

ASIAN INFLUENZA IN SOUTH AFRICA

A LABORATORY AND CLINICAL STUDY OF AN OUTBREAK ON THE SIMMER AND JACK MINE

M. WESTWOOD, B.Sc.

South African Institute for Medical Research

P. SMIT, M.B., CH.B., D.T.M. & H.

Group Research Medical Officer, New Consolidated Gold Fields

D. OBERHOLZER, M.B., CH.B.

Assistant Senior Medical Officer, Simmer & Jack Mine

In South Africa in 1957 influenza first occurred during the late autumn and early winter months—April to June—when medical practitioners reported an increase in respiratory illnesses amongst the European population. Unfortunately, as influenza is not a notifiable disease statistical support is not available but the outbreak appeared to be of epidemic proportions and specimens were received in the laboratory from all provinces of the Union.

Virus was isolated from 3 of these specimens and from the lung exudate of a woman who died suddenly of a fulminating pneumonia on 20 June. The strain isolated was the same as an Influenza A-prime strain isolated in Holland in 1956 and designated by the World Influenza Centre A/Nederlands/36/56.

This outbreak appeared to have no effect on the course of the epidemic of Asian influenza which followed a few weeks later. The Asian strain of influenza virus had appeared in Hong Kong and Singapore in April 1957 and spread rapidly throughout the East. The first intimation of its occurrence in South Africa was from the gold mines near Johannesburg,

where large numbers of the African labour force were suddenly attacked by a mild respiratory illness resembling influenza. Laboratory confirmation followed soon after the mine medical officers had provided material for investigation.

As this virus was a new antigenic variant it was anticipated that influenza might reach pandemic proportions and precautionary measures were taken by all health authorities to control the spread of the disease. Provision was made for the hospitalization, nursing and feeding of large numbers of patients and for the vaccination of medical officers and nursing staff.

This report covers the epidemic amongst 109,961 African labourers employed by the three Mining Groups, New Consolidated Gold Fields, Anglo-Vaal, and General Mining, with a more detailed report on the Simmer & Jack Mine and the laboratory findings in 6 cases studied.

This epidemic of Asian influenza was responsible for a great increase in the incidence of respiratory infections in the African labour force of the gold mines, as is shown in Fig. 1. The epidemic was sudden in onset and of about

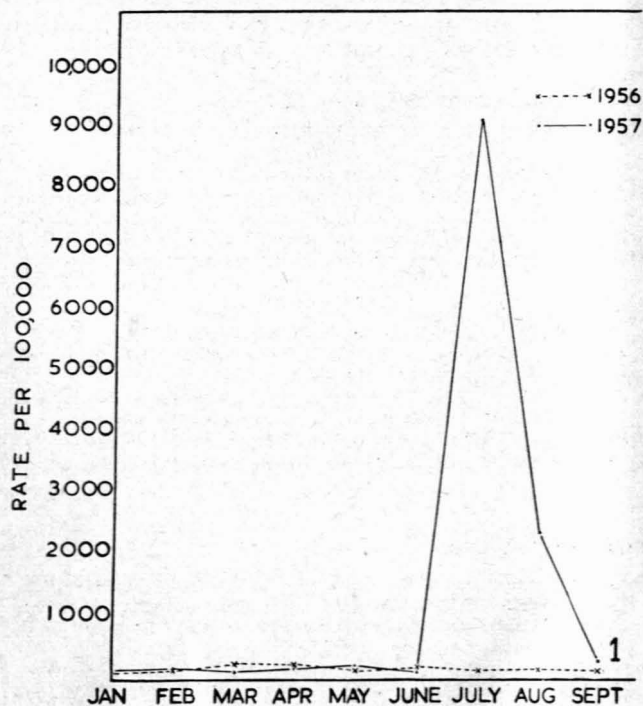


Fig. 1. Influenza in the gold-mining industry.

