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not include *Proteus*, *Providencia*, and *Pseudomonas* spp. Plasma and urinary levels are modest. Efficacy data are largely for community infections, with modest numbers of bacteraemias. More T than C pts died, and more experienced septic shock, but the imbalances were not statistically significant. GI AEs were common (cSSSI >cIAI>C), but usually mild or moderate; nonetheless, some pts do not tolerate T. Methods to improve GI tolerability are not identified. Increased PT/ PTT and bilirubin/ jaundice occur, the latter in predisposed cIAI pts. Increased blood urea and abnormal wound healing likely reflect an anti-anabolic effect.

Conclusion: The benefit-risk ratio is favorable in cSSSI and cIAI. Candidate pts include those with polymicrobial surgical wound infection, cSSSI complicating diabetes mellitus, cIAI such as diverticulitis or biliary infection, and allergy to/intolerance of other therapies. More data are needed on the role of T in therapy of nosocomial infection, bacteraemia, and infection caused by *Acinetobacter* spp. and ESBL-producing organisms.

29.015 Antiviral Effects of Novel Phenoxazines, Phx-1 and Phx-2 on Poliovirus and Porcine Parvovirus

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Background: We found that novel phenoxazines such as 2-amino-4, 4a-dihydro-4a, 7-dimethyl-3H-phenoxazine-3-one (Phx-1) and 3-amino-1, 4a-dihydro-4a, 8-dimethyl-2H-phenoxazine-2-one (Phx-2) exert antimicrobial, anticancer and immunosuppresive effects. It may be interesting to study preventive effects of these phenoxazines on viruses.

Methods: Phx-1 and Phx-2 were obtained by the reaction of 2-amino-5-methylphenol or 2-amino-4-methylphenol with bovine hemoglobin. Antiviral effects of Phx-1 and Phx-2 on poliovirus and porcine virus were examined after treatment of Vero cells or ESK cells with Phx-1 and Phx-2 for 1 hour at 37C. Antiviral effects of these phenoxazines were examined for other viruses such as simian virus 40, herpes simplex virus-1, Sindbis virus and vesicular stomatitis virus.

Results: Phx-1 and Phx-2 suppressed the proliefation of poliovirus in Vero cells and that of porcine parvovirus in ESK cells at concentrations between 0.25 ug/ml and 2 ug/ml, when the cells were treated with these phenoxazines for 1 h and then inoculated with these viruses. The proliferation of otehr viruses in the host cells was not affected by these phenoxazines.

Conclusion: Present result may suggests that Phx-1 and Phx-2 may be useful to prevent the proliferation of poliovirus and porcine parvovirus infection.

29.016 Inhibition by Thyme Oils of Growth, Aflatoxin Production and Ultrastructural Alterations of *Aspergillus parasiticus*

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Background: Some Aspergillus species are are responsible for many cases of food and feed contamination. Aflatoxin producing fungi grow rapidly on a variety of natural substrates and consumption of contaminated food feedstuffs can pose serious health hazards to human and animals. The use of natural antimicrobial compounds is important not only in the preservation of food but also in the control of human and plant diseases of microbial origin.

Methods: The antifungal effects of essential oils from Thymus eriocalyx and Thymus x-porlock were studied with special reference to the inhibition of Aspergillus parasiticus growth and aflatoxin production. Minimal inhibitory (MIC) and minimal fungicidal (MFC) concentrations of the oils were determined. The oils analyzed by GC and GC/MS for their chemical constituents. Ultrastructural alterations of the fungus were studied under Transmission Electron Microscope.

