Consequences and Management of Pain in Herpes Zoster

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Postherpetic neuralgia (PHN) is a common complication of herpes zoster, particularly in the elderly and in persons with severe symptoms at presentation. Unless varicella vaccination reduces the incidence of herpes zoster and attenuates the risk and/or severity of complications, PHN will continue to result in significant suffering and remain a consumer of health care and related social support resources. Although there have been useful advances in the management of PHN (e.g., the use of the anticonvulsant gabapentin), some cases remain intractable. Prevention remains the preferred strategy, and antiviral drugs are the most well established means of preventing the development of pain. Other interventions require further evaluation (nerve blocks, acute-phase tricyclic antidepressant or anticonvulsant use). Because prevention of PHN requires early recognition and prompt management of patients presenting with herpes zoster, public education and dissemination of information to all health care personnel involved with the disease are essential.

The most debilitating symptom of herpes zoster is the associated pain, which commonly occurs in the acute (rash) phase and can persist to become chronic for months or even years [1–3]. Herpes zoster pain has a major impact on patients’ quality of life (QoL). Once postherpetic neuralgia (PHN) is established, it can be difficult to manage effectively, making this complication the most compelling reason to treat herpes zoster. Early treatment with antiviral agents reduces the incidence and duration of prolonged zoster-associated pain [4–6]. However, barriers to early treatment must be removed. The benefits and optimum use of a number of interventions for the prevention and treatment of chronic zoster-associated pain have yet to be determined, but options include analgesics, tricyclic antidepressants, nerve blocks, and anticonvulsants. Social, psychological, and environmental factors also influence a patient’s perception of pain and the ability to cope with pain and discomfort [7].

A coherent management strategy must be developed for each patient with PHN. Pain is a biopsychosocial phenomenon, and all components of the triad should be addressed for care to be effective. Here I discuss the phenomenon of zoster-associated pain, its impact on patients and meaning for health care providers, and current strategies for preventing and treating chronic pain following herpes zoster.

Epidemiology of Herpes Zoster and PHN

The incidence of herpes zoster and its direct relationship to age has been estimated from prospective and retrospective population studies. There is no indication that the incidence has fallen with time but there are reasons to expect the converse. Increasing longevity (leading to a natural decline in cell-mediated immunity) and rising numbers of patients who are immunocompromised, either because of disease (e.g., human immunodeficiency virus infection) or therapy (e.g., organ transplantation or rheumatoid arthritis), may be expected to increase the incidence of herpes zoster. The impact of child and adult vaccination against varicella-zoster virus (VZV) on the prevalence of herpes zoster and PHN remains to be determined, although epidemiologic investigation of US sentinel sites shows a clear reduction in the incidence of varicella with universal childhood vaccination.

An early UK study (1947–1962) demonstrated an incidence of herpes zoster of 3.4 per 1000 population per year, with a direct relationship to age such that the incidence in those in their eighth decade of life was 10 per 1000 per year [8]. A US survey conducted at a similar time reported an incidence of 1.31 per 1000 [2], but more recent figures indicate that the overall incidence has risen to 2.9 per 1000 [9]. The annual incidence of herpes zoster was recently reported to be 4.8 per 1000 in Iceland [10] and 4.8 per 1000 in France [11].

PHN has been variously defined as pain persisting from 1 month after rash onset, pain persisting after rash resolution, pain at 3–6 months after the acute episode, and pain differing from acute pain [12]. The lack of consensus on when acute pain ends and chronic pain begins matters little to the patient but makes comparisons between different epidemiologic and efficacy studies difficult. The development of a zoster international data standard to permit meaningful analysis of data from different sources has been proposed [13]. Recently, phase-specific
analysis has separated herpes zoster pain into three phases: acute, subacute, and chronic. The subacute and chronic phases comprise the PHN stage [14]. This methodology allows the effect of treatment on a specific phase to be assessed while controlling for the effect of other variables.

