Varicella Pneumonitis in Adults: Frequency of Sudden Death

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Primary Chickenpox Pneumonia in
the adult was first described by War-ing and associates' in 1942 and the subse-
quently literature includes reports of at least
150 cases.

The treacherous nature of this disease
and its significant mortality rate are
repeatedly emphasized by most observers.
Less fully appreciated, however, is the
remarkable frequency with which sudden
death occurs. Death has been described as
"sudden if it comes reasonably quickly un-
der circumstances when its immediate ar-
rial is unexpected." A total of 23 fatal-
ities from adult varicella pneumonitis have
been reported and in 15 instances, death
occurred suddenly (Table 1).

Thirteen adult patients with varicella pneu-
omonitis have been studied at the Palo
Alto-Stanford and San Mateo County Hos-
itals (Table 2). We will describe the two
instances of sudden death in detail and re-
view the clinical, laboratory, radiologic,
and nonspecific therapeutic features of this
disease.

Case Reports

Case 1

A 43-year-old man (Case 6, Table 2) entered
the hospital on November 23, 1959 complaining
of vesicular skin lesions of the chest and abdo-
men and painful "spasms" of the abdominal and
low back musculature of four days' duration.
Two weeks prior to admission, one of his chil-
dren had developed varicella; another child de-
volved the disease simultaneously with the pa-
tient. He stated no prior history of varicella. Di-
hydrocodeinone and meperidine had not con-
trolled the severe muscular pains.

The patient was a well-developed, well-nour-
ished white man who appeared acutely ill. A
maculopapular rash was seen over the upper tho-
rax, abdomen, neck and head, and in the or-
opharynx. The pulse rate was 92 per minute, the
respiratory rate 22, and the blood pressure 140/80.
Oral temperature was 38.4°C. (101.3°F.). No other
abnormalities were noted.

A chest x-ray film taken at the bedside on
the day of admission revealed confluent patches and
strands of increased density in the upper one-half
of the left lung field (Fig. 1a).

On the second hospital day (the fifth day of
illness), the back pain was less severe though
the patient still required narcotic administration.
New crops of vesicles appeared and were noted
for the first time on the palmar and plantar skin
surfaces. The patient complained of moderate
epigastric and substernal pain, but commented
that these pains were "just a nuisance" com-
pared to the back pains. Mild nausea was also
noted on the evening of this day. Oral intake
was supplemented with 2000 ml. of intravenous
fluids daily. The intake on the second hospital
day was 2160 ml. and urine output was 1900 ml.

At 8 p.m., on the second hospital day, the pa-
tient complained of mild chest discomfort on
deep inspiration and began to cough with expec-
toration of pink frothy sputum in small amounts.
A few persistent rales were detected at the left
lung base.

Eight hours later, in the early morning of the
third hospital day, the sixth day of disease, there
was an abrupt increase in pulse rate, respiratory
rate, and temperature (Fig. 2). When examined
at 8:30 a.m., the patient was mildly disoriented
and dysnpeic and demonstrated a severe cough
productive of large amounts of pink frothy sput-
um. The entire skin rash had become hemor-
rhagic. A clysis containing hydrocortisone was
ordered, but before it was prepared at 8:40 a.m.,
the patient became incoherent and cardiac arrest
occurred with apnea evident shortly thereafter.
Open chest cardiac massage was instituted with-
out avail, and the patient was pronounced dead
at 9:35 a.m.

On the day of admission, packed cell volume
was 51 per cent; hemoglobin 15.9 gm. per cent;
white blood count 9,500/mm³; platelets were
adequate on the differential smear which re-
vealed 87 per cent neutrophils and 10 per cent
mononuclear cells. On the second hospital day,
the serum amylase was 110 units (normal 20-
### Table 1—Fatalities Reported from Varicella Pneumonitis

