In the Literature

Can We Prevent Linezolid-Associated Anemia and Thrombocytopenia?


The most frequently encountered adverse effects of linezolid therapy are anemia and thrombocytopenia, both of which are observed mostly in individuals receiving the drug for >2 weeks, and both of which are generally reversible after discontinuation of treatment. This effect appears to be the result of bone marrow suppression, possibly as a consequence of inhibition of mitochondrial protein synthesis resulting in impairment of cellular proliferation [1]. The finding of ringed sideroblasts in the bone marrow of some patients with linezolid-associated anemia has raised the consideration that pyridoxine, which has a putative role in mitochondrial function, may play a preventive or therapeutic role. Such a role of pyridoxine supplementation was suggested by a report of reversal of anemia and thrombocytopenia in 2 patients who were given this B complex vitamin [2]. A subsequent uncontrolled, retrospective cohort study, however, found a high incidence of both anemia and thrombocytopenia, despite administration of pyridoxine, in 24 patients with osseous infections who received therapy for a median period of 3.5 weeks [3]. Soriano and colleagues have now examined the effect of pyridoxine and other factors on linezolid-associated hematological toxicity in a prospective, non-randomized, cohort controlled study.

All 52 of the patients who were studied, most of whom had osseous infection, were treated with standard doses of linezolid. The first 24 patients receiving linezolid alone, and the next 28 received linezolid plus pyridoxine (200 mg daily). The 2 treatment groups were comparable at baseline. The median durations of linezolid administration were 55.5 days and 50.8 days, respectively, in the 2 groups. A baseline glomerular filtration rate <50 mL/min was associated with an increased risk of thrombocytopenia (P = .02). Pyridoxine administration was not demonstrated to provide a benefit; the cumulative probabilities of thrombocytopenia and anemia did not significantly differ between the groups. Linezolid treatment was discontinued because of the occurrence of a platelet count <100 × 10^9 platelets/L in 12.5% of those who received the antibiotic alone and in 14.2% of those who received it with pyridoxine. Linezolid treatment was discontinued because of severe anemia (hemoglobin concentration, <8 g/L) in 12.5% and 3.5% of patients, respectively (P = .24). Thus, the accumulated evidence suggests that pyridoxine supplementation does not reduce the risk of the hematologic toxicity of linezolid.

On the other hand, rifampin treatment may play a protective role. Seventeen of the 52 patients received rifampin with linezolid for treatment of retained infected orthopedic implants. Cox regression analysis identified concomitant rifampin use as the only factor independently associated with a reduced risk of thrombocytopenia (hazard ratio, 0.37; 95% CI, 0.14–0.98). No factor was identified in association with anemia. The reason for the apparent protective effect of rifampin is unknown, but it has been speculated to be associated with a proposed rifampin-enhanced transport of linezolid [4]. Thus, although rifampin may provide protection from adverse hematologic effects, it may do so by reducing exposure to linezolid, with a consequent potential reduction in antibacterial efficacy.

References

Projecting Bacteria into Space


The US space program has long demonstrated concern regarding the possibility of bringing an alien microbial invader back from extraterrestrial locations and has acted by putting objects brought back to earth, such as moon rocks, in quarantine for prolonged periods while they were examined. In some cases, as part of the continuing search for extraterrestrial life forms, the scientists are actually hoping to find microorganisms in such samples. If such forms were found, it would have to be determined with certainty that they were not simply contaminating organisms from the earth’s microbiota. Such contamination could occur after the object was brought to earth, but it could also result from contamination from elements of the spacecraft itself. To guard against this, as well as against contaminating extraterrestrial sites with alien microorganisms from earth, rigorous procedures are used to minimize biological contamination of all spacecraft components. Moissi and colleagues have examined the efficacy of these procedures by searching for microbial flora by molecular techniques in clean spacecraft assembly rooms at 3 geographically distant sites (the Jet Propulsion Laboratory in Pasadena, California; the...
Kennedy Space Center in Cape Canaveral, Florida; and the Johnson Space Center in Houston, Texas).

Nine clone libraries from within the facilities and 3 libraries from the surrounding air were created. Randomly selected clones were sequenced directly or examined by restriction fragment–length polymorphism analyses. A broad range of bacteria were identified at each site, with all major bacterial phyla represented. The differing external environmental characteristics surrounding the facilities (humid and swampy or dry and desert-like) did not appear to affect the biodiversity of the identified flora, yet the bacterial communities significantly differed between sites. The only genera common to all 3 sites were Acinetobacter, Deinococcus, Methylbacterium, Sphingomonas, Staphylococcus, and Streptococcus. Staphylococci were the most widespread, having been detected in every sample location except one. These same organisms have been readily recovered in the International Space Station, and it can be speculated that some of those organisms originated in the clean assembly rooms on earth.

Overall, the types of bacteria identified may be considered in 2 broad groups: bacteria that colonize or infect humans and bacteria that can maintain themselves in the harsh, nutrient-poor clean room environment. The latter may be considered oligotrophs (i.e., organisms adapted for growth in the presence of minimal nutrients that are capable of absorbing trace amounts from air or substratum). Some of these organisms have been demonstrated to survive decontamination procedures, including UV and γ irradiation, further explaining their presence. Although it is unlikely that contamination can be completely eliminated, an understanding of the range and depth of organisms present at these sites may allow improved microbial control and an improved understanding of organisms that we are bringing into space, as well as some that appear to have come from space.

**Not All Transmissible Diseases Are Infectious—The Devil Knows**


The Tasmanian devil, which earned its name as the result of its blood-curdling nocturnal screams, is under threat of extinction as the result of a tumor that is spread between the animals by biting. Fatal facial tumors began appearing in these carnivorous marsupials in 1995 in the northeastern region of Tasmania and spread rapidly, with a subsequent 90% decrease in the incidence of sightings of the animals in that area and a >50% decrease on the island as a whole. Animals affected by these ulcerating tumors generally die in 3–6 months.

When the tumor first began killing these carnivorous marsupials, a variety of hypotheses were generated to explain the phenomenon, with the leading early candidate being that it was due to transmission of a herpesvirus. Subsequent studies, however, failed to identify an associated microorganism, making the transmissible nature of Devil Facial Tumor, which is restricted to this single species, puzzling. On the basis of the presence of complex chromosomal rearrangements, the tumors appear clonally identical among the animals, which do not appear to mount any immune response against them. In fact, the devils demonstrate a lack of alloreactivity between lymphocytes of different individual animals, indicating a lack of major histocompatibility diversity, a finding confirmed by genotyping.

Thus, these island-confined animals are highly inbred and, as a consequence, exhibit a marked lack of genetic diversity, resulting in a lack of a histocompatibility barrier between individuals. The facial tumor is transmissible among the devils, not because of the presence of an infectious agent, but because it is acting like transplanted tissue from a highly genetically related donor. The devils, having tumor cells transferred into bite wounds, do not recognize the transplanted cells as foreign and do not reject them. The resultant successful transplant grows without restraint and eventually leads to the death of the recipient, a fate that potentially confronts the entire species.

DOI: 10.1086/524690