Susceptibility to autoimmune disease explained?
It is well known that susceptibility to autoim-
mune diseases such as multiple sclerosis and
uveitis varies depending on the genetic back-
ground of the individual, but the mechanism
whereby this occurs is unknown. Although
conventional teaching has it that potentially
autoreactive T lymphocytes are deleted in the
thymus during development, more recent find-
ings have indicated that there are small
numbers of autoreactive T cells present in the
periphery and which have presumably escaped
deletion in the thymus. The extent of thymic
deletion of autoreactive T lymphocytes is
dependent in some part on the expression of
self antigens in the thymus and it has been
shown that self antigens, such as retinal and
CNS proteins, previously considered to be
organ specific, are expressed at low levels in the
thymus. Their expression in the thymus is
thought to be important for the induction of
tolerance and thus protection from autoim-
mune disease. A recent paper (Nature Medicine
2000;6:56–61) has reported a further twist to
this tale. Proteolipid protein (PLP) is a major
protein of myelinated nerve fibres and immuni-
sation of animals with this protein combined
with adjuvant produces a demyelinating disease
with similarities to multiple sclerosis. PLP is
composed of a number of antigenic peptides
(epitopes) and some of these are expressed in the
thymus on thymic epithelial cells. Intrathymic
expression of PLP was largely restricted to
the shorter splice variant of PLP, known as
DM20. Expression of DM20 by thymic epithe-
lium was sufficient to confer T cell tolerance
not only to DM20 but to all other epitopes of
PLP in a strain of disease resistant mice. In
contrast, this major T cell activating epitope
was expressed only in the central nervous
system specific PLP, but not in the thymus, of
disease susceptible mice. The authors suggest
that the absence of this antigen from the
thymus prevented susceptible mice developing
tolerance to the disease and offers an explana-
tion for the exquisite susceptibility of the latter
strain of mice to experimental autoimmune
encephalomyelitis. They further suggest that
as PLP expression in the human thymus is also
restricted to the DM20 isoform, these findings
have risk implications for multiple sclerosis.

NSAIDS may be toxic to cornea
Recent reports suggest that some non-
steroidal anti-inflammatory drugs may be
toxic to the cornea especially if used fre-
quently or intensively. As reported in
Eyenet, a report by Laslo Dosa indicated that
an accommodating intraocular lens that would
cope with the problem of presbyopia. In the
recent edition of Eyenet, a report by Laslo
Dosa indicated that an accommodating in-
traocular lens is in phase I clinical trials. Made
of a “new, unique blend of silicone” it is
placed vaulted posteriorly against the vitreous
face and hinges forward just outside of the
optic on the haptic to allow maximum forward
movement for near vision. The lens moves
forward about 1 mm accounting for about 2
dioptres of accommodation, according to
Stephen Slade who is conducting the trial.
The current study involves 16 eyes in 15
patients who had mature cataracts.

Minimising leakage from blood vessels
Several retinal diseases are characterised by
leakage from retinal and/or choroidal vessels.
The resulting macular oedema is a major
cause of visual loss in diseases such as diabetic
retinopathy, posterior uveitis, and age related
macular disorders. In some of these diseases
growth factors such as vascular endothelial
growth factor (VEGF) are strongly implicated
not only in the growth of new vessels but also
in the initial leakage from these vessels. Indeed,
VEGF was first identified as an inducer of vascular leakage in tumours and
inflammatory conditions before it was recog-
nised as an angiogenic factor. More recent
studies have identified other growth factors
such as angiopoietin 1 and 2 and Tie 1 and 2
in regulating new vessel growth, and several
research programmes are directed at deter-
mining the role of these novel factors in
conditions such as retinopathy of prematurity
and diabetic retinopathy. A recent study has
shown in transgenic mice overexpressing angio-
opoi etin or VEGF that, while both growth
factors can induce new vessel growth, angi-
opoi etin prevents vascular leakage, in contrast
with VEGF which has the opposite effect (Sci-
ence 1999;286:2511–14). In addition, inflam-
matory agents were unable to induce leakage
in vessels in Ang1 overexpressing mice. In
strains of mice which were bred to coexpress
Ang1 and VEGF there was an additive effect
on angiogenesis but leakage resistant vessels
are also typically seen in Ang1 alone transgenic
mice. The authors suggest that selective use of
Ang1, therefore, may be useful for reducing
microvascular leakage in diseases in which the leakage results
from chronic inflammation and in diseases in
contrast with diabetic retinopathy in which
inhibition of VEGF might be preferable.

3% of homeless have TB
The UK charity Crisis indicated that there
appeared to be a rise in the incidence of TB in
homeless individuals after opening their
Crisis Open Christmas shelter during December
1999. Apart from the fact that there was an
increase in the number of visits by 20% to 878
compared with the same period in 1998, the
rise in TB incidence from 1/50 of this group to
1/33 reflected a worrying trend. Crisis is the
UK national charity for single homeless
people—and is, those with no legal rights to
housing. It researches, develops, and partners
schemes to provide help where it is most
needed at whatever stage of homelessness—
from emergency help on the streets, through
hostel accommodation, permanent housing,
and resettlement support.

Uveitis patient information group
Uveitis, particularly posterior uveitis (better
termed posterior segment intraocular infor-
mation), is a surprisingly common cause of
visual loss in all age groups and estimates of
incidence suggest that it is as frequent a cause
of visual handicap as diabetic retinopathy.
Despite this, very little information concern-
ing uveitis is available generally and especially
to the public at large or even to patients with
sight threatening posterior segment intraocu-
lar inflammation. This is partly due to the
wide spectrum of clinical entities which can be
categorised as posterior segment intraocular
inflammation and the tendency for causes of
blindness to be recorded by the specific clini-
cal entity rather than the generic “uveitis” or
“intraocular inflammation” title. However,
much of these conditions respond to appro-
appropriate and adequate therapy and, in
many cases, despite the clinical heterogeneity,
the treatment approach follows similar princi-
ples. Patients with uveitis would benefit from
information on this complex set of conditions
and a new patient information group, the
Uveitis Information Group, has been estab-
lished with a website address for interested
individuals including healthcare professionals
and patients (www.uveitis.net).

Eprints
Publishing scientific literature will dramati-
cally change in the near future. This is mainly
because of the effects of the internet. Recent
developments include the “eprint”, which is a
posting of a completed study on a website
before submission for peer review. Eprints are
already the norm in other scientific fields such
as high energy physics and astronomy, and are
coming fast to medicine. The BMJ has
already launched its eprint server on the inter-
et and many specialist journals are likely to
follow suit, including the BJO. In a sense this
sort of publishing will be a return to the early
days of printed journals when formal peer
review was rare if it occurred at all and peer
review meant comment by letters to the editor
from the readership. Eprints will be accompa-
nied by the full peer reviewed article appear-
ing later in the journal if accepted.