spinal fluid is an important cause of morbidity. The 10 significant perivascular deposits (eight patients) noted in the present series represent a minimum assessment of the occurrence of the complication, since information on this aspect was available in only a proportion of cases. Of considerably greater significance in this context was the development of progressive cauda equina lesions after direct injection of Thorotrast into cerebrospinal fluid spaces. After injection into the ventricles thorium diffuses rapidly and spreads throughout the cerebrospinal system. It tends to collect in the more dependent parts of the ventricles, in the basal cisterns, on the choroid plexus, and most of all in the sacral cul-de-sac. The particles of thorium settle out and gradually become incorporated within the ependymal lining of the ventricles and the surface layer of the arachnoid membrane.

The serious sequelae after deposition in the sacral cul-de-sac have been amply demonstrated in the present series. Seven out of 10 patients surviving five years after Thorotrast administration developed progressive cauda equina lesions. Four (possibly five) of six subsequent deaths among these patients were the direct consequence of interference with bladder innervation. Taken as a whole the evidence pointing to thorium as the cause of cauda equina lesions appears conclusive and is consistent with the previous demonstration (Reeves and Stuck, 1938) of other hazards, such as hydrocephalus and damage to cranial and spinal nerve roots, after the prolonged exposure of neural tissue to thorium, and with similar cases which have been described by Hughes (1953) and by Dale and Love (1967). It is quite plain that Thorotrast should never be injected into the cerebrospinal fluid or into a cavity likely to communicate with cerebrospinal pathways. It is also fortunate that ventriculography or myelography with Thorotrast, never used with confidence, was so soon and so firmly abandoned.

Summary

All patients (168) known to have received Thorotrast in the course of clinical investigation in a department of surgical

neurology have been followed up and their current or final status at 1 January 1966 or later established. A total of 137 patients received Thorotrast by intra-arterial injection during the years 1933 to 1955. While their subsequent mortality experience reflected the diseases, mainly cerebrovascular, bringing them under investigation, it was notable that there were 12 deaths from cancer (including four primary liver tumours) among the 109 who survived more than one year after Thorotrast administration.

Between 1935 and 1941 27 patients received Thorotrast by direct injection into the ventricular system or subarachnoid space. Seventeen of these patients died within five years as a direct result of the disease bringing them under investigation. Seven of the 10 five-year survivors subsequently developed progressive cauda equina lesions, six of which have proved fatal.

We are pleased to acknowledge our indebtedness to Professor Norman Dott for generous co-operation and help throughout and to Dr. Kate Hermann for her continued interest in the investigation. We are deeply indebted also to the late Mr. Peter Ascroft for his careful definition of the population under study. Miss A. Fotheringham, Mrs. E. Goldenberg, and Miss C. M. Jones undertook the considerable task of tracing patients. Our thanks are due to them and the many doctors who provided information about their own patients.

REFERENCES

- Ascroft, P. B., and Maccabe, J. J. (1962). *J. roy. Coll. Surg. Edinb.*, **7**, 221.
 Buckton, K. E., Langlands, A. O., and Woodcock, G. E. (1967). *Int. J. Radiat. Biol.*, **12**, 565.
 Dale, A. J. D., and Love, J. G. (1967). *J. Amer. med. Ass.*, **199**, 606.
 da Silva Horta, J., Abbott, J. D., da Motta, L. C., and Roriz, M. L. (1965). *Lancet*, **2**, 201.
 Gardner, D. L., and Ogilvie, R. F. (1959). *J. Path. Bact.*, **78**, 133.
 Hughes, R. (1953). *Proc. roy. Soc. Med.*, **46**, 191.
 Langlands, A. O., and Hermann, K. (1967). *J. clin. Path.*, **20**, 892.
 Langlands, A. O., and Williamson, E. R. D. (1967). *Brit. med. J.*, **3**, 206.
 MacMahon, H. E., Murphy, A. S., and Bates, M. I. (1947). *Amer. J. Path.*, **23**, 585.
 Maltby, G. L. (1964). *New Engl. J. Med.*, **270**, 490.
 Reeves, D. L., and Stuck, R. M. (1938). *Medicine (Baltimore)*, **17**, 37.

