Effective Influenza Treatment

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An effective treatment is the best response to an infectious epidemic. Currently, for influenza and many other viral infections, corticosteroids are the best treatment. In fact, corticosteroids have been used successfully in the treatment of influenza for over 50 years. The reason that corticosteroids are such an effective treatment is that they directly relieve the symptoms caused by influenza. But most importantly, corticosteroid therapy does not just reduce a patient's suffering, corticosteroids keep patients alive.

In the event of an epidemic of severe influenza, precautions such as a vaccine and antiviral treatments such as Tamiflu will be inadequate to avoid influenza-related deaths. An influenza vaccine cannot be relied on because it requires long lead times to develop, test and manufacture, and its effectiveness is limited due to problems in matching strains, disappointing immune system priming and incomplete population coverage. Tamiflu is not a dependable drug to save lives because it is minimally effective, must be given early in an infection to even produce this poor relief and there are influenza strains that are resistant to Tamiflu.

Corticosteroid treatment has been shown to be an effective therapy for influenza and other viral infections. Below is a list of some excerpts of medical journal articles describing the good results attained by using corticosteroids in the treatment of viral respiratory illnesses. Also pertinent to the use of corticosteroids is my 2004 article explaining why corticosteroids are an effective treatment for many viral infections, "Molecular Mimicry in SARS—Implications for Corticosteroid Treatment and Prophylaxis" (available at http://www.query.com/terp/MM_of_ACTH_in_SARS.html). Essentially, viral infections induce a corticosteroid deficiency that causes many symptoms. Corticosteroid supplements counteract this deficiency, which alleviates the accompanying symptoms.

Among its many functions, corticosteroids are an anti-inflammatory agent. When a virus induces deficient corticosteroid levels in someone suffering from a respiratory infection, the person's inflammatory processes will not be suitably inhibited and the inflammation may become overwhelming. If this goes on too long, the person will die from respiratory distress. Basically, they will drown from the fluid in their lungs because of an imbalance between the body's inflammatory and anti-inflammatory responses. Corticosteroid therapy restores this balance in people suffering from respiratory infections. This is just one way that corticosteroids keep sick people alive.

Nobody needs to die from the flu. If someone dies from an influenza infection, it is because they have not received the proper treatment. Proper treatment includes sustained corticosteroid supplements, at a sufficient dosage and instituted without delay. Corticosteroids are a safe, inexpensive, effective treatment for influenza infections. Corticosteroids should be used in coordination with vaccines and antiviral drugs to protect people from needless suffering from influenza infections.

Please join me in recognizing corticosteroids as an important treatment for many common diseases. Furthermore, corticosteroids should be recommended as a primary treatment for influenza infection. It is the only treatment currently available to avoid massive suffering and mortality from a virulent influenza epidemic.

Excerpts from medical journal articles describing the results attained by using corticosteroids in the treatment of viral respiratory illnesses

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Influenza

Plaza de los Reyes M, Cruz-Coke R. Influenzal pneumonia treated with cortisone and antibiotics. *Lancet* 1957;2:845

This hospital has 1131 beds, with 362 in the department of medicine. We received in July and August of this year 365 cases of postinfluenzal pneumonia. These patients were treated with a combination of penicillin, streptomycin, and tetracycline in high doses, with analeptics [central nervous system stimulants], oxygen, and cardiac stimulants in the most severe cases. But the mortality in this series was 22%. In each case the cause was confirmed by necropsy.

In view of this very high mortality, we began treatment with cortisone, together with antibiotics, in the worst cases. 100 mg. of cortisone was given daily for five to ten days. The 7 cases so treated had bilateral postinfluenzal pneumonia, confirmed by radiographic examination.

All the patients were very ill; some had underlying chronic disease (coronary-artery sclerosis with cardiac failure in 2, bilateral pulmonary tuberculosis in 1, cirrhosis of the liver in 1, and diabetes in 1). Treatment for three to five days without cortisone had been unsatisfactory, and the patients were in a very poor condition. With cortisone the course of the acute disease changed dramatically in twenty-four hours: temperature, pulse-rate, and respiration-rate returned to normal, and severe hypotension was terminated. In the next seventy-two hours the acute bilateral infection subsided, and the underlying chronic disease was restored to its pre-influenzal state. In this section of the hospital there were no further deaths.

The most dramatic case was that of a 22-year-old man with bilateral pulmonary tuberculosis. He came into hospital with bilateral pneumonia. Temperature 104º F, respiration-rate 64 per min., pulse-rate 188 per min., and blood-pressure 90/50 mm Hg. He was treated with bed rest, streptomycin, isoniazid, penicillin, tetracycline, leptazol, lanatoside C ('Cedilanid'), and oxygen. On the fourth day of treatment he had a haemoptysis [coughing up blood] of 250 ml. and appeared to be dying. 100 mg. of cortisone daily apparently saved his life in twenty-four hours: within seventy-two hours he was completely recovered from the acute disease.