Although PHN is the most common complication of herpes zoster, there are fewer data on the relative frequency of PHN than on the incidence of the disease overall. The proportion of patients with herpes zoster still experiencing pain 4–5 weeks after rash crusting was reported as 28.4% in one study [15]. In another UK retrospective study, 15% still had pain 3 months after rash appearance [16]. At 1 year, about 5%–10% of patients still had pain; spontaneous resolution of PHN after this duration is limited [16]. In a meta-analysis, 25% of placebo-treated cases of herpes zoster reported pain at 6 months [4]. A small study in Iceland [10] reported incidences of pain of 19.2%, 7.2%, and 3.4% at 1, 3, and 12 months after rash onset, respectively, but this isolated study may significantly underestimate the magnitude of the problem in other countries. Not all studies have included data on pain severity, thereby increasing the difficulty of comparing studies.

Effect of PHN on the Patient

The impact of PHN falls on patients, their caregivers, and on health care providers. The burden includes both personal suffering and use of health care and social or community support resources. The quality of the pain when examined by using the McGill pain questionnaire [17, 18] was described by patients as tender, burning, throbbing, stabbing, shooting, and/or sharp. Allodynia, or pain following stimuli not normally overtly painful, is described by a majority of patients [19]. Patients with prolonged PHN often have ongoing disturbances in physical and psychosocial functioning [20–23]. In severe cases, PHN can lead to drug dependency, depression, and even suicide [11].

The Nottingham Health Profile (NHP), a generic health-related QoL measure, was used to assess the impact of herpes zoster on overall health status, including patients' energy levels and ability to sleep [5, 24]. Herpes zoster rash severity was significantly associated with pain, impairment of physical mobility, and sleep, but the correlations were not large. Herpes zoster pain, measured at week 8, correlated best with the QoL variables, and had a significant association with all of them. The NHP dimensions that correlated most significantly with herpes zoster pain measures were pain (Spearman correlation coefficient, 0.42–0.50), energy (0.34–0.38), and sleep (0.32–0.38). The impact of pain at week 8 was similar to days 14 and 30 and was higher than the impact from week 12 onward.

A US study in 50 acute zoster patients (mean age, 70 years; range, 54–94) applied the Wisconsin brief pain inventory, which is now used widely to assess pain and its impact on activities of daily living [25]. Interference with all measured modalities (particularly work and general activity, but also mood, sleep, and enjoyment of life) became significant (score ≥3) when pain was scored as 3 on a 0–10 numeric rating scale and severe at a pain score of ≥4. This adds credence to the belief that pain ratings of ≥3 should be considered indicative of significant PHN. The same study observed the impact of herpes zoster on QoL by using a standard questionnaire, the Medical Outcome Study Short Form 36 (SF-36) QoL evaluation, every 2 weeks for 2 months after disease onset. The effects of herpes zoster were particularly apparent in the domains of physical functioning, emotional functioning, and vitality. At week 8, scores from the zoster patients rebounded to near mean scores for the general population of similar age in most domains except for role functioning (physical and emotional). During the peak of the episode, the impact of herpes zoster on QoL is at least as great as that seen with chronic diseases such as congestive heart failure, diabetes, myocardial infarction, and clinical depression [26].

A large study in France produced similar findings [11]. In total, 9088 patients (mean age, 56.2 years; median, 61) consulted physicians for acute herpes zoster (8103 patients), PHN (pain persisting after rash healing, 935 patients), or other complications (visceral or neurologic complications other than rash and PHN, 50 patients). Each patient completed an SF-36 questionnaire at the physician's office. Pain-related disruption of life during the week prior to presentation was more severe for the patients evaluated for PHN. For the overall herpes zoster patient population, all QoL scores were decreased in comparison with those of a French reference population matched by age and sex; the lowest value was 41 of 100 (vitality) and the highest was 72 (social functioning; figure 1). The patients presenting with PHN had the lowest values for all dimensions (figure 1). In particular, scores for physical functioning and role functioning (i.e., emotional) showed substantially larger decreases in the PHN group than in other patients. Patients with opthalmic zoster were more likely to report that their pain was severe and permanent (46% vs. 40%, P < .001).

