

# Science Digest

Contributed by Michael Legge

## ABO blood type and severe trauma

The ABO blood group system is established by complex carbohydrates on red cell surfaces and the vascular endothelium as well as other cells and tissues. In recent years, research has implicated ABO blood type as a risk factor for various diseases including cancer, myocardial infarction and venous thromboembolism with the latter being rare in individuals with blood group O. In addition, the association of ABO blood groups and the risk of bleeding has been reported in the past. In the present research from Japan the association between the difference of ABO blood group and the outcome of severe trauma was investigated by a retrospective observational study (1). From a total of 901 patients comprising of type O, 32%; type A, 32%; Type B, 23% and type AB, 15%; blood group O was associated with the highest mortality (28%) compared with 13% for all other ABO blood groups. Transfusion volumes did not affect the data. The researchers noted that previous research has indicated that blood group of patients have 25 to 30% lower plasma von Willebrand factor (VWF) compared with those with other ABO blood groups which would increase the risk of haemorrhage. Previous research has shown that the highest levels of factor VIII and VWF were identified in: A<sub>1</sub>A/A<sub>1</sub>B/BB genotypes with intermediate levels in: A<sub>1</sub>/O and BO genotypes with the least in O/O genotype.

## Antibiotic resistant typhoid in Pakistan

Spread through contaminated water up to 22 million cases of *Salmonella typhi* occur each year. If left untreated, typhoid fever can lead to intestinal haemorrhage and perforation of the bowel killing up to 15% of infected individuals, and estimates are that 200,000 people die each year. During the last six months over 2000 people have been infected with the XDR *S. typhi* strain (2). According to the National Health Institute in Islamabad the only oral antibiotic effective for the XDR strain is azithromycin. Alternatively, intra-venous antibiotics may be effective but are too expensive in low income communities. Vaccination programmes are underway but the situation is expected to get worse before any improvement. It is believed that the XDR strain emerged from *S. typhi* due to multiple antibiotic use and the possible plasmid transfer from *E. coli* with a drug resistance gene(s). International travelers from Pakistan have returned with XDR strain infections.

## A novel approach to microbiology

Recent research from the USA has developed a novel microbial identification system based on biochip technology (4). The researchers developed a fully integrated, miniaturized semiconductor biochip with closed tube chemistry detection system. The biochip was capable of performing multiplex amplification and sequence analysis with the capacity to perform comprehensive mutation analysis on up to 1000 sequences or strands simultaneously in less than two hours. In trials comparing conventional techniques with the biochip, the biochip correctly identified multiple DNA and RNA respiratory viruses using clinical samples as well as 54 drug resistance-associated mutations in six genes of *Mycobacterium tuberculosis*, all of which were correctly identified by next generation sequencing. The chip (8x8mm) is mounted on a circuit board (2x8cm) with fluidic ports and the data analysed using application software via a USB port.

## Review of human papilloma virus (HPV) vaccination in males

Although human papilloma virus (HPV) infections are largely asymptomatic with the virus being cleared in the majority of cases, it still remains the most commonly sexually transmitted microorganism. Overall, approximately 10% of HPV infections persist and about 3% result in epithelial dysplasia and 1% result in cancer. Currently there are more than 200 different HPV types and these have been classified as high and low risk viruses. Of these there are two HPV types classified as high-risk cancer causing with HPV 16 and 18 the most common. In women about 100% of cervical cancers are attributable to high risk HPV types and in men approximately one third of penile cancers and 90% of oral cancers are attributable to high risk HPV types. Currently, a number of HPV vaccines are available: the bivalent against HPV 16 and 18; the quadrivalent against HPV 6,11,16 and 18, and a non-avalent which adds protection against a further five high risk HPV types. Whilst most industrialised countries have introduced female HPV vaccination, only five countries, including Australia, have introduced male HPV vaccination. In the review from Belgium, researchers identified 5196 articles, seven randomised control trials and three non-randomised studies and assessed them for efficacy, effectiveness and safety of HPV vaccinations in males of any age (3). Vaccine efficacy against permitting existing anogenital HPV infections was 49.9% and 88% for persisting oral HPV16 infections. Patients that were seronegative and PCR-negative had the highest degree of HPV vaccine induced protection from which the authors concluded that the use of the vaccines was most effective in HPV-naïve males prior to sexual activity.

## Platelet counts during pregnancy

In uncomplicated pregnancies platelet counts of less than  $150 \times 10^3/\text{mm}^3$  are considered to be gestational thrombocytopenia. This occurs in about 5 to 10% of women at the time of delivery with a general acceptance that it initially starts around mid-second to third trimester. Complications of pregnancy such as pre-eclampsia may also be associated with thrombocytopenia. Recent research has investigated platelet counts in uncomplicated pregnancies over a four-year period in women aged between 15 and 44 years over the period of their pregnancies and up to 12 weeks post-partum (5). A total of 7,351 women had sufficient data for analysis and of these 4,568 had uncomplicated pregnancies and 2,586 had pregnancy related complications. Those with pre-existing thrombocytopenia disorders totaled 197. In the uncomplicated pregnancies, the mean platelet count was  $250 \times 10^3/\text{mm}^3$  in the first trimester,  $230 \times 10^3/\text{mm}^3$  in the second and  $217 \times 10^3/\text{mm}^3$  in the third. At mean post-partum time of 7.1 weeks, a mean platelet count of  $264 \times 10^3/\text{mm}^3$  was found. Although a similar trend was observed in the pregnancy related complications, the platelet counts were significantly lower. The authors concluded that all pregnancies had gestation related platelet decreases, which, with the exception of the pre-existing thrombocytopenia conditions, return to normal non-pregnancy levels post-partum.

