Characterization of epitope-specific anti-RSV antibody responses after natural infection and after vaccination with FI-RSV

Antibodies against the fusion (F) protein of respiratory syncytial virus (RSV) play an important role in the protective immune response against this important respiratory virus. Strikingly, vaccination with FI-RSV exclusively resulted in the induction of poorly neutralizing antibodies against postfusion-specific antigenic site I, although antigenic sites I, II and IV were efficiently displayed in FI-RSV. The apparent immunodominance of antigenic site I in FI-RSV likely explains the low levels of neutralizing antibodies upon vaccination and challenge, and may play a role in the vaccination-induced enhancement of disease observed with such preparations. Mpr1 (sigma1278b gene for proline-analog resistance 1) protects yeast cells from various oxidative stresses, mediates the l-proline and l-arginine metabolism by acetylating l-Δ(1)-pyrroline-5-carboxylate.

In unanesthetized, spontaneously hypertensive rats the decrease in blood pressure and heart rate produced by intravenous clonidine, 5 to 20 micrograms/kg, was inhibited or reversed by nalozone, 0.2 to 2 mg/kg. Logistic regression analysis revealed that infusion time was significant (p = 0.0004; odds ratio = 0.974) and increasing the IP infusion time of bupropion HCl 120 mg/kg was associated with a 91% reduced odds of convulsions at infusion times of 15 to 90 min compared to bolus injection. The hypotensive effect of 100 mg/kg alpha-methyldopa was also partially reversed by naloxone. Naloxone alone did not affect either blood pressure or heart rate. In brain membranes from spontaneously hypertensive rats clonidine, 10(-8) to 10(-5) M, did not influence stereoselective binding of [3H]-naloxone (8 nM), and naloxone, 10(-8) to 10(-4) M, did not influence clonidine-suppressible binding of [3H]-dihydroergocryptine (1 nM). The time course and concentration-effect relationship of terbutaline-induced hypokalemia was studied, using computer-aided pharmacokinetic-dynamic modeling. In spite of higher terbutaline concentrations after oxprenolol pretreatment, the hypokalemia was almost completely antagonized by the beta 2-blocking action. Previous experiments in this laboratory have shown that microinjection of methyldopa onto the ventrolateral cells of the B3 serotonin neurons in the medulla elicits a hypotensive response mediated by a projection descending into the spinal cord. It is concluded therefore that, unlike the ventrolateral B3 cells which mediate a methyldopa-induced hypotension via descending projections, the midline serotonin B3 cells in the medulla contribute to the hypotensive action of methyldopa, either by way of an ascending projection which does not pass through the median forebrain bundle, or through a projection restricted to the caudal brainstem. A single case report suggests that yohimbine may be used to treat the sexual side effects of clomipramine. These findings indicate that in spontaneously hypertensive rats the effects of central alpha-adrenoceptor stimulation involve activation of opiate receptors. Animals which received over six courses of doxorubicin demonstrated the electrocardiogram (ECG) changes, decrease of blood pressure and high-grade histopathological cardiomyopathy, while animals which were terminally sacrificed after the SM-5887 administration did not show any changes in ECG, blood pressure and histopathological examinations.

Based on the strong enhancement effect of nucleic acids on resonance light scattering of dequalinium chloride, the determination method for micro amounts of nucleic acids has been developed. Hepatitis B virus (HBV) infection can cause chronic liver disease which is associated with increased risk of liver cirrhosis, liver failure and liver cancer. Clearance of HBV infection requires effective HBV-specific immunity, however the immunological mechanisms that determine the development of effective HBV-specific immunity are poorly understood. Dendritic cells (DC) play a pivotal role in the regulation of anti-viral immunity. Here, we investigated the interaction between HBV surface antigen (HBsAg), the main envelop glycoprotein of HBV, and BDCA1+ myeloid dendritic cells (mDC).Exposure of peripheral blood-derived BDCA1+ mDC to HBsAg resulted in strong DC maturation, cytokine production and enhanced capacity to activate antigen-specific CTL. By using neutralizing antibodies, crucial roles for CD14 and TLR4 in HBsAg-mediated BDCA1(+)mDC maturation were identified. Concordantly, HBsAg-mediated DC maturation required FCS or human plasma, naturally containing soluble CD14 (sCD14). Intriguingly, HBsAg-induced DC maturation was significantly reduced in umbilical cord blood-plasma that contained less sCD14 than adult plasma, indicating that sCD14 is an important host factor for recognition of HBsAg by DC and subsequent DC activation. A direct interaction between sCD14 and HBsAg was demonstrated by using ELISA. Moreover, sCD14-HBsAg complexes were detected both in vitro and in serum of HBV-infected patients. Abundance of sCD14-HBsAg complexes varied between chronic HBV disease stages and correlated with activation of BDCA1+ mDC in vivo.We conclude that HBsAg activates BDCA1+ DC via a sCD14-dependent mechanism. These findings provide important novel insights into initiation of HBV-specific immunity and facilitate development of effective immunotherapeutic interventions for HBV.

