Science Digest

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Face masks

With the advent of SARS-CoV-2 transmission across the world, the use of face masks in everyday life has become part of the 'norm' to reduce viral transmission. While this is a generally accepted process, getting to that point has a long and convoluted history. In an article published in 2020, a group of German authors map the history and value of face masks from around the middle ages to present times (1). Historical records indicate the use of "beak masks" covering the full face with a beak -like feature allegedly filled with herbs and spices to prevent the miasma (bad air widely believed to be the source of infections). These masks made their appearance in engravings during the European bubonic plagues. Although a small number of the masks still exist, there is modern doubt about whether the "beak-doctors" actually existed. Up to and including the 19th century (when antiseptic surgery was introduced) there are no records of face masks being used and a major complication of surgery at that time was "hospital gangrene" associated with surgical techniques and the miasma concept. At the turn of the 20th century nose and face coverings were gradually introduced with the discovery of droplet infections but they were not in common use with strong opposition. However, by 1920 the use of face masks is documented in the USA and Germany. Even after the First World War the use of face masks was not generally accepted by physicians but nurses wore them. By the 1940s washable and sterilisable face masks became available and by the 1960s the use of paper and fleece masks was introduced in the USA. There is still ongoing research relating to the overall value of face masks in reducing hospital infections and the authors indicate that face mask efficiency in the SARS-CoV-2 pandemic should be scientifically researched.

Evaluation of commercial RT-qPCR diagnostic kits for SARS-CoV-2

With the rapid appearance and spread of SARS-CoV-2 in 2020, the need for rapid and reliable test kits was a priority. In a recent publication from China the authors indicate that many of the commercial test kits may not have undergone full and independent evaluation (2). In this publication five commercial RT-qPCR test kits for SARS-CoV-2 produced in China were evaluated (Da An, Liferiver, Kinghawk, eDiagnosis, and Maccura Biotechnology). The authors used the following performance criteria : coincidence rate, limit of detection (LoD), cross reactivity, precision and anti-interference, and the use of clinical samples. The coincidence rate was 100% for all kits except Liferiver (95%). Three kits had LoD of 250 copies/ml (Da An, eDiagnostics, Maccura) and 1000 copies for Liferiver. Kingshawk failed to detect the advertised 500 copies/ml. Cross reactivity for all kits was negative. Da An and Liferiver and eDiagnostics demonstrated higher sensitivity to the nucleocapsid gene than the open reading frame. Anti-interference was positive for all kits. Two kits, Da An and Liferiver, had excellent diagnostic specificity and sensitivity; however, Kinghawk failed to pass the use of COVID-19 RNA liquid performance verification product using droplet RT-PCR combined with fluorescence quantitative PCR. In conclusion, the authors discussed that this work will help provide guidance for clinical laboratories when selecting test kits and for manufacturers to optimise their test kits.

Metabolic and lipid biomarkers in SARS-CoV-2 patients

Although SARS-CoV-2 is primarily a respiratory infection, there is increasing evidence that other physiological and biochemical parameters are affected as a result of the viral infection. A recent publication from Germany has investigated metabolic and lipidaemic markers in both SARS-CoV-2 infected patients and non-infected controls using a NMR-metabolomics approach (3). A feature of SARS-CoV-2 infections is that it can lead to multi-organ damage, as well as neurological symptoms and vascular damage, including thromboembolism. In this publication the authors investigated whether there was a common underlying molecular mechanism that could be detected using metabolic profiles. Using serially collected serum samples over seven days from aged-matched SARS-CoV-2 infected patients in ICU and non-infected controls the samples were analysed by NMR. From the analysis data for 39 metabolites and 112 lipoproteins were obtained. The SARS-CoV-2 patients demonstrated metabolic dysregulation with significant increases in phenylalanine, glucose, and formic acid and significant decreases in glutamine, histidine, and lactic acid. Significant dyslipidaemia was identified in the SARS-CoV-2 patients with increases in triglycerides, small sized VLDL particles (VLDL-2,-3, and -4), and IDL, all of which are atherogenic. Cholesterol levels in VLDL, LDL and HDL were also elevated, and the authors indicated that certain VLDL and LDL sub-classes favour viral membrane fusion events and therefore an alternative entry into cells. Interestingly, patients with SARS-CoV-2 positive antibodies but without acute infections were found to have similar results to the non-infected controls. In conclusion, the authors comment that their results are typical of a pre-cachetic, catabolic state, hepatic damage, and severe dyslipidaemia, but lacks sufficient data for SARS-CoV-2 biomarkers underlying the disease processes.

Why do babies smell?

