Two Tales of *Cytauxzoon felis* Infections in Domestic Cats

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Summary: *Cytauxzoonosis* is an emerging infectious disease that affects wild felids as well as the domestic cat; it is caused by the apicomplexan protozoan parasites belonging to the genus *Cytauxzoon*. *Cytauxzoon felis* is the species of major concern, whose transmission occurs via the bite of an infected tick. *Cytauxzoonosis* of the domestic cat has historically been considered uniformly fatal, with a short course of illness, and most domestic cats die within 9 to 15 days postinfection. However, increasing evidence of domestic cats surviving *C. felis* infection suggests the existence of different strains with various levels of pathogenicity. Although wild felids are considered natural reservoirs for this parasite, a number of studies suggest that domestic cats that have survived nonlethal infections may serve as an additional reservoir. The current article comprehensively reviews the parasite and its life cycle, geographic distribution, genetic variability, and pathogenesis, as well as host immunology and the diagnosis, treatment, and prevention of infection in the domestic cat. This information should provide a basis for better understanding the parasite as well as the pathogenesis of the disease.

The Role of Antibiotics in Modulating Virulence in *Staphylococcus aureus*

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Summary: *Staphylococcus aureus* is often involved in severe infections, in which the effects of bacterial virulence factors have great importance. Antistaphylococcal regimens should take into account the different effects of antibacterial agents on the expression of virulence factors and on the host’s immune response. A PubMed literature search was performed to select relevant articles on the effects of antibiotics on staphylococcal toxin production and on the host immune response. Information was sorted according to the methods used for data acquisition (bacterial strains, growth models, and antibiotic concentrations) and the assays used for readout generation. The reported mechanisms underlying *S. aureus* virulence modulation by antibiotics were reviewed. The relevance of *in vitro* observations is discussed in relation to animal model data and to clinical evidence extracted from case reports and recommendations on the management of toxin-related staphylococcal diseases. Most *in vitro* data point to a decreased level of virulence expression upon treatment with ribosomally active antibiotics (linezolid and clindamycin), while cell wall-active antibiotics (beta-lactams) mainly increase exotoxin production. *In vivo* studies confirmed the suppressive effect of clindamycin and linezolid on virulence expression, supporting their utilization as a valuable management strategy to improve patient outcomes in cases of toxin-associated staphylococcal disease.
Impact of Childhood Malnutrition on Host Defense and Infection

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Summary: The global impact of childhood malnutrition is staggering. The synergism between malnutrition and infection contributes substantially to childhood morbidity and mortality. Anthropometric indicators of malnutrition are associated with the increased risk and severity of infections caused by many pathogens, including viruses, bacteria, protozoa, and helminths. Since childhood malnutrition commonly involves the inadequate intake of protein and calories, with superimposed micronutrient deficiencies, the causal factors involved in impaired host defense are usually not defined. This review focuses on literature related to impaired host defense and the risk of infection in primary childhood malnutrition. Particular attention is given to longitudinal and prospective cohort human studies and studies of experimental animal models that address causal, mechanistic relationships between malnutrition and host defense. Protein and micronutrient deficiencies impact the hematopoietic and lymphoid organs and compromise both innate and adaptive immune functions. Malnutrition-related changes in intestinal microbiota contribute to growth faltering and dysregulated inflammation and immune function. Although substantial progress has been made in understanding the malnutrition-infection synergism, critical gaps in our understanding remain. We highlight the need for mechanistic studies that can lead to targeted interventions to improve host defense and reduce the morbidity and mortality of infectious diseases in this vulnerable population.

Intrinsic Maturational Neonatal Immune Deficiencies and Susceptibility to Group B Streptococcus Infection

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Summary: Although a normal member of the gastrointestinal and vaginal microbiota, group B Streptococcus (GBS) can also occasionally be the cause of highly invasive neonatal disease and is an emerging pathogen in both elderly and immunocompromised adults. Neonatal GBS infections are typically transmitted from mother to baby either in utero or during passage through the birth canal and can lead to pneumonia, sepsis, and meningitis within the first few months of life. Compared to the adult immune system, the neonatal immune system has a number of deficiencies, making neonates more susceptible to infection. Recognition of GBS by the host immune system triggers an inflammatory response to clear the pathogen. However, GBS has developed several mechanisms to evade the host immune response. A comprehensive understanding of this interplay between GBS and the host immune system will aid in the development of new preventative measures and therapeutics.
The Role of BAFF System Molecules in Host Response to Pathogens