Four cases of acute flaccid paralysis caused by slightly evolved (Sabin-like) vaccine polioviruses of serotype 2 were registered in July-August, 2010 in an orphanage of Biysk (Altai Region, Russia). The Biysk cluster of vaccine-associated paralytic poliomyelitis (VAPP) had several uncommon, if not unique, features (1). Until this outbreak, Sabin-like viruses (in distinction with more markedly evolved vaccine-derived polioviruses, VDPV) were reported to cause only sporadic cases of VAPP. Consequently, VAPP were not considered to require outbreak-type responses. However, the Biysk outbreak completely blurred the borderline between Sabin-like viruses and VDPV in epidemiological terms (2).

Andes virus (ANDV) is associated with a lethal vascular leak syndrome in humans termed hantavirus pulmonary syndrome (HPS). To determine whether alveolar macrophages play a role in HPS pathogenesis, alveolar macrophages were depleted in an adult rodent model of HPS that closely resembles human HPS. Syrian hamsters were treated, intratracheally, with clodronate-encapsulated liposomes or control liposomes and were then challenged with ANDV. Treatment with clodronate-encapsulated liposomes resulted in significant reduction in alveolar macrophages but depletion did not prevent pathogenesis or prolong disease. These data demonstrate that alveolar macrophages may play a limited protective role early after exposure to aerosolized ANDV, but do not directly contribute to hantavirus disease pathogenesis in the hamster model of HPS.

The outcome of the Selenium and Vitamin E Cancer Prevention Trial, demonstrating harm and no preventive activity of selenomethionine and α-tocopherol for prostate cancer, and the lack of approval by the US Food and Drug Administration for the use of 5α-reductase inhibitors to prevent prostate cancer have cast doubt about the future of chemoprevention of prostate cancer. This article attempts to critically assess whether the notion that chemoprevention of prostate cancer has no future is warranted. Risk of prostate cancer is modifiable and chemoprevention of prostate cancer, particularly fatal/lethal cancer, is both needed and possible. However, the approach to prostate cancer chemopreventive agent development has not followed a rational and systematic process.

Inflammation of the adrenal glands is caused by autoimmunopathies or infections and can induce adrenal insufficiency. Autoimmune lymphocytic adrenalitis is often combined with other autoimmune diseases and the most frequent cause of Addison's disease; however, it only becomes clinically apparent when more than 90 % of the adrenal cortex has been destroyed. Histological features are characterized by lymphoplasmacytic inflammation leading to an increased destruction of adrenocortical tissue but less severe courses can also occur. The second most frequent form of adrenalitis is adrenal tuberculosis, showing typical granulomatous findings that are nearly always caused by spreading from a tuberculous pulmonary focus. Other bacterial as well as viral infections, such as Epstein-Barr virus (EBV), cytomegalovirus (CMV) and others, generally affect the adrenal glands only in patients with immunodeficiency disorders. In these infections, the adrenal cortex and medulla are frequently involved to roughly the same extent. Although surgical specimens from inflammatory adrenal lesions are extremely rare, the various forms of adrenalitis play an important role in the post-mortem examination of the adrenal glands for clarification of unclear causes of death (e.g. death during an Addisonian crisis).

