VLA-4 or LPAM-2 participates, for example, in the inflammatory response in asthma but does only contribute to a minor extent if at all to the homing of lymphocytes to Peyer's patches.²

ICAM-3, a member of the immunoglobulin superfamily and constitutively expressed on lymphocytes and intradermal Langerhans' cells, should be added to the list of counter-receptors of LFA-1 since it has been cloned already in 1992.⁴

CD21, TAPA-1, Leu-13, and CD19 form a complex on the surface of B lymphocytes that upon crosslinking transmits signals into the cell but has not been identified to function as a ligand for $\beta 4$ integrins in adhesive interactions.⁵

A recently described novel LAD syndrome termed LAD type 2 deserves being mentioned.⁶ This complex syndrome is characterised by recurrent bacterial infections with high neutrophil counts, mental retardation, short stature, and the Bombay blood phenotype. The analysis at the molecular level revealed the lack of expression of Sialyl-Lewis X (sialylated form of CD15), the carbohydrate ligand of the leucocyte adhesion molecules E-selectin and P-selectin, on haemopoietic cells. Due to this defect neutrophils are no longer capable of adhering to endothelial cells using the E- and P-selectin pathway which initiates the transmigration of immunocompetent cells through the blood vessel. The underlying mechanism leading to the deficiency of Sialyl-Lewis X probably is a general defect in the fucosylation of glycoproteins and carbohydrates. The disturbance of the fucose metabolism would also explain the Bombay blood phenotype and may lead to the understanding of the other components of the syndrome as, for example, the mental retardation.

NORBERT WAGNER
Institute for Genetics,
Division of Immunology,
University of Cologne,
Weyertal 121,
D-50931 Cologne,
Federal Republic of Germany

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Dr El Habbal and Professor Strobel comment:

We thank Dr Wagner for his interesting comments on our review on leucocyte adhesion deficiency (LAD) which focused on clinical presentation and management.¹ We did not intend to discuss extensively the interspecies homology of adhesion molecules and, for example, did not include the cadherins² as a fourth family of adhesion molecules.

Our review was based on 'consensus' data published, and single reports, however interesting in their own right, were not included

and ICAM-3 and the recently described novel 'LAD type 2' were consequently not discussed. We did not associate LPAM-1 with CD28 as Dr Wagner states. It is B7 (CD80) (and not $\beta 7$ as erroneously printed in our table 1) which associates with CD28. We apologise for this misprint. His comments on LPAM-1 and LPAM-2 are correct, but they apply to mouse integrins only.

VLA-4 is not recognised to be abnormal in LAD. The VLA family of integrins are expressed as heterodimers, composed of a variable α (CD49a, b, c, d, e, f) and a constant β chain (CD29). Human VLA-4 (CD49d) is known to be 'promiscuous' and known to associate with either $\beta 1$ and $\beta 7$ integrin subunits. In the mouse CD49d can pair with $\beta 7$ or $\beta 1$ chains to generate LPAM-1 and LPAM-2. In humans, LPAM-1 shares homologies with $\beta 1$ and $\beta 6$ integrins, as stated.³

Dr Wagner's remarks on P-selectins and E-selectins, as well as his comments on a signal transduction complex (CD21, TAPA-1, Leu-13, CD19) are interesting but not relevant to the topic of our review.

LAD is a key example where astute clinical observations (combined with basic research) have led to an exponential increase in our understanding of the role of cellular adhesion pathways in innate and adaptive immunity ('copora non agunt nisi fixata', Paul Ehrlich).

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Migration of fine bore Silastic catheter to pulmonary artery

EDITOR,—We wish to report a serious complication that arose during insertion of a long line, which was to be used to administer intravenous antibiotics to a 12 year old boy with cystic fibrosis. A fine bore Silastic neonatal catheter (Epicutaneo-Cava-Catheter model No 2184, Vygon) was used. This model has a detachable Silastic indwelling catheter that is inserted through a supplied 19 gauge needle. The proximal end of the catheter contains a short metal rod that is anchored within the distal end of the external supply line to prevent migration once sited. After venepuncture of the left basilic vein the catheter, unattached to the supply line, was threaded through the needle. The catheter was almost fully advanced so that the distal end might lie in a satisfactory position within the great veins. The needle was then removed from the vein and disengaged from the catheter by threading it over the proximal end. At this point the catheter was lost to vision and when the needle was fully removed, the proximal end was still not visible. Chest radiography revealed the metal proximal tip of the catheter to be lying in the right pulmonary artery. The catheter itself was radiolucent. We presume that dynamic venous flow and negative intrathoracic pressure caused aspiration of the whole catheter into the circulation. Subsequently, the patient underwent general anaesthetic and cardiac catheterisation. The

catheter was successfully removed intact using a snare wire during a difficult and lengthy procedure.

