stimulated lymphocytes. The most promising results so far have come from raising antisera to lymphokines from various sources[26-28]—with considerable immunochemical ingenuity. Recently assay techniques have been simplified and improved.[29]

Conflicting reports about the nature and properties of lymphokines have engendered despair among immunologists and cynicism among clinicians. Nevertheless, the matter is one of crucial importance. As a practical illustration, the common clinical problem of recurrent herpes lesions may result from the defective production of lymphokines in response to infection by herpes simplex virus.[30] Fundamental research on the structure of immunoglobulin illuminated the entire subject of immediate hypersensitivity, hitherto an area of equal confusion. Characterising the molecules by which lymphocytes interact with other lymphocytes and different cell types will transform our understanding of cell-mediated immunity and provide the proper basis for experimental and clinical observations.

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Otosclerosis

As surgical techniques to restore hearing in otosclerosis have advanced over the last 20 years there has been a renewed interest in its aetiology, histopathology, and histochemistry. Nevertheless, our knowledge of this condition goes back over 200 years. Valsalva[1] first described fixation of the stapes in anatomical dissections, and the term otosclerosis was introduced by von Tröltsch, who believed that a "catarrhal" condition caused immobility of the stapes. Toynbee[2] actually studied postmortem specimens and as long ago as 1857 recognised that ankylosis of the stapes could produce deafness.

Otosclerotic deafness occurs clinically in about 2% and histologically in 10% of the white population but is much rarer in negroes. Women are affected twice as often as men. Altmann[3] proposed constitutional, local, and systemic aetiological factors, but most authorities regard otosclerosis as an autosomal dominant[4] hereditary disorder. Chromosome studies have shown normal karyotypes, and there is no evidence of linkage with the ABO, MN, or Rh blood groups.[5] Cartilage rests and mechanical stresses and strains associated with development of the temporal bone[6] may explain the incidence of otosclerotic foci at particular sites, while hormonal changes and vascular insufficiency may be systemic activating factors.

Pathological studies of otosclerosis have recognised four phases[3]: osteoclastic activity forming large spaces in the bone marrow; replacement of absorbed bone by blue-staining web-like tissue; a later infiltration of this material by increasing numbers of fibrils; and finally deposition of lamellar bone around blood vessels. This schema implies that cellular bone is found more commonly in the earlier phases. Nevertheless, when Wright[5] examined 401 specimens removed during stapedectomy for otosclerosis she found that just under a quarter showed, surprisingly, avascular necrosis rather than cellular bone formation. There was no apparent relation between cellular reactive lesions and a shorter history of deafness. Other evidence suggesting the aetiological importance of ischaemia was the presence of fat emboli in the stapes mucosal vessels and intravascular rouleaux formation.

Pregnancy and childbirth are known to lead to clinical deterioration of otosclerosis in many cases, and Wright explained this on a basis of vascular insufficiency and emboli during and after labour. She listed other causes of ischaemia as fat emboli associated with fractures, cholesterol emboli in older people, sickle-cell anaemia, platelet thrombosis, head injuries, and air embolism. The results of recent electron-microscopic[7] and biochemical studies suggest that the release of enzymes derived from histiocytes within otosclerotic foci results in lysis and resorption of bone and cartilage. On this theory, if the enzymes remain in the vicinity of a focus close to the oval window then the stapes will become fixed, while spill of these proteases into the perilymph may lead to vertigo or sensorineural deafness. High concentrations of oestrogens are known to increase the fragility of lysosomal membranes, providing another explanation of the progression of the deafness in pregnancy.

Surgical techniques for otosclerosis evolved in the latter part of the nineteenth and early twentieth centuries,[8-10] but it was Lempert[11] who reintroduced the fenestration operation and established the use of the operating microscope and specialised instrumentation for middle ear surgery. The standard operation for correcting the conductive deafness is a partial or total stapedectomy with substitution by natural tissue or foreign materials. Experienced stapedectomists can expect initial success rates[12] of over 95%, and the complication of early sensorineural hearing loss should occur in under 2% of cases. Late deterioration in hearing after stapedectomy may be conductive or sensorineural. The recurrence of conductive deafness may be dealt with by further surgery, and the results should be comparable to those of primary operations.[13] Early deterioration of hearing should be taken seriously, as a perilymph fistula may have occurred, and this must be treated early both to minimise the risk of progressive deafness and to prevent meningitis.

