Progress in
CLINICAL MEDICINE

PROGRESS IN CLINICAL MEDICINE

Editors

RAYMOND DALEY

M.A., M.D. Cantab., F.R.C.P.

Physician to the Cardiac Department,
St Thomas's Hospital.
Consultant Cardiologist,
King Edward VII Hospital for Officers.
Consultant Physician and Cardiologist,
Chelsea and Kensington Group of Hospitals

and

HENRY MILLER

M.D., F.R.C.P.

Honorary Consulting Neurologist,
Royal Victoria Infirmary,
Newcastle upon Tyne

SIXTH EDITION

1971

CHURCHILL LIVINGSTONE
EDINBURGH AND LONDON

First Edition 1948
Reprinted 1948
Second Edition 1952
Third Edition 1956
Fourth Edition 1961
Reprinted 1963
Fifth Edition 1966
Reprinted 1967
Sixth Edition 1971

International Standard Book Number 0.7000.1486.1

Printed in Great Britain
by T. & A. Constable Ltd, Edinburgh

Preface to the Sixth Edition

THE purpose of this book has remained unchanged since its first appearance 22 years ago. It aims to describe current developments in internal medicine in a manner intelligible and useful to the general physician and the post-graduate student.

Recent progress has blurred the outline of the traditional disciplines. New developments in genetics and immunology are relevant in every speciality. Psychiatry is increasingly neurochemical, and computerization now begins to permeate every field of medicine.

Our first edition was traditional in concept and arrangement, but like its immediate predecessor this volume bespeaks a constant struggle to embody contributions of basic science into the clinical armamentarium. The reader will find a more extended consideration of medical computerization, a comprehensive review of the invasion of clinical medicine by immunology, and a succinct presentation of the present status of transplant surgery. Where duplication occurs it is entirely intentional: the different approaches of the neurologist and immunologist to myasthenia are illuminating. The more traditional aspects of medicine have not been overlooked, though it would be fair comment to say that the focus of the book is now as biochemical as it is clinical. The editors hope that their pleasure in assembling a series of outstanding reviews will be shared by their readers.

RAYMOND DALEY AND HENRY MILLER
London and Newcastle upon Tyne

Contributors

J. I. S. BAYLISS, M.A., M.D.CANTAB., F.R.C.P.
Physician to H.M. The Queen; Physician and Endocrinologist, Westminster Hospital, London.

R. Y. CALNE, M.A.CANTAB., M.S.LOND., F.R.C.S.ENG.
Professor of Surgery, University of Cambridge; Fellow of Trinity Hall.

C. A. CLARKE, C.B.E., F.R.S., SC.D., M.D., F.R.C.P., F.R.C.O.G.
Professor of Medicine and Director of the Nuffield Unit of Medical Genetics, University of Liverpool; Consultant Physician, Liverpool Royal Infirmary and Broadgreen Hospital, Liverpool.

P. H. CONNELL, M.D., M.R.C.P., D.P.M.
Physician, The Bethlem Royal Hospital and the Maudsley Hospital.

BRIAN CREAMER, M.D.LOND., M.R.C.P.
Physician to St. Thomas's Hospital.

RAYMOND DALEY, M.A., M.D.CANTAB., F.R.C.P.
Physician to the Cardiac Department, St Thomas's Hospital; Consultant Cardiologist, King Edward VII Hospital for Officers; Consultant Physician and Cardiologist, Chelsea and Kensington Group of Hospitals.

G. HAMILTON FAIRLEY, D.M., F.R.C.P.
Director of Imperial Cancer Research Fund, Medical Oncology Research Unit at St Bartholomew's Hospital, London, E.C.1., Consultant Physician, St Bartholomew's Hospital, London, E.C.1., and the Chester Beatty Research Institute, Royal Marsden Hospital, Sutton, Surrey.

