July 2014.

STUDY SELECTION:

Randomized, controlled trials and observational studies of screening and treatment.

DATA EXTRACTION:

One investigator abstracted data, and a second investigator confirmed; 2 investigators independently assessed study quality.

DATA SYNTHESIS:

No study directly assessed benefits and harms of screening versus no screening. For subclinical hypothyroidism (based on thyroid-stimulating hormone levels of 4.1 to 11.0 mIU/L), 1 fair-quality cohort study found that treatment of subclinical hypothyroidism was associated with decreased risk for coronary heart disease events versus no treatment. No study found that treatment was associated with improved quality of life, cognitive function, blood pressure, or body mass index versus no treatment. Effects of treatment versus no treatment showed potential beneficial effects on lipid levels, but effects were inconsistent, not statistically significant in most studies, and of uncertain clinical significance (difference, -0.7 to 0 mmol/L [-28 to 0 mg/dL] for total cholesterol levels and -0.6 to 0.1 mmol/L [-22 to 2 mg/dL] for low-density lipoprotein cholesterol levels). Treatment harms were poorly studied and sparsely reported. Two poor-quality studies evaluated treatment

of subclinical hyperthyroidism but examined intermediate outcomes. No study evaluated treatment versus no treatment of screen-detected, undiagnosed overt thyroid dysfunction.

LIMITATION:

English-language articles only, no treatment study performed in the United States, and small trials with short duration that used different dosage protocols.

CONCLUSION:

More research is needed to determine the clinical benefits associated with thyroid screening.

PRIMARY FUNDING SOURCE:

Agency for Healthcare Research and Quality.

PMID: 25347444 [PubMed - in process]

6.

J Pediatr. 2015 Jan;166(1):119-24. doi: 10.1016/j.jpeds.2014.09.006. Epub 2014 Oct

8. Long-term outcomes in children with congenital heart disease: National Health Interview Survey. Razzaghi H, Oster M, Reefhuis J.

Abstract

OBJECTIVE:

To assess the extent of long-term morbidity in children with congenital heart disease (CHD).

STUDY DESIGN:

We used data from the 1997-2011 National Health Interview Survey to study long-term outcomes in children aged 0-17 years with CHD. Parents were asked whether their child was diagnosed with CHD. We assessed for comorbidities, including autism/autism spectrum disorders; healthcare utilization, including number of emergency room visits; and daily life aspects, including number of days of school missed. These outcomes were compared between children with and without reported CHD using ORs and χ^2 statistics.

RESULTS:

The study included 420 children with reported CHD and 180 048 children without CHD, with no significant between-group differences in age and sex. The odds of reporting worse health and more than 10 days of school/daycare missed in the previous year were 3 times higher for the children with CHD compared with those without CHD. Children aged 2-17 with CHD were more likely than those without CHD to have had a diagnosis of autism spectrum disorder (crude OR, 4.6; 95% CI, 1.9-11.0) or intellectual disability (crude OR, 9.1; 95% CI, 5.4-15.4). The rates of emergency room, home, and doctors' office visits were significantly higher in the children with CHD.

CONCLUSION:

Reported adverse outcomes were more prevalent in the children with CHD. Our findings, particularly those regarding neurodevelopmental outcomes, may be helpful for parents, healthcare providers, and others in assessing the specific needs of children and teenagers with CHD.

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PMID: 25304924 [PubMed - in process]

7.

Nature. 2015 Jan 15;517(7534):327-32. doi: 10.1038/nature13997. Epub 2014 Dec 3. **The African Genome Variation Project shapes medical genetics in Africa.** Gurdasani D, Carstensen T, Tekola-Ayele F, Pagani L, Tachmazidou I, Hatzikotoulas K, Karthikeyan S, Iles L, Pollard MO, Choudhury A, Ritchie GR, Xue Y, Asimit J, Nsubuga RN, Young EH, Pomilla C, Kivinen K, Rockett K, Kamali A, Doumatey AP, Asiki G, Seeley J, Sisay-Joof F, Jallow M, Tollman S, Mekonnen E, Ekong R, Oljira T, Bradman N, Bojang K, Ramsay M, Adeyemo A, Bekele E, Motala A, Norris SA, Pirie F, Kaleebu P, Kwiatkowski D, Tyler-Smith C, Rotimi C, Zeggini E, Sandhu MS.

