included in the analyses. Heritability of 24 hour sodium intake was estimated using a variance components model (SOLAR). After adjustment for age, sex, income and province effects, the heritability was 0.30±0.1. Shared environments did not account significant contribution. We concluded that although salt intake is mediated through diet and meals are shared among families, genetic predisposition will play an important role in controlling salt intake.

ANTENATAL CARE FOR TWIN AND TRIPLET PREGNANCIES: SUMMARY OF NICE GUIDANCE IN THE UNITED KINGDOM

M. D. Kilby

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice.

The National Guidance published in September 2011[1] for the UK includes recommendations on care to:
Determine gestational age and chorionicity.

Screening for fetal anomalies and chromosomal anomalies.

Screening for TTTS and management of monochorionic twin and monochorionic/dichorionic triplet pregnancies.

Monitoring for preterm birth and intrauterine growth restriction.

Indications for referral to a tertiary Fetal Medicine Centre.

Timing of Birth.

[1]Visintin, C., et al. (2011). Antenatal care for twin and triplet pregnancies: summary of NICE guidance. BMJ, 343, d5714.

CO-TWIN PROGNOSIS AFTER SINGLE FETAL DEATH: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: To perform a systematic review and meta-analysis of the effects on the surviving twin of single fetal death comparing monochorionic to dichorionic twins to report the rates of co-twin death, preterm delivery, and neurologic morbidity in the surviving fetus.Data Sources: MEDLINE (inception-December 2010), EMBASE (inception-December 2010), The Cochrane library (inception-December 2010), Web of Science (inception-December 2010), and British Nursing Index (inception-December 2010) were searched electronically. Methods of Study Selection: Selected studies had more than five cases of single fetal death with reports of co-twin death, neurologic morbidity, or both co-twin death and neurologic morbidity. They also must have defined the gestational age of single fetal death and chorionicity. Tabulation, integration and *Results:* The search yielded 1,386 citations. Full manuscripts were retrieved for 204 and 22 were included in the review and meta-analysis. Twenty manuscripts were used to calculate overall summary statistics for monochorionic and dichorionic twins showing rates of co-twin death after single fetal death (15% compared with 3%), rates of preterm delivery after single fetal death (68% compared with 54%), the rate of abnormal postnatal cranial imaging after single fetal death (34% compared with 16%), and the rate of neurodevelopmental impairment after single fetal death (26% compared with 2%). Odds ratios (ORs) were calculated from 16 manuscripts. There was no significant difference reported between preterm delivery of monochorionic or dichorionic twins (OR 1.1, 95% confidence interval [CI] 0.34–3.51, P = .9). After single fetal death, monochorionic twins had higher odds of an abnormal cranial imaging after delivery, this was not significant (OR 3.25, 95% CI 0.66-16.1, P = .12). After single fetal death, monochorionic twins were 4.81-times more likely to have neurodevelopmental morbidity (95% CI 1.39-16.6, P<.05). *Conclusion:* Monochorionic twins are at significantly increased odds of co-twin demise and neurodevelopmental morbidity after single fetal death.

LINKAGE DISEQUILIBRIUM INFORMATION WITHIN MONOZYGOTIC TWIN PAIRS - A RATIONALE FOR GENOTYPING TWINS

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Recently genome-wide association studies have become a standard gene mapping method, but MZs have been either considered to be redundant or treated as unrelated individuals after randomly selecting one cotwin. It has been a common sense in academia that monozygotic twin (MZ) pairs, although they have unique strengths in detecting non-genomic etiology, do not contribute to gene mapping studies. It is indeed true for linkage analysis, but resemblance of phenotypes between MZ cotwins does include information about linkage disequilibrium (LD) between the genetic markers and postulated disease-susceptibility loci (DSL) when the concordance/discordance rates are compared across genotypes. The authors attempted to formulate a method to detect association and suggest several ways of applying the information using triglyceride and hypertriglyceridemia as a model phenotype. Genome-wide association test findings from the Healthy Twin Study, Korea which do not utilize MZ concordance information were compared with the tests of MZ concordance only from 493 MZs with genetic markers It is natural to assume that if allele D (wild type allele is +) is in LD with true DSL, MZ twins with genotype DD or D+ should have more diseases, and thus concordance rate than those with ++ genotype. Numerically, the observed concordance rate of MZ twins will exceed the expected concordance rate under null hypothesis of non-association (Equation 1) where "A*A"—the proportion of MZ with both affected, "U*U"—the proportion of MZ with both unaffected,

