CLINICAL EXPERIENCE

Successful Immunotherapy of Acute Viral Infections with a Virus Vaccine

JOSEPH B. MILLER MD

101 Jordan Lane, Mobile, AL 36608, USA

Abstract
Since 1968, I have been providing relief in 30 min for patients with acute influenza, as well as for patients with all five types of herpes virus infection seen in my practice. Relief occurs more rapidly than from any antibiotic or anti-viral treatment available. This remarkable response has been obtained by subcutaneously injecting a small skin test determined dose of ordinary influenza virus vaccine. The rapid relief response to influenza virus vaccine constitutes the first specific and rapidly effective anti-viral treatment for any established virus infection. It is unusually safe, rapidly effective, globally available, broadly applicable, and very economical. Because there are 21 vaccines available now, and more to come, this could be the discovery that opens the door to a new era of rapid relief dose therapy with many vaccines. It is important that this be confirmed scientifically. Influenza and herpes virus infections cause much pain, suffering and death world-wide. No comparable therapy is available for any of these infections. Influenza kills thousands of people every year, and some world-wide epidemics (pandemics) have killed millions. Herpes viruses can cause painful fever blisters, eye-destroying ocular herpes, newborn-killing genital herpes, the severe pain of shingles, and the many debilitations and dangers of mononucleosis and chickenpox. Herpes viruses are oncogenic, i.e. they have a tendency to change normal cells into cancer cells. Several cancers, including Hodgkin’s disease, multiple myeloma, and Kaposi’s sarcoma, have been recently reported by many respected investigators to probably be induced by herpes viruses. Is it possible that the incidence of these cancers could be decreased by early treatment of the herpes virus before it has had an opportunity to induce malignant change? This clinical finding has revealed the existence of a simple means of calling into action a rapidly effective disease-fighting mechanism that has not been known or utilized until now. Learning the molecular mechanism of this response could lead to new knowledge about human immunology and bring relief to many patients for whom little relief has been hitherto available. If the small double-blind studies now under way confirm my clinical observations, they could lead to many larger studies and the potential for benefits in numerous additional diseases.

INTRODUCTION
During the influenza epidemic of 1968–69, I found that I could provide complete or near-complete relief in 30 min for patients acutely ill from influenza [1–3]—faster than from any antibiotic or anti-viral medication for any bacterial or viral infection. I obtained this remarkable relief response by subcutaneously injecting ordinary influenza virus vaccine in a small or diluted dose, determined for each patient by an intradermal skin test.
Then it became evident that these individualized doses of influenza virus vaccine could also provide the 30 min relief response in most patients with all five types of herpes virus infection seen in my practice [4–8]. The herpes virus infections which have responded have consisted of herpes simplex 1 (fever blisters), herpes simplex 2 (genital herpes), herpes zoster (shingles), varicella (chickenpox), and Epstein–Barr virus infections, which cause infectious mononucleosis and chronic Epstein–Barr virus infection [9]. I have had no opportunity in my practice to study other types of herpes virus infection such as cytomegalovirus infections.

In both influenza and herpes, symptoms do return, typically at 4–6 hour intervals the first day, then usually at progressively longer intervals such as 8, 12 and 24 hours in the following days. Each recurrence of symptoms can be relieved in minutes at home by self-administration of the relieving dose. In order to steadily decrease and finally eliminate the inflammatory process, the injections are repeated with each return of the symptoms until the symptoms no longer recur.

In influenza, even the fever typically clears the first day, usually after about the third injection, and the entire illness is usually clear after 3 days. In fever blisters, where the inflammatory process is visible, the lesions can usually be seen to clear completely within 3 or 4 days. In genital herpes, the average response rate has been about 70%, with higher rates in females than males. In influenza and fever blisters, the response rate has exceeded 90%.

In untreated shingles, skin lesion clearing is variable. So, in any individual patient, I have been unable to determine if the healing time of the skin lesions is reduced. Usually, however, the severe shingles pain is markedly reduced from the first few injections, typically with little or no further need for narcotics or pain relievers other than possibly acetaminophen or a topical preparation for the blistered skin. It is important that the injections be repeated with each pain recurrence until the pain no longer recurs. This may take 1, 2, or 3 weeks. Thus far, no patients who have been treated on this schedule have developed post-herpetic neuralgia.

In shingles, the earlier the treatment, the better the response rate. About 80% of shingles patients have responded when treatment was begun while the skin lesions were present. Treatment begun in the first few days is most effective. Post-herpetic neuralgia, a painful condition that can persist for life, has responded in about 30% of patients treated within 1 year, and in 10% when treatment was instituted beyond 1 year. These percentages are low, but still better than with any other approach, and those who respond are grateful to be released from a life of constant pain. And if relief dose therapy for shingles becomes mainstream, physicians will undoubtedly institute therapy earlier for a higher percentage of patients obtaining relief during the acute attack and possibly a lower percentage of patients with post-herpetic neuralgia.

In mononucleosis, the severe sore throat and malaise usually clear the first day. Again, for complete control, the injections are repeated with each symptom recurrence, including malaise, until the symptoms no longer recur. In chronic Epstein–Barr virus infection, relief has been maintained by long-term therapy.