Abstract

Given the importance of Africa to studies of human origins and disease susceptibility, detailed characterization of African genetic diversity is needed. The African Genome Variation Project provides a resource with which to design, implement and interpret genomic studies in sub-Saharan Africa and worldwide. The African Genome Variation Project represents dense genotypes from 1,481 individuals and whole-genome sequences from 320 individuals across sub-Saharan Africa. Using this resource, we find novel evidence of complex, regionally distinct hunter-gatherer and Eurasian admixture across sub-Saharan Africa. We identify new loci under selection, including loci related to malaria susceptibility and hypertension. We show that modern imputation panels (sets of reference genotypes from which unobserved or missing genotypes in study sets can be inferred) can identify association signals at highly differentiated loci across populations in sub-Saharan Africa. Using whole-genome sequencing, we demonstrate further improvements in imputation accuracy, strengthening the case for large-scale sequencing efforts of diverse African haplotypes. Finally, we present an efficient genotype array design capturing common genetic variation in Africa.
PMID: 25470054 [PubMed - indexed for MEDLINE] PMCID: PMC4297536 [Available on 2015-07-15]

8.

N Engl J Med. 2015 Jan 8;372(2):124-33. doi: 10.1056/NEJMoa1408932. Epub 2014 Nov 14. **Gestational hypertension and preeclampsia in living kidney donors.** Garg AX, Nevis IF, McArthur E, Sontrop JM, Koval JJ, Lam NN, Hildebrand AM, Reese PP, Storsley L, Gill JS, Segev DL, Habbous S, Bugeja A, Knoll GA, Dipchand C, Monroy-Cuadros M, Lentine KL; for the DONOR Network.

Abstract

BACKGROUND:

Young women wishing to become living kidney donors frequently ask whether nephrectomy will affect their future pregnancies.

METHODS:

We conducted a retrospective cohort study of living kidney donors involving 85 women (131 pregnancies after cohort entry) who were matched in a 1:6 ratio with 510 healthy nondonors from the general population (788 pregnancies after cohort entry). Kidney donations occurred between 1992 and 2009 in Ontario, Canada, with follow-up through linked health care databases until March 2013. Donors and nondonors were matched with respect to age, year of cohort entry, residency (urban or rural), income, number of pregnancies before cohort entry, and the time to the first pregnancy after cohort entry. The primary outcome was a hospital diagnosis of gestational hypertension or preeclampsia. Secondary outcomes were each component of the primary outcome examined separately and other maternal and fetal outcomes.

RESULTS:

Gestational hypertension or preeclampsia was more common among living kidney donors than among nondonors (occurring in 15 of 131 pregnancies [11%] vs. 38 of 788 pregnancies [5%]; odds ratio for donors, 2.4; 95% confidence interval, 1.2 to 5.0; $P=0.01$). Each component of the primary outcome was also more common among donors (odds ratio, 2.5 for gestational hypertension and 2.4 for preeclampsia). There were no significant differences between donors and nondonors with respect to rates of preterm birth (8% and 7%, respectively) or low birth weight (6% and 4%, respectively). There were no reports of maternal death, stillbirth, or neonatal death among the donors. Most women had uncomplicated pregnancies after donation.

CONCLUSIONS:

Gestational hypertension or preeclampsia was more likely to be diagnosed in kidney donors than in matched nondonors with similar indicators of baseline health.

(Funded by the Canadian Institutes of Health Research and others.).

PMID: 25397608 [PubMed - indexed for MEDLINE]

9.

N Engl J Med. 2015 Jan 22;372(4):331-40. doi: 10.1056/NEJMoa1403489. **Causes and timing of death in extremely premature infants from 2000 through 2011.**

Patel RM, Kandeler S, Walsh MC, Bell EF, Carlo WA, Laptook AR, Sánchez PJ, Shankaran S, Van Meurs KP, Ball MB, Hale EC, Newman NS, Das A, Higgins RD, Stoll BJ; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network.

Abstract

BACKGROUND:

Understanding the causes and timing of death in extremely premature infants may guide research efforts and inform the counseling of families.

