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Neural Blockade for Diagnosis and Prognosis

A Review

Quinn H. Hogan, M.D., Stephen E. Abram, M.D.†*

CONTENTS

THE popularity of neural blockade as a diagnostic tool in painful conditions is due to several features especially characteristic of chronic pain. Specifically, pain is purely subjective, and the conditions are, in most cases, inexactly defined, with uncertain pathophysiology. Social, emotional, financial, and legal factors compound the complexity of chronic pain. To clarify these challenging clinical situations, diagnostic blocks are used to determine the pathophysiology of clinical pain, the site of nociception, and the pathway of afferent neural signals. Information gained from blocks may then be applied to the choice of medicines, therapeutic blocks, or surgical therapy, and may also be used to anticipate the response to neuroablative therapies.

However, the interpretation of even properly performed procedures is rarely simple. Few blinded and controlled studies exist that tested the use of these alluring methods. There has been no critical examination of the theoretic basis on which diagnostic blockade rests, nor an evaluation of the published support for the diagnostic use of neural blockade. In the first part of this review, physiologic, anatomic, and psychosocial issues that influence the quality of information from diagnostic blocks are examined. In the second section, data regarding the diagnostic utility of the various blockade proce-

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* Associate Professor.

† Professor.

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Address correspondence to: Quinn Hogan, M.D., Department of Anesthesiology, Pain Management Center, Froedtert East, 9200 West Wisconsin Ave., Milwaukee, Wisconsin 53226.

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dures are analyzed. No attempt is made to analyze the evidence for therapeutic use of these blocks.

Neurophysiologic Issues

The diagnostic use of neural blockade rests on three premises. First, pathology causing pain is located in an exact peripheral location, and impulses from this site travel *via* a unique and consistent neural route. Second, injection of local anesthetic totally abolishes sensory function of intended nerves and does not affect other nerves. Third, relief of pain after local anesthetic block is attributable solely to block of the target afferent neural pathway. The validity of these assumptions is limited by complexities of anatomy, physiology, and psychology of pain perception and the effect of local anesthetics on impulse conduction.

Nociceptor Activity

Although pain perceived in somatic structures is generally associated with activation of nociceptors,[1] peripheral nerve activity associated with pain perception also may arise from injured nerves independent of nociceptor activity.[2,3] Dorsal root ganglia of injured nerves participate in abnormal impulse generation.[2] Blockade of such nerves proximal to the injured segment but distal to the dorsal root ganglion may not relieve pain if spontaneous activity continues at the level of the dorsal root ganglion. This may lead to the false assumption that the injured nerve is not responsible for the patient's pain.

Nerve blocks are usually interpreted in terms of their effect on afferent neural activity, but important efferent traffic must be considered. Impulse generation arising from an injured nerve fiber is likely to be propagated both orthodromically toward the spinal cord and antidromically toward the innervated tissues. For instance, bursts of sural nerve activity are recorded during straight leg raising in a patient with S-1 radiculopathy.[4] Although not proved in all experimental models,[5] antidromic activity from injured sensory nerves may cause peripheral tissue release of substance P and perhaps other substances, such as bradykinin, histamine, 5-HT — prostaglandins that may change the threshold of nociceptors by direct and indirect means.[6] Therefore, nerve block distal to the primary site of nerve pathology may alter pain perception by interrupting antidromic impulses, contrary to the common assumption that axonal function must be interrupted proximal to the area of injury to provide relief. Peripheral blockade of the sciatic nerve has been shown to provide profound relief of pain for patients with documented lumbosacral radiculopathy,[7,8] perhaps by blocking antidromic impulses that arise from the nerve root or dorsal root ganglion and are propagated to the periphery, producing changes in nociceptor sensitivity.[9]

Sympathetic Contributions

When sympathetic motor activity is blocked during diagnostic procedures, such as with most peripheral and central nerve blocks, sympathetic influences on sensory mechanisms should be considered. Receptors at the terminals of C fibers from an injured nerve become excited during sympathetic stimulation or norepinephrine application and show enhanced responsiveness to irritating stimuli.[10] At the site of the nerve injury, sympathetic efferent impulses may depolarize nociceptive afferent fibers (ephaptic transmission), potentially producing both orthodromic and antidromic activity. Increased sympathetic activity or high levels of norepinephrine increase discharge rates of spontaneous impulses arising from neuromas,[11,12] and injection of epinephrine in the vicinity of neuromas in patients with pain aggravates pain.[13]