The typical prostration or semi-stuporousness that some adults have with chickenpox has improved markedly within 30 min after the first injection, and no new chickenpox lesions have emerged. Again, the injections are repeated for each recurrence of malaise until it no longer recurs, typically for about 1 week. In children with chickenpox, the itching of the skin lesions has cleared after the first injection, and no new skin lesions have occurred. The old lesions scab over and heal in about 3 days. The signal for using repeat injections in children has been recurrent itching of the old lesions. Each injection clears the itching in 30 min. In both adults and children, a single daily injection has usually been sufficient to maintain relief after the first 2 or 3 days.
THE VALUE OF CLOSELY SPACED INJECTIONS

Influenza may be complicated by such conditions as emphysema, chronic obstructive pulmonary disease, hypertension, congestive heart failure, compromised kidney or liver function, diabetes, primary influenzal pneumonia, and many others. Elderly patients with these conditions are the ones most likely to succumb to influenza and its complications.

Severe herpes virus infections, such as destructive lesions of an eye, could rapidly lead to grave situations such as loss of the eye. In such a patient, it is desirable to repeat the treatment injections before symptoms recur, such as on a schedule of every 3 hours day and night the first day or two, then at progressively longer intervals as healing proceeds. This type of schedule provides a much better opportunity to rapidly reverse the inflammatory and necrotizing processes, and in ocular herpes, to prevent loss of the eye.

With correct dosage, multiple closely spaced injections have provided greater benefit, not adverse reactions. If an adverse reaction should occur, it would probably not be due to the close spacing of injections but to a change in the patient’s dosage-need level. Immediate retesting can quickly determine the new treatment dose. Administration of this dose will eliminate the symptoms of the ‘adverse reaction’ in 30 min and restore the ongoing beneficial response.

TREATMENT APPARENTLY DECREASES INFLAMMATION AND INCREASES IMMUNITY

Pain relief is of great importance in itself. But this treatment does not just relieve symptoms such as pain. The progression of the entire inflammatory process (characterized by edema, erythema, and local heat, as well as pain) is also markedly inhibited. When visible tissue necrosis has been present, as in herpes of the lip or eye, the necrotizing process can be seen to be quickly halted and reversed. Furthermore, if a relief dose is administered during the prodromal paresthesia, consisting of symptoms such as tingling and numbness of the lip, that has, in this patient, invariably been followed in the past by the development of a fever blister, the tingling and numbness will usually be cleared in 30 min, and the fever blister will usually not appear. Typically, the single timely relief dose will abort the attack and prevent the occurrence of both inflammation and necrosis. The need for a second or third such injection is infrequent.

Apparently, immunity is often enhanced as well. For example, most patients who have had severe recurrent attacks of fever blisters, lasting up to 2 weeks almost every month for several years, begin noting that recurrences quickly become much less frequent and less severe if they are treated for each recurrence. Some are continuing to be completely or near-completely recurrence free for 20 or more years as of this writing.

DETERMINATION OF THE APPROPRIATE TREATMENT DILUTION

Preparing the Testing Dilutions

Testing to find the relief dose for influenza or herpes virus infections is accomplished with five vials of 1:5 serial dilutions of influenza virus vaccine (Fig. 1).

The concentrate vial contains full strength influenza virus vaccine. Each successive vial is five times weaker than the preceding vial. Thus vial number 1 contains a 1:5 dilution of the concentrate, number 2 contains 1:25, number 3 contains 1:125, and number 4 contains 1:625.
Performance of the Intradermal Test

The effective dose for each patient is initially determined by intradermally injecting into the deltoid area, 4 or 5 cm apart, in a vertical row, 0.05 ml of concentrate and the four 1:5 serially diluted vaccine suspensions. In general, stronger dilutions tend to produce wheals which grow 2 mm or more in average diameter and thereby become positive, whereas weaker dilutions tend to produce wheals which grow less than 2 mm and thereby become negative. In almost 100% of such tests, the strongest of these dilutions that produces a negative wheal with 0.05 ml test volumes is the dilution that provides the 30 min relief response—a highly repeatable, objective endpoint that correlates very well with subjective relief.

The strongest negative wheal dilution is also described as the maximal intradermally tolerated dilution, as it produces a negative wheal (and all weaker dilutions invariably produce negative wheals) and the next stronger dilution produces a positive wheal (and all dilutions stronger than this produce positive wheals). Although figures vary from year to year, the strongest negative wheal dilution has typically occurred on concentrate in approximately 25% of tests, on dilution number 1 in 50%, on dilution number 2 in 15%, on dilution number 3 in 7%, and on dilution number 4 in 3%.

TEST PROCEDURE FOR SPECIAL PATIENTS

Tests are not performed on patients with a history of asthma, anaphylaxis, laryngeal edema, egg sensitivity, or significant reaction to previous exposures to influenza virus vaccine or any of its ingredients. If judgement dictates an overriding need in such cases, extreme caution should be observed and all preparations made in advance for handling possible severe test responses.