MAX. M. GLATT, M.D., M.R.C.P., D.P.M.
Consultant Psychiatrist, St Bernard's Hospital and the Paddington Clinic and Day Hospital; Consultant in Charge, Regional Alcoholism and Addiction Unit of the North-West Metropolitan Regional Hospital Board; Honorary Consultant Physician, Department of Psychological Medicine, University College Hospital, London; Visiting Psychotherapist, H.M. Prison, Wormwood Scrubs.

R. HALL, B.SC.DUNELM, M.D.DUNELM., F.R.C.P.
Professor of Medicine at the University of Newcastle upon Tyne; Physician, Royal Victoria Infirmary, Newcastle upon Tyne.

P. HUDGSON, M.B., M.R.A.C.P.
Consultant Neurologist, The General Hospital and the Royal Victoria Infirmary, Newcastle upon Tyne.

M. C. G. ISRAËLS, M.D.,MANCH., M.SC., F.R.C.P.
Professor of Clinical Haematology, University of Manchester and Physician to the United Manchester Hospitals.

D. N. S. KERR, M.B.EDIN., M.SC.WIS.
Professor of Medicine and Physician to the Royal Infirmary, Newcastle upon Tyne.

E. G. KNOX, M.D., M.R.C.P.
Professor of Social Medicine, University of Birmingham.

M. H. LESSOF, M.A., M.D., F.R.C.P.
Physician and Clinical Immunologist, Guy's Hospital, London.

W. A. LISHMAN, B.SC., M.D., M.R.C.P., D.P.M.
Consultant Psychiatrist, The Bethlem Royal and Maudsley Hospitals; Senior Lecturer, Institute of Psychiatry, London.

D. M. McLEAN, M.D.MELBOURNE, F.R.C.PATH., F.R.C.P. CANADA.
Professor of Medical Microbiology, University of British Columbia, Vancouver B.C., Canada.

H. MILLER, M.D., F.R.C.P.
Honorary Consulting Neurologist, Royal Victoria Infirmary, Newcastle upon Tyne.

A. S. RUSSELL, M.A., M.R.C.P.
Senior Medical Registrar, West London Hospital.

T. B. STRETTON, M.B., CH.B., M.R.C.P.
Consultant Physician and Senior Lecturer in Medicine, the Royal Infirmary, Manchester.

Contents

1 Clinical Virology

DONALD M. McLEAN

VIRUS CLASSIFICATION. LABORATORY DIAGNOSIS. MEASLES. RUBELLA. MUMPS

VIRUS CLASSIFICATION

VIRUSES are living organisms whose sizes range from 20 to 300 nanometers (nm) diameter and which replicate only inside living cells of susceptible host tissues. The laboratory cultivation of viruses therefore depends on their ability to induce microscopically visible changes in tissue cultures or characteristic clinical syndromes following inoculation into experimental animals. At present the only transmissible agents causing disease in man which have not been cultivated with certainty in the laboratory are the viruses of infectious hepatitis and serum hepatitis.

The complete infectious unit (virion) is composed of nucleic acid surrounded by a protein shell (capsid) which is composed of subunits (capsomeres) (Pereira and Valentine, 1967). For some viruses, the capsid is surrounded by an outer membrane (envelope), which contains protein and lipid, principally of host origin.

Viruses pathogenic for man are classified among the animal viruses. These comprise one of four main categories of viruses, according to the phylum of hosts which they infect; vertebrate animals, insects, bacteria, angiosperm plants. The animal viruses are subdivided (Andrewes and Pereira, 1967) into groups primarily on the basis of their known physicochemical properties. Within each group they are further subdivided into serotypes or "virus species" according to their antigenic constitution. Individual strains of virus belonging to the same serotype may show important differences in other attributes. For example the development of the disease, mumps, may follow exposure of a susceptible human to a clinical case, but development of antibody occurs without clinical illness after injection with the Jeryl Lynn attenuated strain of mumps vaccine (Weibel *et al.*, 1967). Table 1.1 lists 11 groups of viruses which are pathogenic for man