In uninjured tissues, it is well accepted that sympathetic supply can modulate sensory responses,[14] but the role of this mechanism in producing pain is less certain. Mechanoreceptor sensitivity is heightened by increases in sympathetic discharge rates, and aberrant central processing of these signals by sensitized wide dynamic range (WDR) neurons in the dorsal horn may result in the allodynia present in certain cases of reflex sympathetic dystrophy.[14] There is growing recognition of a sympathetic component in the inflammatory response, especially in joints.[15] Apart from its obvious peripheral effects, some reports also have documented analgesia by an undefined central mechanism after sympathetic block.[16,17] Pain relief after peripheral block may be due to interruption of any of these efferent mechanisms rather than somatic sensory fibers.

Spinal Processing

Whatever the contribution of receptor, neuropathic, or sympathetic mechanisms, activity in nociceptive afferent fibers is subject to further, variable processing in the spinal cord. The balance between large and small fiber inputs is an important determinant of the response of dorsal horn neurons to noxious stimulation.[18] Conceivably, loss of large fiber activity after peripheral or neuraxial blockade could increase dorsal horn cell activ-

ity, particularly if there is preservation of C-fiber input, producing a paradoxical increase in pain. Conversely, it is likely that mechanical allodynia in neuropathic pain states is conveyed by large fiber (Aβ) input.[19] A diagnostic block that interrupted small, but not large, fibers could fail to relieve touch-evoked pain even if the remainder of the extremity is insensitive to nociceptive or thermal stimuli, whereas selective large fiber block would create the opposite effects.[20,21]

In addition to segmental influences on dorsal horn function, descending pathways modulate the response of spinal cord neurons to sensory stimuli.[22] Because these tracts lie superficially in the cord, they are susceptible to blockade by intrathecally administered local anesthetics, possibly leading to disinhibition of nociceptive transmission. The relative effect of the drug on afferent pathways *versus* descending inhibitory tracts would then determine the analgesic effect of a subarachnoid block. Descending cerebral influences may obscure findings during a diagnostic test by producing analgesia in response to stress, independent of the specific nature of the block. Intense pain from the procedure may diminish the perceived severity of the original pain by stimulating descending inhibition of nociceptive transmission (noxious counterirritation),[23] creating the illusion that neural blockade directly relieved the pain. Conversely, descending modulation may be stimulatory and produce pain independent of sensory input. Dubner *et al.*[24] demonstrated, in primates, that nonpainful signals (flashing light) can be associated with nociceptive stimuli (heat probe) by conditioning with simultaneous presentation. Eventually, the light alone can result in firing of secondary nociceptive neurons and presumably the sensory experience of pain. In this setting, diagnostic blocks that produce no relief may suggest a diagnosis of malingering or psychiatric disease when, in fact, descending influences are generating sensory activity.

Convergence and Referred Pain

Many second-order neurons in the spinal cord respond to a variety of input from primary afferents with either visceral and somatic receptive fields, an example of convergent input.[25] In other instances, convergence is the result of primary afferent C-fibers that have both visceral and cutaneous collaterals.[26] When afferent input arises from both somatic and visceral structures or from separate somatic foci, the perception of pain may depend on a level of combined neuronal activity from both components. Interruption of one limb of the convergent inputs may be sufficient to provide complete pain relief, leading to false assumptions about the source of the pain. For instance, a patient with pain of pancreatic cancer may have nociceptive inputs from splanchnic nerves plus from myofascial pain in the paravertebral muscles. Infiltration of a painful trigger point in the affected muscle may reduce the combined input to a level below the pain threshold, and the mistaken interpretation would be that the pain is entirely somatic, without any visceral source.