We have used this type of line successfully for a number of years. The manufacturers inform us that this complication has occurred once before worldwide. They also stated that adherence to the instructions included with the line, updated in April 1992, should prevent this complication. The instructions state that, after advancing the catheter through the needle to the desired position, 'the catheter should then be fixed in its final position by applying slight pressure beneath the needle tip and the needle is then withdrawn ...'. However, there is no warning in the instruction leaflet of the potential complication reported here, although we gather that this will be highlighted in future.

The use of short and long indwelling venous catheters is known to carry a small risk of embolism to the heart and great vessels and has in the past led to both serious morbidity and mortality due to thrombus formation, infection, and perforation.¹ For these reasons, attempted removal of embolised catheters or fragments is recommended. This has been achieved by thoracotomy^{2,3} or by cardiac catheterisation.^{4,5}

Embolism has been more commonly reported with use of the 'catheter in needle' cannula where during insertion the needle shears off the distal part of the catheter.^{1,6} This complication has led to widespread use of 'needle in catheter' forms of cannulas, although these are not free from risk of fracture and embolism.⁷ Embolism due to disconnection of the catheter from the supply line has also been described^{1,7} and most catheters now in use have undetachable external hubs to prevent this problem. The catheter used in this reported case has neither of the above safety features. For such lines to be used safely, it is necessary to ensure that throughout insertion the line is at all times both visible and held externally.

I M DOUGHTY
T J DAVID
University Department of Child Health,
Booth Hall Children's Hospital,
Charlestown Road,
Blackley,
Manchester M9 2AA

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Prophylaxis or modification of varicella by oral acyclovir after household exposure

EDITOR,—In his commentary on our paper Dr Conway raised several concerns about the use of oral acyclovir in varicella infection.¹ We do believe that varicella should be

prevented or treated if safe and effective methods are available. In Japan, most (probably all) children when they develop varicella visit their doctor because parents know that children with the disease are often uncomfortable, febrile, irritable, and unhappy and they look to doctors to prevent or reduce these problems. There is also an increasing number of children who receive a live varicella vaccine, which costs approximately 10 000 yen (about £65) in Japan. More than 200 000 children received the vaccine in 1993, which clearly indicates a strong parental need to have their children free from the disease.

Dr Conway questions whether a rise in antibody titre from <4 to 8 reflects seroconversion. We believe it is an obvious seroconversion and a significant (a fourfold) increase in the antibody titres, which would surely be supported by clinical virologists. We followed up children who did not show seroconversion and found that most of them had antibody activity two to three months later (unpublished data), which suggests that administration of acyclovir in the incubation period tends to postpone development of immune response to the virus. We also found that immunity to the virus persisted for at least one year in most of the children treated with acyclovir (unpublished data). It is therefore possible that the actual seroconversion rate is higher than reported. As suggested by Dr Conway the optimal dose of acyclovir that prevents the disease but induces virus immunity should be established.

It is unlikely that immunity in children treated with acyclovir tends to decline or diminish, thereby creating a risk of more severe varicella or early zoster later in life. Reduced frequency and severity of the skin rash in children treated with acyclovir suggests that the drug prevents or reduces blood borne dissemination of the virus and infection of skin with the virus.²⁻⁴ Possibly, the drug suppresses replication of the virus in the lung, liver, spleen, and other organs before or during the second viraemia.⁵ Many of the children given acyclovir developed the virus antibodies and most of them had no signs and symptoms of varicella. All this suggests that subclinical infection is occurring. As fluorescent antibody to membrane antigen assay measures antibodies to glycoproteins or late antigens of the virus, it is reasonable to consider that a limited virus replication conferred specific memory to the virus in the immune system of children treated with acyclovir. Moreover, it is likely that the immunity will persist for a long time, as subclinical infection in a natural setting and infection with live varicella vaccine provide a long lasting immunity to the virus and protect the infected individual from the disease.⁶

Little is known about the mechanism by which the virus establishes latency in sensory ganglia. However, it is generally believed that the virus may arrive at the sensory ganglia not only via a nerve but also via the haematogenous route during the viraemic phase of varicella. It is unlikely that acyclovir treatment during the incubation period predisposes the host to a higher risk of reactivation of disease (herpes zoster), as there was protection against rash and probably a reduced degree of viraemia in treated patients.