TABLE 1.1

Classification of Viruses affecting Man according to Chemical and Physical Criteria (adapted from Andrewes and Pereira, 1967)

Virus group	Particle size (nm)	Nucleic acid	Symmetry	Number of capsomers	Enveloped or naked	Common viruses which infect man
Herpesvirus	100–150	DNA	Cubic	162	Enveloped	Herpes simplex, varicella
Adenovirus	70–90	DNA	Cubic	252	Naked	Adenovirus
Papovavirus	30–50	DNA	Cubic	72	Naked	Warts
Poxvirus	200–300	DNA	Helical?	—	Enveloped	Variola, vaccinia
Myxovirus	80–120	RNA	Helical	—	Enveloped	Influenza
Paramyxovirus	140–250	RNA	Helical	—	Enveloped	Mumps, measles
Arbovirus	20–100	RNA	Cubic	?	Enveloped	St Louis, Powassan
Picornavirus	20–30	RNA	Cubic	42	Naked	Poliovirus echovirus
Reovirus	60–90	RNA	Cubic	92	Naked	Reovirus
Rhabdovirus	100–150	RNA	Helical	—	Enveloped	Rabies
Rubella	120–280	RNA	Cubic	?	Enveloped	Rubella

TABLE 1.2

Viruses commonly associated with Syndromes in Man

Syndrome	Viruses found regularly	Virus group
Respiratory tract infection	Influenza	Myxovirus
	Parainfluenza, respiratory Syncytial	Paramyxovirus
	Adenovirus	Adenovirus
	Rhinovirus	Picornavirus
Pleurodynia	Coxsackievirus B	Picornavirus
Mouth lesions	Herpesvirus hominis	Herpesvirus
	Coxsackievirus A	Picornavirus
Rash: maculopapular	Measles	Paramyxovirus
	Rubella	Ungrouped
	Echovirus	Picornavirus
CNS: meningitis	Mumps	Paramyxovirus
	Coxsackievirus B, echovirus	Picornavirus
CNS: encephalitis	St Louis, Powassan	Arbovirus
Tropical fevers	Dengue, chikungunya	Arbovirus
Eye infections	Trachoma, inclusion blenorrhea	Chlamydia
	Vaccinia	Poxvirus
	Herpesvirus hominis	Herpesvirus

according to whether: (i) the virion contains ribonucleic (RNA) or deoxyribonucleic acid (DNA) as the only form of nucleic acid; (ii) the internal protein subunits are arranged in cubic or helical symmetry; (iii) the virion is enveloped or naked.

At the bedside however, the clinician must be familiar with the range of viruses which are likely to be associated with the patient's illness (Table 1.2). In several instances, for example the picornaviruses, one agent such as echovirus 9 may be associated with diverse syndromes such as maculopapular rash and aseptic meningitis. On the other hand, syndromes such as acute laryngotracheobronchitis may be associated with a wide range of agents including myxoviruses such as influenzavirus A2, paramyxoviruses such as parainfluenzavirus 1 and measles virus, and a member of the herpesvirus group, varicella.

REFERENCES

ANDREWES, C. H. & PEREIRA, H. G. (1967). *Viruses of Vertebrates.* 2nd ed. London: Baillière, Tindall and Cassell.

PEREIRA, H. G. & VALENTINE, R. C. (1967). Morphological and antigenic sub-units of viruses. *Brit. med. Bull.*, **23**, 129.

WEIBEL, R. E., STOKES, J., BUYNAK, E. B., WHITMAN, J. E. & HILLEMAN, M. R. (1967). Live, attenuated mumps-virus vaccine. 3. Clinical and serologic aspects in a field evaluation. *New Engl. J. Med.*, **276**, 245.