Financial Impact of Zoster-Associated Pain

Although data for the actual costs of management of both herpes zoster and PHN could theoretically be collected for different health care settings, at present most estimates involve some form of mathematical modeling. The cost of failure to prevent PHN is significant for both patient suffering and health care costs. Estimates of disease prevalence and evaluation of disease management from specialist centers permit estimates of lifetime and episode costs. Several authors have estimated costs of managing PHN from a UK national health care perspective. In the United Kingdom in 1994, the lifetime cost of managing PHN was estimated to be £770 (∼$1120) per patient. Annual national spending on PHN was estimated to be £4.8–£17.9 million
Figure 1. Medical outcome study short form 36 quality-of-life evaluation. This 36-item questionnaire elicits information for 8 dimensions believed to reflect a person’s perceptions of his/her quality of life, each scored 0–100 from worst to best perception: 1, limitations in physical activities because of health problems (physical functioning); 2, limitations in usual role activities because of physical health problems (role physical); 3, bodily pain; 4, general health perceptions; 5, vitality (energy and fatigue); 6, limitations in social activities because of physical or emotional problems (social functioning); 7, limitations in usual role activities because of emotional problems (role emotional); 8, general mental health (psychological distress and well being). PHN, postherpetic neuralgia. Data from [11].

(∼$7.0–$26 million) [27]. A more recent study estimated the total cost of treating herpes zoster in England and Wales at £47.6 million (range, £33.5–£73.8) or about $69.2 million (range, $48.7–$107.3 million/year) (1998 costs) [28]. Over £32.6 million (∼$47.4 million) was estimated as attributable to acute zoster and £15 million (∼$22 million) to management of PHN. Other costs associated with PHN in the United Kingdom and United States include antiviral drugs prescribed in primary care (£12.3 million (∼$17.9 million)) of the acute zoster, hospitalization (£14 million (∼$20 million)), and physician consultations (£6 million (∼$8.7 million)).

K. Higa in Fukuoka, Japan (personal communication), provides intensive inpatient management with continuous epidural administration of local anesthetic for patients with severe acute herpetic pain. He estimates the cost of hospitalization for this treatment (average hospital stay, 22 days) is 520,000 yen (∼$4000), of which 150,000 yen (∼$1150) is paid by the patient. Clearly, cost comparisons between different social and health care systems are virtually impossible.

Smith and Roberts [29] used a Markov decision model to estimate the incremental cost-effectiveness of treating severe acute zoster in all patients and milder zoster in patients ≥50 years old. Effectiveness of treatment was measured in quality adjusted life years (QALY). It was assumed for the purposes of this study that antiviral therapy did not alter PHN incidence but decreased PHN duration. For severe acute herpes zoster, the additional cost per QALY gained by treatment with valacyclovir was $21,000 (if treatment had no effect on PHN) down to $15,300 if treatment decreased PHN duration by 20%. With famciclovir, the respective costs per QALY gained were $28,100 and $20,700. Thus, it is economically viable (cost per QALY = $50,000) to treat mild acute herpetic zoster with famciclovir if it reduces PHN duration by 20% or with valacyclovir if PHN duration is reduced by 10%. Both agents were considered cost effective in patients ≥50 years old and for all adults presenting with severe herpes zoster.

Challenges for Physicians

Prompt treatment of herpes zoster with acyclovir, famciclovir, or valacyclovir can reduce the duration, and perhaps the incidence, of PHN [4–6]. However, the evidence for antiviral therapy is largely restricted to patients presenting within 72 h of the appearance of rash. General awareness of herpes zoster among the elderly must be raised in order to encourage older people with a painful unilateral rash to consult their physician as soon as possible. In a European survey of 236 patients, 48% said that they would have consulted sooner if they had known about herpes zoster [19].