In these patients, the same intradermal test procedure can be employed but with the use of 0.01 ml rather than 0.05 ml test volumes. The 0.01 ml volume is difficult to visualize on the syringe, so is defined as the volume required to produce a 4 mm wheal (0.05 ml usually produces a 7 mm wheal). With a little practice, the technician can accurately inject just sufficient volume to produce the 4 mm wheal. The use of 0.01 ml volumes is much less likely to induce symptoms, and any symptoms that do arise should be milder and briefer.

Once the strongest negative wheal dilution is determined with 0.01 ml volumes, 0.05 ml of this dilution is administered. If a negative wheal is thereby produced, it verifies that this is indeed the treatment dilution. However, when this 0.05 ml injection has produced a positive wheal, as it has in 11% of such tests, 0.05 ml of the next weaker dilution has been injected and, thus far, has invariably produced a negative wheal and relief, and has been the effective treatment dose.
VERIFYING THE DOSE

When the initial intradermal testing reveals what appears to be the strongest negative wheal dilution, 0.05 ml of this and the next stronger dilution are again injected intradermally. If, in 10 min, the stronger dilution produces a positive wheal and the weaker dilution produces a negative wheal, the weaker dilution has been verified as the strongest negative wheal dilution, and has been confirmed to be the appropriate treatment dilution. Then 0.10 ml of the strongest negative wheal dilution is self-administered subcutaneously in the office by the instructed patient. Any symptoms present should markedly subside or completely clear in 30 min. Infrequently, a second or third such injection is required for complete eradication of symptoms. If the symptoms do not improve, or indeed worsen, it is usually because the wrong dilution has been administered. Immediate retesting is indicated to find the true relieving dilution, which is almost always the strongest negative wheal dilution. Obviously, to find the strongest negative wheal dilution, it is necessary to first find the weakest positive wheal dilution (Figs 2 and 3).

UNDERDOSE WORSENING AND SEVERE SHINGLES PAIN

Neither an overdose dilution nor an underdose dilution will be a satisfactory treatment dilution even if test symptoms clear temporarily on them during testing. Even on a true relieving dilution, symptoms from preceding injections can emerge or worsen somewhat for a few minutes before they clear. Although wheals usually reach their peak at 10 min (rarely at 15 min) and should be evaluated at that time, symptoms of influenza and herpes virus infections usually require about 30 min to completely clear.

Paradoxically, in this system of intradermal testing, symptoms can be worsened with ‘underdose’ dilutions, i.e. negative wheal dilutions that are weaker than the relieving dilution, as well as with ‘overdose’ dilutions, i.e. positive wheal dilutions. Underdose worsening can be severe and progress rapidly. This requires administering consecutively stronger dilutions at intervals of 10 min or less, until a positive wheal is produced, then

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**FIG. 2.** Superficial intradermal injection of 0.05 ml produces a wheal of approximately 7 mm average diameter (6×8, 5×9, etc.). Growth in average diameter of 2 mm or more in 10 min is typical of a positive wheal. Growth of less than 2 mm in average diameter is typical of a negative wheal.
administering the next weaker dilution to end with the strongest negative wheal dilution and relief.

In patients with severe shingles pain, underdose reactions can induce marked worsening of the pain which the relief dose may not be able to overcome. In testing these patients, the use of underdoses can be avoided by injecting 0.01 ml of a single concentration at a time, at 10 min intervals, beginning with concentrate. When the first negative wheal dose with 0.01 ml is reached, 0.05 ml of that dilution should be administered. If this produces a negative wheal, it is the relieving dilution. A second or third such relieving injection may be required for maximal relief in severe shingles. If the 0.05 ml dose should produce a positive wheal, 0.01 ml and then (if negative) 0.05 ml of the next weaker dilution should be used and this should be the relieving dilution. To avoid underdose worsening, no dose weaker than the strongest negative wheal dilution should be used.

Patients with severe shingles (and other severe illnesses) may enter the office so weak and in such severe pain that they are unable to undergo testing without an analgesic. These have benefited from the administration of a hydrocodone acetaminophen capsule and lying down or reclining for testing. The analgesic and reclining position will not provide relief but can increase postural security and reduce the anxiety and pain enough to allow time for finding and administering the relieving dose.

In summary, the final result depends upon the production of a contiguous positive wheal/negative wheal pair, the negative wheal being produced by the next weaker dilution than the one that produced the positive wheal.

DISTINCTIONS BETWEEN POSITIVE AND NEGATIVE WHEALS

Misreading the wheals is the most common error in testing. Therefore, it is critical to learn to distinguish a positive from a negative wheal, as defined for this test. Failure to do so will result in failure to provide relief. Another common error is injecting too deeply into the epidermis. A maximally superficial injection is required to allow proper wheal growth and morphology.

All intradermal injections produce wheals which, at the moment of injection, are markedly blanched, hard, and raised, like a circular disc cemented to the skin. If at 10 min
these characteristics are retained or have increased, this is typically a positive wheal. Erythema of the wheal or surrounding skin may occur but does not necessarily denote positivity in this system of testing. If, however, in 10 min all these characteristics have definitely diminished and the wheal is flesh-colored (not blanched), and softer or flatter than originally (not as hard and raised), this is typically a negative wheal (Fig. 2).

