

INFLUENZA EPIDEMIC IN SINGAPORE CHILDREN

CLINICAL IMPRESSIONS

BY

YE OH OON SWEE, M.B., B.S.

AND

HELEN DOURADO, M.B., B.S.

From the Paediatric Unit, the General Hospital, Singapore

An epidemic of influenza swept over Singapore during May, 1957, and spread to the Federation of Malaya. Though both children and adults were affected, only the children who were admitted into the paediatric unit of the General Hospital, Singapore, are discussed here. It must be emphasized that during the influenzal epidemic only the severe cases, especially those with fits, were admitted. The less severe cases were treated in the out-patient department.

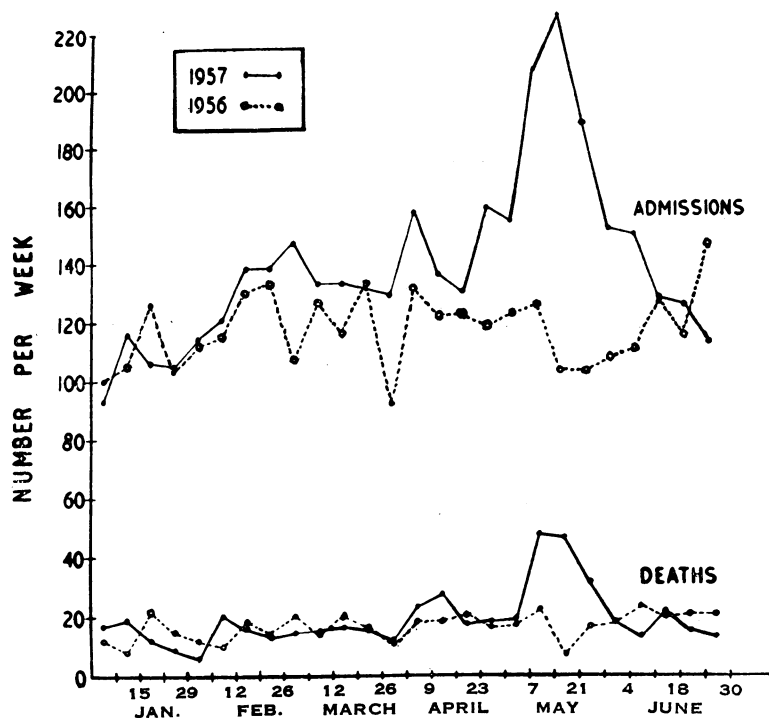
The 250 cases of influenza diagnosed clinically are discussed. In nine cases virus studies were done (see Table II). Often a history was obtained of other members of the family being affected with milder forms of the disease. To ensure an accurate clinical record the medical staff of the paediatric unit met frequently during and after the epidemic.

The increase in the number of admissions and deaths during the epidemic can be seen from the Chart and Table I.

The rise in the number of deaths can be explained by the large number of admissions, as the mortality rate remained about the same.

TABLE I.—Number of Weekly Admissions and Deaths (January–June, 1957)

Date	Admissions	Deaths	Date	Admissions	Deaths
January 1–7	93	17	April 2–8	157	23
" 8–14	116	19	" 9–15	136	27
" 15–21	106	12	" 16–22	130	17
" 22–28	105	9	" 23–29	159	18
" 29–			" 30–		
February 4	114	6	May 6	154	19
" 5–11	121	20	" 7–13	206	47
" 12–18	139	16	" 14–20	224	46
" 19–25	138	13	" 21–27	187	31
" 26–			" 28–		
March 4	147	14	June 3	151	18
" 5–11	133	15	" 4–10	149	13
" 12–18	133	16	" 11–17	127	21
" 19–25	130	15	" 18–24	125	15
" 26–			" 25–30	112	13
April 1	129	12			



Showing the increase in the number of admissions and deaths during the epidemic, as compared with the corresponding period in 1956.

Clinical Manifestations

Age.—The maximum incidence occurred in the 1–5-year age group, though the youngest child affected was 21 days old.

Sex.—No discrepancy in the sex distribution was noticed.

Symptoms.—The onset was typically sudden, the disease reaching its maximum intensity in one to two days. The attack often started with a mild dry irritative cough, followed by a sudden onset of high fever, unassociated with rigors. Vomiting was common in younger children and occurred soon after taking feeds. Fits were very common. In 110 out of 250 cases fits were the prominent feature and were often the symptom that induced the parents to bring the child to hospital. The fits occurred suddenly and lasted for several minutes; repeated attacks one after the other were the rule rather than the exception.