Results: The oils from the above plants were found to be strongly antimicrobial and inhibitory to aflatoxin production. Static and lethal effects of the above oils against A.parasiticus were at 250 and 500-1000ppm of the oils respectively. Aflatoxin production was inhibited at 250ppm of both oils with that of T.eriocalyx being stronger inhibitor. The oils analyzed by GC and GC/MS lead to identification of 18 and 19 components in Thymus eriocalyx and Thymus x-porlock oils respectively. The profile of the oil components from Thymus eriocalyx was similar to that of Thymus x-porlock in almost all the compounds but at different concentrations. The major components of Thymus eriocalyx and Thymus x-porlock oils were Thymol (64.3, 30.7%), beta-phellandrene (13.2, 39.4%) and Cis Sabinene hydroxide (8.4, 9.7%) respectively. Transmission electron microscopy (TEM) of A. parasiticus exposed to MIC level (250 ppm) of the oils showed irreversible damage to cell wall, cell membrane and cellular organelles.

Conclusion: Substitution of currently used antifungal and aflatoxin inhibiting chemicals by natural compounds such as thyme is recommended.

29.017 Search for Antimicrobial Peptides Among Natural Toxins and Venoms

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Background: Burkholderia pseudomallei are the causative agent of melioidosis. It is intrinsically resistant to many antibiotics. Consequently, there is an urgent need to search for alternatives to synthetic antibiotics.

Methods: A large library of natural toxins and venoms from snakes, scorpions, spiders and purified PLA2s including ammodytoxin, crotoxin A, crotoxin B, daboiatoxin, taipoxin, mulgatoxin, melttin, α-bungarotoxin and Mojave toxin were screened for their antimicrobial activity against a wide variety of organisms by disc-diffusion method.

Results: The crotoxin B(CB) showed broad spectrum of activity against S. aureus, P. aeruginosa, E. aerogenes, E. coli and B. pseudomallei. However the CB and daboiatoxin exerted strong antimicrobial activity against S. aureus and B. pseudomallei. The enzymes were further studied their MIC by MH broth dilution assay at 0.5-0.0315 μM. Enzymes, CB (MICs 0.0125 μM) and daboiatoxin (MICs 0.25 μM) showed strong bacterial inhibition at the lowest dilutions. SEM showed membrane pore formation. Hemolytic property was assayed using human erythrocytes; the enzymes did not show any toxic effect compared to control.

Conclusion: This antibacterial profile of snake venom PLA2s reported may be useful agents against drug resistant microorganisms of B. pseudomallei.

Pathogenesis caused by B. pseudomallei was also studied by infection with human macrophages as well as in mice and guinea pig models after intra peritoneal injections. Also postmortem specimens from infected pigs were studied by Light microscopy, TEM as well as SEM. A complete evolution of the pathogenesis of the organism from entering the macrophage to abscess formation in animal models will be presented using all the microscopic methods.

29.018 Adverse Events During Pegylated Interferon/ Ribavirin Combination Therapy in Patients with Chronic Hepatitis C

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Background: To evaluate the effects of adverse events on the course of therapy with pegylated interferon/ribavirin in patients with CHC.

Material and Methods: 89 patients with CHC are treated with pegylated interferon/ribavirin at the Clinic. 45/89 with CHC (19 pts with C1 and 26 pts with C3), were analyzed. Seventy subjective and 3 objective adverse events were taken into account. The methods used were questionnaire and standard laboratory investigations.

Results: 63 adverse events were observed in more than 10% of the patients, and 10/63 in more than 50%. More than 50% of the patients with C1 infection experienced 18 adverse events, and only 2 were present in less than 10% of the patients. Nine adverse events occurred in more than 50% of the patients with C3 infection, and less than 10% experienced only 6 adverse events. Discontinuity/dose modification was done in 7 patients (15, 6%); in two because of severe neutropenia, in two because of anemia, in one patient due to neutropenia and thrombocytopenia, in one patient as a result of thrombocytopenia, and in one because of prominent subjective reactions. From total 89 patients with ongoing combination therapy pegylated interferon/ribavirin, the therapy was stopped in 12 (13, 5%); in 5 (5, 6%) as a result of serious adverse events.

Conclusion: adverse events are present in large number and in significant proportion of patients treated with pegylated interferon/ribavirin. The length of therapy, according the HCV genotype, has some influence on the percentage of the reported adverse events, as well as the number of patients in which they appear. It should be noticed that all of the reported adverse events disappeared one month after end of treatment.