Plasticity

Sensory processing is not stable but depends on preceding events, a phenomenon called neuronal plasticity. Small fiber (nociceptive) activity initiates a series of events in the dorsal horn that leads to heightened responsiveness of second-order neurons that are activated by noxious stimuli.[27-29] Sensitization in response to noxious stimulation is known to affect WDR neurons, which ordinarily respond at very low firing rates to nonnoxious inputs and at high firing rates to nociceptor activity. After sensitization, these cells may respond to nonnoxious stimuli at sufficiently high firing rates to cause pain perception (allodynia). High-threshold specific neurons also may demonstrate sensitization.[27] It is impossible to predict responses to local anesthetic blockade of afferent impulses under conditions of dorsal horn sensitization. Afferent blockade of conditioning stimuli could lead to normalization of dorsal horn responsiveness and profound, prolonged relief. In other circumstances, however, spinal sensitization might persist independent of afferent activity, with little or no change in pain.

Pain and abnormal sensation after injury is often found in a distribution that is inconsistent with any nerve or root, such as an entire limb or a stocking or glove pattern, possibly leading to the diagnosis of psychoneurosis rather than a neurologic condition. Injury to a single peripheral nerve may, however, create allodynia in adjacent territories innervated by other nerves, due to altered central processing of afferent signals from the uninjured as well as injured nerve.[30] Blockade of the uninjured nerve will relieve pain within the borders of its innervation. The likely but erroneous interpretation would be that the blocked nerve had been injured, which may lead to injection therapy or surgical neurolysis. Analgesia may outlast the duration of local anesthetic neural blockade by hours or days,[31] leading to speculation that pain is psychosomatic or factitious. Possibly, a period of interruption of nociceptor activity may lead

to temporary reversal of the sensitization of spinal cord neurons. Once the peripheral generator recommences, a period of hours or days may go by before sufficient dorsal horn sensitization occurs to reestablish perception of pain.

Decreased afferent input also can lead to functional changes in the dorsal horn. After periods of deafferentation, cells that respond to noxious stimulation become hypersensitive to remaining afferent inputs, and their receptive field may expand.[32] Denervation may additionally produce sufficient sensitization of WDR neurons that nonnoxious stimulation, including stimuli from outside the original receptive field, can produce pain. Blockade of such stimulation could falsely indicate the site of pathology. Alternatively, blockade of an injured nerve may not provide relief of pain and allodynia if the receptive field of sensitized dorsal horn neurons has spread beyond the distribution of the injured nerve, again leading to the mistaken conclusion that the injured nerve is not involved. Denervation of peripheral afferent fibers has been shown to cause dramatic functional changes in responses of WDR neurons in the dorsal horn.[33]

Conclusion

Current neurophysiologic evidence does not support the direct inference of pathogenic mechanism, site, or transmission pathway from observations during neural blockade. Complex physiologic events may confound the simple interpretation of diagnostic blocks.

Local Anesthetic Issues

Intensity of Blockade

Diagnostic and prognostic blocks are accomplished by the action of local anesthetics on nerves. It has long been recognized that neural blockade is not an all-or-none response. For instance, analgesia is usually evident earlier, and to a greater extent, than loss of perception of mechanical stimuli after peripheral neural blockade. If pain relief follows sympathetic blockade, lack of anesthesia to touch does not assure that pain relief is by sympathetic interruption, because a subtle somatic block could produce analgesia without anesthesia, resulting in pain relief independent of a sympathetic mechanism.[34] In the opposite sense, apparent intense blockade with complete insensitivity to touch and pain is nonetheless not a complete afferent blockade, because studies of different types of blocks with various agents uniformly demonstrate incomplete elimination of somatosensory potentials evoked by stimulation of the anesthetized region.[35] If pain continues after a diagnostic block, one cannot be certain that the injected pathway is not involved, because neural blockade is often not absolute.

The variable and partial nature of local anesthetic effects is also evident in blockade of efferent sympathetic activity. Skin conduction responses, a manifestation of sympathetic action at sweat glands, is often present in areas of apparently complete somatic blockade,[36] and skin warming has been noted in the center of a truncal band of segmental epidural anesthesia.[37] During total thoracolumbar epidural anesthesia, circulating norepinephrine levels decrease by only approximately 60%[38] or not at all,[39] which indicates persistent sympathetic synaptic release. These considerations weaken the predictive value of sympathetic blocks, unless monitoring confirms the loss of sympathetic activity in the affected area concurrent with the onset of relief.