In most studies, antiviral therapy was administered within 72 h of the appearance of rash; however, there is some evidence that later therapy may still have benefits. Immunocompromised
patients, older patients, those with ophthalmic zoster, and patients forming new lesions after 72 h may all benefit from treatment outside what has come to be regarded as the normal “treatment window” for zoster. Acyclovir administered as late as 7 days after onset of cutaneous lesions confers a beneficial prophylactic effect with respect to the ocular complications of herpes zoster ophthalmicus [30]. During an observational study of valacyclovir, there was no loss of impact on pain or allodynia if this is a consideration of physicians treating patients with persistent pain or abnormal sensations.

Diagnosis. Diagnosis of herpes zoster in the prodromal period can be extremely difficult as the rash is a pathognomonic feature. However, a painful prodrome is predictive of PHN and, if this is a consideration of physicians treating patients with unexplained pain, treatment during the prodrome might reduce the incidence of PHN. In a small study, a majority of elderly patients presenting to primary care physicians with acute localized unilateral pain did not develop herpes zoster during the following 28 days [32]. Therefore, empiric antiviral therapy should only be offered if there is a high index of suspicion that the patient has a zoster prodrome, but it is appropriate to ask such patients to return promptly if a rash appears. In addition to delays enforced by symptomatic uncertainty, delays are often incurred between patients requesting and receiving appointments to see the doctor at any stage in presentation.

Predicting those at risk. To make the best use of limited resources, antiviral therapy should be targeted to those most at risk of long-term pain. Age at presentation is the best-established predictor for risk of PHN [33], but a number of other prognostic factors can be assessed when the patient presents. Risk factors for prolonged pain were assessed in several clinical trials of acyclovir, valacyclovir, famciclovir, and netivudine. Advanced age, prodromal pain, and severe acute pain each independently predispose patients to prolonged zoster-associated pain [34]. Two studies also identified rash severity as a significant predictor of risk of PHN [35, 36].

In contrast to previous epidemiologic studies, women were no more likely to suffer PHN than men in these analyses. An apparent association between sex and long-term pain may be because more women are in higher age groups. Confirmation of advanced age and the intensity of prodromal or acute pain as prognostic factors were obtained in a large observational study of valacyclovir [31]. In addition, ophthalmic zoster and preexisting neurologic disorders were also identified as highly significant risk factors for prolonged abnormal skin sensations in herpes zoster in this study. Available guidelines for antiviral agents strongly advise their use in older patients, those with ophthalmic zoster, and in younger patients presenting with severe acute symptoms [37, 38].

Prevention of PHN. The extent to which antiviral drugs licensed for treatment of acute herpes zoster reduce the incidence of PHN or shorten the duration of zoster-associated pain differs somewhat by the way data are analyzed. By meta-analysis of acyclovir trials on an intent-to-treat basis, acyclovir accelerates cessation of zoster-associated pain, including PHN [4]. The effect on pain resolution is more pronounced in elderly patients. Valacyclovir (1000 mg 3 times/day) resolved zoster-associated pain 34% faster than acyclovir (800 mg 5 times/day) in patients over age 50 in one trial [5]. Famiciclovir (250 mg 3 times/day) is as effective as acyclovir for shortening zoster-associated pain and may provide greater benefit when treatment is initiated within 48 h of the appearance of rash [38, 39]. At higher doses (500 or 750 mg 3 times/day), reductions in duration of pain compared with placebo reduced proportions of patients with pain at some time points [6, 36]. Table 1 shows the effects of the 3 antiviral agents on the incidence of pain at 3 and 6 months.

The prodrugs valacyclovir (1000 mg 3 times/day) and famciclovir (500 mg 3 times/day) were compared directly in patients over age 50 [40]. No significant differences were detected in the time to resolution of zoster-associated pain, PHN, clinically significant pain, or abnormal sensations.