Acquired Cytomegalovirus Infection*

GUN CARLSTRÖM, M.D.; JÖRAN ALDÉN, M.D.; SVEN BELFRAGE, M.D.; GRETA HEDENSTRÖM, M.D.
 LARS HOLMBERG, M.D.; FOLKE NORDBRING, M.D.; GÖRAN STERNER, M.D.

Brit. med. J., 1968, **2**, 521-525

The role of the cytomegalovirus group as pathogen for the foetus has been well documented since the isolation of the first cytomegalovirus strains and the consequent development of virological methods of diagnosing the disease. Infection in utero is contracted from a mother, generally without clinically recognized disease. The congenital infection has been described as a generalized disease which may resemble congenital toxoplasmosis, neonatal hepatitis, or neonatal sepsis. It has usually been regarded as a very serious illness, but recent observations indicate that various degrees of severity may occur. Jaundice, petechial rash, hepatosplenomegaly, microcephaly, and mental retardation are common manifestations (Weller and Hanshaw, 1962).

Little is known about the clinical features of postnatally contracted cytomegalovirus infections. Before the use of virological techniques the recognition of these infections depended on the microscopical detection of typical inclusion-bearing cells. Such cells were found at post-mortem examination of adults with conditions complicating malignant and chronic

debilitating diseases. Wong and Warner (1962) reported 14 such cases and reviewed 41 others in the literature. Diseases known to alter the resistance of the host to infection were prevalent and the majority of cases were treated with corticosteroids. The possibility of a reactivation of dormant virus has been discussed. Common clinical manifestations of such secondary cytomegalovirus infections were ulcerative gastroenteritis, pneumonitis, or generalized disseminated disease. The complication of cytomegalovirus infection in debilitating diseases and in immunodepressive therapy has now in some cases been verified by means of virological techniques (Hanshaw and Weller, 1961; Carlström, 1966; Craighead *et al.*, 1967).

Reports on postnatally contracted cytomegalovirus infection occurring without connexion with debilitating diseases are scarce, but the development of virological diagnostic methods

* From the Department of Clinical Bacteriology, Section of Virology, Karolinska Sjukhuset, Stockholm, and the Departments of Infectious Diseases of Falun, Malmö, Göteborg, Uppsala, and Danderyd Hospitals.

seems to have opened up this field. Data are now accumulating and slowly delineating the epidemiological pattern and clinical picture of postnatally contracted cytomegalovirus infections.

Rowe *et al.* (1958) presented evidence indicating a common occurrence in children of postnatal cytomegalovirus infections with a subclinical course. Hanshaw *et al.* (1965) reported a chronic type of hepatitis clinically significant in postnatally acquired cytomegalovirus infection.

Recently reports have appeared indicating postnatally acquired cytomegalovirus infections running the course of an acute febrile illness. Klemola and Kääriäinen (1965) found cytomegalovirus to be the aetiological agent in cases which on account of the haematological findings were referred to the group of infectious mononucleosis. These cases differed from the common type of infectious mononucleosis in having a negative heterophil agglutination reaction and in lacking

exudative pharyngitis and enlargement of the lymph nodes. Fever lasting two to three weeks was the dominating clinical symptom. The occurrence of the same syndrome after surgery and transfusion has been connected with cytomegalovirus (Kääriäinen *et al.*, 1966). Recently Carlström *et al.* (1968) presented evidence of cytomegalovirus infection complicating open-heart surgery and transfusion with fresh blood. Long-lasting fever and involvement of the lungs dominated the clinical picture. Heart, liver, and spleen were also affected, and there was an increase in the number of atypical lymphocytes.