Physical Examination.—The temperature ranged from 100 to 105° F. (38.7 to 40.6° C.), though hyperpyrexia of 105 to 107° F. (40.6 to 41.7° C.) was not unusual. Flushing of the skin was common, and in a few cases patches of erythematous weals of varying sizes, resembling urticaria, were seen. The throat was frequently red and granular. Nasal discharge was not very common and conjunctival injection was seen in only a few cases. The pulse was usually rapid, and a few cases showed peripheral circulatory collapse. Clinically the lungs were usually clear, but in a third of the cases crepitations and rhonchi revealed bronchitis and bronchopneumonia. The abdomen was soft and not tender, the liver and spleen were usually not enlarged, though in a few cases the spleen was just palpable and disappeared when the fever subsided.

The lymph nodes were not enlarged. In the central nervous system, drowsiness was a common feature, while those children with fits were often admitted in coma. Neck rigidity was not infrequent and Kernig's sign was positive in a few cases. Transient fine involuntary tremors of the hands were also seen in a few cases.

Investigations.—The total white-cell count was often normal, though in the first one or two days leucopenia, and in the next few days leucocytosis, were noted. A lumbar puncture was done in all cases presenting with fits, and in all the cerebrospinal fluid was normal. A radiograph of the chest was normal or showed increased hilar markings. In cases complicated by bronchopneumonia patchy opacities were seen. Serological tests on paired sera were done on nine cases. The first specimen (acute serum) was taken on the day of admission, and the next specimen (convalescent serum) 6–16 days later. By the haemagglutination inhibition tests, using the influenza type A/Singapore 1/57 strain, which was isolated from an adult during the same epidemic, five cases were positive and four were negative (see Table

II). Some of the cases giving a negative result may have been due to a different strain.

TABLE II

Case No.	Age	Acute Serum	Convalescent Serum
1	3 years	Positive (7)	Positive (14)
2	9 months	Negative (8)	" (20)
3	2 years	" (8)	" (19)
4	11 months	" (4)	" (20)
5	2 years	" (3)	" (13)
6	3 "	" (4)	Negative (10)
7	1 year	" (2)	" (9)
8	3½ years	" (4)	" (11)
9	3 "	" (2)	" (12)

Figures in parentheses represent the day of illness on which blood specimens were taken.

Course.—The fever lasted three to five days and convalescence was rapid in the uncomplicated cases.

Variations According to Age

Some features were more common in certain age groups than in others.

Neonatal Period.—Very few infants under 1 month were admitted into the hospital with influenza.

Infants.—Vomiting of feeds was common, associated with parenteral diarrhoea in some cases.

1-5 Years.—This age group suffered the brunt of the disease and included the largest number of severe cases with a high mortality. 151 of the 250 cases belonged to this age group, and of the 30 deaths 20 were in this group. Fits were characteristic and often followed one another in rapid succession. Peripheral circulatory collapse was the presenting feature in a few cases, and might even develop during stay in hospital. The onset was sudden. The child was comatose. The pulse was not palpable, and the blood pressure could not be recorded. The axillary temperature might be normal, but the rectal temperature was 105 to 107° F. (40.6 to 41.7° C.). The mortality in these cases was very high.

5-10 Years.—These children often complained of headache and general body aches. Constipation and profuse sweating were common. Epistaxis was almost confined to this group. The bleeding was so severe in some cases as to cause alarm, and often the blood from the nose was swallowed, and vomited later as coffee-ground material. Vomiting of clots of blood was seen in a few cases.

Pulmonary Complications

Persistent cough was the commonest complaint among the cases followed up as out-patients. Bronchitis and bronchopneumonia were seen in a third of the cases. These responded to sulphonamides or antibiotics. Two cases of lobar pneumonia were observed.

Lung Abscess.—There were three cases. A 5-year-old girl had cough and pain in the left chest for one week before admission: she had an abscess and consolidation of the lingula. A 6-year-old boy, with a history of fever and cough for nine days and breathlessness for four days, had consolidation and multiple abscesses in the right upper lobe. An 8-year-old boy had fever, breathlessness, and cough productive of blood-tinged sputum for 40 days. He had an abscess in the right lung which had burst and produced an empyema. It was interesting to note that these cases developed symptoms during the last two weeks of the epidemic.

Unilateral Empyema.—There were two cases. One case, referred to above, was the result of an abscess bursting into the pleural cavity. A 7-year-old girl after a week of fever and three days of cough and pain in the right chest was admitted with empyema on the right side.

Bilateral Empyema.—Two boys, 8 and 9 years old, were admitted with bilateral empyema. One gave a five-day history of fever and cough before admission, the other gave a three-day history. The onset and symptoms in both were very suggestive of influenza.

Neurological Complications

Tremors.—A 3-year-old girl had influenza with fits and bronchopneumonia. She gradually improved. On the tenth day of the illness she had coarse tremors and ataxia of all limbs, and this persisted till her discharge on the 28th day. A month later, in the follow-up clinic, the tremors had disappeared, but her legs were weak. The cerebrospinal fluid examined on the 2nd and 19th days was normal.