In testing with influenza virus vaccine, an important characteristic of wheal development is average wheal growth in 10 min. A positive wheal almost always grows 2 mm or more in average diameter in 10 min. A negative wheal almost always grows less than 2 mm, if at all (Fig. 3). The final designation of a wheal as positive or negative requires evaluation of all these characteristics, namely growth, blanching, hardness, elevation, and disc-like appearance.

For technician practice in inspecting, palpating, and measuring for wheal evaluation, one can intradermally inject 0.05 ml of phenolated saline diluent. At the moment of injection, this wheal will be blanched, hard, raised, and disc-like, resembling a positive wheal. Ten minutes later, however, it will have lost these characteristics and will have grown less than 2 mm, resembling a negative wheal, due to absorption of some of the saline. One can also demonstrate a positive wheal by intradermally injecting 0.05 ml of 10% glycerine. This wheal will have all the characteristics of positivity at 10 min as well as at injection, and will have grown 2 mm or more, because of the hygroscopic action of glycerine, holding and drawing additional fluid into the wheal.

POST-TEST TREATMENT

Once the treatment dose has been established in the office, the patient or a member of the family can be taught to give the injections at home for relief whenever symptoms return. The patient can be provided with syringes and a vial containing the number of such treatment doses needed. Because a small amount of vaccine can leak out of the skin after some subcutaneous injections, a dose of 0.1 ml (rather than 0.05 ml) of the relieving dilution is used in therapy. This also facilitates patient accuracy, as the 0.1 ml mark on the syringe is easier to visualize.

Because the influenza virus vaccine is constituted differently each year, the current vaccine must be used for influenza treatment each year. On the other hand, herpes infections have apparently been relieved equally well with each of the influenza virus vaccines that have been available each year.

THE IMPORTANCE OF INFLUENZA

The influenza virus has been known to cause epidemics for at least 400 years. Influenza epidemics have caused an average of 30,000 excess deaths annually in the USA, much more in some years. For example, during the Asian Flu virus epidemic of 1957–58, an estimated 78,000 excess deaths occurred. It has been estimated that at least 10–30% of the population—and possibly up to twice that many—become infected in an epidemic. In institutions such as schools, as many as 50–60% may develop the illness [10].

Influenza causes a tremendous amount of absenteeism. The maintenance of vital utilities and services in a community or a military group may be seriously curtailed by the rapid spread of the epidemic. The economic cost of the 1968 pandemic (world-wide epidemic), which was not considered a major pandemic, was estimated to exceed $3.9 billion [11].

Over two-thirds of the deaths occur in patients 65 years of age or older. The following conditions, among others, predispose individuals to such risk: (1) heart disease; (2) chronic pulmonary disease; (3) hypertension; (4) chronic liver or kidney disease; (5) diabetes; (6) chronic severe anemia such as sickle cell disease; (7) older persons, particularly those over
65 years of age; (8) conditions which compromise the immune mechanism, including AIDS, certain malignancies, chemotherapy, therapy with other immunosuppressive drugs, and, to a lesser extent, long-term daily high-dose cortisone therapy [12]. Our population is aging, so this will be an increasing problem in the future. Is it possible that relief-dose therapy might help many of these?

Thirty-two world-wide pandemics have occurred. In the pandemic of 1918–19, 549,000 excess deaths were recorded in the USA and 21 million deaths worldwide [13]. That pandemic killed twice as many people as had World War I. It was said to have killed more Americans in a single year than died in battle in World War I, World War II, the Korean War, and the Vietnam War [14]. ‘If such a plague came today, killing a similar fraction of the U.S. population, 1.5 million Americans would die, which is more than the number killed in a single year by heart disease, cancer, strokes, chronic pulmonary disease, AIDS, and Alzheimer’s disease combined’ [14]. Furthermore, ‘it is probably the largest number of people dying over that period of time from an infectious disease. The next comparable event would be to go back to the fourteenth century and the Black Death’ [14]. ‘Even today, with the exquisite advances of molecular biology in the pharmaceutical industry, viral diseases—and influenza in particular—are largely untreatable’ [14].

THE IMPORTANCE OF HERPES

Herpes viruses are everywhere, they do much harm, and they tend to persist or recur repeatedly for life. More than 50 herpes viruses are known to infect 30 vertebrate species [15–17]. The human herpes viruses, a group of DNA viruses, includes herpes simplex viruses types 1 and 2, varicella zoster virus, cytomegalovirus, Epstein–Barr virus and human herpes viruses 6, 7, and 8 (Table 1). They cause substantial morbidity and mortality among infants and children as well as adults [18].

Herpes Simplex Virus Type 1

Dr Albert Sabin, developer of the oral polio vaccine, has stated that herpes simplex virus type 1, commonly called the fever blister virus, is one of the most common, most painful, and most recurrent afflictions of mankind [19]. Herpes simplex virus type 1 causes painful ulcerative lesions of the lips, mouth, throat, face, ears and eyes, and can also cause infections of the brain. Infection of the lips and face (such as fever blisters) is very common, occurring in 20–40% of the population [20, 21]. This virus also causes herpetic gingivostomatitis in small children, with fever and painful ulcers of the mouth, tongue, and throat [22, 23]. The children refuse to eat or drink for nearly 2 weeks and may have to be monitored carefully for the danger of dehydration.