Chronic obstructive pulmonary disease (COPD) affects roughly 10% of the global population and is growing in prevalence annually. COPD is characterized by progressive non-reversible narrowing of airways mainly due to cigarette smoking. Therapeutic interventions aimed at altering this progressive disease course can largely be grouped into pharmacological or non-pharmacological therapies. The focus of this paper is on the non-pharmacological aspects of COPD management, reviewing the current literature to provide an evidence-based management approach. Non-pharmacological therapies reviewed in this article include the implementation of comprehensive care models utilizing a coordinated multidisciplinary team, tele-monitoring and patient-centred approach to optimize COPD care and improve compliance. Preventing progression of COPD via smoking cessation remains of paramount importance, and newer therapeutic options including electronic cigarettes show promise in small studies as cessation aids. COPD has systemic manifestations that can be ameliorated with the enrollment in pulmonary rehabilitation programmes, which focus on exercise endurance to improve dyspnoea and quality of life. Advanced therapeutics for COPD includes lung volume reduction surgery for a pre-specified cohort and minimally invasive bronchoscopic valves that in recent reviews show promise. Lastly, patients on maximal COPD therapy with progressive disease can be referred for lung transplantation; however, this often requires a highly selected and motivated patient and care team. Survival rates for lung transplantation are improving; thus, this procedure remains a viable option as more expertise and experience are gained.

Depression is a chronic disease with a high prevalence that normally is episodic and an average episodic duration of 16 weeks. The aim of this study is to analyze the correlation between symptomatic progression (appearance, maintenance, remission of different symptoms) and the evolution of the diagnosis of depression (onset, maintenance, and remission) in a cohort of patients diagnosed with and without major depression. A prospective cohort study was performed with a one year follow-up in which a random sample of 741 subjects attending primary care was interviewed. Diagnosis of depression was made according to DSM-IV criteria and symptoms presented were analyzed. These subjects were reevaluated at 6 months and 12 months. Depressed mood state, decreased interest or anhedonia and symptoms related to sleep (insomnia or hypersomnia), agitation, feeling of guilt, fatigue or energy loss, are consistent with the diagnosis. The rest of the symptoms display an evolution independent of the diagnostic trends. In Primary Care, it is important to know which are the key symptoms in the evolution of the diagnosis in order to achieve full remission of depression and avoid maintenance of residual symptoms that can become prodromal.

The HIV epidemic in Peru is concentrated in men who have sex with men and transgender women, who have an estimated prevalence > 10%, while the overall population prevalence remains < 1%. Because MSM and TW account for >60% of new infections, it is crucial to understand the full HIV continuum of care for these key populations. We performed a review of the peer-reviewed scientific and grey literature to determine the proportion of HIV-infected MSM and TW in Peru who are diagnosed, linked to and retained in care, taking antiretroviral therapy, and who have attained virologic suppression. Of the estimated 613,080 MSM and TW in Peru in 2015, approximately 63,981 are HIV-infected. Only 24.0% of HIV-infected MSM and TW are aware of their diagnosis, 15.6% are retained in care, 13.6% are on antiretroviral therapy, and 12.0% have achieved adequate virologic control. The largest drop-off in the HIV care continuum occurs at the first step: diagnosis of HIV. Improving HIV serostatus awareness among MSM and TW is crucial to controlling Peru's HIV epidemic. In the era of 'treatment as prevention', understanding the full HIV care continuum may help guide efforts to curb transmission and reduce HIV-related morbidity and mortality.

The prognostic value of the tumour response to induction chemotherapy (IC) for long-term survival outcomes after intensity-modulated radiation therapy in nasopharyngeal carcinoma (NPC) remains unknown. We retrospectively reviewed 1811 consecutive patients with newly diagnosed NPC treated using IMRT, and 399 eligible patients with pre- and post-induction chemotherapy magnetic resonance images were recruited. The clinicopathological features of patients with different tumour responses were compared using the Chi-square test or Fisher's exact test. Prognostic value was assessed using a multivariate Cox proportional hazards model. After IC, 101/399 (25.3%) patients had a complete tumour response overall (CR), 262 (65.7%) had a partial response (PR) and 36 (9.0%) had stable disease (SD). The 4-year disease-free survival (DFS), overall survival (OS), distant metastasis-free survival (DMFS) and locoregional relapse-free survival (LRRFS) rates for CR vs. PR vs. SD were 90.0% vs. 79.0% vs. 58.2% (CR vs. PR: P1 = 0.007; CR vs. SD: P2 < 0.001; PR vs. SD: P3 = 0.004), 95.7% vs. 88.7% vs. 70.2% (P1 = 0.017, P2 < 0.001, P3 = 0.005), 92.0% vs. 87.4% vs. 74.3% (P1 = 0.162, P2 = 0.005, P3 = 0.029) and 95.9% vs. 88.8% vs. 81.8% (P1 = 0.024, P2 = 0.006, P3 = 0.268), respectively. Multivariate analysis identified that the tumour response to IC was an independent prognostic factor for DFS, OS and LRRFS.

