serum intravenously. Two and a half years after her illness she was normal both mentally and physically.

The prognosis, both as to life and the possibility of any sequalæ is not necessarily unfavourable because there has been long delay in instituting adequate therapy.

SUMMARY

1. Influenzal meningitis will continue to have a high mortality rate during the early months of life, until a more effective treatment has been discovered.

2. In view of the high mortality rate in all patients with this disease until a few years ago it is advisable that every patient should be given both sulfatherapy and serotherapy as soon as a diagnosis has been made.

3. An early diagnosis and the prompt administration of adequate treatment is of great importance. However, complete recovery does take place sometimes when there has been a delay of weeks before adequate therapy has been given.

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RÉSUMÉ

La méningite à *H. influenzæ* demeure toujours très meurtrière lorsqu'elle survient durant les premiers mois de la vie, du moins, lorsqu'elle est traitée par les moyens en usage à la date de parution de ce rapport (juin 1946). Il s'agit de donner au malade une quantité suffisante de sulfamidés et d'y adjoindre, selon l'indication, la sérothérapie spécifique à la dose convenable. On n'oubliera jamais d'associer le sérum glucosé à 5% dans tous les cas, comme médication adjuvante de soutien. Le diagnostic précoce est de première importance, cependant, un certain délai n'est pas incompatible avec la guérison. JEAN SAUCIER

The leech should always be busy about things belonging to his craft. He must always be talking about it or studying it or be writing or praying, for the use of books brings a doctor a good reputation because it is both noticed by others and he himself becomes wiser thereby. And besides all this it is profitable to him that he be found always sober, for drunkenness destroys all virtue and brings it to naught, as sayeth a wise man, "Drunkenness destroys whatsoever wisdom teaches". Let him be content in strange places with the meats and drinks found there, using moderation in everything. For the wise man says "As it is good to be moderate in everything that is, so without moderation everything that is perisheth".—Master John of Arderne.

INFECTIOUS MONONUCLEOSIS—COMPLICATIONS*

Francis S. Brien, M.B.

London, Ont.

INFECTIOUS mononucleosis is world-wide in its prevalence. It usually attacks children and young adults. Ordinarily it is not difficult of recognition, and complications are stated by many writers to be exceptional. This paper is concerned with some of the problems in diagnosis and with certain complications.

Serial blood counts and heterophile antibody agglutination tests may be necessary to establish the diagnosis. Absorption tests will eliminate false-positive Paul-Bunnell reactions, a particularly useful procedure if horse serum has been administered previously to the patient. The typical cell of infectious mononucleosis is a large abnormal lymphocyte, often with an indented nucleus, and a pale-staining zone in the cytoplasm immediately about the nucleus. Vacuoles are commonly seen in the cytoplasm which may show projecting processes. All variations between this cell and a normal lymphocyte may be seen. Characteristic changes in the blood and the appearance of enlarged lymph glands may be delayed for as long as several weeks after the onset of symptoms.

The Wassermann reaction in the blood may be transiently positive in a small proportion of cases. Should this occur in a patient with generalized lymphadenopathy and a macular or maculo-papular type of eruption, admittedly an uncommon combination in infectious mononucleosis, confusion with secondary syphilis may take place, unless the blood smear be carefully studied, and the heterophile agglutination test be performed. German measles, with its posterior cervical adenitis, transient rash, and lymphocytosis, likewise may cause difficulty in diagnosis. Scarlatiniform, nodular, vesicular, urticarial, hæmorrhagic, and polymorphous eruptions have been recorded. In 1920, two cases were admitted to a London (England) fever hospital with a presumptive diagnosis of typhus that subsequently proved to be infectious mononucleosis. Acute leukæmia at its onset may constitute a very real difficulty in

* Department of Medicine, Faculty of Medicine, University of Western Ontario. Department of Medicine, Victoria Hospital, London, Ont.

differential diagnosis, but the leucocytosis is usually far in excess of that of glandular fever and the cell type more uniform. Hæmorrhages into the mucous membranes and skin are nearly always present in acute leukæmia. Anæmia is progressive, and the issue fatal. The heterophile agglutination test is negative.

