Summary

The insulin equivalence of aspirin has been determined in 14 diabetics with insulin requirements of 12 to 112 units of insulin zinc suspension daily.

Nine patients, who were well controlled with insulin, also had good responses to aspirin. The largest quantity of I.Z.S. replaced completely with aspirin was 48 units; the largest reduction in insulin requirement was 72 units in the patient receiving 112 units daily.

Five patients who were poorly controlled with insulin were not materially improved by aspirin therapy. It was concluded that aspirin was most effective in patients who responded well to insulin, and vice versa. The findings in patients well stabilized with insulin also suggested that the higher the insulin requirement the greater was the amount of hormone that may be replaced by aspirin.

These results place salicylate in the class of promising oral antidiabetic substances, and should stimulate investigations to remove its undesirable effects and to find out how it acts.

Our thanks are due to Miss M. McCombie, of the dietetic department of the Western Infirmary, for supervision of the diets, and to the staff of the unit for invaluable technical assistance.

REFERENCES

- Benedict, S. R. (1911). *J. biol. Chem.*, **9**, 57.
 Lehmann, H., and Silk, E. (1952). *Biochem. J.*, **50**, xxxi.
 Manchester, K. L., Randle, P. J., and Smith, G. H. (1958). *Brit. med. J.*, **1**, 1028.
 Reid, J., Macdougall, A. I., and Andrews, M. M. (1957). *Ibid.*, **2**, 1071.
 — Watson, R. D., and Sproull, D. H. (1950). *Quart. J. Med.*, **19**, 1.
 Trinder, P. (1954). *Biochem. J.*, **57**, 301.

RESPIRATORY VIRUS INFECTIONS IN THE GLASGOW AREA

BY

N. R. GRIST, M.B., B.Sc., F.R.C.P.Ed.

AND

R. G. SOMMERVILLE, M.B.

Sir Maurice Bloch Fellow in Virology

From the Virus Laboratory, University Departments of Bacteriology and Infectious Diseases, Ruchill Hospital, Glasgow

This paper summarizes further investigations of acute respiratory illnesses during two years after the period dealt with in a previous report (Grist *et al.*, 1957). In addition to observations during the epidemic of Asian influenza, further evidence was found of infections with adenoviruses and with agents related to the Sendai virus (Kuroya *et al.*, 1953).

Materials and Methods

Over 1,000 cases were investigated during the period July, 1956, to April, 1958. Most of these were patients admitted to adult and baby pneumonia wards; over 200 were adult cases seen in general practice (Blair *et al.*, 1959). Serological tests of paired sera were made in most cases, but virus isolation was attempted with necropsy material from 32 cases and with throat swabs, garglings, or stools from a number of other cases in hospital, general practice, or seen by public health officers.

Technical methods have been described previously (Grist *et al.*, 1957). So far as was possible, haemagglutination inhibition (H.I.) tests with Asian (A/Singapore/4/57), A-prime (A/Scotland/1/53), and A/PR8 influenza virus were performed in addition to routine complement-fixation (C.F.) tests on sera collected after February, 1957.

Adenovirus Investigations

Rising C.F. antibody titres were shown by 10 patients whose main features are summarized in Table I. Most of these patients had respiratory illnesses, but Case 2

TABLE I.—Cases With Evidence of Adenovirus Infection

No.	Age (Years)	Clinical Features	Adenovirus C.F. Titres	
			"Acute" Serum	"Convalescent" Serum
1	<1	Bronchitis ..	<2	8
2*	2	"Glandular fever" ..	<8	32
3*	3	Pneumonia ..	32	128
4	3	" ..	<4	8
5†	3	Tonsillitis ..	8	64
6	5	Bronchitis ..	<2	8
7	28	Rhinitis ..	<2	16
8	45	Pharyngitis ..	<2	16
9	54	"Influenza" ..	<2	16
10	61	Pharyngoconjunctivitis	8	32

* Monotypic type 2 neutralizing antibody response.

† Type 3 adenovirus isolated from stool.

presented gingivo-stomatitis with ulceration of tongue and exudative tonsillitis, enlarged tender cervical and axillary lymph nodes, and palpable spleen. The blood showed leucocytosis of 15,000 per c.mm., with 65% lymphocytes. The Paul-Bunnell test was negative on three occasions. The throat swab contained normal mixed bacterial flora. The illness did not respond to penicillin, but resolved slowly over a fortnight. Neutralization tests showed no antibodies to adenovirus types other than type 2, which gave titres of 8 and 16 in consecutive sera. A monotypic type 2 adenovirus response was also given by Case 3 (N.T. titres <8 and 32). Neutralizing antibodies to several adenovirus types were developed by three adults tested, the major responses being to type 7 (Case 7), type 2 (Case 9), types 2 and 3 (Case 10). Type 3 adenovirus was isolated from Case 3.

