[haematologica reports]
2005;1(5):44-45

Monoclonal antibodies. How do they change the pattern of infections in lymphoproliferative diseases?

B.E. de Pauw

Department Blood transfusion and Transplant Immunology, University Medical Center St Radboud, Geert Grooteplein Zuid 6. NL-6525 GA Nijmegen, The Netherlands

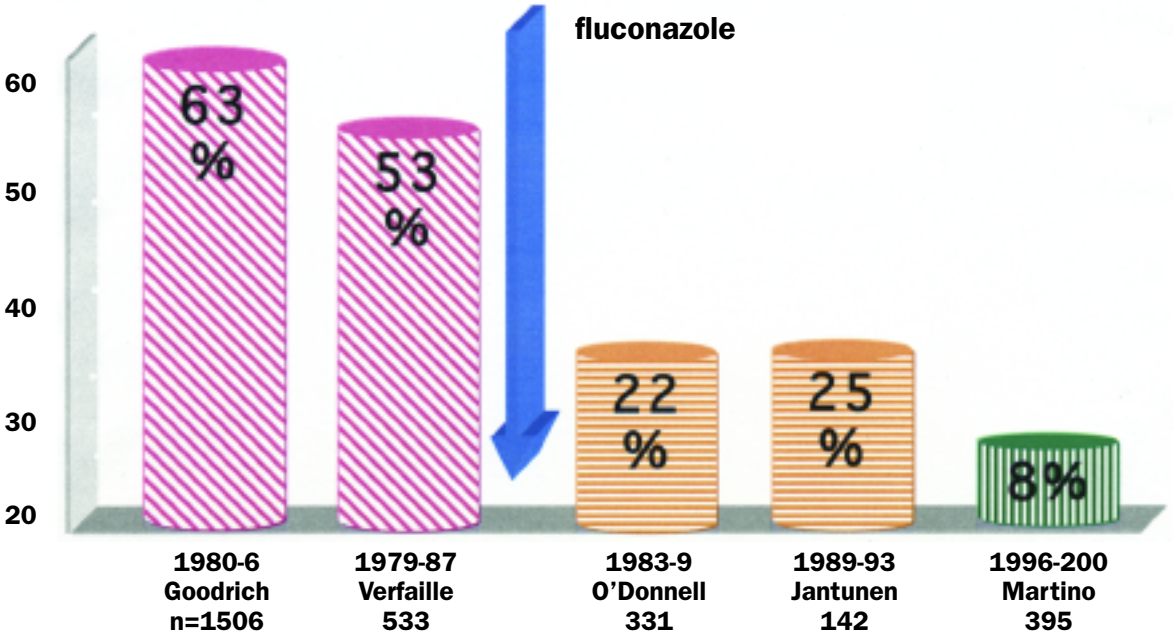
Opportunistic infections have always been pitfalls on the road of progress in the treatment of diseases that are accompanied by compromised host defences. Because of the severe morbidity and mortality associated with these infections, they have become substantial challenges for the clinicians who offer such patients care. With medical progress, the number of immunocompromised patients is still steadily climbing and it has become evident that deficiencies in host defences mechanisms are multiple as well as changing in harmony with alterations in treatment modalities for underlying diseases. Some of the major factors that facilitate infections by fungi are summarised in Table 1. The spectrum of opportunistic pathogens will shift as anti-leukemic and anti-lymphoma therapy become more intensive and when bone marrow transplant practices evolve. Initially bacterial infections were most problematic. However, as strategies to control bacterial infections improved, viruses demanded more attention from the clinicians but the associated morbidity declined due to advances in rapid diagnostics and the introduction of effective antivirals such as acyclovir and ganciclovir. Today, opportunistic fungi have become the most frequent and dangerous pathogens. Since the 1980's the rate of nosocomial invasive fungal diseases has doubled without any sign of slowing during the 90's. During the past two decades we have even observed an increased incidence of invasive fungal infections in patients who are not in an end stage of their underlying disease. Yeasts and moulds now rank amongst the 10 most frequently isolated pathogens and approximately 7% of all febrile episodes can be attributed definitely to these microorganisms.

The relative incidence of the various fungal infections depends on geography as well as on medical practices and local conditions. Candida and Aspergillus species remain the prominent fungal pathogens. A recent study highlights, that even patients treated with nonmyeloablative allogeneic transplantation (or "minitransplants") to reduce transplant-related toxicity, are at high risk of contracting an invasive fungal infection. These unexpected infections were again associated with, an as yet unexplained, recurrent neutropenia after engraftment in this new treatment modality. Under normal circumstances, the intact epithelial surfaces of the gastrointestinal tract will prohibit invasion by micro-organisms and the mucociliary barrier of the respiratory tract prevents aspiration of fungal cells and spores, while, in contrast, dead or damaged tissue creates a nidus for infection. With the growing use of potent immunosuppressive purine analogues, fludarabine, pentostatin and cladibrine, and anti-T and anti-B cell antibodies, such as rituximab and campath, in the management of lymphoreticular malignancies, in combination with increasing emphasis on dose intensity, the number of patients at risk has almost reached levels encountered in recipients of allogeneic stem cell grafts.

Table 1. Factors facilitating emergence of invasive fungal infections. Increasing age of patients

- More complex therapeutic interventions
- More patients are given cytotoxic therapy
- Intensification of cytotoxic regimens
- More central venous lines hyperalimentation
- Increased use of immunomodulating therapy
- Decreased mortality from other causes

(Improved diagnostic techniques as indirect cause of increased awareness)


fluconazole
60
50
40
30
20
63 %
53 %
22 %
25 %
8%
1980-6 Goodrich n=1506
1979-87 Verfaille 533
1983-9 O'Donnell 331
1989-93 Jantunen 142
1996-200 Martino 395