Differential Block

The variable effects of local anesthetics on fibers conveying different functions is termed differential block. If it were possible to predict and control the neural modalities that are blocked, disease mechanisms could be discerned by selectively interrupting sympathetic or somatic fibers. This goal has proved elusive, and the physiologic mechanisms that result in differential effects of local anesthetics have been shown to be complex.[40] Most commonly cited is the importance of fiber size,[41] which predicts that small, nonmyelinated C fibers are the most sensitive to local anesthetics, followed by small myelinated B fibers, whereas large myelinated A fibers are the most resistant. Despite the appealing simplicity of this model, it has not withstood the test of time. Further study[42-44] showed that the intrinsic sensitivity of nerve fiber types to local anesthetics is probably $A \geq B > C$. Problematic for the use of local anesthetics in diagnosis, however, is the great range conduction speed and, therefore, fiber size within a fiber type, and the lack of correlation of size and necessary anesthetic concentration for blockade (C_M) within the group.[42,45] The overlap of C_M between different groups "appears to negate any possibility of obtaining steady state differential interruption" by local anesthetics.[42] Difference in diffusion barriers of the various fiber types probably explains a large part of clinically evident differential effects.[46] Despite the inherent greater resistance of C fibers to blockade, they are exposed to a higher local

anesthetic concentration early in the onset of the block because of more rapid diffusion.[47] Only an incompletely selective differential block results from the different rates of penetration, however, because partial A fiber block has already occurred by the time C fiber activity has been abolished.

To prevent conduction, at least three nodes of Ranvier in succession must be blocked completely.[48] If local anesthetic is limited in longitude, large fibers with long internodal distances may lack exposure to three nodes, whereas smaller fibers have the necessary three nodes exposed and are blocked. At concentrations that produce incomplete sodium channel blockade, the influence of exposure length extends several centimeters, and C_M is inversely related to exposed nerve length.[49] These phenomena dictate that anesthetic potency and the degree of differential effects varies with the length of nerve exposed, an added variable that is hard to control.

Further subtle influences on local anesthetic action may cloud the interpretation of diagnostic blocks. Sodium channel closure by local anesthetics depends on nerve use. The block that develops when the axon is firing at very low rates (tonic block) is less intense than the block that develops while the nerve is active (phasic block). Local anesthetic will affect more completely those fibers that are most active. The spectrum of anesthetic effects will, therefore, depend on the pattern of activity of the subject's various neuron types when the diagnostic block is undertaken. Because the earliest perturbation of nerve function at very low anesthetic concentrations is prolongation of the latent interval for refiring,[45] information encoded with bursts will be transformed into a more uniform signal. By this means, incomplete local anesthetic block may cause sensations to change without terminating transmission.

We conclude that consideration of the subtle, complex, and variable action of local anesthetics should inspire caution in the interpretation of blocks.

Systematic Effects

Local anesthetic is absorbed from the site of injection during diagnostic blockade, raising the question of a systemic analgesic contribution. At local anesthetic blood concentrations that are insufficient to produce side effects in humans (*e.g.*, 1–5 μg/ml lidocaine), there is little or no appreciable effect on impulse conduction in normal peripheral nerves[50–53] or on cutaneous C-fiber terminal function.[50] Likewise, local anesthetics have little or no analgesic effect in animal models of acute nociception.[50] However, there is considerable evidence that systemically administered local anesthetics affect spontaneous and mechanically stimulated impulse generation arising from injured nerves.[51–53] Nontoxic doses of systemic local anesthetics also depress spinal transmission of nociceptive inputs,[50,54] but the principal effect of systemic local anesthetics on neuropathic pain is peripheral.[55]

There have been several clinical reports of the efficacy of intravenous lidocaine in patients with neuropathic pain.[52,54,56–58] Whereas some cite very transient effects,[52,57] others indicate analgesic effects that last several days or longer.[56,58] Doses of local anesthetic required to relieve neuropathic pain are generally 1–3 mg/kg. It would be unlikely, therefore, that a selective nerve root block with 3 ml 1% lidocaine (30 mg) would produce pain relief by a systemic effect. In contrast, a lumbar sympathetic block using 15 ml 1% lidocaine might relieve neuropathic pain at a location distant from the site of injection.