<table>
<thead>
<tr>
<th>Sex, Age</th>
<th>Day of Cutaneous Disease on Which</th>
<th>Admission</th>
<th>Reference and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>M, 40</td>
<td>4</td>
<td>8</td>
<td>15,250 Pos.</td>
</tr>
<tr>
<td>M, 35</td>
<td>4</td>
<td>Not 4</td>
<td>None</td>
</tr>
<tr>
<td>M, 29</td>
<td>1</td>
<td>Not 4</td>
<td>None</td>
</tr>
<tr>
<td>M, 42</td>
<td>4</td>
<td>5</td>
<td>7 8,550 Pos.</td>
</tr>
<tr>
<td>F, 24</td>
<td>2</td>
<td>3</td>
<td>4 &quot;Normal&quot; Pos.</td>
</tr>
<tr>
<td>F, 19</td>
<td>1</td>
<td>4</td>
<td>4 38,000 Pos.</td>
</tr>
<tr>
<td>F, 26</td>
<td>1</td>
<td>Not 5</td>
<td>None</td>
</tr>
<tr>
<td>F, 23</td>
<td>2</td>
<td>4</td>
<td>18 6,800 Pos.</td>
</tr>
<tr>
<td>F, 34</td>
<td>4</td>
<td>6</td>
<td>6 None</td>
</tr>
<tr>
<td>M, 71</td>
<td>5</td>
<td>10</td>
<td>10 14,400 None</td>
</tr>
<tr>
<td>M, 41</td>
<td>4</td>
<td>5</td>
<td>7 12,500 Pos.</td>
</tr>
<tr>
<td>F, 26</td>
<td>2</td>
<td>3</td>
<td>4 12,800 Pos.</td>
</tr>
<tr>
<td>M, 44</td>
<td>4</td>
<td>4</td>
<td>5 None</td>
</tr>
<tr>
<td>F, 27</td>
<td>3</td>
<td>4</td>
<td>4 8,550 None</td>
</tr>
<tr>
<td>M, 34</td>
<td>3</td>
<td>3</td>
<td>3 12,450 None</td>
</tr>
</tbody>
</table>

*Fitz et al.*—The patient reported cough and dyspnea on the 4th day of skin rash; immediate hospitalization advised, but patient died in ambulance on way to hospital.

*Fitz et al.*—During the evening of the 4th day of illness, the patient became so dyspneic that he sat up in a chair in his living room, where he was found dead the next morning.

Fitz _et al._—After a progressively downhill hospital course, the patient died on the 7th day of the disease.

*Fish*—The heart beat became very rapid and irregular and the patient died suddenly. Central adrenal softening noted at necropsy.

*Fish*—After developing shock shortly after admission, the patient continued to deteriorate and died 22 hours after admission.

*Fish*—The husband called a physician on the fourth day of his wife's illness to ask if the previously prescribed cough medicine could be making her drowsy. Two hours later he called again to report her death.

*Fish*—After slight improvement in the pulmonary condition of the patient, massive hemorrhage, shock, and oliguria were experienced. Irreversible renal damage was the cause of death.

*Frank*—The patient was admitted in extreme respiratory distress; cyanosis developed; the skin rash became hemorrhagic and the patient died soon after admission.

*Eisenbud*—No definite diagnosis was made; chest x-ray film was not obtained; no specific therapy was given and 12 hours after admission severe dyspnea and cyanosis suddenly developed and the patient died.

*Rizz et al.*—Critically ill, the patient suddenly became restless, more dyspeptic and expired. Underlying lymphosarcoma.

*Krugman et al.*—The patient rapidly became worse and died 24 hours after admission.

*Krugman et al.*—On the 2nd day of respiratory symptoms, the patient developed pulmonary edema and died.

*Hunnincut and Berlin*—The hospital course was rapidly downhill and the patient expired 18 hours after admission.

*Bailey and Gaitlin*—Patient steadily deteriorated and died 20 hours after admission.
40 units) and urinalysis was normal, except for microhematuria (attributed to catheterization), one plus proteinuria, and a specific gravity of 1.031. On the morning of demise, the urinalysis indicated a specific gravity of 1.021 with a trace of proteinuria, microhematuria, slight pyuria, and a few hyaline and granular casts. The blood studies obtained one-half hour before death revealed a packed cell volume of 70 per cent; hemoglobin 21.1 gm. per cent; red blood count 8,080,000/mm.\(^3\); white blood count, 26,450/mm.\(^3\) with 83 per cent neutrophils including 24 band forms, and 17 per cent mononuclear cells; platelets were adequate on the differential smear.