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Describing new syndromes

The classification and study of developmental abnormalities start with identifying disease entities. This often relies on the definition of a composite picture from several variables including the clinical appearances, aetiology, pathogenesis, treatment, and prognosis of a sample of those affected. This method is and has been very useful—with the caveat that it should be applied cautiously to prognosis, which in developmental disease may lead to a self-fulfilling prophecy.

Recently Garlinger *et al*[1] have used this approach to try to distinguish between a complete and a partial trisomy in Down's syndrome and so to identify a recognisable new clinical entity, partial trisomy 22. They relied on one case of their own and 16 derived from published reports. The children ranged in age from newborns to 17 years. The delineation of a new clinical entity in this context requires attention to continuous variables such as IQ, linear growth, craniofacial asymmetry, the interorbital space, the slant of orbital fissures, length of philtrum, the siting and configuration of external ears, and the size of mandible. The authors state, "The facial features of our case 1 show a striking resemblance to those of other translocation cases—mild coarseness of features with a broad nose and a long philtrum." These features are difficult to measure and in the absence of objective methods photographs are invaluable to capture the clinical observer's concept. The photographs published in support of the new syndrome are far from convincing, however, and the other publications cited refer to children of widely different ages and states of nutrition, which again makes comparison very difficult. Furthermore, Garlinger *et al* clustered together major system abnormalities to imply a commonality of aetiology that can be misleading. Thus they advance diverse skeletal variations such as scoliosis, hypoplasia of the middle phalanx, and overgrowth of the medial femoral condyle as constant variables occurring in the partial trisomy. They emphasise, and correctly so, the difficulty in identifying a single small acrocentric chromosome; and yet they categorise two cases[2 3] as examples of partial trisomy though this disagrees with the original authors' interpretation. In such circumstances they should surely have justified their own assessment.

What, we may ask, is the justification of such criticism of a single article in a specialist journal? There are two general principles at issue. Firstly, labelling as a result of categorisation may create real problems for the individuals so affected. Garlinger *et al* designated as mentally retarded 14 of the 17 children described, though six were aged less than $2\frac{1}{2}$ years and three others under 4 months. Mental retardation is a pejorative term to many professionals and families, and, though patients with autosomal chromosome abnormalities are at high risk for developmental delay and ultimately mental retardation, it serves no good purpose to lump them all together. Labelling in this manner is all too frequent in medical publications and has contributed to the number of children who function at the retarded level because they are expected to do so.

Secondly, professional meetings and gatherings are replete with accounts of new syndromes based on anecdotal information about unusual or flawed children. These reports generally lack evidence based on clinical measurement using techniques and values of the kind compiled by David Smith,[4] William Nyhan,[5] and others. In the absence of such objective data high quality clinical photographs are absolute requirements. Investigators and editors should be as critical in their publication of clinical data and photographs as they are of laboratory values.

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Pemphigoid

Of the many questions about pemphigoid that remain to be answered, two are of current interest. The first concerns the relation between the three syndromes in the adult to which the term pemphigoid is applied. The second is the pathogenic significance of the autoantibodies in pemphigoid.

The term pemphigoid was coined in France during the nineteenth century, probably by Besnier, and applied by him and by Colcott Fox in London to a bullous eruption, which should be differentiated from pemphigus.[1] The diagnostic criteria, however, were clinical and differed from country to country in accordance with strikingly divergent concepts and classifications of the bullous diseases. The systematic histological study of these diseases was undertaken by A Civatte of Paris, but as the second world war was in progress his findings were at first little known outside France. After the war they were continued and extended by investigators in many countries. Lever in Boston had independently differentiated what he called bullous pemphigoid from pemphigus, also on histological grounds. Subsequent histological refinements confirmed the further differentiation, usually clinically obvious, of pemphigoid from dermatitis herpetiformis. The discovery of the latter's association with jejunal abnormalities was followed by a report of the absence of these in pemphigoid.[2]

A new dimension was then added to the study of bullous diseases by developments in immunopathology, and in particular by immunofluorescence techniques. The histological distinction between pemphigus and pemphigoid was reinforced by the finding[3–5] of circulating autoantibodies to different zones of the skin. Immunofluorescence is seen in the intercellular spaces in pemphigus while in pemphigoid it occurs at the basement membrane zone. In dermatitis herpetiformis the diagnostic feature is the presence of granular deposits, consisting largely of IgA, at the tips of the dermal papillae.