LABORATORY DIAGNOSIS

Although clinical inspection is frequently sufficient to establish the viral aetiology of conditions such as measles, mumps and chickenpox, knowledge of the syndromes which are usually associated with virus infections, and the particular virus groups which are commonly implicated (Table 1.2), will permit rapid and accurate confirmation of the infecting agent by laboratory procedures. In syndromes such as aseptic meningitis which occurs during winter and in the absence of involvement of the salivary glands, laboratory diagnostic procedures are essential to determine whether the infecting agent is mumps virus or a picornavirus. During the normal winter upsurge of measles and rubella in Temperate Zone communities, it is vitally important to establish by laboratory means whether an exanthem in a child is due to measles or rubella virus, when the mother is in her first trimester of pregnancy. In the Tropics, where undifferentiated fevers due to arboviruses occur commonly, laboratory techniques frequently provide the only means of

differentiation between yellow-fever virus which may cause fatal disease in some subjects, and dengue or chikungunya viruses which induce less severe illness.

Laboratory diagnosis of virus infections depends upon two general methods; direct and indirect. Direct methods involve: (i) isolation of virus from the site at which the pathological process is occurring, for example mumps virus from the cerebrospinal fluid (CSF) in cases of aseptic meningitis (McLean *et al.*, 1967); (ii) observation of virions in electron micrographs of secretions or exudates stained negatively with phosphotungstic acid (Doane *et al.*, 1967), for example mumps virus in CSF; or by observation by light microscopy of characteristic changes in epithelial cells from scrapings of vesicles following staining with Giemsa, for example, multinucleate (Tzanck) cells with acidophilic intranuclear inclusions in chickenpox. Direct methods establish the causative virus in the patient's illness immediately, without recourse to tests on additional specimens. Indirect methods involve the demonstration of a conversion of the patient's antibody status against a particular virus from negative to positive during convalescence, or at least a fourfold increment in antibody titre in those subjects who had detectable antibody at the time the initial blood sample was secured.

Suggestive evidence that a particular virus has induced a disease, for example coxsackieviruses in aseptic meningitis (McLean, 1966), may be obtained by the isolation of this agent from a site in the body, such as the faeces, which is remote from the area at which the pathological process is occurring. Since some subjects, especially residents of warm climates, may excrete coxsackieviruses in the faeces without developing overt illnesses (Cook *et al.*, 1969; Pelon *et al.*, 1966), additional confirmatory evidence must be sought, usually by detection of antibody conversion, to show that this virus infected the patient at the time of illness.

Whenever possible, direct methods should be employed to identify the causative virus in an illness. Collection of appropriate specimens depends upon knowledge of the pathogenesis of the disease. In addition, indirect methods should regularly be used as confirmatory evidence when direct methods elucidate the viral aetiology, or to provide suggestive information regarding the type of causative agent if direct methods yield negative results. Selection of the optimum laboratory techniques for virus isolation and serology depends on knowledge of the range of susceptible host tissues and types of antibody detected most readily. The range of laboratory tests for viral infections is shown in Table 1.3.

Specimens for attempts at virus isolation should be collected as soon as possible after onset of illness. These include CSF from any case of suspected involvement of the central nervous system; faeces or rectal swabs plus throat washings from patients with syndromes involving the CNS, serous membranes or musculoskeletal system; throat washings, swabs or naso-

pharyngeal secretions from cases of respiratory disease; and scrapings of the base of lesions, or samples of vesicle fluid, from subjects with vesicular exanthemata or enanthemata. Serum derived from 1 to 5 ml of whole clotted blood should be obtained from each patient on two occasions—the first as soon as possible after onset of symptoms and the second at least one day after the temperature has returned to normal. This is usually two to seven days after collection of the initial serum sample, but for some tests such as the complement-fixing antibody response to arbovirus infection, it is advisable to collect an additional serum sample three to four weeks after onset of illness.