Psychosocial Issues

Even though diagnostic blocks are motivated by a desire to obtain specific, convincing data, the procedure is also, inevitably, a complex social interaction. Whereas the physician may seek pathophysiologic information, the patient may be looking for reassurance, confirmation of their suspicions or proof to persuade doubting family members, certification of their disability for legal and financial reasons, or may simply wish to please the physician. These purposes may enter into the patient's reporting. To diminish ambiguities created by these psychosocial factors, a physician might choose to inject a placebo, an inert substance with no known pharmacodynamic effect. Interpretation of a favorable response to a placebo is problematic. Patients obtain relief from placebos administered during acute pain approximately one third of the time,[59] but obtain relief from chronic pain in approximately two thirds of cases after administration of a placebo.[60,61] For instance, in patients with causalgia, 3 ml of subcutaneous normal saline relieved spontaneous pain in 68% of patients, and also relieved mechanically induced allodynia in 56% and Tinel's sign (a tingling sensation in the distal end of a limb during percussion of the injured nerve) in 67%.[62] Probability of analgesia from a placebo is proportionate to the intensity of pain.[63] No personality features predict a placebo response,[64] individuals are not consistent in

being responders or nonresponders, and most individuals will eventually respond to a placebo if administered repeatedly.[65] Placebo action may be as intense as the active agent, usually mimics the active agent in dose-response and time-effect relations,[66] and may develop over as prolonged an interval as 60 min.[67,68] Injections, like surgery, are especially potent placebos compared with pills.[66] The same problems that accompany intentional placebo use make it difficult to determine whether analgesia after a diagnostic block with an active agent is, nonetheless, a placebo response. The potency and frequency of the placebo effect is underestimated by the majority of physicians and nurses.[69]

Psychologic theory that explains placebo response focuses on the subject's expectations[70] and on conditioning.[71] In the context of diagnostic blocks, the expectation of a favorable response may make analgesia more likely. Most subjects can be trained to have a placebo response,[72] and a placebo response is more likely if the test with the active agent precedes the placebo administration.[73,74] It is evident that the physician's convictions play a large role in generating placebo responses, and that, even in carefully blinded protocols, unintended communication from the examiner to the subject takes place.[66,75] On a neurophysiologic level, the placebo response is a demonstration of descending modulation of nociception. Evidence of an opiate mechanism includes the antagonism of placebo analgesia with naloxone,[76,77] and documentation of increased cerebrospinal fluid endogenous opioid activity after a placebo response, but not if there was no response.[78]

Compelling evidence with regard to placebo responses leads to the conclusion that the ambiguity created by these responses is a major impediment to the valid use of neural blockade for diagnosis.

Anatomic Issues

The use of blocks for diagnosis and prognosis depends on an assumption of anatomic consistency. Nerve structures are expected to be found in predictable places and to have predictable connections, but there are important limitations to these assumptions. Most anatomic parameters show variability about a norm.[79] Surface and palpation landmarks are unreliable indicators of deep structures, which is borne out by a 50% accuracy in guessing vertebral level of needle placement without x-ray imaging.[80,81] In a variety of injection procedures, accurate needle placement requires imaging.[82,83] Idealized textbook descriptions of anatomic structures hold in only approximately 50-70% of actual subjects,[84] including segmentation of vertebrae[85] and distribution of nerve roots to the intervertebral foramina.[86-88]

Separation of somatic input into a discernible segmental pattern is a fundamental concept that underlies many diagnostic blocks. There is, however, variability in the formation of segmental spinal nerves and their peripheral distribution. Multiple interconnections of adjacent rootlets and roots are found within the dural sac in all subjects, with between 3 and 9 such intersegmental anastomoses at the upper cervical region and a similar number at the lumbosacral level.[89,90] The pattern of spinal nerve contributions to the limb is highly inconsistent. The distribution of spinal nerve root fibers to the skin has been mapped using zoster eruptions, residual sensation after sectioning the roots on either side of an intact segment, absent sensation after root section or anesthesia, vasodilatation during stimulation of roots, or pain with nerve root compression and visceral disease.[91] The dermatome diagrams these methods produce show considerable disagreement, especially in the extremities. Also, extensive overlap between consecutive peripheral dermatomes is evident because the division of an individual root rarely produces an appreciable loss of sensibility.[92] As a consequence, the sensory innervation of a particular site cannot be assigned, with certainty, to any segmental level, and sensory changes after local anesthetic injections near the vertebral column are variable. There is also segmental inconsistency in the motor innervation of the extremities. Marked departure from the usual distribution of L5 and S1 motor fibers is found in 16% of subjects,[93] in whom stimulation of a root produces movement typical of the other root.