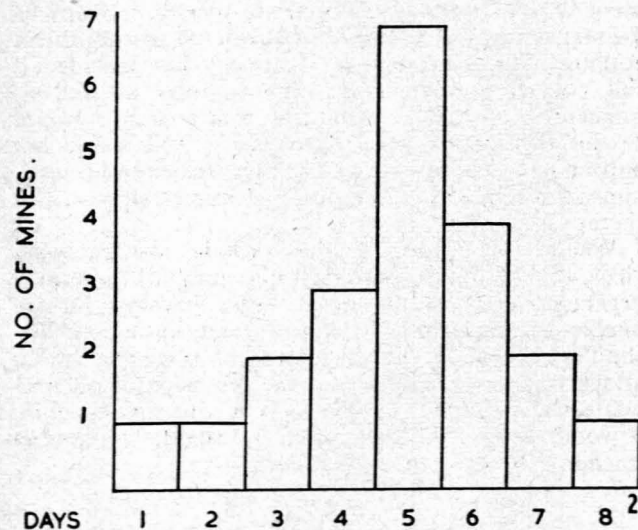


Fig. 2. Showing day on which maximum number of cases occurred (by mines).

4 weeks' duration. Fig. 2 shows the day on which the maximum number of cases occurred at each of the 21 mines in this group. It can be seen that while in one mine the peak of admissions was on the 1st day, in most of them the peak was on the 5th day.

During an epidemic of this nature it is difficult to distinguish between true influenza and other respiratory illnesses without laboratory confirmation of each case. For this reason only those cases which were detained for 24 hours or longer have been included in this report, although it is fully realized that many of the one-day illnesses were cases of influenza. Table I illustrates the morbidity rates on the various mines, and it is

TABLE I. INCIDENCE OF INFLUENZA AT 21 MINES

Mine	Total Complement	Cases of Asian Influenza	% of Complement with Influenza
A	6,581	1,102	16.74
B	5,283	480	9.08
C	5,563	646	11.61
D	5,047	218	4.32
E	4,267	279	6.54
F	5,426	948	17.47
G	2,798	281	10.04
H	1,157	90	7.78
I	6,668	494	7.41
J	1,562	180	11.52
K	681	75	11.01
L	7,777	963	12.38
M	4,833	396	8.19
N	8,373	1,780	21.24
O	11,771	2,731	23.20
P	2,241	501	22.36
Q	7,175	1,809	25.21
R	6,718	704	10.48
S	6,794	1,414	20.81
T	1,957	168	8.58
U	7,289	1,757	24.10
Total ..	109,961	17,034	15.49

% hospitalized=58.8, rest bedded in Compound.

interesting to note the marked variation irrespective of the size of the mine. There appears to be no obvious explanation for this variation; a study of the period of employment and the area of tribal origin of the individuals appeared to be of no significance.

The clinical picture in most cases was similar. The patients complained of cough—usually non-productive—pain in the chest, headache, sore throat, and generalized body pains; a number of the patients felt depressed and showed loss of appetite. Pyrexia in most cases was of sudden onset, varying between 100°F and 104°F, and had dropped by the 2nd or 3rd day of illness. In 75% of cases clinical findings were *nil* apart from fever. More severe cases appeared to predominate later in the epidemic; these showed chest signs and prostration was great, while epistaxis was frequently noted. Relapses were few and may possibly be accounted for by superimposed infections. Most cases were discharged between the 3rd and 6th days, but a few were detained for 14 days.

Only 3 deaths were reported; autopsy showed one of these to be due to lobar pneumonia and 2 to bronchopneumonia. These may well have been primary cases of influenza but no laboratory confirmation was sought

CLINICAL HISTORIES OF THE 6 CASES STUDIED

Case 1. Coy. no 11048

Temperature on admission 102°F, rose to 103°F the following day but dropped to normal by the 3rd day. Complained of headache and chest pains, there were no physical signs on examination. Discharged after 8 days in hospital. Gargles and blood samples

were obtained on the 3rd day of illness, when the temperature was 101.4°F.

Case 2. Coy. no. 13058

Temperature on admission 100°F, dropped to normal on the 3rd day of illness and rose again on the 4th day. Complained of chest pains and cough. There were no physical signs on examination. Was discharged after 7 days in hospital. Gargles and blood samples were taken on the 3rd day of illness.