METHODS:

We analyzed prospectively collected data on 6075 deaths among 22,248 live births, with gestational ages of 22 0/7 to 28 6/7 weeks, among infants born in study hospitals within the National Institute of Child Health and Human Development

Neonatal Research Network. We compared overall and cause-specific in-hospital mortality across three periods from 2000 through 2011, with adjustment for baseline differences.

RESULTS:

The number of deaths per 1000 live births was 275 (95% confidence interval [CI], 264 to 285) from 2000 through 2003 and 285 (95% CI, 275 to 295) from 2004 through 2007; the number decreased to 258 (95% CI, 248 to 268) in the 2008-2011 period (P=0.003 for the comparison across three periods). There were fewer pulmonary-related deaths attributed to the respiratory distress syndrome and bronchopulmonary dysplasia in 2008-2011 than in 2000-2003 and 2004-2007 (68 [95% CI, 63 to 74] vs. 83 [95% CI, 77 to 90] and 84 [95% CI, 78 to 90] per 1000 live births, respectively; P=0.002). Similarly, in 2008-2011, as compared with 2000-2003, there were decreases in deaths attributed to immaturity (P=0.05) and deaths complicated by infection (P=0.04) or central nervous system injury (P<0.001); however, there were increases in deaths attributed to necrotizing enterocolitis (30 [95% CI, 27 to 34] vs. 23 [95% CI, 20 to 27], P=0.03). Overall, 40.4% of deaths occurred within 12 hours after birth, and 17.3% occurred after 28 days.

CONCLUSIONS:

We found that from 2000 through 2011, overall mortality declined among extremely premature infants. Deaths related to pulmonary causes, immaturity, infection, and central nervous system injury decreased, while necrotizing enterocolitis-related deaths increased. (Funded by the National Institutes of Health.).

PMID: 25607427 [PubMed - indexed for MEDLINE]

10.

N Engl J Med. 2015 Jan 29;372(5):407-17. doi: 10.1056/NEJMoa1404595.

Less-tight versus tight control of hypertension in pregnancy. Magee LA1, von Dadelszen P, Rey E, Ross S, Asztalos E, Murphy KE, Menzies J, Sanchez J, Singer J, Gafni A, Gruslin A, Helewa M, Hutton E, Lee SK, Lee T, Logan AG, Ganzevoort W, Welch R, Thornton JG, Moutquin JM.

Abstract

BACKGROUND:

The effects of less-tight versus tight control of hypertension on pregnancy complications are unclear.

METHODS:

We performed an open, international, multicenter trial involving women at 14 weeks 0 days to 33 weeks 6 days of gestation who had nonproteinuric preexisting or gestational hypertension, office diastolic blood pressure of 90 to 105 mm Hg (or 85 to 105 mm Hg if the woman was taking antihypertensive medications), and a live fetus. Women were randomly assigned to less-tight control (target diastolic blood pressure, 100 mm Hg) or tight control (target diastolic blood pressure, 85 mm Hg). The composite primary outcome was pregnancy loss or high-level neonatal care for more than 48 hours during the first 28 postnatal days. The secondary outcome was

serious maternal complications occurring up to 6 weeks post partum or until hospital discharge, whichever was later.

RESULTS:

Included in the analysis were 987 women; 74.6% had preexisting hypertension. The primary-outcome rates were similar among 493 women assigned to less-tight control and 488 women assigned to tight control (31.4% and 30.7%, respectively; adjusted odds ratio, 1.02; 95% confidence interval [CI], 0.77 to 1.35), as were the rates of serious maternal complications (3.7% and 2.0%, respectively; adjusted odds ratio, 1.74; 95% CI, 0.79 to 3.84), despite a mean diastolic blood pressure that was higher in the less-tight-control group by 4.6 mm Hg (95% CI, 3.7 to 5.4). Severe hypertension ($\geq 160/110$ mm Hg) developed in 40.6% of the women in the less-tight-control group and 27.5% of the women in the tight-control group ($P < 0.001$).

CONCLUSIONS:

We found no significant between-group differences in the risk of pregnancy loss, high-level neonatal care, or overall maternal complications, although less-tight control was associated with a significantly higher frequency of severe maternal hypertension. (Funded by the Canadian Institutes of Health Research; CHIPS Current Controlled Trials number, ISRCTN71416914; ClinicalTrials.gov number, NCT01192412.).

