

and nonepithelial tumors (lymphoma, sarcoma etc.) have to be considered. Standard therapy for DTC is total thyroidectomy including central lymph node dissection. Additional unilateral neck dissection should be considered in T2 to T4 tumors and is mandatory in suspected or proven regional lymphatic spread. Limited radicality meaning lobectomy or even subtotal resection in occult tumors is adequate for small encapsulated papillary (<1 cm; T1) and microinvasive follicular (<1 cm; T1) tumors with no necessity of additional radioiodine therapy. MTC might be sporadic (SMTC, unifocal) or familial (FMTC, multifocal) requiring thyroidectomy always and neck dissection unilaterally in SMTC and bilaterally in FMTC. Genetic screening allows early detection of the disease and thus thyroidectomy only seems to provide appropriate radicality. In ATC radiochemotherapy is the treatment of choice and operation is rarely indicated and only suitable for decompression or debulking.

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### Introduction to tumour immunology and cancer vaccines

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Since the turn of the century there have been many attempts to try to induce remissions in tumours by stimulating the immune system. Perhaps the grandfather of clinical application was William Coley, a New York Surgeon who noticed that patients with severe septicemia sometimes underwent remission of their tumours. Whilst trying to identify the active component of the infection, he came up with a bacterial cell wall mixture which subsequently became known as 'Coley's Toxins'. Other investigators tried a variety of autologous and allogeneic cell based vaccines with limited success.

More recently the use of cell based vaccines has been re-visited under the guise of gene therapy. Autologous tumours are difficult to grow and stabilize on an individual basis and allogeneic vaccines have been considered by a number of investigators. The use of cells allows one to present a variety of tumour antigens to the immune system. Boon and his colleagues have identified several tumour antigens recognised by cytotoxic T-cell lymphocytes from patients at the peptide level and a number of new antigens

have been defined and their epitopes and HLA associations documented. This has led to a number of studies using peptides such as MAGE, MART and tyrosinase with a variety of antigen presenting techniques such as culture dendritic cells.

What is urgently needed is parameters to know which patients to treat, what immune parameters are required in order to ensure a response and perhaps most importantly when to stop treatment with a specific protocol. The technology to address these questions is now available and it only remains to apply the most appropriate ones to the correct clinical questions.

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### Current developments in the treatment of chronic myeloid leukemia

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Currently, allogeneic bone marrow transplantation (BMT) is the only curative treatment available, but is only applicable in a minority of patients ( $\pm 20\%$ ) for whom a HLA identical related or unrelated donor can be found and who are under the age of 50–55 years. Results have improved over the last 10 years, largely due to a reduction of transplant related mortality. The relapse rate after BMT depends on the number of T-cells in the graft and recently it has become clear that an established relapse after BMT can be treated effectively by donor lymphocyte infusion (DLI) without the addition of chemotherapy.

Patients, lacking an allogeneic donor, are currently treated with Interferon-Alpha (IFN- $\alpha$ ) and/or Hydroxyurea. IFN- $\alpha$  has been shown to prolong survival, but the beneficial effects of IFN- $\alpha$  seem to be restricted to a subgroup (15–20%) of patients, who achieve a major cytogenetic response.

Current treatment protocols are designed to improve the number of cytogenetic responders by combining IFN- $\alpha$  with chemotherapeutic agents, such as low-dose Cytarabine. Autologous stem cell transplantation followed by IFN- $\alpha$  may also improve survival and several approaches are underway to address the value of that treatment modality.