Case 3. Coy. no. 12584

Temperature on admission was 104°F, dropped to normal after 2 days. Was discharged after 6 days in hospital. Gargles and blood samples were obtained on the 2nd day of illness.

Case 4. Coy. no. 2036

Temperature on admission 102°F. Dropped to normal by 3rd day. Complained of chest pains, headache and cough. No physical signs on examination. Was discharged after 6 days in hospital. Gargle and blood obtained on 2nd day of illness.

Case 5. Coy no. 12601

Temperature on admission 101.2°F. Dropped to normal by 2nd day. Complained of chest pains, cough and headache. Was discharged after 5 days in hospital. Gargle and blood were obtained on the 1st day of illness.

Case 6. Coy. no. 10029

Temperature on admission 101.2°F dropped to normal by 3rd day. Complained of chest pains, headache and cough. Was discharged after 6 days in hospital. Gargle and blood obtained on 1st day of illness.

All cases were treated with 1 c.c. of Flocillin daily.

Fig. 3 shows temperature chart from case 1 (Coy. no. 11048).

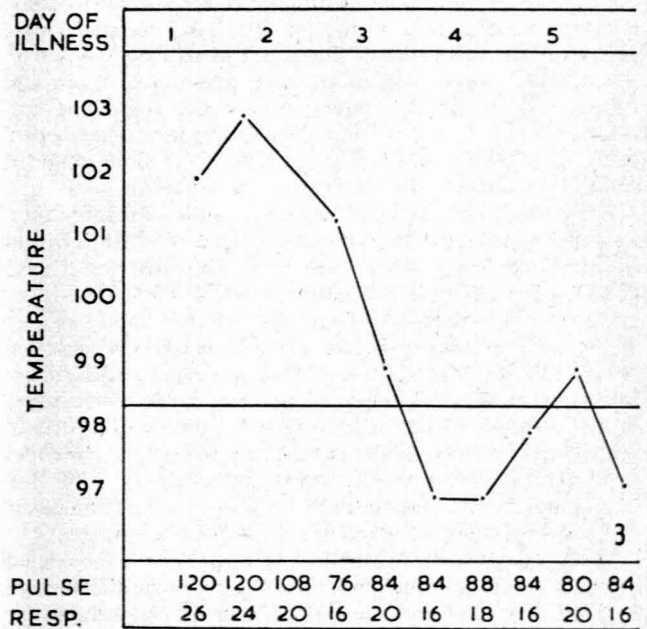


Fig. 3. Temperature etc., case 1 (Coy. no. 11048).

no. 11048), the only case which gave negative results by haemagglutination-inhibition titration of acute and convalescent sera. Egg inoculation and tissue culture of this gargle did not yield virus. Fig. 4 shows the temperature chart of case 6 (Coy. no. 10029), from whom virus was isolated on the first day of illness.

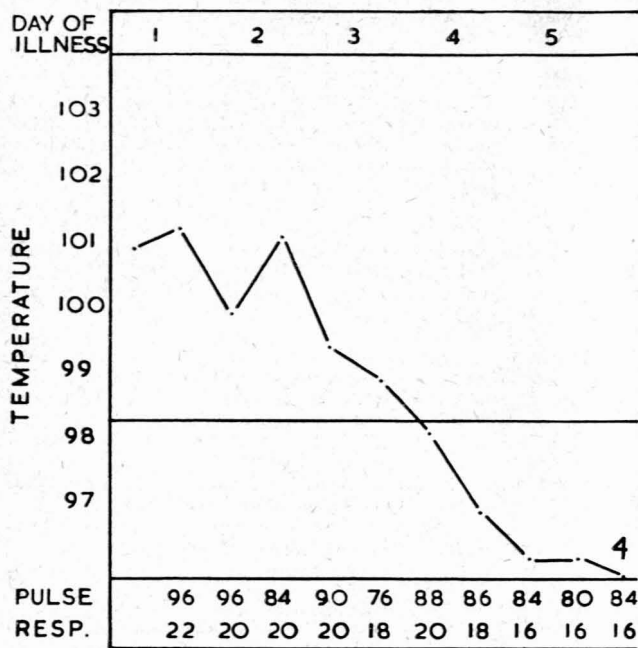


Fig. 4. Temperature etc., case 6 (Coy. no. 10029).