YOSHIZO ASANO
SADAO SUGA
TETSUSHI YOSHIKAWA
Department of Paediatrics,
Fujita Health University School of Medicine,
Toyoake, Aichi 470-11,
Japan

TAKAO OZAKI
Department of Paediatrics,
Showa Hospital,
Konan, Aichi,
Japan

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Simultaneous pulmonary infection with respiratory syncytial virus and human cytomegalovirus

EDITOR,—Respiratory syncytial virus (RSV) is the major cause of acute lower respiratory tract illness in infants and young children. The presentation and subsequent course of RSV bronchiolitis may be atypical in the presence of a simultaneous infection with other viral agents.^{1,2} During the winter 1991-2, we studied children hospitalised for respiratory disease in a paediatric unit in Marseille. All patients were tested for viral infections and an information chart was made to determine the prevalence of multiple viral isolates and to assess the impact of dual infections on the severity of clinical disease.

Between December 1991 and February 1992, 405 children were hospitalised for respiratory disease. In all cases, nasopharyngeal wash specimens were taken on admission to the paediatric unit and simultaneously submitted to human cytomegalovirus isolation and respiratory virus fluorescent antibody staining. For human cytomegalovirus isolation, specimens were inoculated on human embryonic lung fibroblasts and a monoclonal antibody directed against the immediate early antigen (E13, Biosoft, Clonatec, France) was added 48 hours later to detect viral antigen expression. Simultaneously, indirect immunofluorescence assay was performed directly on nasopharyngeal secretions, using monoclonal specific antibodies against several viruses: RSV, influenza A virus, influenza B virus, parainfluenza virus type 1, 2, and 3 (Monofluo kit, Pasteur, France), and adenovirus (Biosoft, Clonatec, France).

The following information was obtained for each patient: age, sex, history and clinical symptoms, other infections, duration of hospitalisation, socioeconomic status, and ethnic group.

From the 405 children hospitalised for bronchiolitis or respiratory disease, 195 (48%) presented viral infection: 165 were positive for RSV, 30 were positive for human cytomegalovirus, and 20 were simultaneously infected with RSV and human cytomegalovirus.

Given the frequency of RSV-human cytomegalovirus coinfection in our series (10%), we studied these 20 children. The sex ratio was 1:1 and they were aged 1 month to 8 years. Fourteen of them were less than 4 months old, hence they may have had congenital or perinatal human cytomegalovirus infection. However, six were from 6 months to 8 years old. One child had oral candidosis and one was simultaneously infected with *Haemophilus influenzae* and rotavirus, one had a history of pneumonitis, but all were without underlying disease. Most of them were from low socioeconomic groups. Three were of Spanish extraction, seven were North Africans, and two were black children. No specific clinical situation was correlated with the coinfection: five had fever over 39°C, four had severe bronchiolitis or pneumonitis requiring corticotherapy. But the severity of the children's illness was demonstrated by the duration of hospitalisation: the average was 6.6 days compared with 3.2 days in RSV isolated infection.

We especially noted the frequency of RSV-human cytomegalovirus simultaneous infections in the children hospitalised for lower respiratory tract disease. But the exact role of human cytomegalovirus in bronchiolitis remains unclear^{3,4} and further clinical and biological investigations should be undertaken.

CHRISTINE M ZANDOTTI
XAVIER N DELAMBALLERIE
CATHERINE VIGNOLI
JEAN-MARC GARNIER
University Timone Hospital,
13385 Marseille,
France

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Carers as children

EDITOR,—Aldridge and Becker in their article comment that there is uncertainty as to how many child carers there are.¹ We have recently completed two population based surveys into the health and social care needs assessment of people with multiple sclerosis in Bradford and Huddersfield. We surveyed over 500 people who agreed to volunteer. Of those surveyed over 20% between the districts indicated that their children helped with either domestic or personal care.

A further random sample of 192 were interviewed by face to face interviews. Approximately 40% of those with children under 16 years felt that their children helped more than they normally would with personal care. However, from the parents' point of view it did not all seem to be bad. Approximately 40% felt that the multiple sclerosis had had little or no effect on their