Drains are commonly used after abdominal wall reconstruction (AWR) to prevent seroma formation. Drain management is subjective, and the merits and drawbacks of drains are not well understood. After receiving Institutional Review Board approval, we queried our prospectively maintained surgical database for AWR cases from 2009 to 2012 to ascertain if the number of days postoperatively that drains are left in place impacts the incidence of surgical site complications. Number of drains, drain duration, wound complications, and interval to development of complications were recorded. Wound complications were defined as superficial cellulitis, seroma, hematoma, superficial infection, and deep infection. Among 117 AWRs, we investigated the 64 cases with Centers for Disease Control grade one wound classification. Longest drain duration varied widely (2-171 days postoperatively; mean = 22 days). Cases were divided into four groups based on duration prior to removal of all drains: ≤7 days (n = 18), 8 to 14 days (n = 16), 15 to 28 days (n = 18), or ≥29 days (n = 12). No significant relationship was found between incidence of seroma/hematoma and days postoperatively of last drain removal. Wound complications increased linearly with drain time. Using logistic regression to adjust for obesity (body mass index >35kg/m(2)), drain duration >2 weeks and operative time >220 minutes, only body mass index >35 remained an independent predictor of wound occurrence, P < 0.05. Wound complications occur frequently after AWR. Wound infections occur more commonly among patients with drains in place for more than 2 weeks. Strategies to reduce drain duration require furthermore investigation.

Group B streptococci (GBS) cause severe invasive disease in both neonates and adults. Understanding the epidemiology of GBS provides information which can include determining prevalence rates of disease in defined populations and geographic regions, documenting the success of GBS screening programs and understanding antimicrobial susceptibility patterns. In Alberta, only invasive neonatal GBS (iGBS) disease is notifiable to health authorities. We performed a surveillance study of iGBS in Alberta, Canada from 2003 to 2013. Over the 11 years, the incidence rate of disease increased from a low of 3.92 to a high of 5.99/100,000. The capsular serotypes (CPS) found in order were CPS III (20.3%), CPS V (19.1%), CPS Ia (18.9%), CPS Ib (12.7%), CPS II (11.1%), CPS IV (6.3%) and nontypable GBS (9.4%). Rates of early onset disease (0-7 days) increased from 0.15/1000 (2003) to 0.34/1000 (2013). Rates of late onset disease (>7 days to 90 days) also rose from 0.15/1000 live births (2003) to 0.39/1000 (2013). Alberta also experienced an increase in CPS IV isolates from 2 cases (2003) to 24 cases (2013) of which the majority were hvgA positive (86.6%). The predominant MLST in 2013 was ST-459. Erythromycin resistance rose from 23.6% to 43.9% in 2013. Clindamycin resistance also increased from 12.2% to 32.5%. In summary, Alberta, Canada has experienced an increase in GBS disease. The increase includes both neonatal and adult disease. CPS IV cases have also notably increased during the surveillance period as well as antimicrobial resistance to erythromycin and clindamycin.

Family history of rheumatoid arthritis (RA) is a proxy for an individual's genetic and, in part, environmental risk of developing RA, and is a well-recognized predictor of disease onset. Although family history of RA is an old concept, the degree of familial aggregation of RA, whether it differs by age, sex, or serology, and what value it has for clinical decisions once a diagnosis of RA has been made remain unclear. New data have been emerging in parallel to substantial progress made in genetic association studies. In this Review, we describe the various ways that familial aggregation has been measured, and how the findings from these studies, whether they are based on twins, cohorts of first-degree relatives, or genetic data, correspond to each other and aid understanding of the aetiology of RA.

The predation of cysts and oocysts in 15 ciliate species from water and sewage samples collected in Campinas, São Paulo, Brazil were verified under laboratory conditions. The ciliated protozoan species were selected based on their mode of nutrition, and only bacterivorous and suspension-feeders were considered for the experiments. The species Blepharisma sinuosum, Euplotes aediculatus, Sterkiella cavicola, Oxytricha granulifera, Vorticella infusionum, Spirostomum minus, and Stentor coeruleus ingested cysts and oocysts, the resistance forms of Giardia spp. and Cryptosporidium spp., respectively. This is the first time that the ingestion of Giardia cysts by ciliated protozoa has been reported. These findings may contribute to a better understanding of the biological removal of these pathogens from aquatic environments.