LABORATORY INVESTIGATIONS

Material. On 19 July gargles and blood samples were obtained from patients in the Simmer & Jack Mine Hospital; 6 cases were chosen, 2 on the 1st day, 2 on the second day, and 2 on the third day of illness. The patients gargled in saline, which was added to an equal quantity of broth and transported to the laboratory in a flask containing ice. Gargles which could not immediately be investigated were stored at -20°C . Further samples of blood were obtained from these patients after an interval of 3 weeks.

Egg Inoculation. The gargles, after addition of antibiotics, were inoculated into the amniotic cavities of 12- or 13-day-old embryonated hen's eggs, which were incubated for 5 days at 37°C . For allantoic inoculation 10- or 11-day-old embryonated eggs were used. All fluids were given 4 blind passages in the amniotic cavity before being discarded as negative.

Tissue Culture. In addition, 0.5 ml. of the gargle was inoculated into each of 3 tubes of monkey kidney monolayer cultures from which the growth medium of Lactalb. hydrolysate + 5% horse serum had been removed. The tubes were then returned to the revolving wheel at 37°C for 30 minutes before the addition of 1.5 ml. of maintenance medium consisting of Parker 199 without serum.

Mouse Inoculation. Mice of 8-10 g. weight were inoculated by the intranasal route under light ether anaesthesia with 0.05 ml. of undiluted allantoic fluid from 4th and 5th passage material. The toxicity of the strains was investigated by the method of Henle and Henle,¹ by (1) the intravenous inoculation of 1 ml. quantities of undiluted infected allantoic fluid, (2) by intracerebral inoculation of 0.03 ml. quantities of undiluted infected allantoic fluid, and (3) by intraperitoneal inoculation of 1.0 ml. quantities of infected allantoic fluid.

Haemagglutination and haemagglutination-inhibition titrations were carried out in plastic trays with a chick red-cell suspension of 0.25% in saline.

Virus Strains and Antisera. The A/Singapore/1/57 strain used as the Asian influenza prototype strain was obtained from the World Influenza Centre, Mill Hill, London. Ferret antiserum to the strain was obtained by intranasal inoculation of a 10^{-2} dilution in broth-saline. The ferrets were bled before inoculation and again 2 weeks later. Other virus strains and their antisera were obtained from Phillips-Roxane, Antwerp, and consisted of (1) A/Nederlands/36/56 and (2) B/Denmark/2/53 or B/Australia/43.

Sera were treated with *V. cholerae* enzyme according to the method of Mulder *et al.*²

RESULTS

Virus was obtained from only 2 cases, viz. case 5 (Coy. no. 12601), and case 6 (Coy. no. 10029), from whom gargles had been obtained on the first day of illness. These strains were found to conform in general characteristics to those studied by Jensen³ and Meyer *et al.*⁴

Amniotic Inoculations. Guinea-pig and human group-O red blood-cells were not used to test the first harvest of amniotic fluids, which were negative when tested with fowl red blood-cells. The harvest from the 2nd passage, however, showed haemagglutination with all three types of red blood-cells. These fluids were then diluted in broth and inoculated into the allantoic cavity of 10-11 day eggs. The fluids harvested after 2 days' incubation at 37°C were of low titre. Further passage yielded fluids giving a titre of 1:160 or 1:320. After 3 or 4 allantoic passages it was noted that 50% or more of the inoculated eggs were dead before harvesting. The embryos were invariably covered with petechial haemorrhages, and congestion of the cerebral sinuses were frequently seen. Bacteriological controls of the egg contents were sterile.