"Obs()"—observed rate, "prevalence"—prevalence rate among general population or study participants This can be further formulated by a trend test assuming additive model, or reduced tests assuming dominant model. Extended models can be constructed such as a logistic regression model allowing covariate adjustment or multiple linear regression calculating the sum of covariance between the cotwins for continuous traits. Formula : logit[p(A*A)] = a×covariates + ß × num(allele D) + e : additive model logit[p(A*A)] = a × covariates + ß×I(allele D exists) + e : dominant model where ß×num(allele D)+E numbers of allele D, ß × (allele D exists) + E1 if allele D exists, else 0. When we applied the multiple logistic regression test with 5.83 mmol/L as a cut-off for hypertriglyceridemia, 10 markers out of 26523 SNPs in chromosome 11 which exceeded p<10-3 showed p-value of 0.0003
>0.001. When we consider p-value of 0.05, 0.1, 0.15, 0.2 and 0.3 as cut-off for the MZ test and p-value of 10–3 and 10–4 as cut-off for GWAS results, the sensitivity/specificity of the MZ tests ranged 0.26
>0.56 for sensitivity and 0.69
>0.95 for specificity. Our findings show a way to extract LD information from MZ concordance or resemblance when one of cotwin was genotyped. Because the MZ resemblance is independent of other information conventionally used for GWAS, it can be combined with other results. The test can be also used to screen markers to alleviate the burden of multiple testing with appropriate threshold. Given that the MZ will be ever popularly applied for various omics studies, the addition of genomic information will facilitate multi-omics study in twin research.

THE RELATIONSHIP BETWEEN THE INTERPREGNANCY INTERVAL AND THE CHANCE OF NATURAL DIZYGOTIC TWINNING

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Background: The role of high parity on a higher rate of dizygotic twins, even when corrected for maternal age, is not understood. One consequence of higher parity is a shorter interpregnancy interval. Our study aims to investigate if interpregnancy interval is related to dizygotic twinning rate. *Methods:* For the purpose of this study, we extracted information about interpregnancy intervals from the database of the Perinatal Registry of the Netherlands over the years 2000-2006 about the reported natural conception pregnancies of all multiparous singleton. We took male/female twins to ensure dizygosity. The interpregnancy intervals were divided in periods of three months (0-<3, 3-<6, until 33-<36 months). For each category the frequency of opposite sex twin pairs was computed. *Results:* From a total of 331.279 deliveries, 328.399 were singleton pregnancies and 2.880 women had a natural conception dizygotic twin pair pregnancy. The lowest rate of opposite sex twin pairs (0,57%) was found with an interpregnancy interval of 6-9 months and it increased significantly to the highest rate (1,06%) with an interpregnancy interval of 18-<21 months followed by some decline. *Conclusions:* Opposite sex twin pair rates seem to relate to interpregnancy interval with a relatively high chance shortly after delivery followed by a progressive decline and a subsequent rise. We suggest that lactation and contraceptive behavior during this period may be of importance. Absence of such information in the data base limits the possibility to confirm this.

ASSOCIATION BETWEEN NICOTINE DEPENDENCE AND MAJOR DEPRESSION: ROLE OF DOPAMINE RECEPTOR GENE VARIANTS

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Modifying genetic influence on the association between major depressive disorder (MDD) and nicotine dependence (ND) has been investigated in a limited number of studies. The aims of this study were to investigate (1) association between lifetime DSM-IV diagnoses of ND and MDD among Finnish adult ever smoking twins; (2) magnitude of shared genetic factors influencing this co-morbidity; and (3) association of dopamine receptor genes with these phenotypes. The study sample was ascertained from the Finnish Twin Cohort study. Twin pairs born 1938-1957 and concordant for cigarette smoking history were recruited along with their family members, as part of the Nicotine Addiction Genetics consortium. Phenotype analysis was based on 1296 twins with data on both ND and MDD diagnoses. Individual level multiple logistic regressions were applied for the affected/non-affected phenotypes adjusted for sex, age, and alcohol use. As pair wise analysis we examined the cross-twin cross-trait correlations showing preliminary evidence on common genetic vulnerability. Further, we conducted bivariate Mx models for ND and MDD in 112 monozygotic and 410 dizygotic pairs. The genetic study sample consisted of 1428 individuals from 735 families (mean age 55.6 years). A total of 70 tagging SNPs within the dopamine receptor genes (DRD1-5) were genotyped and analyzed for association for MDD diagnosis, number of DSM-IV depression symptoms, ND, as well as the co-morbidity of MDD and ND. Individuals with ND diagnosis had significantly higher likelihood for lifetime MDD (OR = 2.51, 95% CI 1.83-3.46, p = 7.6e-09). High genetic correlation (rA = 0.70) derived from a bivariate twin model suggested that shared genetic influences might underlie this association. We detected a significant association between the rs2399496 at the 5' end of DRD3 gene and the