The cost of applying preventive therapies can be reduced if risk factors for development of PHN are heeded. Antiviral medications are expensive in terms of unit cost but require administration for only 7 days. In addition, their beneficial effects are not limited to reduction in incidence and duration of PHN. They also reduce acute pain and hasten rash healing and, in ophthalmic zoster, reduce complications involving the eye.

Oral steroids may add to the benefit of antiviral therapy for

### Table 1. Proportions (%) of patients (aged ≥50 years) with persisting pain in controlled trials of antiviral therapies for herpes zoster [4–6, 36, 40].

<table>
<thead>
<tr>
<th>Drugs compared</th>
<th>Acyclovir (800 mg 5×/day, 7–10 days) vs. placebo</th>
<th>Valacyclovir (1000 mg 3×/day, 7 days) vs. acyclovir</th>
<th>Valacyclovir (1000 mg 3×/day, 7 days) vs. famciclovir (500 mg 3×/day, 7 days)</th>
<th>Famiciclovir (500 mg 3×/day, 7 days) vs. placebo</th>
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<tr>
<td><strong>PHN pain</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>At 3 months</td>
<td>25 vs. 54&lt;sup&gt;a&lt;/sup&gt;</td>
<td>31 vs. 38&lt;sup&gt;b&lt;/sup&gt;</td>
<td>32 vs. 34&lt;sup&gt;c&lt;/sup&gt;</td>
<td>34.9 vs. 49.2</td>
</tr>
<tr>
<td>At 6 months</td>
<td>15 vs. 35&lt;sup&gt;b&lt;/sup&gt;</td>
<td>19.9 vs. 25.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>19 vs. 19&lt;sup&gt;d&lt;/sup&gt;</td>
<td>19.5 vs. 40.3&lt;sup&gt;d&lt;/sup&gt;</td>
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<sup>a</sup> P < .05 from 95% confidence interval (CI) for the relative risk (RR) for the difference between treatments.

<sup>b</sup> GlaxoSmithKine data on file.

<sup>c</sup> P = .84 from 95% CI for the RR for the difference between treatments.

<sup>d</sup> P = .08 from 95% CI for the RR for the difference between treatments.
Reducing the acute pain of herpes zoster but have no effect on the development of PHN [41, 42]. In a placebo-controlled trial, 201 herpes zoster patients were randomized to acyclovir, prednisone, both, or neither for 21 days. Treatment was initiated within 72 h of rash onset. No differences in pain incidence were found at 3 or 6 months, but acute pain resolution was more rapid in the acyclovir plus prednisone group than in the placebo group [42]. In the larger study [41], there was an excess of adverse events in the steroid groups despite exclusion criteria that avoided recruitment of patients at greatest risk of such events (e.g., dyspepsia, hypertension, diabetes).

Other treatments have been proposed to reduce the risk of chronic pain when initiated during the acute phase of disease. Interventions that decrease pain, inflammation, and tissue damage during the acute phase of herpes zoster may attenuate peripheral nociceptor sensitization and central hyperexcitability, which in turn, may lessen the likelihood that PHN will develop. It is likely that sympathetic or somatic nerve blocks during the acute phase of herpes zoster may not only control acute pain but also reduce PHN [43, 44]. There is some evidence (largely from uncontrolled studies) that sympathetic nerve blocks may provide considerable pain relief during acute herpes zoster, but there is little support for an effect on the incidence of PHN [45]. Nerve blocks as described by Higa et al. [43] and Pasqualucci et al. [44] carry a potential for risk, although adverse events were few in either study, and utilize considerable resources.

**Treatment of established PHN.** Drugs used for established PHN, which may be required for many years, vary in cost, effectiveness, and side-effect profile (table 2) [46]. Moreover, in many patients, trials of more than one medication may be necessary. Tricyclic antidepressants remain an important treatment for patients with PHN. These drugs have an analgesic effect in chronic neuropathic pain that is independent of their antidepressant effect. Both amitriptyline and desipramine relieved PHN when compared with placebo in randomized trials [47]. Although amitriptyline is relatively inexpensive, therapy is often discontinued because of side effects, some serious. In a double-blind crossover trial that compared amitriptyline and nortriptyline, nortriptyline was as effective as amitriptyline for relieving PHN, but was better tolerated [48]. No placebo-controlled studies have examined the effectiveness of selective serotonin reuptake inhibitors in the treatment of PHN.

