



**Karolinska  
Institutet**

**Institutionen för Medicin, Solna**

# **Aetiology and infection susceptibility in neutropaenic patients**

**AKADEMISK AVHANDLING**

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## ABSTRACT

Increasingly intensive antineoplastic regimes have been effective in the treatment for haematological malignancies, but as effective as it is in limiting neoplasm of the malignant cells, bystander damage occurs equally to cells of the immune system and epithelial cells of the mucosa. Infectious complications following chemotherapy reflect this situation.

The relationship between leukocytopenia and infection risk, in the form of bacteraemia and fungaemia was first suggested by Bodey and colleagues and since then, many studies have followed establishing the breadth of pathogens in relation to neutropenia. However, lymphocytes are also concurrently, markedly reduced suggesting that viraemia should also be considered in the repertoire of infectious complications with these iatrogenic neutropenic patients. Reactivation of latent DNA viruses, for example, members of the *herpesviridae* family, and respiratory viruses have been reported in severely immunosuppressed patients after haematopoiesis stem cell transplantation (HSCT) but less so in patients that have been administered comparatively less aggressive chemotherapeutic treatment used against hematological malignancies. Since fever in these patients is sometimes the only indication of infection due to their immunosuppressed state, we not only determined the prevalence of viral infections in the iatrogenic neutropenic adult patient we also related our findings to fever manifestation. Indeed, an association between virus detection and fever was observed, suggesting viral contribution to 30% of neutropenic febrile episodes in our study cohort.

In addition to immune cell depletion, disruption of the gastrointestinal mucosa is another major side-effect since it can lead to microbial translocation from the large reservoir of bacterial microflora we harbour in our bowels. Elevated plasma endotoxins and sCD14 was observed in the bacteraemic episodes as well as in the episodes with fever of unknown origin (FUO). So, together with the 33% of the febrile episodes attributed to clinically documented bacteraemia and 30% attributed to viruses, we propose that aside from drug and tumour fever, a part of the remaining 37% of febrile neutropenic episodes could be attributed to microbial translocation of bacterial products from the gut.

Acellular components of the immune system, such as the acute phase protein, mannose-binding lectin (MBL) have been suggested to be important in a similar cohort and that the use of replacement MBL therapy could be administered to reduce duration of febrile neutropenic episodes. We however, did not observe any associations between MBL and infection type or frequency and add to the reports casting doubts on the benefit of recombinant therapy in the iatrogenic neutropenic adult.

In conclusion, we have added to the panorama of infectious agents and bacterial products implicated during febrile neutropenic episodes in the adult iatrogenic patient and have further discouraged suggestions for MBL replacement therapy.