During the course of infectious mononucleosis many subclinical cases occur, as has been amply demonstrated by studies on the blood. Convalescence may be very protracted, and relapses are not uncommon. Asthenia is often marked. The abnormal blood picture and enlarged glands may persist for weeks or months. Eosinophilia is frequently encountered during the convalescent period, commonly constituting about 5% of the differential count, and occasionally attaining values as high as 15 to 20%.

Evidence of possible effects of infectious mononucleosis on the heart is extremely scant. Bradshaw, in 1931, reported the case of a young girl of 17, who was felt to have a normal heart previously, and six weeks after recovery from an attack of mononucleosis was found to have definite clinical evidence of mitral stenosis. Surely, in view of our present knowledge of the pathogenesis of rheumatic endocarditis, no one would seriously entertain the thought that such a mitral lesion was a result of the glandular fever. In their report of an extensive epidemic in an American army post, Wechsler, Rosenblum and Sills record the unexpected discovery of a markedly prolonged P-R interval in an otherwise typical case. They carried out electrocardiographic studies on over 200 patients in their series and found significant abnormalities (abnormal T waves, prolonged P-R interval, or both) in 23%. In some of these the electrocardiograms were known to be normal before the infectious mononucleosis developed. In most, the abnormalities were of short duration, in others, they were persistent for months. No specific change was encountered. It is possible that in certain of their cases infectious mononucleosis was complicating rheumatic fever. In the two fatal cases that I shall presently describe no gross pathological changes were present in the heart, but microscopically, small accumulations of mononucleosis cells were found in the heart muscle and just under the endocardium.

Though cough was a common symptom, pulmonary findings were present in only 30 of the 556 cases reported by Wechsler and his co-workers. They took the form of diffusely scattered rhonchi and fine râles. X-ray studies showed mottling indistinguishable from that seen in so-called atypical pneumonia. These lesions rapidly cleared. In none of their cases could enlarged mediastinal glands be demonstrated in the films. This is similar to my own experience. It is impossible to state whether the acute bronchitis or pneumonia is a part of the disease itself or a complication due to secondary invaders. Increased heterophile antibodies have been reported in cases of atypical pneumonia, unaccompanied by mononucleosis or abnormal lymphocytes in the blood smear.

The incidence of renal involvement varies greatly in the literature. In 65 cases Bernstein found no evidence of this complication. Tidy and Morley reported an incidence of 6% in their 270 cases. In Wechsler's series 3% had abnormal urinary findings. Albuminuria, red blood cells, occasionally macroscopic hæmaturia, and hyaline and granular casts, have been reported. They occurred either at the onset or within the first few days of the illness, and were of short duration, usually disappearing within seven to ten days. Œdema, elevation of blood pressure, nitrogen retention, and other evidence of impaired renal function have not been recorded. Tubular degeneration and interstitial infiltration with mononuclear cells were present in the kidneys of both of my two patients dying from splenic rupture.

The liver may be palpably enlarged in the absence of clinical jaundice. When the latter is present the liver is nearly always definitely enlarged and tender. Latent jaundice is not uncommon. Glandular enlargement may precede or appear simultaneously with the icterus, or follow it after an interval. The clinical picture is very like that of the ordinary case of infectious hepatitis, and, as in the latter, the depth of jaundice may be very variable. Both the clinical features and liver function tests indicate that the jaundice of infectious mononucleosis is due to a diffuse hepatitis, and not secondary to obstruction by enlarged lymph nodes, as has been suggested by several authors. Support for this statement comes from liver biopsy performed on cases of infectious mononucleosis and from autopsy studies on fatal cases. In these, degenerative changes in the liver cells, and marked foci of mononucleosis

cells were seen in the liver sinusoids and portal areas.