We think that the good results with cortisone were due to correction of an acute adrenal insufficiency, which may have been the underlying cause of the high mortality.

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Rotem CE. Influenzal pneumonia treated with cortisone and antibiotics. *Lancet* 1957;2:948

I was much interested in the letter from Dr. Plaza de los Reyes and his colleagues (Oct. 26) and their successful use of cortisone in critically ill patients. A similar observation was made here.

Influenza was fairly severe in the Midlands, and from August to October about 150 patients with post-influenza pneumonia were admitted to this hospital. We were struck by the severe toxicity and extensive involvement of the lungs. In spite of intensive treatment with antibiotics, oxygen, and cardiac stimulants there was a mortality of 10%—all in patients with other underlying conditions such as chronic bronchitis and emphysema or valvular heart-disease. Observing the "shock-level" blood-pressure and lack of resistance, we first used 100 mg. hydrocortisone intravenously in 2 obviously moribund patients who had pronounced heliotrope cyanosis [dusky blue-gray to lavender pallor of the face, lips and ears due to the shortage of oxygen]. The result was dramatic.

A few days later the following patient was seen:

A woman, aged 28, previously in good health, para 3 [number of previous births], 6 months pregnant, was admitted with pneumonia involving the whole of the right lung and the left upper lobe. Temperature 104º F., heliotrope cyanosis. After 48 hours' treatment with large doses of antibiotics, analeptics, and oxygen, she appeared moribund. Prednisolone 10 mg. was given initially, and then 5 mg. t.d.s. [3 times/day] 24 hours later she was afebrile and not cyanosed, and there was some air entry over all the affected lobes. 3 days later she was able to get up.

It was then decided to use prednisolone in average doses (15 to 30 mg. daily) in severely ill patients with extensive pulmonary involvement, toxicity, and low blood-pressure. Without exception the results were gratifying.

It appears that in these cases prednisolone is as effective as cortisone, not only correcting adrenal insufficiency but also helping to absorb exudate [fluid discharged from cells].

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Excerpts from medical journal articles describing the results attained by using corticosteroids in the treatment of viral respiratory illnesses (Influenza continued)

Greaves IA, Colebatch HJ, Torda TA. A possible role for corticosteroids in the treatment of influenzal pneumonia. *Aust N Z J Med* 1981;11(3):271-6

A 52-year-old woman with severe influenzal pneumonia developed increasing hypoxaemia [subnormal oxygenation of the blood] on the sixth and seventh hospital days. Hydrocortisone (250 mg intravenously) was given on the seventh day and the arterial oxygen tension increased within two hours. Clinical improvement continued with further steroid therapy.

We observed that the administration of a corticosteroid during the acute phase of her illness led to increased arterial oxygenation, and a second course of corticosteroid during the convalescent period was followed by accelerated recovery of lung function.

On the seventh day the patient was given hydrocortisone succinate (250 mg) as an intravenous bolus dose. The PaO_2 [arterial oxygen tension] increased within two hours and her fever resolved over the same period.

Increasing hypoxaemia and fever developed on the sixth and seventh days, and both features decreased after a single dose of hydrocortisone succinate.

SARS

Zhao Z, Zhang F, Xu M, Huang K, Zhong W, Cai W, et al. Description and clinical treatment of an early outbreak of severe acute respiratory syndrome (SARS) in Guangzhou, PR China. *J Med Microbiol* 2003;52(8):715-720

The best response (no deaths) was seen in the group of 60 patients receiving early high-dose steroids and nasal CPAP (continuous airway positive pressure) ventilation; the other three treatment groups had significant mortality....Early administration of high-dose steroids and CPAP ventilation appears to offer the best supportive treatment with a reduced mortality compared with other treatment regimens.

The 60 cases in group D were treated with methyl prednisolone if fever did not resolve within 3 days. Dosage for the steroid was chosen according to the area of pulmonary infiltrates: 160 mg day^{-1} if one lobe was involved, 320 mg day^{-1} if more than one lobe was involved. A substantial proportion of cases (36/60) had temperature resolution within 1-3 days after starting treatment. Fifteen of 60 needed an increased dosage of the steroid from 160 to 320-720 mg day^{-1} to maintain respiratory physiological parameters and to control temperature. None of the group D patients needed mechanical ventilation and all of them recovered and were discharged from the hospital.

Because the response of different groups of patients to different therapeutic regimens has been documented, we are able to suggest that the early and aggressive use of steroids combined with non-invasive ventilatory support should offer the best hope for a favourable outcome.

Chickenpox (Varicella Virus)

Thompson CA, Cantrell FP. Chickenpox pneumonia treated with prednisolone: a case report. *Ann Int Med* 1958;49(5):1239-46

A 31 year old white housewife was admitted to the hospital on March 17, 1957, complaining of cough, fever, blood-tinged sputum and vesiculopustular skin lesions [elevations of the skin containing clear fluid or pus]. One of her children had had chickenpox two weeks previously, and another developed a rash coincident with the onset of the patient's illness.