PMID: 25629739 [PubMed - indexed for MEDLINE]

11.

Am J Obstet Gynecol. 2015 Jan;212(1):94.e1-7. doi: 10.1016/j.ajog.2014.07.023.

Epub 2014 Jul 18. **Antenatal magnesium sulfate exposure and acute cardiorespiratory events in preterm infants.** De Jesus LC, Sood BG, Shankaran S, Kendrick D, Das A, Bell EF, Stoll BJ, Laptook AR, Walsh MC, Carlo WA, Sanchez PJ, Van Meurs KP, Bara R, Hale EC, Newman NS, Ball MB, Higgins RD; Eunice Kennedy Shriver National Institute of Health and Human Development Neonatal Research Network.

Abstract

OBJECTIVE:

Antenatal magnesium (anteMg) is used for various obstetric indications including fetal neuroprotection. Infants exposed to anteMg may be at risk for respiratory depression and delivery room (DR) resuscitation. The study objective was to compare the risk of acute cardiorespiratory events among preterm infants who were and were not exposed to anteMg.

STUDY DESIGN:

This was a retrospective analysis of prospective data collected in the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network's Generic Database from April 1, 2011, through March 31, 2012. The primary outcome was DR intubation or respiratory support at birth or on day 1 of life. Secondary outcomes were invasive mechanical ventilation, hypotension treatment, neonatal morbidities, and mortality. Logistic regression analysis evaluated the risk of primary outcome after adjustment for covariates.

RESULTS:

We evaluated 1544 infants <29 weeks' gestational age (1091 in anteMg group and 453 in nonexposed group). Mothers in the anteMg group were more likely to have higher education, pregnancy-induced hypertension, and antenatal corticosteroids, while their infants were younger in gestation and weighed less ($P < .05$). The primary outcome (odds ratio [OR], 1.2; 95% confidence interval [CI], 0.88-1.65) was similar between groups. Hypotension treatment (OR, 0.70; 95% CI, 0.51-0.97) and invasive mechanical ventilation (OR, 0.54; 95% CI, 0.41-0.72) were significantly less in the anteMg group.

CONCLUSION:

Among preterm infants age <29 weeks' gestation, anteMg exposure was not associated with an increase in cardiorespiratory events in the early newborn period. The safety of anteMg as measured by the need for DR intubation or respiratory support on day 1 of life was comparable between groups.

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12.

J Pediatr Surg. 2015 Jan;50(1):44-9. doi: 10.1016/j.jpedsurg.2014.10.028. Epub 2014 Dec 7. **An extracorporeal artificial placenta supports extremely premature lambs for 1 week.** Bryner B, Gray B, Perkins E, Davis R, Hoffman H, Barks J, Owens G, Bocks M, Rojas-Peña A, Hirschl R, Bartlett R, Mychaliska G.

Abstract

PURPOSE:

The treatment of extreme prematurity remains an unsolved problem. We developed an artificial placenta (AP) based on extracorporeal life support (ECLS) that simulates the intrauterine environment and provides gas exchange without mechanical ventilation (MV) and compared it to the current standard of neonatal care.

METHODS:

Extremely premature lambs (110-120days; term=145d) were used. AP lambs (n=9) were cannulated (jugular drainage, umbilical vein reinfusion) for ECLS. Control lambs (n=7) were intubated, ventilated, given surfactant, and transitioned to high-frequency oscillatory ventilation. All lambs received parenteral nutrition, antibiotics, and steroids. Hemodynamics, blood gases, hemoglobin, and circuit flows were measured.

RESULTS:

Four premature lambs survived for 1 week on the AP, with one surviving 6 days. Adequate oxygenation and ventilation were provided by the AP. The MV lambs survived 2-8 hours. Each of these lambs experienced a transient improvement with surfactant, but developed progressive hypercapnea and hypoxia despite high airway pressures and HFOV.

CONCLUSIONS:

Extremely premature lambs were supported for 1week with the AP with hemodynamic stability and adequate gas exchange. Mechanically ventilated lambs succumbed within 8hours. Further studies will assess control of fetal circulation and organ maturation on the AP.

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