abdominal aorta), there was no difference in survival compared with the group with GCA without large-artery complication. Survival of patients with GCA and large-artery stenosis was not different from that of those with GCA without large-artery complications.

**Conclusions:** Large-artery involvement is common in GCA. The protective effect of cranial symptoms and of a higher sedimentation for large-artery stenosis may be explained by earlier appropriate therapy with glucocorticosteroids of patients presenting with these findings. Overall, the mortality in the whole group of patients with GCA with large-artery complications was similar to that observed in patients with GCA without large-artery complications. However, thoracic aortic dissection in GCA is associated with a markedly increased mortality. Increased awareness of large-artery involvement in GCA, particularly its association with rather early occurring aortic dissection, may decrease associated morbidity and mortality.

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**OP25. NEW GLUCOCORTICOIDS: SELECTIVE GLUCOCORTICOID RECEPTOR AGONISTS, NO-GLUCOCORTICOIDS AND LONG-CIRCULATING LIPOSOMAL GLUCOCORTICOIDS**

F. Buttgereit
Department of Rheumatology and Clinical Immunology, Charité University Medicine, Berlin, Germany

Our understanding of the actions of glucocorticoids has greatly increased in the last few years. The various genomic and non-genomic mechanisms of glucocorticoid action provide interesting and sometimes very advanced starting points for the development of optimised glucocorticoids and glucocorticoid receptor ligands. SEGRAs, NO-glucocorticoids and long-circulating liposomal glucocorticoids are examples to be mentioned in this regard.

**Selective glucocorticoid receptor agonists (SEGRAs):** Currently glucocorticoid receptor ligands are being developed that cause predominantly transrepression but not transactivation. These drugs are called selective glucocorticoid receptor agonist ligands (SEGRAs) and are thought to have an improved safety/efficacy profile. In vivo investigations and clinical trials will have to define whether SEGRAs will, as ‘improved glucocorticoids’, enter clinical medicine in the near future.

**NO-glucocorticoids:** Recent experimental observations prompt the assessment of the clinical impact of another new class of glucocorticoid drugs, NO-glucocorticoids, which are able to release low levels of nitric oxide. They have been shown to be endowed with enhanced anti-inflammatory properties and reduced side effects. The prototype of these new steroids, 21-NO-prednisolone, is much more potent than prednisolone in models of acute and chronic inflammation but does not activate primary osteoclast activity (whereas prednisolone does). However, more studies are needed to confirm that NO-glucocorticoids will be effective as anti-inflammatory agents in clinical practice.

**Long-circulating liposomal glucocorticoids:** The anti-inflammatory effectiveness of glucocorticoids can be improved by the additional benefits of the non-genomic actions of high glucocorticoid concentrations. On this basis, the successful use of long-circulating liposomal glucocorticoids has recently been reported which accumulate at sites of inflammation. This leads to very high glucocorticoid concentrations at e.g. the inflamed joint (but accompanied by low plasma concentrations with perhaps a lower rate of side effects) which is the key factor explaining the observed strong therapeutic effect.

**Conclusions:** These new GCR-ligands and the administration of liposomes are very promising approaches that will hopefully soon be available in clinical practice to improve the benefit/risk ratio and well-being of patients being treated. Another intriguing issue is the study of membrane bound glucocorticoid receptors (mGCR). These surface receptors are suggested to mediate rapid nongenomic effects and have been found to be upregulated in active rheumatoid arthritis. The number of monocytes expressing mGCR is significantly correlated with disease activity. Therefore, drugs binding selectively to the mGCR may in future also prove to be of therapeutic value but the functions of mGCR must first be investigated in detail.

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**OP26. THERAPY IN VASCULITIS**

D. Jayne
Addenbrooke's Hospital, Cambridge, UK

The treatment of vasculitis has developed empirically with the introduction of corticosteroids and their subsequent combination with immune suppressive drugs, especially cyclophosphamide. Over the last fifteen years, prospective multi-centre studies have helped determine optimum drug regimens and have attempted to design regimens according to disease extent and severity. Common features of these trials have been the high rates of treatment toxicity reported and the risk of disease relapse when treatment is reduced or withdrawn. These are the two principal targets for newer therapeutics. Furthermore, current regimens are not necessarily effective at restoring the patient to their pre-morbid state of health and the apparent disease remission seen by physicians is not reflected in normalisation of quality of life. Subclinical disease activity may persist, although this is difficult to study without improved biomarkers of disease. Current studies are exploring alternative immune suppressives, such as myco-phenolate mofetil and deoxyspergualin, and the optimal duration of therapy.

Two newer therapeutic approaches have taken advantage of recombinant antibody technology and drugs developed for more common, and profitable, indications. Lymphocyte depletion aims to remove autoreactive lymphocytes and thereby control disease. Anti-thymocyte globulin and anti-CD52 (CAMPATH-1H) have had the effect of depleting T cells and both strategies have been effective in vasculitis. This confirms a T cell role in the pathogenesis of vasculitis but these drugs are associated with high levels of intercurrent infection and have never entered routine use. B cell depletion with Rituximab has been surprisingly effective in autoimmunity and has emphasised a role for B cells in supporting autoreactive T cell activity. Several studies in ANCA associated vasculitis have reported high rates of success and other vasculitides are now being studied. B cell depletion appears to be safe and to lead to prolonged remission, re-treatment seems to be uncomplicated and effective. The other strategy has been cytokine depletion especially with agents blocking tumor necrosis factor (TNF). Results in small vessel vasculitis have been conflicting with short term studies suggesting benefit and larger, longer term studies not finding any sustained effect. Uncontrolled studies in giant cell arteritis and Takayasu's disease have been promising and it will take some time to clarify the optimal indications, therapeutic agent dose and duration of therapy for TNF blockade in vasculitis.

With the development of large clinical trial databases during the 1990s longer term follow-up studies are now feasible in vasculitis. Preliminary results have revealed increased mortality and increased cardiovascular risk but there is no clear indication of an increase in malignancy. It will be important to determine how current therapeutic strategies influence longer term outcomes and whether additional interventions are required to reduce these increased risks.