Tissue Culture. Slight cytopathogenic changes were observed in the two cultures 10029 and 12601 on the 3rd day of incubation. These consisted of a scattering of small rounded cells distributed throughout the cell sheet. The changes were not progressive and no more than one-quarter of the tissue was involved by the 6th day of incubation, when

TABLE II

	Haemagglutination-Inhibition Titres with 4 Agglutinating Doses of				
	10029	12601	A/Sing. 1/57	A/Ned. 36/56	B/Aus. 43
Serum 10029					
Acute phase	0	0	0	192	384
Convalescent phase	576	96	1,536	192	384
Serum 12601					
Acute phase	0	0	0	0	0
Convalescent phase	384	192	768	48	192
Serum 2036					
Acute phase	0	0	0	0	384
Convalescent phase	1,536	0	1,152	0	384
Serum 12584					
Acute phase	0	0	0	0	0
Convalescent phase	96	0	768	0	0
Serum 13058					
Acute phase	0	0	0	0	0
Convalescent phase	384	24	1,536	6	96
Serum 11048					
Acute phase	0	0	0	0	0
Convalescent phase	0	0	0	0	0
Normal ferret serum	0	0	0	0	0
A/Sing. 1/57 ferret antiserum	768	192	3,072	0	0
A/Nederlands/36/56 antiserum	0	0	0	768	0
B/Australia/43 antiserum	0	0	0	0	384

the cultures were discarded. Media were changed on the 3rd or 4th day of inoculation and the fluids tested for haemagglutination with human group-O red blood-cells, guinea-pig red blood-cells, and fowl red blood-cells. Haemagglutination was demonstrated at 4°C in the culture fluids from the two gargles which later yielded virus in egg culture.

Antigenic Analysis. Table II shows the results of the H.A.I. tests used for typing the strains, and for titration of the acute-phase and convalescent-phase sera. As will be seen, case 1 (Coy. no. 11048) was the only one in which a rise in antibody titre to the strain A/Singapore/1/57 was not demonstrated. All other sera showed a marked antibody titre in the convalescent phase although virus was isolated only from the two cases from which gargles had been obtained on the first day of illness.

Mouse Inoculations: (1) *Pathogenicity.* The strains were not pathogenic for mice when inoculated by the intranasal route. Minimal lesions only were induced on serial passage.

(2) *Toxicity.* There was no indication that the strains were toxic for mice when inoculated by the intracerebral, intravenous or intraperitoneal routes.

SUMMARY

An epidemic of influenza amongst the African labourers in a group of gold mines is described.

Laboratory investigations have shown the strain responsible to be identical with those isolated in the Far East, of which the prototype strain is A/Singapore/1/57.

Preliminary studies of the biological properties of the virus in tissue culture and mice are described.

Our thanks are due to Dr. Clifton, Group Medical Officer, New Consolidated Goldfields, for permission to carry out this study and to publish our findings, and to Dr. J. H. S. Gear for criticism and help in writing this paper.

APPENDIX

Since this paper was submitted for publication evidence has been obtained which suggests that the Asian strain of influenza is still present amongst the African workers on the mines. From 14 November 1957 a steady increase of daily admissions of patients with mild respiratory diseases was noted. From an admission rate of one or two per day the number steadily increased until a peak was reached on 23 November, when 12 patients were admitted. The numbers then declined slowly until 4 December, after which the admission rate was again one or two per day. Serological studies of acute- and convalescent-phase sera from patients on the Simmer & Jack Mine, admitted between 18 and 28 November, showed that many of these patients had antibodies to Asian influenza in the convalescent-phase sera while the acute-phase sera were negative. The greatest percentage of positive results were found amongst new recruits who had been resident on the mine for a period of 2 months or less.

REFERENCES

1. Henle, G. and Henle, W. (1946): *J. Exp. Med.*, **84**, 623.
2. Mulder, J., de Nooiper, I. and Brans, L. M. (1952): *Antonie v. Leeuwenhoek*, **18**, 128.
3. Jensen, K. E. (1957): *J. Amer. Med. Assoc.*, **164**, 2025.
4. Meyer, H. M., Hilleman, M. R. *et al.* (1957): *Proc. Soc. Exp. Biol. (N.Y.)*, **95**, 609.