A chest film obtained 30 minutes before death indicated marked spread of the diffuse confluent nodular densities throughout both lung fields (Fig. 1b).

On necropsy examination, microscopic study of the skin lesions showed a generalized uniform reaction in the vesicles, which were filled with homogenous pink-staining material containing polymorphonuclear cells, round cells and epidermal cells containing type A intranuclear inclusion bodies. Pulmonary edema without significant polymorphonuclear cells, but considerable hemorrhage and a few intranuclear inclusion bodies were seen in the lungs. Culture of the lung parenchyma revealed a heavy growth of hemophilus and a few colonies of Klebsiella-aerobactor and nonhemolytic streptococci. Cardiac hypertrophy of mild degree was present. Multiple ulcers of the esophagus, 2-5 mm. in diameter were noted throughout its course and in these no inclusion bodies were found. The adrenal glands were normal in appearance grossly, but lipid depletion was noted microscopically.

**CASE 2**

A 24-year-old Caucasian housewife, five months pregnant (Case 11, Table 2), was seen at home by her family physician on the tenth day of illness, complaining of dyspnea and severe cough of "several days" duration. A diffuse skin rash considered typical of varicella had been present for five or six days prior to examination. Physical examination revealed no other abnormalities; particularly, examination of the chest was unremarkable. An antissuive preparation was prescribed and the patient was instructed to contact her physician immediately if her condition worsened. Hospitalization was not advised.

Early the following morning, the patient's husband awakened to find his wife vomiting and severely dyspneic. Her respiratory distress worsened and the local fire department and private physician were summoned. In spite of vigorous resuscitative attempts, the patient was pronounced dead on arrival at the hospital emergency room. No laboratory procedures or radiographic studies were obtained before death.

The coroner's necropsy revealed the typical skin rash of varicella without hemorrhagic

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**Table 1 (Cont'd)**

<table>
<thead>
<tr>
<th>Sex, Age</th>
<th>Respiratory Signs</th>
<th>Onset</th>
<th>Admitted</th>
<th>Patient Expected</th>
<th>WBC (\times 10^9)</th>
<th>Chest X-ray</th>
<th>Reference and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>M, 32</td>
<td>4</td>
<td>5</td>
<td>7</td>
<td>8,900</td>
<td>Pos.</td>
<td></td>
<td>Rotter and Collins—Cyanotic on admission, with bilateral rales. Deteriorated steadily despite intensive therapy.</td>
</tr>
<tr>
<td>F, 32</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>9,200</td>
<td>Pos.</td>
<td></td>
<td>Claudy—During hospitalization, patient gradually worsened and expired quietly.</td>
</tr>
<tr>
<td>F, 32</td>
<td>?</td>
<td>5</td>
<td>5</td>
<td>Not reported</td>
<td></td>
<td></td>
<td>*Hackel—Six months pregnant. Died 14 hours after therapy started.</td>
</tr>
<tr>
<td>M, 36</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>15,500</td>
<td>Pos.</td>
<td></td>
<td>Lander—Gradual downhill course. Presumed cause of death acute hemorrhagic leukoencephalitis, though clinical and pathological signs of pneumonitis were present.</td>
</tr>
<tr>
<td>F, 35</td>
<td>?</td>
<td>5</td>
<td>6</td>
<td>None</td>
<td>None</td>
<td></td>
<td>*McLachlan—Died less than 24 hours after admission.</td>
</tr>
<tr>
<td>M, 34</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>Not reported</td>
<td>Pos.</td>
<td></td>
<td>Nicolaides—Admitted comatose. Progressive downhill course.</td>
</tr>
<tr>
<td>M, 26</td>
<td>?</td>
<td>2</td>
<td>7</td>
<td>Not reported</td>
<td></td>
<td></td>
<td>Trimble—Course not reported.</td>
</tr>
<tr>
<td>F, 34</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>Not reported</td>
<td></td>
<td></td>
<td>*Johnson and Nelson—Underlying Hodgkin's disease. Dyspneic, cyanotic. Collapsed and died on day of admission.</td>
</tr>
</tbody>
</table>