Anticonvulsants have traditionally been used for the management of neuropathic pain. In a randomized double-blind, placebo-controlled trial, patients received gabapentin up to 3600 mg a day and had pain measured on a Likert scale from 0 (no pain) to 10 (worst possible pain) [49]. There was a statistically significant reduction in average daily pain score from 6.3 to 4.2 points with gabapentin compared with a change from 6.5 to 6.0 points in subjects randomized to receive placebo ($P < .001$). It was recently shown that a reduction of 2 points on a 0–10 numeric rating scale for pain indicates significant benefit [50]. McGill pain questionnaire results were also better ($P < .001$) and QoL was significantly improved as demonstrated by SF-36. Somnolence, dizziness, ataxia, peripheral edema, and infection were all more frequent in the gabapentin group. These findings were confirmed in a study of 334 patients [51]. Gabapentin is as effective for managing neuropathy as tricyclic antidepressants [52] and has a better adverse-event profile (both in frequency and severity of events) but is significantly more expensive. The lack of drug interactions associated with gabapentin is a useful asset in elderly patients who frequently take concomitant medication.

Better understanding of the correct use of opiate analgesics in chronic benign pain [53] and the development of practical methods of applying local anesthetic drugs to the skin [54, 55] have further improved therapy for established PHN. The US Food and Drug Administration recently approved a lidocaine patch for treatment of PHN. Several double-blind vehicle-controlled studies have been performed in patients with PHN and allodynia [54, 55]. The majority of patients treated with the lidocaine patch reported moderate or greater pain relief.

Historically, strong opioid drugs (e.g., morphine) were believed to be ineffective in reducing neuropathic pain. Clearly, this is not so, and opioids such as morphine, oxycodone, and methadone are in routine use for PHN. In a placebo-controlled crossover trial of 38 patients with PHN receiving an average of 45 mg of controlled-release oxycodone [56], patients treated with oxycodone had significantly greater pain relief and reductions in allodynia and disability. At what stage in the hierarchy of treatments opioids should be tried remains controversial, but their use must be encouraged, at least in patients not responding to such drugs as amitriptyline and gabapentin. Opioids vary in cost (table 2); there is no evidence regarding their relative value.

Although sympathetic nerve blocks may be effective in relieving pain during acute zoster, these blocks do not appear to provide prolonged relief in patients with long-standing PHN [45]. A recent publication by Kotani et al. [57] shows impressive long-term benefit for patients with intractable PHN from intrathecal (subarachnoid) injection of methylprednisolone. However, this technique carries serious ethical considerations in view of the significant perceived risk of the technique (a possible cause of arachnoiditis) and the clear statement from the manufacturer that this drug should never be injected in-

### Table 2. Approximate cost of treatment of postherpetic neuralgia in the United Kingdom based on typical effective dosages.

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<tr>
<th>Drug</th>
<th>Dosage/24h</th>
<th>Monthly cost*</th>
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<tr>
<td></td>
<td>UK£</td>
<td>US$</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>50 mg</td>
<td>1.88</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>50 mg</td>
<td>13.89</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>1800 mg</td>
<td>95.00</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20 mg</td>
<td>23.00</td>
</tr>
<tr>
<td>Methadone</td>
<td>15 mg</td>
<td>5.60</td>
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* Calculated from British National Formulary [46] and converted to US$.
trathecally. Patients in this study were followed for 2 years and had magnetic resonance imaging of the spinal cord, and no case of arachnoiditis was identified. Additional controlled trials are needed to compare the efficacy and tolerability of tricyclic antidepressants, gabapentin, the topical lidocaine patch, and controlled-release opioid analgesics (used singly and in combination in the treatment of patients with PHN).