The present paper reports epidemiological, clinical, and laboratory data in 11 cases with acutely acquired cytomegalovirus infection recognized in Sweden during the last two years and diagnosed by virus-serological methods.

Material and Methods

Clinical Material. — Initially, diagnostic studies of cytomegalovirus were attempted in febrile diseases of unknown origin showing different kinds of clinical manifestations. Upper and lower respiratory tract symptoms, gastrointestinal disorders, meningoencephalitis, urinary tract infections, influenza-like diseases, parotitis, vaginitis, conjunctivitis, and atypical exanthematous diseases were studied. Particular attention was paid to the clinically well-defined but aetiologically unexplored syndromes of hepatitis and mononucleosis. The patients were admitted to the departments of infectious diseases in Swedish hospitals from June 1965 to October 1967. Paired acute and convalescent sera were examined for cytomegalovirus antibodies at the Virus Laboratory of Karolinska Sjukhuset. As this was the only Swedish laboratory using diagnostic methods for cytomegalovirus, the material has been collected from different parts of the country and should be representative of virologically recognized cases of acquired cytomegalovirus infections in the whole of Sweden.

Virological techniques used in the diagnostic tests for cytomegalovirus were those described by Carlström (1965). In complement fixation

X) Highest twofold serum dilution giving complement fixation taken as complement fixing titre (C.F.T.)
Highest fivefold serum dilution giving neutralization taken as neutralizing titre (N.T.)
Titres are expressed as dilution factors
N.d. Not done

Relevant data in 11 patients with acquired cytomegalovirus (C.M.V.) infection.

tests and neutralization tests the Ad. 169 strain of cytomegalovirus was used. In most cases it took a long time to transport the specimens to the laboratory, and therefore attempts to isolate virus were seldom made, serological cytomegalovirus tests being the diagnostic method of this study. Paired acute and convalescent sera were tested simultaneously, and a fourfold rise in titre was taken as significant. All sera were tested at twofold dilution steps, 1/2 being the lowest dilution. Positive Paul-Bunnell tests were read after absorption with guinea-pig kidney tissue and bovine erythrocytes. A single titre less than 1/160 was regarded as negative.

Results

Paired acute and convalescent sera from 135 patients with different infectious diseases were examined for a rise in cytomegalovirus antibody titre. Owing to our own observations, and to reports appearing during the course of this study (Hanshaw *et al.*, 1965; Klemola and Kääriäinen, 1965), there was a tendency to select cases particularly with clinically atypical hepatitis and Paul-Bunnell-negative mononucleosis. In some of these patients, and in some others with long-lasting febrile illnesses, there was a significant rise in titre of cytomegalovirus antibodies. In all, 11 serologically positive cases were found. The relevant data of these cases are summarized in the Chart, where age in years and date of onset of symptoms are recorded. The different clinical patterns of the cytomegalovirus-positive patients are further described in separate case histories. Normal findings are not listed. The Paul-Bunnell test was negative in all cases.

Case Reports

Case 1.—At the end of July 1966 high fever, micturition, sore throat, proteinuria, and elevated E.S.R. Treated with sulpha and penicillin but remained febrile. During next four weeks tired, moderate upper respiratory symptoms, proteinuria, and anaemia. On September 2 relapse with chills and 40.1° C. Admitted to Uppsala Hospital seriously ill, with redness of the throat and marked hepatosplenomegaly. Hb 8.6 g./100 ml., 58% of 6,600 W.B.C. mononuclear without pathological appearance, E.S.R. 126 mm./hour, and thymol turbidity 5 units. Afebrile after three days, improved gradually, and discharged after three weeks. Three months later all findings normal except thymol 2.1 units.