Sendai Virus Investigations

Serological tests showed rising C.F. titres in 10 cases whose main features are summarized in Table II. In view of the reported antigenic overlap between Sendai and mumps viruses, sera from these cases were also tested with mumps antigens where possible. The results, summarized in Table III, show various combinations of reactions. Two Cases (Nos. 12 and 19) showed increasing titres of mumps antibody, which in Case 19 were confined to the "V" antigen.

TABLE II.—Cases With Serological Response to Sendai Virus

No.	Age (Years)	Clinical Features	Sendai C.F. Titres		
			"Acute" Serum	Second Serum	Third† Serum
11	1	Bronchitis ..	<2	16	16
12*	2	Pneumonia ..	<4	8	16
13	4	" ..	<8	32	—
14	7	" ..	<4	8	—
15	20+	"Influenza" ..	<8	16	—
16*	20+	Febrile catarrh ..	16	64	—
17	31	Pneumonia ..	<8	16	8
18	49	" ..	<4	16	8
19*	55	" ..	4	64	—
20*	78	" ..	<8	64	—

* Also tested for mumps (Table III).

† Taken in 5th week after onset of illness.

TABLE III.—Cases Tested With Mumps and Sendai Antigens

No.	Age (Years)	Day of Illness when Serum Taken	C.F. Titres with Indicated Antigens		
			Sendai	Mumps "S"	Mumps "V"
12	2	6	<4	—	—
		16	8	<4	<4
		32	16	<16	<16
16	20+	?	16	8	8
		22	64	8	8
19	55	14	4	<4	4
		27	64	<4	32
20	78	3	<8	—	—
		13	64	<4	<4

Influenza Virus Investigations

During the whole period no type B and only one type C infection was detected. No outbreak of influenza was experienced during the winter of 1956–7, and serological evidence of type A infection before the Asian outbreak was limited to one case in October, 1956, and 13 in the period March–May, 1957. No strains of virus were isolated during this period, but H.I. tests showed antibody responses predominantly to A-prime virus. The main Asian influenza epidemic occurred during August–October, 1957, with a minor second wave of infection in January–March, 1958 (Horne, 1957; Grist, 1958a, 1958b). A comparison of these two waves of influenza will be reported separately (Grist, to be published). Sixteen strains of virus were isolated during the first wave and 10 during the second, 12 from post-mortem lung specimens. Serological tests by Dr. A. Isaacs at the World Influenza Centre, and cross-H.I. tests performed in this laboratory, using antisera from fowls immunized by serial intraperitoneal injections, showed no evidence of antigenic variation during the outbreak.

Six cases of suspected influenzal encephalitis were examined: three adults showed no laboratory evidence of infection, and a final diagnosis of cerebrovascular incident was reached in one of these. Influenza infection was confirmed serologically in the following three cases.

Case A.—Male, aged 9 years: "Influenzal" illness for two days in September, 1957, followed by vomiting, convulsions, and delirium for one day. Admitted dehydrated with tracheitis, Babinski sign positive on left side only, reflexes brisk in upper limbs but knee-jerks absent. The cerebrospinal fluid was normal. Improved to full recovery. Type A influenza C.F. titre rose from <8 (day 4) to 64 (day 13).

Case B.—Female, aged 12 years: "Influenzal" illness for four days in October, 1957, followed by recovery for two days, then coma progressing to death on eighth day after first symptoms. Type A influenza C.F. titre was 32 on seventh day. No virus was recovered from brain or lung removed at necropsy, which showed the presence of pneumonia and cerebral oedema with congestion of cortex, midbrain, and pons, and stippling of white matter. Microscopical examination showed no evidence of encephalitis.

Case C.—Female aged 18 years: "Influenzal" illness for one week in April, 1958, recovery for three days, then onset of restlessness and insomnia on ninth day. On admission, found to be hallucinated, inattentive, with slurring speech. Transferred from Ruchill to Stobhill Hospital as suspected schizophrenic, but improved and was dismissed well seven weeks after onset of symptoms. Investigations negative except for type A influenza C.F. titre 128 on both 14th and 24th days of illness.

Discussion

Our findings provide further evidence of the definite but small part played by adenoviruses in the causation

of acute respiratory illnesses in the civilian population. In view of the recognized association between infection by certain adenoviruses and lymphoid hyperplasia, it is of interest that Case 2 indicates that these agents may also contribute to the "glandular fever" syndrome.