When the virus laboratory is located geographically close to the patient, all specimens should be delivered unrefrigerated by messenger immediately after their collection. Specimens submitted for attempts at virus isolations may be held at 4°C in refrigerators in the hospital ward or preferably in the virus laboratory, for testing up to 24 hours after their collection. An exception to this rule is a throat swab from a case of respiratory infection which requires inoculation into tissue cultures at the patient's bedside in order to recover respiratory syncytial virus readily (Tobin, 1963). However, if more than one day is likely to elapse between receipt of a specimen by the virus laboratory and start of the test, the specimen should be stored in a deep freeze at −20°C.

When the laboratory is far from the patient, specimens of CSF, throat washings and scrapings of vesicles should be placed in screw-capped bottles which are then stacked into vacuum jars or expanded polystyrene containers to which ice-cubes or re-usable "Sno-Gel" packs have been added. Containers should be sent to the laboratory by the most rapid means available, so as to arrive there within 24 hours. Avoid shipments which are likely to arrive at the laboratory on Fridays, weekends or statutory holidays. If longer periods of transit are anticipated, pieces of dry ice should be used in place of ice-cubes.

REFERENCES

COOK, I., ALLAN, B. C. & WELHAM. S. (1969). Coxsackieviruses in normal children. *Med. J. Aust.*, **2**, 789.

DOANE, F. W., ANDERSON, N., CHATIYANONDA, K., BANNATYNE, R. M., MCLEAN, D. M. & RHODES, A. J. (1967). Rapid laboratory diagnosis of paramyxovirus infections by electron microscopy. *Lancet*, **2**, 751.

MCLEAN, D. M. (1966). Coxsackieviruses and echoviruses. *Amer. J. med. Sci.*, **251**, 351.

MCLEAN, D. M., LARKE, R. P. B., COBB, C., GRIFFIS, E. D. & HACKETT, S. M. R. (1967). Mumps and enteroviral meningitis in Toronto, 1966. *Canad. med. Ass. J.*, **96**, 1355.

TABLE 1.3

Laboratory Tests appliable to Common Virological Syndromes
(adapted from McLean, D. M. *et al.* (1960), *Canad. J. Pub. Health*, **51**, 94)

Syndrome	Group of causative agent	Virus isolation		Histopathology		Serology	Electron microscopy
		Specimen	Test system	Specimen	Light microscopy		
Central nervous system diseases							
Aseptic meningitis Poliomyelitis	Enterovirus	CSF, faeces, throat swab	Macaca kidney, human amnion, human thyroid, Tissue cultures Suckling mice	Brain	Perivascular cuffing Neuronophagia	NT, CF, HI	*Enterovirus* non-enveloped, 30 nm virions, 42 capsomers *Mumps* enveloped, 150 nm virions, helical nucleocapsid
	Arbovirus	CSF, blood brain	Suckling mice hamster kidney Swine kidney Chick embryo Fibroblast Tissue cultures	Brain	Perivascular cuffing Neuronophagia Glial knots	NT, CF, HI	*Arbovirus* enveloped, 40 nm virions, cubic symmetry
Encephalitis	Rabies	Brain, saliva	Mice	Brain	Fluorescence Negri bodies		*Rabies* enveloped, 150 nm virions, complex symmetry
	Herpesvirus	Brain	Macaca kidney Human amnion Continuous line Tissue cultures	Brain	Eosinophilic intranuclear inclusions	NT, CF	*Herpesvirus* enveloped 125 nm virions, 162 capsomeres
Respiratory disease							
Influenza, coryza, croup, bronchiolitis, bronchopneumonia	Myxovirus Paramyxovirus	Throat swab, Throat washing, Nasopharyngeal suction	Macaca kidney, Continuous line tissue cultures Chick embryo (amniotic)			HI, CF, NT	*Myxovirus and paramyxovirus* enveloped 90–180 nm virions, helical nucleocapsid
	Adenovirus	Throat swab, etc.	Continuous line cultures			NT, CF	*Adenovirus* non-enveloped 80 nm virions, 252 capsomeres
	Chlamydia	Throat washing	Chick embryo (yolk sac)			CF	*Chlamydia* enveloped 300 nm particles
Serous membrane affections							
Pleurodynia Pericarditis	Enterovirus	Faeces or throat swab	Macaca kidney cultures Suckling mice			NT	

TABLE 1.3 (cont'd.)