It is well established that in terrestrial mammals aggressive behaviour can be triggered by odours. Examples of this are female rabbits killing their young if they are tainted of an odour of a strange female, female mice will abort if an odour of a strange male is introduced, and female aggression in pigs can be blocked by androsterone. In humans, a decrease in male testosterone when smelling human tears has been documented. Previous research using chemosignals has identified that brain activity differed between males and females when exposed to identical chemosignals and can modulate aggressive behaviour. Amongst the known chemosignals is hexadecanal, a volatile long chain aliphatic aldehyde metabolic intermediary compound involved in glycolipid metabolism. The mouse cell receptor for this compound is highly conserved across mammals, including humans. In a recent collaborative publication from Japan and Germany, researchers investigated whether hexadecanal influenced human aggression as there were no reports of it being emitted by humans (4). Using validated behaviour techniques men and women were exposed to hexadecanal and controls and aggressive behaviour was blocked in men but triggered in women. They next used brain imaging techniques to validate the initial findings and identified areas of the brain associated with social arousal had significantly different responses when exposed to hexadecanal, correlating to the behavioural studies. Previous research has demonstrated that amongst the odours emitted from babies heads, one of the most abundant is hexadecanal. The authors conclude that as with other mammals, this is a highly conserved chemosignal that could decrease male aggression towards babies and increases female aggression as a protective measure for their babies thereby ensuring survival.

A new and novel role for red blood cells

Red blood cells (RBCs) are solely responsible for transporting and delivering oxygen to all parts of the body and facilitating the removal of carbon dioxide.to the lungs. Mature RBCs are a unique cell-type as they have no nucleus or cell organelles, as well as being flexible withstanding significant shear forces in the circulation. In addition, RBCs are widely considered to be immunologically inert. Recent research from the USA has now provided evidence that brings in to question the immunologically inert status of the RBCs (5). The authors have previously described that RBCs express intracellular Toll-like receptor 9 (TLR9), which is a nucleic acid sensing receptor. In the present publication they now present evidence that TLR9 is expressed on the surface of the RBCs and propose a significant role for RBCs in the immune response. It is known that damaged cells and pathogen DNA is released, which formed part of the inflammatory response and removal had been previously ascribed to white blood cells. Starting with in-vitro work, they demonstrated that human RBCs specifically bound CpG motifs from DNA. When the RBCs with bound CpG were introduced to macrophages they were quickly removed whereas 'free' RBCs were not. This effect was also demonstrated using mice. When they investigated RBCs from patients with sepsis, COVID-19 with anaemia, and compared to COVID-19 only, similar CpG binding was demonstrated in the first two groups but not in the latter. The authors conclude that the TLR9 receptor on RBCs acts as an immune sentinel and during pathological states, such as inflammation, they remove the CpG DNA and present to macrophages for clearance.

Platelets and COVID-19

One of the curious outcomes pf patients with severe COVID-19 infections is the finding that significant thrombocytosis is uncommon. This has been identified in approximately 5% of hospital and 8% of intensive care patients with COVID-19 infections where platelet counts of $100x10^9$/L are frequently found. In a short report from the UK (6) the authors investigated the inconsistency of the coagulationopathy associated with COVID-19 infections, which differs from disseminated intravascular coagulation (DIC). They report that autopsies on COVID-19 infected patients demonstrated microvascular thrombosis throughout the small blood vessels of the lungs and alveolar capillaries., likely to be the end point of inflammation. When the peripheral blood films from COVID-19 patients were examined, all showed macrothrombocytes, dense granules and large proplatelet fragments. They also report large (7 to 30 platelets) aggregates in all ICU patients. These finding were not seen in patients receiving invasive ventilation for other reasons. None of the COVID-19 patients had DIC. The authors conclude that damage to the lungs by COVID-19 results in disordered megakaryocyte fragmentation, which in turn influence the inflammatory response via cytokines and growth factors release. They also consider that mechanical ventilation could aggravate this process resulting in proplatelet cleavage and release of proinflammatory particles.

Breath: another technique for diagnosis

The ability to diagnose diseases using non-invasive techniques was probably first described by Hippocrates (c400BC) who identified that body odours could be associated with certain diseases. In the mid-1800s an association of breath acetone was established as a link to diabetes mellitus. By the 1970s over 200 volatile organic compounds (VOCs) had been identified in breath using mass spectrometry. To date, with modern instruments, over 3500 VOCs have been identified in human breath. It is now accepted that metabolites in breath can not only indicate normal metabolic functions, but also may reflect disease processes within the body. A recent review of breath metabolites to diagnose infections provides a succinct summary of the potential of VOCs in breath to diagnose disease (7). Analysis relies on gas chromatography- mass spectrometry and provides evidence of infectious disease 'fingerprints'. Examples of such infectious disease VOCs 'fingerprints' are provided for influenza, SARS-CoV-2, *Mycobacterium tuberculosis, Pseudomonas aeruginosa,* and *Aspergillus fumigatus.* Additionally, the authors indicate that *Helicobacter pylori* and *Plasmodium falciparum* also demonstrate their own signatures in breath analysis. Each of these diseases has a characteristic breath VOC composition and pattern of up to 10 VOCs. In conclusion the authors indicate that there is the necessity to provide more evidence for clinical translation and propose more research for paediatric breath analysis to identify biomarkers for rapid diagnosis.

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