Herpes simplex virus type 1 also causes prolonged painful ulceration of the throat in adults [24, 25]. These patients suffer excruciating pain whenever they try to chew or swallow ordinary food [26]. Many must subsist on bland, unseasoned foods like plain boiled spaghetti or macaroni, sliding it down their throats with a minimum of swallowing action.

Herpes simplex virus type 1 causes 500,000 cases annually of potentially destructive ocular herpes simplex, and is the leading infectious cause of blindness in the USA [27]. This virus can also attack the brain and cause encephalitis. Herpes encephalitis kills a third of these patients, and half the remainder suffer permanent neurological damage such as cerebral palsy and mental retardation [28, 29]. I have not had an opportunity to treat gingivostomatitis or encephalitis, but most patients with the other syndromes I have described have responded.
Herpes Simplex Virus Type 2

Herpes simplex virus type 2 causes most cases of genital herpes. It is the second most common venereal disease after gonorrhea [30]. At least 50% of the newborns delivered vaginally through herpetic birth canals become infected, and about 50% of these are killed or severely damaged [31–33]. Herpes simplex virus type 2 also causes highly fatal herpetic meningitis [34, 35]. I have not treated infected newborns or meningitis. Genital herpes has responded, with a much higher response rate in females than males.

Varicella Zoster Virus

The varicella zoster virus typically causes varicella (chickenpox) in childhood, then persists for life in nerve cells, and can re-emerge later to cause herpes zoster (shingles). Shingles is an extremely painful, prolonged skin condition afflicting three million patients annually in the USA [36]. In some patients, the pain persists for life (post-herpetic neuralgia) [37, 38]. Varicella zoster infection is ubiquitous. Nearly all persons contract chickenpox before adulthood, and 90% of cases occur before the age of 10 years. Chickenpox can produce severe malaise and prostration, particularly in adults. Primary chickenpox virus pneumonia is highly fatal. Chickenpox can also be fatal if contracted by patients being treated with immunosuppressives or chemotherapeutic agents for conditions such as Hodgkin’s disease, leukemia, and bone marrow or organ transplants, or by patients with inborn immuno-deficiency disorders. It can also be fatal if contracted by patients on high-dose continuous cortisone therapy. Even when none of these conditions exists, the chickenpox virus can kill
by entering the open skin of patients with generalized skin conditions such as allergic eczema or burns. Children with poor nutrition, measles, pertussis (whooping cough), and other debilitating diseases may also succumb to chickenpox.

Reye’s syndrome is a highly fatal disease of children who are given aspirin when they have chickenpox or influenza B virus infections. I have had no opportunity to treat Reye’s syndrome, but chickenpox and influenza B would probably respond. I wonder if the fatal course might be reversed if treatment was initiated early. In general, the more severe the infection, the more closely the treatment injections would need to be spaced.

**Cytomegalovirus**

Cytomegalovirus is a member of the herpes family of viruses [39]. The most serious clinical syndrome caused by cytomegalovirus is congenital cytomegalovirus disease. World-wide, 1% of unborn infants are infected *in utero*. The infants with symptomatic illness (about 0.1% of all births) may have a variety of congenital defects. Twenty per cent of those who have been infected before birth and who appear normal go on to develop sensory nerve hearing loss and/or psychomotor mental retardation. In young adults and children, cytomegalovirus may cause a mononucleosis-like syndrome [40, 41]. In immunosuppressed patients, latent cytomegalovirus may again become active, resulting in highly fatal cytomegalovirus pneumonia. In patients receiving bone marrow transplants, interstitial pneumonia caused by cytomegalovirus (with a mortality rate of 90%) is the leading cause of death [42].

Like other herpes viruses, cytomegalovirus is both ubiquitous and latent. At least 80% of adults have antibody to it from a prior infection. The infection can be contracted *in utero*, in childhood, or in adulthood. The virus has been isolated from saliva, cervical secretions, semen, urine, and white blood cells. Transmission of infection in daycare centers to other children and parents has been shown to occur from asymptomatic excretors [43].

Cytomegalovirus infections have been major problems in the transplantation of bone marrow, hearts, kidneys, and other tissues and organs. That is because immune deficiency such as that in immunosuppression or chemotherapy limits the patient’s ability to keep this virus under control [44]. Cytomegalovirus continues to be one of the most important opportunistic infections associated with HIV infection [45]. I have had no opportunity to treat cytomegalovirus infections.

**Epstein–Barr Virus**

The Epstein–Barr virus, another ubiquitous human herpes virus, causes infectious mononucleosis, characterized chiefly by severe sore throat, profound malaise, fever, and enlarged lymph nodes in the neck. Mononucleosis is common and world-wide. It may occur as a subclinical infection in early childhood or as an overt infection in adolescence. Symptoms usually last 4–6 weeks, but may persist for several months [46].

