

### A new approach to childhood febrile illness

Childhood infections and inflammatory diseases are amongst the most common causes for seeking medical intervention. Often there are challenges in the diagnosis and treatment of childhood infections with the conventional approach is often slow due to the time for culture. Additionally, infections may be in inaccessible sites and conventional samples may fail to identify the infection. A recent publication from a European collaboration may provide a new direction for the diagnosis of childhood febrile illnesses (1). The multi-author publication used whole blood transcriptomic microarray, linked to medical learning incorporating 12 publicly available data sets. This included 1,212 children with 18 infections or inflammatory diseases. A further 411 children were investigated using a new RNA dataset panel. Overall, the 161 transcripts classified 18 disease categories which reflected a specific pathogen and a specific disease as well as predicting broad classes of diseases such as malaria and tuberculosis. The authors concluded that a single panel of RNA transcripts can be used to identify causative organisms resulting in fever in a non-specific laboratory finding from a single blood sample, thereby reducing diagnostic delays and improving antibiotic use.

### Serum potassium and seasonal change

Serum potassium is an important electrolyte with a reference range of 3.5 to 5.3mmol/L depending on the method used. While there is no standard definition of hyper and hypokalaemia, above 5.5mmol/L and below 3.0mmol/L respectively are used as triggers for clinical intervention. Many of the spurious changes in serum potassium concentrations are due to pre-analytical issues such as prolonged tourniquet use and fist clenching. In addition, transport temperature of whole blood can increase serum potassium concentrations and blood collection in winter may also increase this analyte. Medication may also influence the serum potassium concentration and ACE inhibitors are known to increase potassium excretion. ACE inhibitors are a widely prescribed group of medication. In a recent publication (2) the authors investigated the relationship of serum potassium levels in patients prescribed ACE inhibitors and the association with Met Office recorded temperatures using the United Kingdom national anonymised database for general practice. Overall, 10,680,825 serum potassium results were obtained from 5,600,741 prescriptions. Their analysis clearly demonstrated seasonal changes in serum potassium concentrations which was linked to changes in prescribing ACE inhibitors. They conclude that clinicians need to be more aware of seasonal variability and measurement error that has been demonstrated as influencing their prescribing activity.

### Transgender women and prostate cancer

Transgender patients are heavily marginalized despite efforts to reduce health disparities in this group. An area of healthcare frequently overlooked is the susceptibility of cancer in birth organs. Transgender women (assigned male sex at birth) retain their prostates even after gender affirmation surgery and by doing so remain at risk for prostate cancer. Until recently, the medical and scientific literature has been limited, primarily to a few case studies or short reports. A recently published study (3) using medical records over the last 11 years has provided some additional data on this issue. A total of 449 transgender patients were identified with prostate cancer. Of these, 116 never used oestrogen, 17 had used previously used oestrogen and 22 were active oestrogen users at the time of diagnosis. The PSA values and biopsy results were most significant in the group who had not used oestrogens and the lower grade prostate biopsies and PSA values were above the upper cut-offs but lower than the non-oestrogen group. The authors emphasise the necessity for prostate cancer screening for transgender women especially for those who have not used gender-affirming hormone therapies

(GAHTs). However, they further indicate that those using GAHTs need to have improved prostate screening and the overall effect of GAHTs need further research.

### Leftover samples in diagnostic laboratories

Tens of thousands of patient samples pass through pathology laboratories every day that are clinically characterised and provide valuable diagnostic information. For research, new test development, validation studies, quality control etc., many of the leftover samples may provide useful options for secondary use once their primary function has been fulfilled. This should require ethical consideration as a range of data exists such as personal records, age, disease status and family history which may be readily available. Access to and use of such samples could reduce the necessity to recruit new people into a research project. A recent publication from Argentina (4) considers the ethical issues for using leftover samples. The authors consider the three principles of ethics, autonomy, beneficence, and justice. It was considered appropriate to respect the autonomy of the individual as the consent for use was only originally given for a specific use of a sample, therefore efforts should be made to obtain further informed consent. Would the secondary use of the sample cause harm to the individual such as breach of privacy, access to medical information, the risk of harm to integrity. The risk of identifying a significant disease related result should be considered in any consent process. The justification of sample use for the 'greater good' i.e., beneficence, has several historical unethical practices. Collecting samples from vulnerable populations only, especially when their autonomy is compromised is against the principles of justice. The authors conclude that clear informed consent underpins good ethical practice and the individual's right to know. They provide seven recommendations for the use of leftover samples to guide investigators and management of medical laboratories.