Case 2.—Sudden onset of fever, headache, loss of appetite, and after one week dark-coloured urine. Sulphamedication without benefit, and 14 days after onset still 38° C. Admitted to Falun Hospital. Chest x-ray examination showed some scattered cloudy densities basally on both sides. 88% of 9,800 W.B.C. mononuclear. No atypical lymphocytes. E.S.R. 25 mm./hour, thymol turbidity 19.8 units, and serum alanine aminotransferase (AIT) 102 units. Without antibiotic treatment subfebrile after three days, and afebrile and discharged after 14 days. After three months normal laboratory tests and chest x-ray picture.

Case 3.—Onset with headache, fatigue, and later conjunctivitis and sore throat. Temperature gradually rising to 38.5° C. Sulpha and penicillin without benefit. Admitted to Falun Hospital 19 days after onset of disease. 76% of 9,800 W.B.C. mononuclear. No atypical lymphocytes. E.S.R. 20 mm./hour, thymol turbidity 6.5 units, and AIT 60 units. Four days after admission afebrile; dismissed one week later, still with some conjunctivitis but otherwise free of symptoms.

Case 4.—Fell ill with fever and a sore throat and, after two days, a scarlet-fever-like rash. Admitted to the Department of Infectious Diseases, Gothenburg, with 39.1° C., a faint jaundice, and enlarged and tender lymph nodes on neck and in axillae and groins. Chest x-ray films showed a moderate bilateral pneumonitis, which increased and involved both lungs almost completely on the tenth day. X-ray films of the sinuses revealed signs of frontal, maxillary, and ethmoidal sinusitis. W.B.C. count 11,600 on arrival and 23,400 after eight days. In every examined specimen about 90% polymorphonuclear W.B.C. No atypical lymphocytes. E.S.R. 49 mm./hour, serum bilirubin 7.6 mg./100 ml., and serum AIT 94 units. Penicillin and tetracycline without benefit. 39–40° C. for 10 days.

Afebrile after three weeks; dismissed free of symptoms and with normal x-ray picture of lungs.

Case 5.—Gonorrhoea in 1961, and during 1963 three episodes of tonsillitis and fever. Fell ill with vaginal discharge and dysuria, and after three days sore throat with high fever. Five days later admitted to Malmö Hospital with marked tonsillitis and enlarged tender lymph nodes on the neck. 74% of 8,500 W.B.C. mononuclear, many of atypical appearance. E.S.R. 74 mm./hour, AIT 84 units, and thymol turbidity 0.24 extinction unit. Splenomegaly diagnosed by x-ray examination. Throat culture showed heavy growth of β -haemolytic streptococci and *Staphylococcus aureus*. Treated with antibiotics, the tonsillitis, vaginitis, and lymphadenopathy soon improved, but the temperature remained high for 14 days.

Case 6.—A follicular rash persisted for about 24 hours on her right ear and the lower part of the back and was followed by 39° C. and headache. Penicillin without benefit. After 10 days still febrile, and admitted to Uppsala Hospital. 78% of 9,200 W.B.C. mononuclear. No atypical lymphocytes. E.S.R. 28 mm./hour, thymol turbidity 4.5 units, alkaline phosphatase 4.9 units, AIT 64 units, and bilirubin 0.3 mg./100 ml. Afebrile after three weeks and dismissed from hospital in good shape. Fourteen days later laboratory tests normal.

Case 7.—Cystitis in January and March 1966 and gonorrhoea in November 1966. Fell ill with nausea, abdominal pains, fever, and sore throat. Admitted to the Department of Obstetrics and Gynaecology of Gothenburg with 39.5° C. and purulent vaginal discharge. Temperature remained high for 14 days in spite of tetracycline and ampicillin. Transferred to the Department of Infectious Diseases. Enlarged lymph nodes found on neck. Hb 9.2 g./100 ml. 79% of 9,000 W.B.C. mononuclear, some of them atypical. E.S.R. 27 mm./hour, AIT 61 units, AsT 36 units, and thymol turbidity 0.47 extinction unit. Afebrile after 17 days, and rapid improvement with all laboratory tests normal.