Important differences in the peripheral distribution of sympathetic motor fibers are relevant to diagnostic blocks. Preganglionic axons originate only from the T1 through L2 segments. Fibers bound for tissues with cervical or low lumbar and sacral somatic innervation are deployed by the paravertebral chains. Therefore, segmental neuraxial local anesthetic application will block sympathetic innervation to different tissues than are somatically denervated. For instance, a low spinal anesthetic may produce intense sensory block to the feet, ankles, calves, and buttocks (low lumbar and sacral segments) without blocking preganglionic sympathetic fibers to these areas that leave the cord in the L1 and L2 nerve roots. Sympathetic outflow is only weakly segmental, due to the crossing of rami communicantes[94] and extensive divergence of sympathetic activity in the

ganglia. Efferent sympathetic fibers supplying a cutaneous region do not necessarily arrive by the same peripheral nerve as the sensory afferents supplying that area. For instance, the radial aspect of the dorsum of the hand receives sensory and sudomotor innervation *via* the radial nerve, but receives vasomotor innervation from the median nerve.[95] Similarly, the lateral aspect of the foot may receive its sympathetic input from peroneal branches while transmitting sensory information through the sural nerve.[96] We conclude, from the available studies, that the extent of sympathetic blockade after regional anesthetic is poorly understood and difficult to predict.

Limited information is available with regard to the patterns of visceral sensory connections. Visceral receptive fields are large and overlapping, and extensive convergence of afferent traffic is evident at many central nervous system levels.[26] Most visceral pain travels through sympathetic nerves, but afferents from the thoracic organs, the pancreas, and biliary tree ascend in the phrenic nerve as well as passing to the thoracic cord *via* medial branches of the sympathetic chain. From the sigmoid colon, rectum, neck of the bladder, prostate, and cervix of the uterus, most visceral afferent fibers retrace the route of parasympathetic efferent neurons, entering the cord in the posterior roots of S2–S4. A few fibers from these organs ascend in the prevertebral plexuses to enter at L1–L2. Pain not relieved by blocks of sympathetic pathways may still be visceral in origin but transmitted by these nonsympathetic routes.

The role and even presence of nociceptive fibers from the limbs that travel in sympathetic structures has been debated.[97,98] Lumbar sympathetic block prevents the poorly localized dull ache during surgical manipulation of the femoral vein or from lower extremity thrombophlebitis.[99,100] Surgical sympathectomy blocks responses to venous distension in canine lower extremities[101] and almost eliminates the aching and stinging pain from cold exposure of human extremities.[102] Sympathetic block also interrupts pain from mechanical stimulation of the femoral medullary cavity.[103] These observations indicate that afferent sensory impulses travel from vascular structures in the extremities *via* sympathetic pathways that, when blocked by diagnostic sympathetic blockade, could be falsely interpreted as an indication of an efferent sympathetic pathogenesis of pain.[104]

Deep somatic pain from bones, joints, muscles, and fascia shares many features of visceral pain, including poor somatotopic localization, referred pain, and a generalized increase in central nervous system excitability with motor and autonomic reflexes.[97] In addition, the fibers from many deep somatic elements (costovertebral joint, posterior and anterior longitudinal ligaments, annular ligament of the intervertebral disc, and dura) traverse the sympathetic rami and chain.[105,106] It is likely that some pains relieved by sympathetic blocks are unrelated to sympathetic efferent activity (sympathetically maintained pain) and, instead, are deep somatic pains transmitted by sympathetic pathways.[104]

Evidence indicates that anatomic uncertainties with regard to neural connections and structural variability degrades the accuracy of diagnostic information obtained by neural blockade.

Specific Procedures

Commonly used diagnostic blocks are discussed below, with regard to the rationale behind the procedure, including indications for the block. Limitations are reviewed, focusing on sources of error in interpreting results from the injections. Studies of the diagnostic utility of the procedure are then reviewed, with emphasis on documentation of success and measures of the diagnostic value. Conclusions based on the available evidence are then stated. Published reports for review were obtained through Medline search of English language articles and from reference lists in relevant articles and chapters. For brevity, not all articles included in this review are listed in the references.