*Death was sudden or unexpected.*
change. The pericardial sac contained 50 ml of clear yellow fluid; and in each pleural space there was found approximately 300 ml of yellowish turbid fluid. The lungs were noted to be very heavy, of dark red color, and the cut surface exuded a dark red fluid. The pulmonary arteries and bronchi were patent, and the latter contained considerable yellow frothy fluid. Extensive interstitial pneumonitis was noted microscopically. Inclusion bodies were not reported. No bacteriologic cultures were obtained. Aside from a gravid uterus containing a four and one-half month fetus and bilateral hydroureters with minimal hydronephrosis, the remainder of the findings were welcomed.

**DISCUSSION**

A description of the clinical and laboratory status of 25 patients who succumbed from varicella pneumonitis appears in Table 1. This represents a summary and extension of the literature review of Rotter and Collins. The course of illness is briefly described. In 16 of these patients, death was sudden and/or unexpected. In this series of adult fatalities from varicella pneumonitis, 12 were men and 11 were women; the age range was between 19 and 71 years. The majority of cases occurred in the third or fourth decades of life. Of the 11 women, five were pregnant. In all the fatal cases, the cutaneous manifestations of varicella were usually severe. In some patients, as in one of ours, the rash became hemorrhagic. There was early evidence of systemic toxicity. Symptoms suggesting pulmonary involvement occurred between the first and seventh day of the cutaneous disease (median: 3.5 days). Cough, dyspnea, hemoptysis, tachypnea, orthopnea, pleuritic chest pain and cyanosis were common.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, Sex</th>
<th>Day of Illness</th>
<th>Highest Temperature (°F.)</th>
<th>Highest Recorded White Blood Count (per mm³)</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34, M</td>
<td>3</td>
<td>104°, cough, cyanosis</td>
<td>5,400</td>
<td>Feburile until 6th day. Improved slowly on oxygen and salicylates.</td>
</tr>
<tr>
<td>2</td>
<td>29, M</td>
<td>2</td>
<td>102.8°, dyspnea, cough</td>
<td>8,500</td>
<td>Afebrile by 4th day; discharged on 5th day.</td>
</tr>
<tr>
<td>3</td>
<td>32, M</td>
<td>5</td>
<td>101.8°, pharyngitis, dysphagia, rales heard on 6th day</td>
<td>6,000</td>
<td>Rales gone by 7th day; discharged on 8th day.</td>
</tr>
<tr>
<td>4</td>
<td>48, M</td>
<td>3</td>
<td>102.8°, cough, nonpleuritic chest pain; cyanosis, rales on 4th day</td>
<td>5,600</td>
<td>Afebrile by 8th day; chest x-ray clear by 13th day.</td>
</tr>
<tr>
<td>5</td>
<td>35, M</td>
<td>4</td>
<td>104°, cyanosis, wheezes</td>
<td>7,500</td>
<td>Rapid improvement; well by 7th day of illness.</td>
</tr>
<tr>
<td>6</td>
<td>43, M</td>
<td>5</td>
<td>104.8°, tachypnea, tachycardias, rales, disorientation, cough</td>
<td>26,450</td>
<td>Expired suddenly on 6th day.</td>
</tr>
<tr>
<td>7</td>
<td>27, F</td>
<td>4</td>
<td>102°, cough, whitish sputum</td>
<td>4,500</td>
<td>Afebrile by 5th day; discharged 10th day.</td>
</tr>
<tr>
<td>8</td>
<td>29, M</td>
<td>5</td>
<td>103°, rales</td>
<td>6,200</td>
<td>Afebrile by 7th day; discharged 9th day.</td>
</tr>
<tr>
<td>9</td>
<td>25, F</td>
<td>3</td>
<td>101.8°, dyspnea, backache, tachypnea, no rales.</td>
<td>12,650</td>
<td>Seven months pregnant. Discharged 7 days after onset; chest x-ray film still abnormal 6 weeks later.</td>
</tr>
<tr>
<td>10</td>
<td>42, M</td>
<td>4</td>
<td>102°, cough, dyspnea, abdominal pain, rhonchi.</td>
<td>11,300</td>
<td>Discharged 7th day.</td>
</tr>
<tr>
<td>11</td>
<td>24, F</td>
<td>7</td>
<td>?, cough, terminal vomiting, dyspnea.</td>
<td>—</td>
<td>Five months pregnant. Treated symptomatically at home. Expired on 11th day.</td>
</tr>
<tr>
<td>12</td>
<td>31, F</td>
<td>5</td>
<td>101.8°, mild cough.</td>
<td>7,300</td>
<td>Discharged, improved on 8th day. X-ray film abnormal 2 months later.</td>
</tr>
<tr>
<td>13</td>
<td>29, M</td>
<td>4</td>
<td>103°, rales on 5th day.</td>
<td>6,200</td>
<td>Discharged recovered on 9th day.</td>
</tr>
</tbody>
</table>