Case 8.—On anti-ovulation therapy. Fell ill with recurring episodes of high fever, abdominal pains, and diarrhoea. After three weeks admitted to the Surgical Department of Malmö Hospital with suspected appendicitis but moved the next day to the Department of Infectious Diseases. On admission subfebrile and other symptoms had subsided. 75% of 9,500 W.B.C. mononuclear. No atypical lymphocytes. E.S.R. 23 mm./hour, thymol turbidity 0.29 extinction unit, and lactic dehydrogenase 690 units with an increase of fraction III. X-ray examination showed hepatosplenomegaly. Afebrile and discharged some days after admission. Suffered from persistent fatigue and had a relative lymphocytosis for about a month after discharge.

Case 9.—Fell ill with high fever, chills, fatigue, and headache. Gradually developed hepatomegaly and generalized lymphadenopathy, and a week later a follicular rash appeared on feet and body. 8,000 W.B.C., with increase of polynuclear cells. No atypical lymphocytes. Ampicillin without benefit. Admitted to Danderyd Hospital with 15,400 W.B.C., a relative increase of mononuclear cells, and 46% atypical lymphocytes. Thymol turbidity 21 units, AsT 90 units, and AIT 135 units. Improved gradually, afebrile after 23 days, and discharged from hospital after 25 days. One month later no hepatomegaly or lymphadenopathy and normal laboratory tests.

Case 10.—Treated in Danderyd Hospital in 1964 for infectious mononucleosis (tonsillitis, 20,000 W.B.C., lymphocytosis, and atypical lymphocytes. Paul-Bunnell 1/80). From 1964 to 1967 repeated episodes of cystitis. In September 1967 again cystitis and treated with sulpha. After 10 days of sulphamedication 38.5° C. and a maculopapular rash on knees and elbows. Sulpha was discontinued and one week later she was seen at the Infectious Clinic of Danderyd, still febrile and with a persisting rash, slight enlargement of the lymph nodes on neck, and tonsillitis. 83% of 20,400 W.B.C. mononuclear, 46% atypical lymphocytes. Liver tests not made. Kept in bed at home, and was again seen in the clinic after 14 days without clinical signs and with normal haematological data.

Case 11.—In June and August 1967 episodes of proctitis. Improved after treatment with Salazopyrin (sulphasalazine). In the middle of September, still on sulphamedication, he developed general malaise. On October 6 fever and chills. Sulphamedication was discontinued. Soon general muscular pains, cough, and conjunctivitis appeared. Admitted to Uppsala Hospital with 39° C. Blood was found twice in his stools. 70% of 8,100 W.B.C. mononuclear. Some of the lymphocytes atypical. Thymol turbidity 6.7 units, AIT 129 units, and AsT 80 units. Treated with ampi-

cillin. Fever and other symptoms gradually subsided, and after 10 days discharged in good general condition. One month later all laboratory tests normal.

Comment

The relevant clinical and laboratory features of the 11 patients are summarized in Table I.

To study the relation between cytomegalic inclusion disease and infectious mononucleosis, specimens sent to the Bacteriological Laboratory of Karolinska Sjukhuset for Paul-Bunnell test were also tested for complement-fixing antibodies against

TABLE I.—*Clinical and Laboratory Findings in 11 Patients with Acquired Cytomegalovirus Infection*

Pathological liver function tests*	10	Lymphadenopathy	..	..	5
Fever lasting > 2 weeks	9	Rash	..	..	4
Mononuclear cells > 50%	9	Splenomegaly	..	..	4
E.S.R. > 20 mm./hour	8	Hepatomegaly	..	..	3
W.B.C. < 10,000	7	Conjunctivitis	..	..	2
Pharyngitis or tonsillitis	6	Pneumonia	..	..	2
Atypical lymphocytes found	5	Anaemia	..	..	2
		Vaginitis	..	..	2

* One case not examined.