### Endometriosis: a new insight for its origins

Endometriosis results from endometrial like tissue growing outside of the uterus which may attach to abdominal organs. It affects between 10 to 15% of women of reproductive age and a widely accepted cause is retrograde menstruation. However, although most women of reproductive age experience retrograde menstruation, around 85% do not develop endometriosis. Although the endometrial growths are considered benign, the disease results in chronic pain and infertility. The current information indicating that most women do not develop endometriosis suggest that there may be alternative mechanisms underlying this disease process. In a recently published study from Japan, investigators considered whether the bacterial flora from the vagina could contribute to the pathology (5). Amongst the vaginal bacteria previously described there were members of the *Fusobacterium* species, which although a normal commensal in the gastrointestinal tract, are considered to be an opportunistic pathogen. Using a range of molecular techniques, the authors analysed endometrial tissues for the presence for the presence of *Fusobacterium* species and in particular *Fusobacterium nucleatum*, which has a role in carcinogenesis as well as initiating inflammatory responses. A total of 79 women with endometriosis had tissue analysed for *Fusobacterium* species as well as inflammatory markers and these were matched with 79 women who had normal endometrium. When assaying endometrial tissue, they identified 1187 genes that were significantly upregulated and 1804 genes that were specifically down regulated during the menstrual cycle, and 10 genes were specifically upregulated and three downregulated in endometriosis compared to controls. The upregulated genes were related to inflammatory response. When tissue from endometriosis patients was analysed, 64% demonstrated a *Fusobacterium* infection compared to <10% of controls. To

further investigate these findings, they inserted endometrial tissue into mice who subsequently developed endometriosis. Direct infection with *Fusobacterium* but not with other bacterial species resulted in the development of endometriosis. The vaginal swabs from women with endometriosis showed a higher *Fusobacterium* population than the controls. Antibiotic treatment of the *Fusobacterium* infected mice significantly reduced the development of endometriosis. The authors conclude that progress to clinical trials is required to reduce the pathogenesis of endometriosis by *Fusobacterium* infection to develop a treatment for endometriosis.

### Human scent and mosquito guidance

Mosquitos (and possibly sand flies) always seem to 'select' their unsuspecting targets and their presence is known only after their blood meal. This uncanny ability to select their human targets is known to be associated with a series of factors such as visual cues, body heat, humidity, breath carbon dioxide and chemicals emitted from the skin. Whilst sandflies and other biting insects are annoying, a more serious issue is malaria caused by the *Anopheles* mosquito with an estimated 247 million cases and 619,000 deaths worldwide from 2021 data provided by WHO. If there was a better understanding of attractants, it could help reduce the incidence of this disease. In a recent publication (6) an international collaboration investigated what cues guide mosquitos to their blood source. *Anopheles gambiae* has a strong preference for humans and the authors designed an experiment to test and validate mosquito attraction. They constructed a 20 x 20 metre screened fly cage which contained thousands of hungry *Anopheles gambiae* mosquitos who prefer to feed at midnight. Eight one-person tents were erected around the structure containing a single person with each having their own scent which was ducted to the cage to individual heated (37°C) aluminium plates. Over six nights the mosquitos were observed using infra-red cameras. Each tent had the scent analysed to provide individual odour profiles. In total 40 volatile organic compounds were detected of which 15 controlled mosquito

attraction. The most frequently sought odour was a participant with high levels of carboxylic acids which are produced by the sebaceous glands and normal bacterial skin flora. The least attractive, was a person with low levels of carboxylic acids and a high level of eucalyptol which is present in high concentration of eucalyptus. It is also found in foods such as rosemary and sage as well as beauty products and mouth wash. This person was a vegan. The authors also confirmed the 60 metre carbon dioxide cues and both visual and odour cues from 5 to 15 metres. Heat and humidity cues were detected from 0.3 to 0.5 metres. The authors conclude that human scent is the primary attractant and speculate whether these data may provide a mechanism for mosquito control.

### REFERENCES

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