Laboratory Tests appliable to Common Virological Syndromes
(adapted from McLean, D. M. *et al.* (1960), *Canad. J. Pub. Health*, **51**, 94)

Syndrome	Group of causative agent	Virus isolation: Specimen	Virus isolation: Test system	Histopathology: Specimen	Histopathology: Light microscopy	Serology	Electron microscopy
Exanthemata							
Measles	Paramyxovirus	Throat washing Blood	Human amnion, grivet kidney cultures	Lymph node nasal mucosa	Warthin-Finkeldey giant cells	HI, NT, CF	
Rubella	Rubella	Throat washing	Grivet kidney (primary) Rabbit kidney (continuous)			NT, CF	*Rubella* enveloped, 40 nm virions, cubic symmetry
Varicella	Herpesvirus	Vesicle fluid	Human amnion	Vesicle scraping	Acidophilic intranuclear inclusions	CF	
Herpes	Herpesvirus	Vesicle scraping	Suckling mice Continuous line or human amnion cultures	Vesicle scraping	Acidophilic intranuclear inclusions	NT, CF	
Smallpox	Poxvirus	Throat washing blood, vesicle scraping	Chick embryo (chorioallantoic) Macaca kidney Chick embryo Fibroblast	Vesicle scraping	Acidophilic cytoplasmic inclusions	HI, CF, NT	*Poxvirus* enveloped 200 nm virions, complex symmetry
Eye diseases							
Inclusion blenorrhoea, Trachoma	Chlamydia	Conjunctival scrapings	Chick embryo (yolk sac)	Conjunctival scrapings	Basophilic cytoplasmic inclusions	CF	
Tropical fevers							
Yellow fever Tropical fevers	Arbovirus	Blood, CSF, Liver biopsy	Suckling mice Chick embryo Fibroblast cultures Hamster kidney cultures	Liver (yellow fever)	Midzonal necrosis	CF, HI, NT	
Rickettsial diseases							
Q. fever	C. burnetii	Clotted blood	Chick embryo (yolk sac)			CF, A	
Rocky Mountain spotted fever	R. rickettsii	Clotted blood	Male guinea-pig			CF, A	
Rickettsiapox	R. akari	Clotted blood				CF, A	
Typhus	R. prowazekii	Clotted blood				CF, A	
Murine typhus	R. typhi	Clotted blood				CF, A	

Serology: NT = Neutralization test. CF = Complement-fixation test. HI = Haemagglutination inhibition test. A = Agglutination test.

PELON, W., VILLAREJOS, V. M., RHIM, J. S. & PAYNE, F. J. (1966). Coxsackie group B virus infection and acute diarrhoea occurring among children in Costa Rica. *Arch. Dis. Childh.*, **41**, 636.

TOBIN, J. O'H. (1963). The isolation of respiratory viruses from children in hospital in South-East Lancashire. *Proc. roy. Soc. Med.*, **56**, 991.

MEASLES

Differential Diagnosis

Development of a blotchy maculopapular rash involving principally the face and trunk, accompanied by fever and Koplik's spots, nasopharyngeal and conjunctival catarrh, after an incubation period usually of 14 days provide sufficient clinical criteria for the diagnosis of measles (red measles or rubeola). However, laboratory procedures may be required, for example, to establish a diagnosis of measles in an allergic child, a patient taking antibiotics or other medication who develops a rash, in a subject previously vaccinated against measles, or in a leukaemic patient. In the Temperate Zone, during the cooler months, when both measles and rubella spread rapidly through communities, it is often desirable to invoke laboratory tests to distinguish measles from rubella in situations where a pregnant woman or her offspring develops a febrile exanthem.