TABLE II.—*Comparison Between Heterophil Antibodies and Cytomegalovirus Antibodies*

		Paul-Bunnell Test	
		Positive	Negative
Cytomegalovirus antibodies	Present	3*	46
	Absent	35	104

* In these three cases Paul-Bunnell titres were only 1/160.

cytomegalovirus. In the material comprising paired sera from 15 patients no case serologically suggestive of cytomegalovirus infection was found. Single convalescent sera were obtained from 188 patients. The results are shown in Table II. It is seen that cytomegalovirus antibodies were found in about 30% of the cases with a negative Paul-Bunnell test but in only 8% of cases with a positive Paul-Bunnell test. (These positive Paul-Bunnell tests were of low titres.)

In paired sera with significant rise in titre of heterophil antibodies no rise was found in cytomegalovirus titre, and vice versa. The same serological cross test was made with Eaton agent and cytomegalovirus, no correlation being found.

Discussion

The cases of cytomegalovirus infections reported above have some clinical signs in common which delineate a certain pattern of the disease, but there are also various symptoms which produce a complex clinical picture.

The pattern common to most cases was as follows. A long-lasting fever of 38.5–40° C. for two to three weeks. The patients were markedly ill and had liver involvement and elevated E.S.R. The total W.B.C. was generally within normal limits or slightly raised. Most patients had a relative increase of mononuclear cells. Antibiotic treatment was without benefit. One girl was 13 years old; the other patients were aged between 19 and 34 years. The disease did not occur epidemically, but there was possibly a certain accumulation of cases. In all patients the rise in titre of cytomegalovirus antibodies occurred rather late in the disease. It was not found during the first 14 days, but appeared in convalescent sera taken more than three weeks after the onset of symptoms. In two patients there was a continuous rise in titre for another month and in one case for another two months.

All serological tests except those for cytomegalovirus were negative. Paired sera were tested against several viral and bacterial antigens which possibly might occur in diseases running a similar clinical course. Influenza, herpes, respiratory syncytial, enterovirus, Eaton agent, toxoplasma, listeria,

yersinia, salmonella, pasteurella, brucella, and treponema all gave negative results. The Paul-Bunnell test was negative in all cases and cold agglutinins were looked for in five patients but not found.

Most patients had signs of liver involvement such as hepatomegaly, pathological thymol turbidity, and moderate rise of transaminase. Jaundice was recorded in only one patient. The pathological findings all became normal during convalescence. Therefore it seems apparent that there is a correlation between cytomegalovirus infection and liver involvement. However, the frequency and specific nature of liver involvement in cytomegalovirus infection has not been further explored in the present study.

The following symptoms and findings occurred occasionally. Six patients had a sore throat—four of them pharyngitis and two tonsillitis. Five patients had lymphadenopathy. There was marked splenomegaly in four cases. Bronchopneumonia was diagnosed in two cases and was also present in two previous patients (Carlström, 1966; Carlström *et al.*, 1968). It has been a common finding in debilitated patients with terminal complications which on grounds of microscopical examinations have been classified as cytomegalovirus infections. In our material the pulmonary cytomegalovirus involvements on radiological examination have constantly appeared as cloudy bilateral infiltrations (Carlström *et al.*, 1968). Gastroenteritis was present in one case, vaginitis in two, and four patients complained of severe long-lasting headache. Two patients suffered from abdominal pain. Two had conjunctivitis and one had muscular pain. A follicular rash appeared in three cases and a maculopapular rash in one. Atypical mononuclear cells were repeatedly looked for in all cases and found in five. Two patients had more than 20,000 W.B.C. with a predominance of polynuclear cells. Two patients had severe anaemia.

