Science Digest

Contributed by Michael Legge

Gestational diabetes and HbA1c

A common complication during pregnancy is the manifestation of gestational diabetes, which is often associated with both maternal and fetal complications. In addition, it may also be associated with an increased risk for the development of type 2 diabetes later in life. Previous research has indicated that fetal complications may develop prior to the onset and diagnosis of gestational diabetes.

A collaboration between research groups in the USA has published results from case-controlled women from 8-13 weeks' gestation to 34-37 weeks' gestation for HbA1c analysis, which included those who developed gestational diabetes as well as other clinical conditions (1). Those women with a pre-existing elevated HbA1c were excluded from the research. The researchers found that those women who subsequently developed gestational diabetes had significantly elevated HbA1c at 8-13 weeks' gestation compared to those who did not develop gestational diabetes. The initial elevation was consistent through-out pregnancy.

Their conclusion was that women who subsequently develop gestational diabetes later in pregnancy already have impaired glucose homeostasis either prior to, or during early pregnancy and that HbA1c screening in the first trimester may identify at risk pregnancies prior to gestational diabetes onset.

Animal origins of rubella?

Rubella was first described in 1814 and was associated with human fetal congenital defects, miscarriages and stillbirths from the 1940s to 1960s. At present the rubella virus is the only recognized member of the riboviral family *Matonavirdae* (genus *Rubivirus*). Despite effective immunization programs it is estimated that at least 100,000 cases of congenital rubella syndrome occur each year and may persist as a sub-clinical infection in the eye.

Recent research from the USA has identified two relatives of the rubella virus; ruhugu and rustella viruses in common animal species that share identical genomic architecture with the rubella virus (2). The ruhugu virus which is the closest relative of the rubella virus is found in healthy leaf-nosed bats in Uganda and rustella virus, which is an outgroup including rubella and ruhuga viruses, is found in placental mammals and marsupials at a German zoo plus in wild yellow-necked field mice near the zoo. Amino acid sequences of the fusion protein (E1) from all three viruses and two putative T-cell epitopes of the capsid protein of rubella and ruhuga viruses were all moderately to highly conserved. Modelling of E1 homotrimers in the post-fusion state has predicted that both the rubella and ruhuga viruses have a similar host membrane fusion protein capacity. The authors concluded that members of the *Matonaviridae* family have the potential for future zoonotic transmission to cross significant barriers and that rubella had a zoonotic origin.

Relationship of Von Willibrand Factor with bacterial pathogenesis

Von Willibrand Factor (VWF) is an essential factor for normal homeostasis and functions as a mechano-sensitive protein, which is dependent on shear-stress for normal function. VWF is most frequently associated with bleeding disorders, however it is also linked to higher risks of cardiovascular disease. In a recent review of VWF and bacterial pathogenesis the authors describe a mechanism for the pathogenesis of VWF and the inflammatory response (3). Pathogenic bacteria such as *Staphylococcus aureus* and *Streptococcus pneumoniae* can bind circulating VWF and subsequently bind the complex to endothelial cells, which subsequently interferes with normal endothelial cell function as well as platelet recruitment and normal blood coagulation, thereby promoting thrombus formation and occlusion of micro-capillaries. The authors conclude that haemodynamic flow conditions are critical to the bacterial-VWF complex formation but more precise data is still required.

Blood group A1 and acute respiratory distress syndrome

The ABO blood group system is defined by differing carbohydrate structures on red blood cells but the respective complex carbohydrates that define the ABO blood groups are also located on other body cells. In addition to defining ABO blood groups the ABO blood group system has been associated with the susceptibility to certain diseases.

Recent research has extended the association of blood group A1 with the severity of acute respiratory distress syndrome (ARDS) in adults (4). The authors using multiple (750,000) SNPs in the ABO gene, genotyped 3710 individuals divided into 3 cohorts of critically ill trauma and sepsis patients to determine the association of the A1 genotype with ARDS risk. In addition, the authors determined whether an association existed with *FUT2* – defined non-secretors. These lack the ABO antigens on the epithelium but not on the endothelium. In addition, the authors analysed plasma concentrations of endothelium derived glycoproteins.

The overall outcome from this research was that the A1 genotype was associated with a moderate to severe risk of ARDS (relative to blood group) in all three cohorts. The relationship of A1 was strongest with sepsis in non-pulmonary infections. This association persisted in non-secretors tending to indicate that a vascular based mechanism underlies the pathology. Additionally, the authors identified that the A1 genotype was associated with a higher risk of DIC.

Ethics in clinical autopsy

This is a relatively short publication where the authors provide a review of the rationale for an autopsy and a historical perspective relating to the use and progression of the autopsy as well as religious aspects relating to permission and philosophical concepts (5).

The role of relatives of the deceased in various countries is considered linked with consent or the necessity for consent. The use of autopsies in education is considered and interestingly the Australian "Autopsy Practice" document is provided as an example of important ethical aspects relating to the use of the clinical autopsy. Despite the relative brief nature of the review, it is well written, providing a good general overview and is well referenced.

Bilirubin in clinical practice

Bilirubin is a frequently requested analyte in the clinical biochemistry and is an important diagnostic aid from before birth (e.g., fetal blood group incompatibility) through to geriatric management (e.g., liver disease), as well as identifying certain inherited disorders (e.g., Gilbert's syndrome) and as a marker for a range of haemolytic disorders. But how well is this molecule understood?

A published review of bilirubin focused on its use in clinical practice and provides a succinct overview of bilirubin synthesis and links the synthesis to the clinical conditions where is has the most value (6). The review is relatively short, but well written and is well referenced.

AUTHOR INFORMATION

Michael Legge, PhD MRSB FIBMS FNZIMLS FFSc(RCPA), Associate Professor

University of Otago, Dunedin

Correspondence: Michael Legge
Email: Michael.legge@otago.ac.nz

REFERENCES

1. Hinkle SN., Tsai MY., Rowal S. et al. HbA1c measured in the first trimester of pregnancy and association with gestational diabetes. *Sci Rep* 2018;8: 12249.
2. Bennett A, Paskey AC, Ehinger A, et al. Relatives of rubella virus in diverse mammals. *Nature* 2020; 586: 424-428. Correction in: *Nature* 2020; 588: E2.
3. Steinert M, Ramming I, Bergmann S. Impact of Von Willibrand Factor on bacterial pathogenesis. *Front Med (Lausanne)* 2020; 7: 543.
4. Reilly JP, Meyer NJ, Shasaty MGs, et al. The ABO histo-blood group endothelial activation, and acute respiratory distress syndrome risk in critical illness. *J Clin Invest* 2021; 131: e139700.
5. Rugge M, Sacchi D, Cesaro S, et al. *J Clin Pathol* 2020; doi: 10.1136/jclinpath-2020-206793. (Online ahead of print).
6. Fevery J. Bilirubin in clinical practice: a review. *Liver Int* 2008; 28: 592-605