However, mononucleosis can also become chronic and can last for years as chronic Epstein–Barr virus syndrome. This syndrome is characterized by profound weakness, fatigue, muscle pains, sore throat, and fever. It can cause severe incapacitation and require radical limitations of life style, diminution of career and personal goals, and resultant feelings of profound hopelessness and depression. In rare instances, serious or fatal complications may occur [47].

Nearly all adults show positive blood tests, indicating that they have been attacked by this virus at some time. It can be transmitted by exchange of saliva on drinking cups and other objects, and by kissing. Infectious mononucleosis has also been transmitted by blood transfusion, and infections have developed after open heart surgery. Relief doses of influenza virus vaccine have provided much benefit to patients with mononucleosis and
chronic Epstein–Barr virus syndrome. I know of no comparable treatment for these diseases.

In conclusion, the herpes virus is everywhere and forever. After the initial infection, it remains latent in the body and can re-emerge later to cause problems. Virtually everyone in the USA has had chickenpox, acute herpetic gingivostomatitis, roseola, infectious mononucleosis, fever blisters, genital herpes, shingles, or cytomegalovirus infection. Therefore, virtually everyone harbors one or more herpes viruses.

**HERPES AND CANCER**

Can a virus infect a normal cell and transform it into a malignant cell? Can a herpes virus do this? If so, would elimination of the virus by prior immunization or by early treatment of the herpes infection prevent development of the cancer?

A growing and highly respected community of researchers in cancer and infectious diseases believes that micro-organisms—viruses, bacteria, and parasites—play a significant role in cancer, heart disease, diabetes, and other illnesses that are not traditionally regarded as infectious. In many cases, the micro-organisms are ‘co-factors’; that is, to cause cancer, they must be accompanied by another factor such as a weak or suppressed immune system, a chemical exposure, or a genetic predisposition.

More than a dozen herpes viruses have been associated with cancer in man and various animals [19, 48–53]. Sabin and Tarro have linked a herpes antigen with nine different kinds of human cancer [54]. Herpes simplex virus type 1, the fever blister virus, has been associated with cancer of the lips [53]. Wyburn-Mason described cancers of the lips that appeared within fever blisters, as well as in the same site on the lips as preceding fever blisters [55].

Some studies have shown an association between herpes simplex virus type 2 (the genital herpes virus) and carcinoma of the uterine cervix [56]. Recent studies have linked another genito-urinary pathogen, the human papilloma virus that causes genital warts, more closely to these tumors [57, 58]. Cervical dysplasia, a pre-cancerous condition, is caused by infection with the human papilloma virus and strikes 600,000–1,000,000 American women each year. Could the incidence of cervical cancer be reduced by early treatment of cervical dysplasia with relief doses of influenza virus vaccine, a herpes virus 2 vaccine, or a papilloma virus vaccine? Pharmaceutical companies are now working on a papilloma virus vaccine. For patients in whom a herpes virus is incriminated, influenza virus vaccine, of course, is already available for trial.

The Epstein–Barr virus that causes infectious mononucleosis has been consistently linked with Burkitt’s lymphoma (a cancer of lymphocytes) and also with cancer of the nasopharynx. Recent evidence suggests that the Epstein–Barr virus also causes Hodgkin’s disease, i.e. it infects certain cells (dendritic cells) and transforms them into the malignant cells of Hodgkin’s disease [59, 60]. It has also been implicated in the pathogenesis of both B-cell and T-cell lymphomas, and, more recently, certain cancers of the stomach and smooth muscle [60].

Is it possible that relief-dose technology with vaccines such as influenza virus vaccine may be useful not only in treating herpes-associated infections like infectious mononucleosis, but in preventing or treating some herpes-associated pre-malignancies or frank malignancies? I am not alone in putting forward this general concept. Khanna et al. [61] suggest that ‘emerging technologies are at a level where vaccine trials aimed at controlling infectious mononucleosis, post-transplant lymphoproliferative diseases, nasopharyngeal carcinoma and Hodgkin’s disease are justified’.

Another herpes virus, the Kaposi’s sarcoma-associated herpes virus, also known as human herpes virus 8, is now considered to be the probable cause of Kaposi’s sarcoma, and also of some lymphomas [62, 63]. Kaposi’s sarcoma is a cancerous condition prevalent
in patients with compromised immune systems, and has become a scourge of patients with AIDS [64, 65]. This virus is also considered to play a possible etiological role in the pathogenesis of multiple myeloma [66–73]. Sjak-Shie et al. [73] state: ‘A direct or indirect causal effect of HHV-8 (in Kaposi’s sarcoma and multiple myeloma) has enormous implications for the therapeutic benefit of antiviral agents and preventive strategies using vaccines. There is, indeed, preliminary evidence that antiviral therapy in HIV-infected patients reduces the risk of development of Kaposi’s Sarcoma. Clinical improvement in patients with Kaposi’s Sarcoma treated with antiviral agents has also been reported. These observations suggest that future treatment strategies to combat multiple myeloma may include antiviral agents.’