In extreme cases of PHN refractory to other measures, patients and physicians have resorted to surgery. There is anecdotal evidence for skin excision, sympathectomy, dorsal root entry zone lesions, cordotomy, thalamotomy, cingulotomy, and spinal cord and deep brain stimulation [58]. Patients and clinicians involved with specialist zoster clinics are in no doubt regarding the sometimes devastating consequences of PHN and the willingness of those affected to undergo treatment—“do anything” is a frequent exhortation among such patients. A logical and coherent management strategy must be tailored for each patient with PHN, including the possible need to cope with failure of multiple therapies.

Future Directions

An important goal for future research is the development of more effective treatments for PHN. Even so, the superior strategy may be to prevent the establishment of chronic zoster-associated pain before it starts. Prevention would eliminate the disability, psychological distress, and increased health care utilization caused by PHN.

The Oka vaccine is in routine use in the United States for prevention of childhood varicella. Research programs are investigating the effectiveness of adult vaccination to prevent or attenuate herpes zoster [59]. Implications are considerable, particularly in the significant interim period when parts of the population are vaccinated and others are not [60]. The continual exposure of adults to children with varicella has been proposed to boost their immune reaction to VZV and, therefore, to delay herpes zoster. Nevertheless, good uptake of an effective vaccine could mean that long-term, herpes zoster-associated pain will be largely eliminated.

The basic science sector of pain research is far in advance of clinically effective therapies. Knowledge of mechanisms of pain is now very sophisticated [61], and it is likely that drugs of the future will act at sites now beyond the reach of today’s therapeutics. With an increasingly elderly population, a likely priority for pain management clinics is the development of cognitive behavioral programs for PHN patients that are as effective as those available for younger patients with chronic benign pain that is not amenable to curative therapies. Elderly patients with herpes zoster are often lonely and many have experienced negative life events such as bereavement and loss of independence. Anxiety and depression are associated with a worse prognosis for herpes zoster [62], and psychosocial support is important in overall management. Pain is a biopsychosocial phenomenon and all components of the triad should be addressed for care to be effective.

Further research is also required on currently available agents. Combination therapy of antivirals and nerve blocks has begun [63, 64] but prospective, randomized, controlled trials are required, and they must be designed with adequate follow-up so as to determine the long-term effect on pain outcomes. Trials are needed to determine whether the addition of analgesics, anticonvulsants, and antidepressants to early antiviral therapy reduces the risk of PHN further.

Summary

For the individual patient and the health care provider, the cost of the long-term sequelae of herpes zoster (mainly PHN) is high. Pending the anticipated fruits of vaccination and development and refinement of effective therapies for PHN, prevention remains the most effective tool against PHN. The antiviral drugs, particularly the more bioavailable prodrugs, valacyclovir and famciclovir, are well tolerated and of proven benefit in reducing the risk of PHN in patients with herpes zoster. The place of nerve blocks remains unclear despite encouraging publications.

Prevention of PHN, the current best strategy for management, could be enhanced. Public education must be improved so that patients are encouraged to consult as early as possible in order to make the best use of antiviral therapy. In the longer term, vaccination may provide the best accommodation of the disease, both by reduction of varicella from vaccination in childhood and attenuation of herpes zoster by adult vaccination. However, this strategy is in its infancy as far as its effects on zoster, let alone PHN, are concerned. Early use of antidepressants or anticonvulsants in combination with antiviral agents merits further study. Epidural medication carries potential risk as well as benefits and further evaluation is necessary.

PHN causes suffering and disability and its management is often suboptimal. Even with best management, many cases remain intractable. Newer proposed therapies require further evaluation for risk, benefit, and economic cost. PHN is largely a problem of the elderly and the application of principles of cognitive and behavioral pain management for this patient group remains to be developed.

References