Physical examination at the time of admission revealed an acutely and seriously ill young female. The respirations were rapid and labored, with a rate of 36 per minute. The lips, mucous membranes and nail-beds were cyanotic. The patient coughed frequently, raising large amounts of thin, frothy, pink-tinged sputum. The skin was covered with the characteristic vesiculopustular lesions of chickenpox in all states of development. In addition, a few lesions were present on

Excerpts from medical journal articles describing the results attained by using corticosteroids in the treatment of viral respiratory illnesses (Chickenpox continued)

the buccal mucous membranes [inner cheeks]. The pulse rate was 120 per minute, and the blood pressure, 110/60 mm. of Hg. The temperature was 99.4° F. Examination of the lungs revealed no dullness and only a few medium moist rales [bubbling noise] in the left lung base.

During the first 48 hours the temperature ranged between 101 and 104° F. The sputum became even more copious in amount and frankly bloody. By the end of the third day the sputum was thick and tenacious. Moist rales had become audible throughout both lung fields. The patient was still cyanotic, with rapid, labored respirations, tachycardia and intermittent anterior chest pain. At this juncture prednisolone was started in a dosage of 40 mg. per day, divided and given at six-hour intervals. The dose was gradually tapered during the ensuing two-week period. Within 24 hours the temperature had fallen from 103° F. to normal levels. The patient became much less dyspneic [difficulty in breathing], and in general appeared to be greatly improved. The sputum became rusty in color and rapidly decreased in amount. No new skin lesions were noted after prednisolone was started, and those present rapidly regressed. As expected, appetite and mental attitude greatly improved during the early phase of steroid therapy, and at no time were there adverse side-effects from treatment. X-ray three weeks following admission revealed almost complete resolution of the pneumonic process.

Summary: A case of severe chickenpox pneumonia is reported. Therapy with prednisolone was instituted after lack of response to supportive measures and when the patient was desperately ill. Within 24 hours there was marked improvement, and convalescence progressed uneventfully. Steroids seemed to have a decidedly favorable influence on the disease in this instance.

Mer M, Richards GA. Corticosteroids in life-threatening varicella pneumonia. *Chest* 1998;114(2):426-31

Background: Varicella pneumonia that results in respiratory failure or progresses to the institution of mechanical ventilation carries a significant morbidity and mortality despite intensive respiratory support and antiviral therapy.

Fifteen adult patients were evaluated, six of whom received corticosteroids in addition to antiviral and supportive therapy. These six patients demonstrated a clinically significant therapeutic response. They had significantly shorter hospital (median difference, 10 days; $p<0.006$) and ICU (median difference, 8 days; $p=0.008$) stays and there was no mortality, despite the fact that they were admitted to the ICU with significantly lower median ratios between $Pa0_2$ and fraction of inspired oxygen than those patients (n=9) who did not receive corticosteroid therapy (86.5 vs 129.5; $p=0.045$).

Conclusion: When used in addition to appropriate supportive care and early institution of antiviral therapy, corticosteroids appear to be of value in the treatment of previously well patients with life-threatening varicella pneumonia.

This study was initiated after corticosteroids were used in one critically ill patient who was deteriorating despite antiviral and supportive therapy. The response was so clinically significant that their use in subsequent patients who had failed to respond to conventional therapy appeared to be justified.

Of note is the fact that no patient who received corticosteroids died.

Those patients who received corticosteroids in addition to antiviral therapy and broad-spectrum antibiotics made striking recoveries, particularly in terms of gas exchange. There was also rapid radiologic improvement.

Patient 2 was managed initially with a rebreathing mask at 15L/min of oxygen; his PaO_2 was 46.mm Hg and oxygen saturation was 83%. Corticosteroids were begun, and 4 h later the $Pa0_2$ had increased to 71.6 mm Hg with a saturation of 94%. This rate of recovery continued until discharge. The other patients treated with corticosteroids all responded in similar fashion, with extremely rapid improvement.

This study examined the effects of corticosteroids in patients with severe varicella pneumonia who were also receiving acyclovir and broad-spectrum antibiotics. The rapidity of the clinical response in each case was remarkable.

Therapy to date for life-threatening varicella pneumonia has been relatively unsuccessful, consisting primarily of cardiorespiratory support and antiviral therapy. The benefit of the latter, however, is controversial. In a retrospective study of 99 adults with varicella pneumonia prior to and after the availability of acyclovir, no conclusive benefit was demonstrated. This was confirmed by fairly constant mortality statistics for England and Wales from 1967 to 1985, the period in which antivirals were introduced. It is possible, however, that acyclovir may hasten improvement in patients who are less ill and do not require ventilation. Despite the realization that acyclovir has limited efficacy, it is still widely recommended as early primary therapy, particularly in those patients who are extremely ill.

Based upon the clinical observations of this study and the fact that the total dose of corticosteroids used would have minimal side effects, we believe that this therapy should be considered in addition to antiviral therapy and appropriate supportive care in any previously well patient with life-threatening varicella pneumonia.