*Helicobacter pylori* is the bacterium that is now known to cause gastric ulcers. Certain strains of this bacterium, possibly combined with as yet unknown co-factors, are also considered by many researchers to be the cause of two types of stomach cancer [74]. Clinical studies have shown that low grade gastric lymphoma, when confined to the mucosa, may regress after eradication of *H. pylori* from the patient’s stomach with appropriate antibiotics [75, 76].

Can preventive immunization of a virus infection in a community reduce the incidence of a specific cancer in that community? In 1984, all the children of Taiwan, where liver cancer (hepatocellular carcinoma) in children was rampant, were vaccinated against hepatitis B [77]. Twelve years later, a report was published in *The New England Journal of Medicine* describing a remarkable decrease in hepatocellular carcinoma in the children [77]. Combating an infectious disease in that population had reduced the incidence of a specific cancer related to that disease. Dr Anthony S. Fauci, Head of the National Institute of Allergy and Infectious Diseases, said the Taiwan study was very significant. He said, ‘For the first time, it is possible to make absolute associations between some microbes and cancer. The link between hepatitis B and liver cancer is a “slam dunk”. The same is true of human papillomavirus and cervical cancer’ [78].

I mention these microbial–cancer relationships to suggest the possibility that early treatment of certain herpes virus infections might reduce the opportunity for the herpes virus to change normal cells into malignant cells, thereby possibly preventing the occurrence of some specific cancers. These specific cancers might include carcinoma of the lips, carcinoma of the nasopharynx, carcinoma of the cervix (when due to herpes simplex virus type 2), Burkitt’s lymphoma, Hodgkin’s disease, lymphomas, cancers of the stomach and smooth muscle due to Epstein–Barr virus, Kaposi’s sarcoma, and multiple myeloma.

The only herpes-specific vaccine available today is the recently introduced varicella zoster vaccine. To my knowledge, it has not yet been studied, even for chickenpox or shingles, by the relief-dose method. If we had preventive vaccines for the Epstein–Barr virus or the Kaposi’s sarcoma herpes virus, we might find that relief doses of these vaccines could be useful in infections (and cancers?) caused by these oncogenic viruses. What we do have now is the influenza virus vaccine, which has been effective by the relief-dose method in all the types of herpes virus infection in which it has been employed. It seems reasonable to study the possibility that it might also be helpful in reducing malignant transformation of herpes virus infected cells that could lead to cancer. If all patients with herpes virus infections in a study population were treated early and completely with influenza virus vaccine relief doses, it seems likely that many patients would benefit. Would such a study of infections caused by the Epstein–Barr and Kaposi’s sarcoma herpes virus also result in a decrease in the incidence of cancers caused by these viruses?

Would this concept be applicable to relief doses of other vaccines, such as a papillomavirus vaccine for cervical dysplasia, or a hepatitis B vaccine, which is now available, for patients who already have hepatitis B infection? Could such treatment doses not only provide relief for the infection but possibly the prevention of the cancer?
THE NEED FOR DOUBLE-BLIND STUDIES

Although I have used this procedure in office practice since 1968, I have not been able to do the double-blind placebo-controlled studies that need to be done to confirm or deny my clinical experiences. That is what I am seeking to do now.

*Is this rapid relief response in influenza and herpes virus infections important enough to warrant double-blind studies?* Emphatically, *yes.* Here are four reasons:

First, influenza and herpes virus infections occur in high incidence world-wide and they both cause a great amount of human suffering, destructiveness, and death. Furthermore, once the infection has become established, no comparable therapy is available for any of them. So the first reason for studying this system of therapy is to provide relief for these patients.

Second, the successful use of a small dose of a specific preventive vaccine to provide quick therapeutic relief for a patient who already has that specific infectious disease (as exemplified by influenza virus vaccine for influenza virus infections) is a new and important finding in medical therapy. It has not been known before. All these years that we have had preventive vaccines, we did not know that we might have been using them to provide quick relief for sick patients, not just future immunity for currently well patients. Could we have saved some of these patients? Are we not now obligated to confirm this and discover which of the many vaccines available, and those which will become available, can do this?

Third, the successful use of a small dose of one vaccine to relieve patients with an infection from an entirely unrelated virus (as exemplified by influenza virus vaccine for herpes virus infections) is another landmark finding. It needs to be studied. It opens the field even wider for additional knowledge and the possibility of helping a great many more sick people. There are already 21 vaccines available today (see Table 2).

Additionally, if a given killed-virus vaccine is not usable or is not readily adopted for immunization by the general population—such as an HIV vaccine for AIDS—it might still be useful for therapeutic relief in HIV-positive or frank AIDS patients who already have the infection and are desperately seeking help. Furthermore, patients with normal immune mechanisms are routinely immunized with live-virus vaccines, so it should be safe to treat such patients with relief doses of live-virus vaccines. And live-virus vaccines can be converted to killed-virus or other safe vaccines for immunocompromised patients.