The spleen would appear to be palpably enlarged in about one-third of the cases. It may be difficult to feel, and must be persistently sought for by repeated careful examination. Spontaneous rupture of the spleen is of most unusual occurrence. Up to the present there have been ten instances of this complication of infectious mononucleosis reported. Seven occurred in the American army, one in the British, and two, which I should like to describe briefly, on my own wards in a Canadian Army Hospital. These two cases have been reported before the Annual Meeting of the American Association of Pathologists and Bacteriologists, in March 1946, by Dr. J. H. Fisher of London. The abstract of this paper appears in the May, 1946, number of the *American Journal of Pathology*. Both occurred in young Canadians (aged 21 and 24) who were suffering from typical examples of the anginose form of the disease. Rupture took place towards the end of the second week in each instance. It was heralded by steady epigastric pain which preceded collapse by about an hour. The abdomen was uniformly soft on palpation in the first case, and showed slight resistance in the epigastrium and left hypochondrium in the other. The first patient died within a very few minutes of the time I first saw him. A tentative diagnosis of ruptured spleen was made in the second but he died on the operating table, despite energetic measures at resuscitation, before his abdomen was opened.

Autopsy was carried out on both cases. The essential features were as follows: (1) Marked enlargement of the superficial lymph nodes which were soft, grey, moist and succulent in one case, and soft and purplish-red in the other. The mediastinal, para-aortic, mesenteric, and other internal lymph glands were similarly involved. (2) The spleens were both enlarged, one weighing 400 grams and the other 660 grams. The capsules in both had been stripped almost entirely from the underlying pulp, the region about the hilum being the only place where this did not occur. The mechanism would appear to be subcapsular hæmorrhage, which gradually separated the capsule from the pulp, ballooned it up to the point where it burst, so giving rise to massive intraperitoneal hæmorrhage. The splenic pulp was soft, red in one case and greyish-red in the other. (3) The livers weighed 1,700 and 1,900 grams and were soft in consistency. Cut surface showed a pale yellowish-grey mottled appearance with the usual markings rather indistinct. (4) The kidneys were slightly swollen and cut section revealed the appearance of cloudy swelling. (5) The bone marrow appeared to be grossly normal. (6) The main microscopic features were prominent accumulations of mononucleosis cells in most of the viscera, but especially in liver, spleen, lymph-nodes and kidneys. The bone marrow showed no specific changes.

The final complication of infectious mononucleosis to which I wish to refer is involvement of the central nervous system. This may take the form of meningitis, encephalitis, or both. The neurological symptoms and signs may dominate the clinical picture at the onset, to be followed by glandular enlargement, splenomegaly and changes in the blood, or the reverse may be encountered. Pain in the back of the neck is not uncommon in cases with marked posterior cervical glandular involvement, and at times it is accompanied by voluntary rigidity, which simulates that seen in meningitis. It has been reported that clinical signs of serous meningitis may be present with normal spinal fluid findings, and, conversely, that abnormal spinal fluids may be encountered when clinical signs of meningitis are lacking. In one of Wechsler's cases in which severe frontal headache, vomiting, and moderate neck rigidity were present, the initial examination of the spinal fluid revealed 524 white blood cells, 517 of which were lymphocytes, total protein 284 mgm. %, colloidal gold and Wassermann reactions negative. Repeated lumbar punctures were carried out because of recurrent headache, the ninth and final tap being performed 51 days after the first. At this time there were still 64 cells present, 63 of which were lymphocytes, and the total protein was 34.6 mgm. %. In most of the reported cases, the increase in cells has been much less marked: 12, 16, 28, 34, etc., in association with a slight increase in total protein. Nearly all of these cases made a good clinical recovery in about a month. So far I have not encountered any record of chronic neurological sequelæ, but Thomsen and Vimtrup have reported six cases in which death occurred from respiratory paralysis during the acute phase of the disease.

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RÉSUMÉ

La mononucléose infectieuse, affection relativement fréquente, peut se confondre avec la syphilis secondaire, la rubéole, le typhus et la leucémie aigue. L'étude de la formule sanguine tranche habituellement la question. Cette maladie se complique parfois de cardiopathie, de bronchite, d'albuminurie, d'hématurie, de troubles hépatiques et spléniques. Deux cas mortels d'hémorrhagie de la rate sont rapportés. Parfois, les centres nerveux sont touchés et le tableau rappelle alors celui d'une méningo-encéphalite. On devra rechercher toutes les fois que cette affection est soupçonnée les modifications caractéristiques des mononucléaires.