A certain clinical pattern may now be traced in acquired cytomegalovirus infection, but it is very likely that other symptoms, different from those found here, may occur. The principles for selection of cases may influence the clinical picture obtained. In the present instance all kinds of febrile diseases of unknown origin were investigated, but cases with clinically atypical hepatitis and Paul-Bunnell-negative mononucleosis are in the majority. A difference in the principle of selection may account for the discrepancies between findings in this material and that presented by Klemola and Kääriäinen (1965). These authors demonstrated cytomegalovirus infection only in cases classified as Paul-Bunnell-negative mononucleosis of the typhoid-like type with no tonsillitis and no lymphadenopathy, but regularly with atypical lymphocytes in the peripheral blood. Presumably those patients were selected for examination of cytomegalovirus.

In the present material most patients could be clinically diagnosed as having various types of infectious mononucleosis, provided that infectious mononucleosis is defined as a long-lasting febrile disease with relative lymphocytosis, liver involvement, and a variety of other clinical symptoms, and occurring especially in adolescence and among young adults. As this is a rather unspecific clinical picture probably caused by several agents, one of which is cytomegalovirus, it now seems reasonable to attempt a classification of these cases according to cause.

Most of our patients have been markedly ill. This may possibly be due to the collection of material from patients in hospitals and not in outpatient departments. Case 10 was the only exception. Mild diseases have otherwise not been subjected to cytomegalovirus studies, but there is every reason to believe that slight or inapparent cytomegalovirus infections occur rather often.

It is seen in Table II that 30% of patients with a negative Paul-Bunnell test had antibodies against cytomegalovirus—that is, a fairly normal proportion in healthy young adults. Among patients with a positive Paul-Bunnell test hardly any cytomegalovirus antibodies were found. The reason for this possibly negative correlation between cytomegalovirus antibodies

and heterophil antibodies is obscure. The material is small, but one might speculate on the possibility that a past cytomegalovirus infection may protect against infections causing heterophil antibodies, and vice versa.

Serological tests have been the diagnostic method of the present study. Isolation of virus has not been attempted, but still the diagnosis is well documented. In all cases a significant rise in cytomegalovirus antibody titre was demonstrated in the complement-fixation test and in most cases also in the neutralization test. Proper controls were included in all tests. The Ad. 169 strain of cytomegalovirus was used in the complement-fixation test and the neutralization test. The complement-fixation test was the primary screening test, and when a sufficient amount of serum was obtained positive serum pairs were subsequently studied in the neutralization test with positive results. If there are antigenically different cytomegalovirus strains, either just one of these has been present here, or there are different strains with the same antigenic substance in common. Quantitative cross-neutralization tests with different cytomegalovirus strains have so far not been made.

There is hardly any doubt that the patients reported on have had an infection with cytomegalovirus or with an antigenically related agent. It is impossible to state, however, whether this is a primary acute infection or a disease of secondary reactivated type. The possibility of a complex microbiological cause of the disease with some kind of reactivation of a latent cytomegalovirus infection might thus possibly be discussed in some of the patients presented. In Cases 1 and 10 recurring urinary tract symptoms and in Case 11 repeated episodes of proctitis occurred before the definite onset of the actual disease. Cases 4 and 5 ran clinical courses suggestive of bacterial complications. However, in most of the patients the uniformity of the relation between clinical course and serological response seems to contradict the occurrence of a secondary reactivation of a latent cytomegalovirus infection.

Summary

Eleven cases of acquired cytomegalovirus infection occurring in different parts of Sweden and diagnosed by serological methods (complement-fixation test and neutralization test) are reported. A common clinical pattern was characterized by long-lasting fever, liver damage, relative lymphocytosis, raised E.S.R., and a significant rise in complement-fixing and neutralizing cytomegalovirus antibodies occurring more than two weeks after onset. A variety of other symptoms occurred, such as upper or lower respiratory tract infections, lymphadenopathy, anaemia, conjunctivitis, exanthema, gastroenteritis, vaginitis, and severe headache.