Clinical studies of the blocks are variable quality. Important considerations include entrance criteria, study size, and the use of control subjects. The prevalence of placebo responses in patients with pain greatly weakens the relevance of studies in which no control subjects or blinding was used. Where possible, neural blockade tests are evaluated numerically, using standard definitions.[107] The importance of false-positive rate (how often patients without a condition will nonetheless have a positive test) and false-negative rate (how often a patient with disease will have a negative test for it) is evident because they vary inversely with specificity and sensitivity, respectively (Table 1). For many painful conditions, however, a credible standard to document the disease for comparison with test results is unavailable. At worst, the block under scrutiny may be the defining gold standard. For these blocks, numerical values for diagnostic efficacy are elusive. Many studies for obvious ethical reasons obtain operative confirmation of disease only in patients with positive results

Table 1. Ratios Describing Efficacy of Tests

	Disease Present	Disease Absent
Test positive	a	c
Test negative	b	d
Sensitivity (true-positive rate)	=	a/(a + b)
False-positive rate	=	c/(c + d)
Specificity (true-negative rate)	=	d/(c + d)
False-negative rate	=	b/(a + b)
Positive predictive value	=	a/(a + c)
Negative predictive value	=	d/(b + d)

from the diagnostic block. A false-negative rate then is unknown, and the false-positive rate, which requires knowledge of true disease incidence in the entire group, also cannot be calculated. From these studies, only the positive predictive value (frequency of confirming disease in those with a positive test) can be derived.

The proper interpretation of a positive test must take into consideration the prevalence of the condition. For example, a test with a 95% specificity rate will have a positive result in 5% of healthy subjects. If the condition being sought is rare (*e.g.*, occurs in only 2% of the test group), false-positive responses will outnumber true-positive tests, and the majority of positive results will occur in subjects who actually are healthy.

Trigger Point Injection

Rationale. Myofascial pain syndrome is characterized by pain associated with movement of affected muscles and reproduction of pain with palpation of well localized trigger points in the affected muscle.[108] Myofascial syndrome is commonly found in association with other painful disorders, such as facet arthropathy or radiculopathy, and it is often helpful to determine whether a patient's pain is predominantly myofascial, because appropriate treatment may be very different if such is the case. Reproduction of pain during injection into the area and relief of pain after injection for the expected duration of local anesthetic are used to indicate that myofascial pain is at least partially responsible for the patient's pain. Other means of documenting myofascial pain, such as electromyography, have not been proved reliable.[109,110] Muscle tenderness is also seen in fibromyalgia, which differs from myofascial pain syndrome in that tender points in the muscle are much more diffuse and numerous and usually symmetrical, and palpation generally produces local, but not referred, pain.[111] Trigger point injections, particularly if repeated several times, may have therapeutic benefit for myofascial pain syndrome but are generally regarded as ineffective for fibromyalgia.[112] The predictable and selective destruction of mature myocytes by local anesthetic infiltration[113] might be the therapeutic mechanism of long-term response to trigger point injection because it encourages the growth of a new generation of myocytes.

Limitations. Undesired spread to adjacent nerves should be considered in interpreting trigger point injections. Injection of the piriformis muscle is likely to have some effect on the sciatic nerve, which either penetrates or passes deep to the muscle. Doubt regarding the specificity of diagnosis by trigger point injection is raised by reports showing comparable efficacy from less specific techniques, such as needle insertion without injection,[114] and from jet injection of local anesthetic into the skin that overlies trigger points.[115]

Conclusion. Controlled studies have not confirmed the ability of intramuscular local anesthetic injection to identify muscle or fascia as the pain source, although the simplicity of the procedure for superficial muscles is persuasive.

Somatic Nerve Block

Rationale. A common reason to perform diagnostic peripheral nerve blocks is to determine the likelihood of success after surgical decompression or neurolysis of a peripheral nerve. Diagnostic blocks also may be performed before a planned peripheral nerve section, neurolytic block, or cryoanalgesia lesion. Somatic nerve block also may be used to predict outcome after decompression of entrapment neuropathies such as of the digital nerve (Morton's neuroma), the median nerve in the carpal tunnel, the tibial nerve in the tarsal tunnel, and the ilioinguinal and iliohypogastric nerves after herniorrhaphy.