Hemiplegia.—A boy aged 2 years had influenza with fits and bronchopneumonia. He was semicomatose and remained in that state for the next few days. On the sixth day of illness he was noticed to have a spastic hemiplegia on the left side. On the seventh day he was fully conscious. On the tenth day the spasticity had disappeared on the left side but appeared on the right side. This developed into a right flaccid hemiplegia without any hemianopia. On discharge on the 34th day he could move his right upper limb slightly, but was flaccid in the right lower limb. Prior to the illness he was able to walk and to recognize, call, and play with his parents, whereas on discharge he was unable to sit up and ignored his parents completely. The cerebrospinal fluid examined on the 4th, 9th, and 17th days was normal.

Delayed convalescence was seen in the severe cases. Lethargy in the convalescent period was not uncommon. A few children, who prior to the attack of influenza were able to run about, complained of marked weakness of the legs for one to two months after the illness.

Second attacks of influenza were seen in a few cases. The first attack was mild and the child was not taken to see a doctor. The diagnosis was based on a typical history of slight fever, cough, and coryza. The second attack occurred 7 to 10 days later, with a high temperature, and required admission into hospital.

Prognosis and Treatment

The majority of cases did well. Untoward signs were hyperpyrexia, persistent fits, and peripheral circulatory collapse. The majority of deaths occurred in the first 24 hours after admission.

Among the 250 cases diagnosed clinically as influenza there were 30 deaths. Permission for necropsy was obtained in 25 cases, and the post-mortem diagnoses were: influenzal bronchopneumonia in 13 cases, bronchopneumonia in 11 cases, and bronchopneumonia with enteritis in one. It was our impression that many clinical cases of influenza were recorded as bronchopneumonia.

During the period of the epidemic, 1,231 patients were admitted, of whom 196 died. In 175 cases necropsy was performed. The post-mortem diagnoses were as follows: bronchopneumonia, 51; influenzal bronchopneumonia, 24; bronchopneumonia with gastro-enteritis, 13; lobar pneumonia, 10; collapse of lung, 4; acute bronchitis, 3; gastro-enteritis, 25; purulent meningitis, 7; congenital heart, 5; encephalitis, 3; miscellaneous, 30.

No specific drug was found to be effective against influenza. Treatment was mainly symptomatic. The sulphonamides and antibiotics were useful in preventing and treating secondary infections. Cortisone was used for some cases with circulatory collapse. It appeared to be of value in the case of a 4-year-old girl who had peripheral circulatory collapse and hyperpyrexia, and who was in coma for two days.

Case Reports

Case 1. A Typical Case with Fits.—A 3-year-old Indian boy was admitted on May 8, 1957. For three days he had a running nose, and at 10 a.m. on the day of admission he had a sudden onset of high fever. At 10.30 a.m. he had a fit, consisting of clonic spasms with loss of consciousness. At 11 a.m. he had another fit. On examination he was conscious but irritable, and his temperature was 104° F. (40° C.). The throat was red. The pulse was 160 a minute. There was nothing abnormal in the heart, lungs, or abdomen. There was no neck rigidity, and Kernig's sign was negative. Another fit occurred in the ward, and this was controlled by

an injection of paraldehyde. W.B.C. was 13,800 (P. 85%, L. 5%, M. 7%, E. 3%). C.S.F. cells, 1; total protein, 20 mg. per 100 ml.; globulin absent; sugar present; chloride 700 mg. per 100 ml. He was treated with sulphadiazine and alkaline potassium citrate mixture. The temperature subsided to normal on the third day of admission and he was discharged on May 11.

Case 2. Epistaxis as a Presenting Symptom.—A 5-year-old Chinese boy was admitted on May 15 with the complaint of fever for four days, bleeding from the nose the night before admission, and vomiting of dark-coloured material on the day of admission. On examination the temperature was 101° F. (38.3° C.). There was fresh bleeding from the nose. There were no petechiae or ecchymoses in the skin. Nothing abnormal was found in the heart, lungs, abdomen, or nervous system. In the ward he vomited coffee-ground material. The epistaxis was controlled by packing the nose with gauze soaked in adrenaline. W.B.C. was 3,600 (P. 67%, L. 27%, M. 6%, E. 0%). The platelet count was 90,000 per c.mm. and the next day it was 110,000 per c.mm. The temperature became normal and he was discharged on May 17.