Jiro Sakai, Mustafa Akkoyunlu

Summary: The two ligands B cell-activating factor of the tumor necrosis factor family (BAFF) and a proliferation-inducing ligand (APRIL) and the three receptors BAFF receptor (BAFF-R), transmembrane activator and calcium-modulating cyclophilin ligand interactor (TACI), and B cell maturation antigen (BCMA) are members of the “BAFF system molecules.” BAFF system molecules are primarily involved in B cell homeostasis. The relevance of BAFF system molecules in host responses to microbial assaults has been investigated in clinical studies and in mice deficient for each of these molecules. Many microbial products modulate the expression of these molecules. Data from clinical studies suggest a correlation between increased expression levels of BAFF system molecules and elevated B cell responses. Depending on the pathogen, heightened B cell responses may strengthen the host response or promote susceptibility. Whereas pathogen-mediated increases in the expression levels of the ligands and/or the receptors appear to promote microbial clearance, certain pathogens have evolved to ablate B cell responses by suppressing the expression of TACI and/or BAFF-R on B cells. Other than its well-established role in B cell responses, the TACI-mediated activation of macrophages is also implicated in resistance to intracellular pathogens. An improved understanding of the role that BAFF system molecules play in infection may assist in devising novel strategies for vaccine development.

Whole-Genome Sequencing of Bacterial Pathogens: the Future of Nosocomial Outbreak Analysis

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Summary: Outbreaks of multidrug-resistant bacteria present a frequent threat to vulnerable patient populations in hospitals around the world. Intensive care unit (ICU) patients are particularly susceptible to nosocomial infections due to indwelling devices such as intravascular catheters, drains, and intratracheal tubes for mechanical ventilation. The increased vulnerability of infected ICU patients demonstrates the importance of effective outbreak management protocols to be in place. Understanding the transmission of pathogens via genotyping methods is an important tool for outbreak management. Recently, whole-genome sequencing (WGS) of pathogens has become more accessible and affordable as a tool for genotyping. Analysis of the entire pathogen genome via WGS could provide unprecedented resolution in discriminating even highly related lineages of bacteria and revolutionize outbreak analysis in hospitals. Nevertheless, clinicians have long been hesitant to implement WGS in outbreak analyses due to the expensive and cumbersome nature of early sequencing platforms. Recent improvements in sequencing technologies and analysis tools have rapidly increased the output and analysis speed as well as reduced the overall costs of WGS. In this review, we assess the feasibility of WGS technologies and bioinformatics analysis tools for nosocomial outbreak analyses and provide a comparison to conventional outbreak analysis workflows. Moreover, we review advantages and limitations of sequencing technologies and analysis tools and present a real-world example of the implementation of WGS for antimicrobial resistance analysis. We aimed to provide health care professionals with a guide to WGS outbreak analysis that highlights its benefits for hospitals and assists in the transition from conventional to WGS-based outbreak analysis.
Molecular Tools for the Detection and Deduction of Azole Antifungal Drug Resistance Phenotypes in *Aspergillus* Species

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Summary: The incidence of azole resistance in *Aspergillus* species has increased over the past years, most importantly for *Aspergillus fumigatus*. This is partially attributable to the global spread of only a few resistance alleles through the environment. Secondary resistance is a significant clinical concern, as invasive aspergillosis with drug-susceptible strains is already difficult to treat, and exclusion of azole-based antifungals from prophylaxis or first-line treatment of invasive aspergillosis in high-risk patients would dramatically limit drug choices, thus increasing mortality rates for immunocompromised patients. Management options for invasive aspergillosis caused by azole-resistant *A. fumigatus* strains were recently reevaluated by an international expert panel, which concluded that drug resistance testing of cultured isolates is highly indicated when antifungal therapy is intended. In geographical regions with a high environmental prevalence of azole-resistant strains, initial therapy should be guided by such analyses. More environmental and clinical screening studies are therefore needed to generate the local epidemiologic data if such measures are to be implemented on a sound basis. Here we propose a first workflow for evaluating isolates from screening studies, and we compile the MIC values correlating with individual amino acid substitutions in the products of *cyp51* genes for interpretation of DNA sequencing data, especially in the absence of cultured isolates.

**AUTHOR CORRECTION**

Correction for Perry, “A Decade of Development of Chromogenic Culture Media for Clinical Microbiology in an Era of Molecular Diagnostics”

John D. Perry