**Table 2—Summary of Cases Reviewed in This Study**
Severe muscular pains in the thorax and back were frequently reported. Often, these symptoms developed during the initial temperature rise.

Differential diagnosis offers no problem; the only similar cutaneous disease associated with generalized pneumonitis is herpes zoster. Such a case was recently reported* from this institution.

Contrary to the impressions of others,** elevated white blood cell count was often seen in patients succumbing from this disease. The meaning of this is not entirely clear. The viral illness alone might be responsible, as might bacterial superinfection or a combination of the two. Severe dehydration or so called "stress-leukocytosis" syndrome are other possibilities. There did not seem to be any difference in the leucocyte counts of those with rapid demise or those with the more gradual, unremitting deterioration. Differential blood counts showed slight to moderate neutrophilia in most cases. Bacteriologic studies, when performed, rarely revealed the presence of pathogenic organisms in the sputum.

Chest x-ray findings consisted of widespread, bilateral acinodular infiltration, with relative sparing of the lung apices. The lung roots were prominent as a result of overlapping parenchymal densities and slightly prominent hilar lymph nodes. In survivors, complete clearing of these changes occasionally did not occur for several months after recovery. The incidence of this x-ray picture in adult varicella is high. Mermelstein and Freirich* have estimated it to be present in 50 per cent of cases with any respiratory symptoms. However, they were reviewing cases in which the patients were sick enough to require hospital care. The appearance of the chest x-ray film did not allow accurate prognostication as to the ultimate outcome of the disease in most cases. In our 13 cases, all initial chest x-ray films were abnormal, having the typical roentgenologic appearance described by Southard et al., Tan et al.* and others.

While diagnosis usually constitutes no problem in these cases, unawareness of the potentially treacherous nature of this disease often does. A particularly sinister feature is the gross disparity which often exists between the relatively mild signs and symptoms and the potentially fatal consequences of the evolving pathologic picture.

Even when dyspnea and cyanosis are severe, the physical examination of the chest may be entirely within normal limits.*

Figure 1: Chest x-ray films (a) on admission and (b) two days later, just before death in H. G., 43-year-old man (Case 6, Table 2).
In all the fatal cases reviewed, progressive ventilatory insufficiency seemed to be evidenced by increasing tachypnea. High fever is usually but not always present in patients with x-ray evidence of progressive disease. In several of the cases reviewed by Rotter and Collins, oral temperatures were consistently below 101°F. In the first of our two fatal cases, the temperature was falling during the second hospital day, and only rose again in the few hours before death (Fig. 2). The pulse is often described as "invariably rapid," but again, may be normal or increased only as a late portent of impending collapse. Again, in non-fatal cases, tachycardia per se is no accurate qualitative indication of the severity of the underlying pneumonitis.

From these observations, we can conclude that close observation must be given to rectal temperature, pulse, and respiratory rate by the nursing and medical staffs. As a routine procedure, vital signs should be recorded at two-hourly intervals, or more frequently if the situation so dictates. Since specific antiviral therapy is not available, treatment is supportive or directed at the complications of the disease. Oxygen delivered by nasal catheter or positive pressure apparatus is often helpful in relieving dyspnea. Cold steam vaporizers are sometimes successfully employed. Di Mase et al. have used a tank-type respirator with success to improve oxygenation in a seriously ill patient during the critical portion of his disease. The use of hyperbaric oxygenation has recently been suggested to temporarily overcome the effects of the disease-produced alveolar-capillary block. Digitalization may be necessary if congestive heart failure (with or without acute pulmonary edema) supervenes.