Since 1954 (Grist *et al.*, 1957) our tests have revealed altogether 19 cases of antigenic experience with an agent related to Sendai virus. The findings do not prove that these infections were caused by Sendai virus itself, particularly as this virus has been found to share antigens with mumps virus (Gardner, 1957; DeMeio and Walker, 1957), and with haemadsorption viruses of type 2 and perhaps type 1 (Chanock *et al.*, 1958). Since mumps virus also shares antigens with croup-associated virus (Chanock, 1956) and with type 1 haemadsorption virus (Chanock *et al.*, 1958), there is evidence of the existence of a group of myxoviruses with complex antigenic interrelationships. The various types of antibody response shown by our four cases tested with both mumps and Sendai antigens (Table III) may thus reflect the variety of antigenic composition of the infecting viruses, and perhaps also differing previous antigenic experience of such myxoviruses by the four patients.

The general features of the epidemic of Asian influenza in the Glasgow area resembled those reported from other parts of Britain. No antigenic variation of the virus was detected during the course of the outbreak, and the population was apparently immunized so adequately by the main autumn epidemic that only a minor resurgence of infection developed during the later months of winter, which are the usual time of seasonal prevalence of influenza in this area.

Our findings throw no new light on the relationship between influenza and encephalitis, but add another three to the cases in Britain recently reported by Dubowitz (1958), McGill and Goodbody (1958), Stephens and Cappell (1958), Morgan and Pickup (1958), and Dunbar *et al.* (1958).

Summary

Over 1,000 cases of acute respiratory illness were investigated virologically during two years. Ten cases of adenovirus infection were detected; one of these presented the features of glandular fever.

Ten cases developed complement-fixing antibodies to Sendai virus; of four such cases tested with mumps antigens, only two developed antibodies—one to both "V" and "S," one to "V" antigen alone. These findings suggest infection with a myxovirus related to but not necessarily identical with Sendai virus.

Type A influenza virus infections were detected during the autumn epidemic of 1957 and in the early months of 1958. No antigenic variation of the virus was detected. Three cases of encephalitis with serological evidence of influenza were encountered during the outbreak.

We are grateful to our numerous colleagues in hospital, general practice, and public health services for their co-operation; to Dr. A. Isaacs, of the National Institute for Medical Research, for supplying Asian prototype virus and for strain-identification of influenza viruses; to Dr. G. B. S. Roberts, University Lecturer in Pathology of Infectious Diseases, for necropsy findings in encephalitis Case B; to Dr. H. Gillies, of Stobhill Hospital, Glasgow, for clinical details of encephalitis Case C; and to Messrs. C. McLean, H. G. Carson, J. Kerr, and T. Roy for technical assistance during the study.

REFERENCES

- Blair, W., Brown, W. Kerr, Caldwell, W. F., Clarke, A., Dunn, S., Primrose, D., Stewart, T. F., Grist, N. R., and Sommerville, R. G. (1959). *Brit. med. J.*, 1, 422.
- Chanock, R. M. (1956). *J. exp. Med.*, 104, 555.
- Parrott, R. H., Cook, K., Andrews, B. E., Bell, J. A., Reichelderfer, T., Kapikian, A. Z., Mastrotta, F. M., and Huebner, R. J. (1958). *New Engl. J. Med.*, 258, 207.
- DeMeio, J. L., and Walker, D. L. (1957). *J. Immunol.*, 78, 465.
- Dubowitz, V. (1958). *Lancet*, 1, 140.
- Dunbar, J. M., Jamieson, W. M., Langlands, J. H. M., and Smith, G. H. (1958). *Brit. med. J.*, 1, 913.
- Gardner, P. S. (1957). *Ibid.*, 1, 1143.
- Grist, N. R. (1958a). *Hi th Bull. (Edinb.)*, 16, 5.
- (1958b). *Ibid.*, 16, 56.
- Sommerville, R. G., and Carson, H. G. (1957). *Brit. med. J.*, 1, 378.
- Horne, W. A. (1957). *Influenza 1957: Report on the Epidemic in Glasgow*. Corporation of Glasgow, Health and Welfare Department.
- Kuroya, N., Ishida, M., and Shiratori, T. (1953). *Yokohama med. Bull.*, 4, 217.
- McGill, R. J., and Goodbody, R. A. (1958). *Lancet*, 1, 320.
- Morgan, D. M., and Pickup, J. D. (1958). *Brit. med. J.*, 1, 263.
- Stephens, J. H., and Cappell, D. F. (1958). *Lancet*, 1, 381.

ANAEMIA AND POLYCYTHAEMIA IN UNIOVULAR TWINS

BY

MARGARET M. KERR, M.D., D.C.H.