JEAN SAUCIER

HÆMOGLOBIN LEVELS IN CANADIAN POPULATION GROUPS: CHILDREN AND YOUNG WOMEN*

W. W. Hawkins, B.A., M.Sc., H. J. Leeson, M.D., D.P.H. and E. W. McHenry, Ph.D., F.R.S.[C.]

Toronto, Ont.

THE determination of hæmoglobin has been used frequently in nutrition surveys to provide an indication of adequacy of iron intake. Data are often difficult to interpret for three principal reasons: (1) determinations of hæmoglobin are often made by inaccurate procedures, as by using Sahli or Dare hæmoglobinometers; (2) results are expressed frequently as percentages of some standard which is usually not defined; and (3) there is little agreement as to "normal" values. Because of this last difficulty particularly we are reporting hæmoglobin values obtained in three nutrition studies, covering two groups of elementary school children and a group of university women students.

Several recent reports have provided hæmoglobin values for groups comparable to those discussed here. The Medical Research Council of Great Britain has stated[1] that children, 6 to 13 years, in Great Britain had average levels of 12.4 to 12.7 gm. % (recalculated from the published data which were given in terms of a standard of 13.8 gm.). Macy[2] has reported hæmoglobin levels of 11 to 13 gm. % for eight children who had been maintained on a "completely adequate" diet for eight months. The adequacy of the diet should be questioned since values for five other children, who were said to be from indigent families and who were reportedly suffering from malnutrition, were 13 to 16 gm. %. For girls of 15 to 19, who may be compared with younger university students, the Medical Research Council[1] gave an average value of 13.6 gm. %. Ohlson *et al.*[3] studied hæmoglobin levels in 4,550 college women in the north central United States and found a range of 8.5 to 17.5 gm. %, with an average of 13.4. For 864 women students at McGill University, Pedley[4] reported a range of 10.1 to over 15.6 and the highest value was not stated; 77% of the McGill group had values between 12.4 and 14.7 gm. %.

METHOD

Hæmoglobin was determined in 0.02 ml. of finger-tip blood by the cyanmethæmoglobin procedure described by Collier.[5] If the blood is delivered carefully into water from a previously dry clean pipette, the errors in that part of the method can be minimized. Ten 0.02 ml. quantities taken with the same pipette from a sample of oxalated human venous blood showed a 2% variation in hæmoglobin content. A 3.4% variation was found in values for nine determinations on fully flowing blood from a finger-tip puncture. Great care was exercised in taking and measuring the blood samples and we are of the opinion that precision, greater than that stated above, cannot be attained on a routine basis.

It has been our practice in some cases to store diluted bloods in a refrigerator for periods up to four days before determining hæmoglobin. This was justified by experiments conducted by Mrs. Semmons of these laboratories. Portions of the same sample of blood diluted 1:500 were stored, some at room and some at refrigerator temperature, some with and some without the addition of 2 drops of toluene per 10 ml. The hæmoglobin value for refrigerated diluted blood without toluene remained the same for 4 days. Samples stored at room temperature without toluene increased slightly but were only 4% higher on the fourth day. After 4 days values rose for blood stored without toluene at either temperature. The presence of toluene at either temperature appeared to cause increased values within 4 days.

Diurnal variation has been said to be a factor of consequence in hæmoglobin determinations. We have examined this to a limited extent. Seven human subjects were used, four of whom provided samples on two different days. To minimize experimental error, 2.0 ml. of venous blood were used and determinations were done in duplicate. Depending upon the individual, a variation of 1.5 to 9.3% was shown between 9 a.m. and 5 p.m. A typical picture was an increase of 4 to 5% between 9 a.m. and noon, followed by a slight fall in the afternoon. The variation encountered in duplicate samples from 2.0 ml. of the same blood was 1.3 to 1.5%. Mole[6] has examined the data of McCarthy and

* Department of Public Health Nutrition, School of Hygiene, University of Toronto.