Intravenous fluid and electrolyte therapy is important. The large losses attendant to pyrexia, tachypnea, and vomiting should be kept in mind when calculating replacement doses. Intravascular hypovolemia due to increased capillary permeability has been reported in meningococcemia and epidemic hemorrhagic fever; it is possible that such a phenomenon occurs in

![Fulminating Varicella Pneumonia](image)

**Figure 2:** Vital signs during course of hospitalization in patient H. G. (see text). Note sudden increase in heart rate, temperature, and respiratory rate approximate four hours before death.
severe varicella, though this is only conjectural at this time.

Antibiotics are of value only for secondary bacterial infections, and do not alter the basic disease. Though most authors employ them for this purpose, decision to implement antibiotics must be made on an individual basis, and an early sputum culture may occasionally be of value in guiding in the choice of agent used.

Hyperimmune serum in large amounts has been reported to be of value in one patient, but of no value in another. It is relatively expensive and not generally available. The use of gamma globulin has been shown to have some modifying effect in the course of the disease, and may prove to be of value with further study.

Adrenocorticosteroid suppression of the inflammatory reaction is advocated by some but thought to be of no help by others. Supporters of the use of steroids in this setting cite the necropsy findings of Montgomery and Olafsson, who reported “Waterhouse-Friderichsen” type hemorrhage into the adrenal glands of a patient who died of varicella and pulmonary edema. In the series currently reviewed, adrenal “softening” was noted in one patient, and Eisenbud noted varicella involvement of the adrenal gland itself in one patient. In his analysis of 300 fatal cases of meningococcal infection, Daniels has pointed out that functional collapse of the adrenal cortex may occur in the absence of demonstrable organic lesions in the adrenal glands. In patients with varicella pneumonitis in extremis, the use of steroids is probably not contraindicated if one accepts the proposition of Essewein and Didomenico that part of the pathophysiologic picture is one of generalized immunoreactive vasculitis and hemorrhage, which would presumably be favorably affected by corticosteroids.

**Summary**

A review of the literature reveals 23 fatalities from adult varicella pneumonitis to which we add two of our own. In 16 of these (70 per cent) death was “sudden” or “unexpected.”

The often malignant, deceptive, and rapidly changing course of the disease is emphasized and attention is drawn to an appropriate attitude of “watchful expectancy” and “therapeutic alacrity” on the part of the attending physician. The available modes of supportive therapy are reviewed.

**Resumen**

La revisión de la literatura arroja veinte y tres defunciones por varicelovaria en el adulto reportadas hasta hoy, a las que podemos añadir dos observados por nosotros. En diez y seis de estos casos (70 por ciento) la muerte sobrevino “repentina” o “inesperadamente”. In-sistimos en el curso maligno, variado y falaz de esta complicación y recalcallamos la necesidad de mantener una actitud suspicaz y de acometividad terapéutica por parte del médico. Señalamos los recursos disponibles actualmente para su tratamiento.

**Zusammenfassung**

Eine Durchsicht der Literatur ergibt 23 tödlich Abläufe bei Varizellen-Pneumonie des Erwachsenen, zu welchen wir zwei aus unserem eigenen Material hinzufügen. Bei 16 von ihnen, 70%, was der Tod “plötzlich” oder “unerwartet”.

Der oft bösartige täuschend und rasch wechselnde Krankheitsverlauf wird herausgestellt und die Aufmerksamkeit auf ein entsprechendes Verhalten eines “wachsenden Abwartsens” bzw. eines “therapeutischen Eifers” von Seiten des betreuenden Arztes gelenkt. Über die zur Verfügung stehenden Arten einer unterstützenden Therapie wird berichtet.

*Complete reference list will appear in the reprints.*

For reprints, please write Dr. Burton, Graduate School of Public Health, University of Pittsburgh, Pittsburgh.