Serological cross-reactions between cytomegalovirus and many other infectious agents were looked for but not found. The implications of a possible negative correlation between heterophil antibodies and cytomegalovirus antibodies are discussed.

We wish to express our appreciation to Miss Irma Huttenlocher, Miss Gunilla Johansson, and Mrs. Eva Olsson for competent technical assistance.

REFERENCES

- Carlström, G. (1965). *Acta paediat. (Uppsala)*, **54**, 17.
 Carlström, G. (1966). *Svenska Läk.-Tidn.*, **63**, 2135.
 Carlström, G., Belfrage, S., and Swedberg, J. (1968). *Scand. J. thorac. Surg.* In press.
 Craighead, J. E., Hanshaw, J. B., and Carpenter, C. B. (1967). *J. Amer. med. Ass.*, **201**, 725.
 Hanshaw, J. B., Betts, R. F., Simon, G., and Boynton, R. C. (1965). *New Engl. J. Med.*, **272**, 602.
 Hanshaw, J. B., and Weller, T. H. (1961). *J. Pediat.*, **58**, 305.
 Kääriäinen, L., Klemola, E., and Paloheimo, J. (1966). *Brit. med. J.*, **1**, 1270.
 Klemola, E., and Kääriäinen, L. (1965). *Brit. med. J.*, **2**, 1099.
 Rowe, W. P., Hartley, J. W., Cramblett, H. G., and Mastrotta, F. M. (1958). *Amer. J. Hyg.*, **67**, 57.
 Weller, T. H., and Hanshaw, J. B. (1962). *New Engl. J. Med.*, **266**, 1233.
 Wong, T.-W., and Warner, N. E. (1962). *Arch. Path.*, **74**, 403.

Degenerative Changes in the Knee after Meniscectomy

J. P. JACKSON,* F.R.C.S.

Brit. med. J., 1968, **2**, 525-527

Meniscectomy is one of the most frequently performed orthopaedic operations. The immediate results are mostly very satisfactory. Late degenerative changes have been reported, but very little information is available about their frequency or their causes.

Radiographic changes which occur after meniscectomy have been described by various authors. Vandendorp, Bastien, and Vandecasteele (1939) did little more than indicate that changes occurred. Fairbank (1948), however, who examined 107 cases three months to four years after operation, described ridging and flattening of the femoral condyle and narrowing of the joint space. He suggested that these changes might be a precursor of osteoarthritis. He found that they occurred in 37% of patients. His conclusion was "that meniscectomy is not wholly innocuous; it interferes at least temporarily with the mechanics of the joint. It seems likely that narrowing of the joint space will predispose to early degenerative changes, but a connexion between these appearances and later osteoarthritis is not yet established and is too indefinite to justify clinical deductions."

Saugmann-Jensen (1963) reported on 548 patients from the clinics in Copenhagen and found what he referred to as "Fairbank changes" in 23% after four and 38% after 10 to

15 years. He also thought that they were probably early osteoarthritic changes. He reported definite osteoarthritis as occurring in some six patients, though he did not define by what criteria the diagnosis was made.

To obtain a clearer picture of the incidence of degeneration after meniscectomy a series of patients were examined who were operated on at Harlow Wood Orthopaedic Hospital by a number of surgeons. The minimum postoperative period was five years. This allowed a reasonable time for the development of radiographic changes.

The term "degeneration" is used in this article rather than osteoarthritis, since in the first part it is a radiographic analysis. The changes referred to, however, are such that in the presence of pain a diagnosis of osteoarthritis would be acceptable.

The results reported have been submitted to statistical analysis and are considered valid.

Material

A total of 640 knees were reviewed. In 56 cases some of the radiographs were missing and seven were subsequently found to have a follow-up of less than five years. This left a total of 577 knees suitable for study. There were 516 (89%) male and only 61 (11%) female patients. Of these cases 480

* Harlow Wood Orthopaedic Hospital, Near Mansfield, Nottinghamshire.