### A possible portable breast cancer diagnostic chip

According to the American Cancer Society about 40,290 deaths will occur this year due to breast cancer and in New Zealand about 600 deaths per year. Researchers in the USA have developed a microelectromechanical system (MEMS) biochip capable of measuring the mechanical properties of normal and tumour tissues (6). As a tumour progresses the mechanical properties (stiffness or elasticity) of the tumour changes that can be directly related to cancer progression. These changes are due to modification of the extracellular matrix associated with cancer cells. The researchers developed a biochip (10mm diameter) held in a 3D printer holder. Using paraffin blocks of normal and previously classified tumours from breast tissue 2mm plug of tissue was removed de-paraffinized and then placed on the biochip sensor and the electrical conductivity over a programmed temperature range was measured. There was a statistically significant difference between normal and breast cancer tissues and it was proposed that this could be a diagnostic biomarker by using electro-thermo-mechanical properties of tissues.

### Early detection of gestational diabetes

Gestational diabetes is associated with pregnancy complications for the mother, the fetus and the newborn. In addition, a longer-term outcome is the development of type 2-diabetes and cardiovascular disease in the women identified with previous gestational diabetes. Associated with maternal gestational diabetes is the risk of macrosomia and obesity in the children from such pregnancies. Although it can be diagnosed later in pregnancy there is increasing evidence that fetal overgrowth starts early rather than later during the pregnancy before the onset of gestational diabetes. HbA1c is used to screen high-risk pregnancies but not often used to identify any potentially at-risk, but otherwise apparently normal pregnancies. In recent research from the USA HbA1c was measured across all pregnancies from early pregnancy to term (7). Women in the 8-13 week gestation group (the earliest group) who had elevated HbA1c at that stage had a 22% increased risk of developing gestational diabetes. The researchers concluded that early HbA1c was more predictive the area under the curve (AUC) and that impaired glucose homeostasis was evident as early as 8-13 weeks gestation as indicated by HbA1c alone.

### ZIKV in human semen

While ZIKV is transmitted primarily by mosquito bites, there are reports of the disease appearing in non-endemic countries and male-to-female transmission has been reported. In addition, the sexual transmission has been reported to enhance viral dissemination in the female genital tract and transmission to the fetus where ZIKV is known to be teratogenic. Further reports have indicated varying infectious viral load in human semen and it has been proposed that ZIKV may have an affinity for the male genital tract. Research, using animal models for ZIKV infections appear not to simulate the human male genital tract infections. Recent research from France supports the shedding of high viral loads in the male genital tract and has used testicular organ culture techniques to identify potential target tissue areas (8). The researchers identified that macrophages were the most susceptible cells in the testes to ZIKV infections, but the virus also infects and replicates in a wide range of testes somatic and germ cell lines. Semen collected from ZIKV infected men demonstrated an association of ZIKV with spermatozoa, however, the infection had no obvious deleterious effects on morphology and hormone production in culture. There was no significant inflammatory response identified in ZIKV infected men, which the researchers considered that it was the basis for persistent infection and warned for both horizontal and vertical transmission of ZIKV through infected testicular germ lines.

### Significance of low serum bicarbonate

After haemoglobin, plasma bicarbonate is the second most significant buffering system in the blood with minor buffering being provided by phosphate and protein. Generally, serum bicarbonate is associated with acid-base balance and is an important analyte in assessing acid-base balance. Two publications have identified an association with low serum bicarbonate and disease processes independent of acid-base status. The first from the USA using data for 2,287 individuals aged between 70-79 years who were part of a 10 year "Health, Aging and Body Composition Study" (9). The participants were grouped into three serum bicarbonate categories, <23.0 mEq/L; reference group 23.0-27.9mEq/L and high >28.0mEq/L. In the otherwise healthy participants with low serum bicarbonate but normal pH there was a 24% higher mortality risk regardless whether there was metabolic acidosis or respiratory alkalosis. Those with high serum bicarbonate showed no increase in mortality. The second publication from China is a study of 5318 participants aged between 18-70 years in a six-year observational research programme (10). The researchers identified that low serum bicarbonate over a two year follow-up period was associated with a 4% increase risk of developing an impaired fasting glucose, which would lead to insulin resistance and was independent of other risk factors for diabetes. Both research groups considered that monitored bicarbonate therapy might be beneficial in treating low serum bicarbonate to reduce both mortality and morbidity.

### References

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