Haemagglutination inhibition (HI) provides the most convenient procedure for the laboratory diagnosis of measles virus infections. It is essential to collect a serum sample within one day after onset of rash, but even at that early stage of illness, some antibody may be detected (Gresser and Chany, 1963; McLean *et al.*, 1966). Collection of a second serum sample two to four days later, within one day after defervescence, will reveal a fourfold or greater increment of measles antibody. Although measles virus has been recovered by inoculation into tissue cultures of human amnion cells, of the leucocyte fraction of heparinized blood obtained from nine of ten subjects one day after onset of rash (Gresser and Chany, 1963), this procedure is too highly specialized for everyday use.

Complications

(i) General

Despite the low case fatality rate from measles in Toronto, Canada (3/10,000) (Department of Public Health), the United States (1/10,000) (Langmuir, 1962) and Great Britain (2/10,000) (Miller, 1964), and a somewhat higher rate (1·2 per cent) among hospitalized patients in Sydney, Australia (Boughton, 1964a), in Tropical Africa the mortality rate among children hospitalized with measles may range from 5·7 to 21 per cent (Morley, 1969). It seems likely that malnutrition in tropical countries contributes to this

high case fatality rate. Complications have been reported in one of 15 cases of measles in Britain (Miller, 1964). Complications frequently involve the respiratory tract and associated structures, giving rise to acute laryngotracheobronchitis, otitis media and bronchopneumonia. Of 44 deaths among 3601 Australian patients, 27 were due to pneumonia (Boughton, 1964a); but among 1283 West African children, 604 developed pneumonia and 169 (28 per cent) died (Morley, 1969). Encephalitis may affect about one in 700 cases of measles in the community (Greenberg *et al.*, 1955; Miller, 1964) and 4·7 per cent of cases hospitalized with measles (Boughton, 1964b). Febrile convulsions without encephalitis occur in another one of 700 cases in Britain (Miller, 1964), but in West Africa 1·5 per cent of children hospitalized with measles convulsed before admission and 2·9 per cent had convulsions after admission (Morley, 1969).

(ii) **Measles in leukaemia**

Conditions affecting the reticuloendothelial system, such as leukaemia, may predispose to unusually severe attacks of measles resulting in giant-cell pneumonia, with (Mitus *et al.*, 1959) or without (Enders *et al.*, 1959) an antecedent rash. A Toronto patient aged five years who had received corticosteroids and antileukaemic chemotherapy for eight months following a diagnosis of leukaemia, developed extensive bilateral nodular infiltration of the lung field, with some areas of confluent alveolar consolidation, particularly in the left lower lobe from which she died three days subsequently. Syncytial giant cells with acidophilic intranuclear inclusions were observed to outline the alveolar air spaces, some of which were filled with exudate containing mononuclear and giant cells. Measles virus was isolated from the lung tissue (McLean *et al.*, 1966).

Administration of 0·2 ml/kg pooled human gammaglobulin to a leukaemic child aged four years under treatment with corticosteroids and antileukaemic chemotherapy immediately after he became febrile, following household contact with measles, was followed two days later by a mild morbilliform rash and a rising measles antihaemagglutinin titre. However no antibody was detected 261 days after onset of rash. Intramuscular injection of leukocytes, derived from 500 ml plasma obtained from a subject who developed measles seven days previously, into a leukaemic child aged two years who developed clinical and radiological evidence of giant-cell pneumonia 20 days after onset of measles, was followed by satisfactory recovery from pneumonia. This patient, who had no measles antihaemagglutinin before administration of human donor leukocytes, developed a low HI antibody level four days later (McLean *et al.*, 1966). Thus administration of pooled human gammaglobulin, or leukocytes from donors who have recently recovered from measles, may be life-saving procedures in patients with suppression of the reticuloendothelial system who contract measles.