Fourth, this clinical finding has revealed the existence of a simple method for calling forth a rapidly effective natural human disease-fighting, inflammation-reversing, and immunity-enhancing mechanism that has been entirely unknown and unutilized before now. There is no antibiotic or anti-viral treatment available today that provides relief in 30 min, none that eliminates fever in the first 24 hours, as in influenza, and none that antagonizes the entire inflammatory response and produces such rapid healing as demonstrated so clearly in influenza and fever blisters. There is also none that confers the long-term enhancement of immunity as is seen in the markedly reduced frequency of recurrences of fever blister attacks. Learning the molecular mechanism of this response

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**TABLE 2. Injectable vaccines available for 21 diseases**

<table>
<thead>
<tr>
<th>Influenza</th>
<th>Tetanus</th>
<th>Poliomyelitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mumps</td>
<td>Hepatitis A</td>
<td>Plague</td>
</tr>
<tr>
<td>Meningococcal meningitis</td>
<td>Pneumococcal meningitis</td>
<td>Pertussis</td>
</tr>
<tr>
<td>Hemophilus influenza B</td>
<td>Chickenpox</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Rubella</td>
<td>Rabies</td>
<td>Diphtheria</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Measles</td>
<td>Typhoid</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>Yellow fever</td>
<td>Tick borne encephalitis</td>
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</table>
could lead to new knowledge about human immunology and a new basic understanding of how our bodies function, as well as how such beneficial functioning can be brought into play for the greater protection of patients.

SUGGESTED STUDIES

My suggestion is that we first prove or disprove my clinical claims. One obvious study would be relief of acute influenza symptoms in 30 min with influenza virus vaccine, subsidence of fever in less than 24 hours, and clearing of all symptoms in 3 or 4 days.

A second example of a simple research study is rapid pain relief and an accelerated rate of healing of fever blisters with influenza virus vaccine. Objective healing can be confirmed by describing or photographing the lesions of treated patients vs. the lesions of control patients, to compare healing times. Follow-up studies can demonstrate the reduced frequency of recurrences after treatment for several recurrences, as well as abortion of future attacks by using a relief dose during the prodrome.

There could also be studies, not necessarily in this order, of genital herpes, shingles, mononucleosis, chickenpox, chronic Epstein–Barr virus syndrome, Burkitt’s lymphoma, cytomegalovirus infections, and Reye’s syndrome (Table 3). This could possibly lead to studies of the prevention of herpes virus-related malignancies such as multiple myeloma, Hodgkin’s disease, and Kaposi’s sarcoma. And successes with influenza virus vaccine might lead to fruitful studies of other diseases with other vaccines.

Of course, this is much speculation based on limited clinical experience. However, if the first studies are successful, they can open the door to many additional studies, new scientific knowledge, and much benefit for great numbers of patients world-wide. The benefit/risk ratio is favorable.

AN ERA OF IMMUNOBIOPTICS?

The rapid relief response to influenza virus vaccine therapy constitutes the first rapidly effective anti-viral treatment for any established virus infection. It is unusually safe, rapidly effective, globally available, broadly applicable, and very economical.

Is it possible that we may be about to enter an era of immunobiotics, in which many acute viral infections can be successfully controlled and their consequences successfully checked with small relief doses of indicated vaccines? The answer can only come from putting this concept to the test.

<table>
<thead>
<tr>
<th>TABLE 3. Disease conditions for possible relief-dose trials</th>
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<tbody>
<tr>
<td><strong>Viral infections</strong></td>
</tr>
<tr>
<td>Influenza</td>
</tr>
<tr>
<td>Herpes simplex 1 (fever blisters)</td>
</tr>
<tr>
<td>Herpes simplex 2 (genital herpes)</td>
</tr>
<tr>
<td>Herpes zoster (shingles)</td>
</tr>
<tr>
<td>Post-herpetic neuralgia</td>
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<tr>
<td>Infectious mononucleosis</td>
</tr>
<tr>
<td>Chronic Epstein–Barr virus syndrome</td>
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<tr>
<td>Varicella (chickenpox)</td>
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<tr>
<td>Cytomegalovirus infection</td>
</tr>
<tr>
<td>Herpetic gingivostomatitis</td>
</tr>
<tr>
<td>Roseola</td>
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<tr>
<td>Pityriasis rosea</td>
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Would we say, someday, that scientific double-blind studies have been justified if all these concepts and speculations have become reality? To keep certain herpes infections from causing herpes-associated cancers? To prevent herpetic and non-herpetic pre-cancerous conditions from becoming frank cancers? To discover that some of the 21 vaccines already available, and others which will become available, are effective in the diseases for which they have been produced and possibly for some other diseases as well? Or failing all these, to still be able to provide relief and possibly improved immunity in one or more types of herpes virus infection, such as painful fever blisters, eye-destroying ocular herpes infections, infant-killing genital herpes, the severe pain of shingles and post-herpetic neuralgia, the serious and sometimes fatal complications of chickenpox, the debilitating and often prolonged depressing effects of mononucleosis and chronic Epstein–Barr virus infections, the killing and impairing of infants and children who contract cytomegalovirus infections, or the prolonged pain of gingivostomatitis in infants and children? Or even ‘just’ for influenza, or for learning new and hitherto undiscovered ways we can direct our immune system to work for our benefit?

REFERENCES