Case 3.—A 3-year-old Chinese boy was admitted on May 20 at 1 a.m. He had fever and cough for one day, and on the day of admission he passed loose motions on four occasions. He had a fit during the night. On examination he was conscious. The temperature was 104° F. (40° C.). The skin was hot and dry; the throat was red and granular, and the tonsils were enlarged. The pulse was 140 a minute. There was nothing abnormal in the heart, lungs, or abdomen. There was no neck rigidity, and Kernig's sign was negative. W.B.C. was 8,900 (P. 83%, L. 12%, M. 4%, E. 1%). He died the same day at 9.15 a.m. *Necropsy Report* (Dr. C. S. Muir): The heart appeared normal, as were the pharynx and larynx. The trachea was oedematous and showed slight congestion. The right lung showed a violaceous mottling with a large collapsed area 3 by 9 by 3 cm. at the base of the lower lobe. The cut surface showed bronchopneumonic change. The left lung showed bronchopneumonic change. The large intestine showed a few small ulcerated areas about 0.5 cm. across. The liver showed fatty change. The renal tract appeared normal. The pancreas, adrenals, thyroid, and spleen appeared normal. The brain was congested. The cause of death was influenzal bronchopneumonia.

Case 4. Case with Peripheral Circulatory Collapse.—An 8-months-old male Chinese child was admitted on May 20. For the last three days he had diarrhoea, passing watery yellow stools 10 times a day, and for two days had slight fever and vomited his feeds. On examination he was sitting up in bed. His temperature was 101° F. (38.3° C.) and he was not dehydrated. The throat was red and the tonsils were enlarged. There was nothing abnormal in the heart, lungs, abdomen, and central nervous system. On the morning of May 21 the temperature was normal. He was taking his feeds well. The stools were still watery. At 2.10 p.m. he suddenly had peripheral circulatory collapse. He was comatose. There was peripheral cyanosis. The pulse was not palpable. Respiration was rapid and shallow. The axillary temperature was 99° F. (37.2° C.), but the rectal temperature was 107° F. (41.7° C.). In spite of active sponging he died at 2.30 p.m. *Necropsy Report* (Dr. T. Balasingham): The child was well nourished. The heart showed slightly dilated right chamber. The muscle and valves were normal. The mucosa of the larynx and trachea was injected, and the lumen contained excess mucus. The lungs were slightly voluminous and reddish in colour. Both lungs showed patches of bronchopneumonia, and these areas were friable. The mucosa of the bronchi was injected. The spleen was twice the normal size, its capsule being tense. The pulp was swollen, red, and firm. Lymph follicles were indistinct. The liver and kidneys showed cloudy swelling. The stomach and intestines were normal. The mesenteric glands were prominent. The brain was injected. The cause of death was bronchopneumonia, probably influenzal.

Summary

An account is given of the clinical impressions of the influenzal epidemic as seen in 250 cases admitted into the paediatric unit of the General Hospital, Singapore.

The common presenting symptoms were sudden onset of fever, cough, and fits. The 1-5-year age group appeared to be most affected.

The main complications were pulmonary and neurological.

The number of admissions and deaths increased considerably during the epidemic, and the causes of death as revealed by necropsy are given.

There was no specific treatment.

Four typical cases with different features are described.

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RAPID COLORIMETRIC MICRO-METHOD FOR ESTIMATING GLUCOSE IN BLOOD AND C.S.F. USING GLUCOSE OXIDASE

BY

J. E. MIDDLETON, B.M., M.R.C.P.

Lecturer in Clinical Pathology

AND

W. J. GRIFFITHS, Ph.D., B.Sc., A.R.I.C.

Chemical Pathologist

St. Thomas's Hospital, London

The availability of glucose oxidase (notatin), first described by Müller (1928) and studied in detail by Keilin and Hartree (1948a), an enzyme which specifically oxidizes β -glucose to gluconic acid with the formation of hydrogen peroxide, has resulted in the development of rapid qualitative tests for glucose in biological fluids and especially in urine (Adams, Burkhart, and Free, 1957; Luntz, 1957).

The use of this enzyme for the quantitative estimation of glucose has also been described: Keilin and Hartree (1948b) measured the oxygen uptake during the reaction, and Froesch and Renold (1956) the decrease in copper-reducing ability after complete destruction of the glucose by the enzyme. In both these methods the hydrogen peroxide formed was decomposed by catalase. However, while they are accurate these procedures are too time-consuming for routine clinical work.

Keston (1956) and Teller (1956) showed that when peroxidase is employed instead of catalase and a suitable chromogenic oxygen acceptor is added to the system, the colour produced is a measure of the amount of glucose originally present. The commercial urine-testing strips "clinistix" and "tes-tape" utilize this reaction, and Kohn (1957) has described the use of clinistix for the rapid but approximate determination of blood glucose.

The work here described was initiated with the object of devising a rapid and simple enzyme method which could be employed when a large number of blood