From the Paediatric Unit, the Glasgow Royal Maternity and Women's Hospital

The simultaneous occurrence of anaemia and polycythaemia in newborn monozygotic twins was first reported by Herlitz (1941-2), who described two such instances. Klingberg *et al.* (1955) and Bergstedt (1957) have reported similar cases, but none has so far been reported in Great Britain. In the past three years the syndrome has been recognized on four occasions in the Glasgow Royal Maternity and Women's Hospital. It seems worthy of comment, since in severe cases prompt treatment may be required. The findings in the cases previously reported are summarized in Table I, and in

TABLE I.—Summary of Previously Reported Cases

Author	Weight in g.	Sex	Hb	R.B.C. mil./c.mm.	Outcome
Herlitz (1941-2)	1,580	M	50%	1.94	Well at 6 years
	2,580	M	160%	7.02	
	3,030	F	200%	6.86	Died at 2 months. "Bronchitis"
	2,220	F	65%	2.27	
Klingberg <i>et al.</i> (1955)	2,690	F	25.2 g./100 ml.	7.47	Uneventful
	1,770	F	3.7 "	1.85	
Bergstedt (1957)	3,030	F	23.6 "	5.90	Well at 5 months
	1,810	F	13.6 "	3.90	

Table II the peripheral blood values in the present series are given. The following is a short history of the births and clinical findings in the four sets of twins.

Case 1

This patient, a 3-gravida, was delivered spontaneously of twin boys after 37 weeks' gestation. She was known to be rhesus-negative, but no antibodies had been detected. Apart from hydramnios, the pregnancy had been uneventful and the onset of labour was spontaneous.

The first twin, an assisted breech delivery, cried lustily at birth and weighed 2,570 g. The second child, a spontaneous vertex delivery, cried shortly after birth and weighed 2,680 g. This infant looked pale, the spleen tip was palpable, and the liver was enlarged to three fingerbreadths below the costal margin. Examination of the peripheral blood revealed a severe anaemia with a reticulocytosis, and many erythroblasts were to be seen in the film. Since the

mother was known to be rhesus-negative, erythroblastosis foetalis was the presumptive diagnosis. The Coombs test on the cord blood was, however, persistently negative. Despite this finding, an exchange transfusion of 500 ml. was carried out.

The results of the examination of the cord blood of the first twin showed that he also had a negative Coombs test but that the haemoglobin level was remarkably high. Full blood examination confirmed the polycythaemia, but there was no excess of reticulocytes and the blood film was normal. Venesection was considered, but thought to be unnecessary.

The single placenta, which had been retained *in utero* and was therefore not available for inspection when the anaemia was discovered, was quite striking in appearance, in that one half was grossly congested with tortuous vessels, while the other half was pale with collapsed vessels.

Both babies made good progress. The plethoric infant had congested hands and feet for several days, and even on the eleventh day of life the haemoglobin remained very high at 20.5 g. per 100 ml.

Case 2

This patient, a nullipara, was well throughout her pregnancy, went into labour spontaneously after 34 weeks' gestation, and had normal vertex deliveries of twin girls. The first infant weighed 1,470 g. and on admission to the

TABLE II.—Peripheral Blood Values in the Present Series

Case No.	Weight in g.	Sex	Peripheral Blood			
			Hb (g./100 ml.)	R.B.C. (mil./c.mm.)	Retic. (%)	Film
1 {	2,570	M	21.8	8.66	2.3	Occasional erythroblasts
	2,680	M	7.7	2.20	19.0	Very numerous erythroblasts
2 {	1,470	F	20.0	5.57	2.2	Occasional erythroblasts
	1,080	F	8.3	2.28	15.0	Numerous erythroblasts
3 {	3,230	F	19.2	4.61	3.5	No abnormality
	2,190	F	14.1	4.42	7.3	" "
4 {	2,410	F	14.7	4.25	—	—
	2,490	F	21.8	7.00	—	—

premature baby unit was intensely cyanosed and had generalized oedema. The spleen was not palpable, but the liver was enlarged to three fingerbreadths below the costal margin. It was noted that the infant was plethoric compared with its twin, and this was confirmed by examination of the peripheral blood (Table II). Although the baby's colour improved with oxygen, respirations were never well established. At 3 hours her condition deteriorated. Venesection of 30 ml. of blood did not produce any improvement, and she died four hours after delivery. At necropsy there was congestion of all organs, the brain showing the presence of numerous small haemorrhages in the subependymal region.

The second twin weighed only 1,080 g. and cried shortly after birth. She was strikingly pale compared with her sister, and examination of the peripheral blood confirmed the anaemia. The Coombs test was negative.

Four and a half hours after delivery a transfusion of 40 ml. of blood was given into the umbilical vein. Her condition was satisfactory, considering the weight, until she was 13 hours old. Thereafter she had frequent apnoeic attacks and died at 18 hours. At necropsy there was some congestion of cerebral vessels, haemorrhage in the left adrenal gland, and widespread hyaline membrane formation in the lungs.

The placenta in this case was similar to that of the first, one side being grossly congested while the vessels of the other half were collapsed.

Case 3

This patient, a 4-gravida, was well throughout her pregnancy and went into labour spontaneously at term. The first twin was a spontaneous vertex delivery and cried at birth. She weighed 3,230 g. and was admitted to the well-baby nursery. At the age of 12 hours she was transferred