Limitations. Relief of pain after blockade of the appropriate nerve does not necessarily confirm the diagnosis of neuropathy at that site. There may be a nociceptive source of pain within the distribution of the blocked nerve, or there may be a neuropathic source of pain proximal to the site of block (*e.g.*, radiculopathy or plexopathy) that may be relieved by the procedure.[7,9]

Studies. The diagnostic use of injection of lidocaine and steroid has been examined in patients suspected to have carpal tunnel syndrome.[116] The test identified most patients with the disease, demonstrated subsequently at surgery (sensitivity rate 85%), but it indicated

lack of carpal tunnel syndrome in only 38% of those surgically negative (specificity). Even when peripheral local anesthetic nerve block produces profound relief, there is poor prediction of long-term relief after neuroablative procedures.[117]

Conclusion. Relief of the peripheral block may help to predict response to neural decompression, but has unproved prognostic value in predicting response to neuroablation.

Visceral Nerve Block

Rationale. It may be helpful to distinguish whether thoracic, abdominal, or pelvic pain is due to pathology of visceral elements or somatic (body wall) structures. If it can be established that pain is visceral in origin, treatment may be directed toward exploration of abdominal or pelvic organs or toward denervation of visceral structures if untreatable malignancy is the source of the pain.

The celiac plexus or the splanchnic nerves proximal to their joining the celiac plexus can be blocked when it is unclear whether abdominal pain is of visceral origin, such as occurs with pancreatitis, distension of the hepatic capsule, or cholecystitis, or of somatic origin, as in the case of entrapment of an intercostal nerve or pain of muscular origin. In such cases, it is helpful to compare the response of celiac or splanchnic block to that of intercostal block or local infiltration of the abdominal wall and to that of placebo injection.

A prognostic celiac or splanchnic block may be performed before neurolysis for treatment of pancreatic cancer, because celiac plexus blocks may be relatively ineffective when local tumor spread and resultant inflammation are extensive. Blockade of the afferent innervation of the pelvic viscera by superior hypogastric plexus block has been used mainly to predict the response to subsequent neurolytic blockade.

Limitations. Systemic local anesthetic effects may be especially important for these procedures, because relatively large volumes are used. Such volumes also may predispose to spread of anesthetic to somatic nerves.

Conclusion. Despite the lack of studies documenting prognostic benefits of visceral blocks, it would seem prudent not to pursue neuroablative techniques in the absence of relief from local anesthetics.

Sacroiliac Injection

Rationale. It is probable that the sacroiliac joint can be the source of acute or chronic pain, because the joint is well innervated.[118] Stimulation by injection of radiographic contrast into the joint in subjects without complaints of back pain produces pain in the immediate area, often also in the surrounding gluteal area, and occasionally into the posterior thigh and knee.[119] Diagnostic criteria for determining a sacroiliac origin of low back pain are uncertain. Gaenslen's maneuver (provocation of pain in a diseased sacroiliac joint by hyperextension of a hip over the side of the bed while a prone patient holds their hip and knee flexed) or compression of the apex of the sacrum with the patient prone on a firm surface may reproduce the pain, but the specificity of this test in unknown. Other physical examination maneuvers frequently indicate disease in asymptomatic individuals.[120] Typically, there is tenderness over the sacrum just medial to the posterior superior iliac spines. Computed tomography (CT) scans of the joint may show erosions, narrowing of the cartilaginous portion of the joint, and bony sclerosis of the adjacent ilium. However, the normal anatomy of the joint shows asymmetry of cartilage thickness (thinner on the iliac side) and cartilage-covered irregularities in the bony surfaces that interlock with reciprocal depressions on the opposite surface, enhancing joint stability.[121] Such changes are more prominent in men, and, with age, there is a predictable thickening of the capsule, roughening of the cartilage, and growth of marginal osteophytes.[122] For these reasons, it is often difficult to identify pathologic changes in sacroiliac joints and the extent of the sacroiliac contribution to back pain.

Local anesthetic injection of the sacroiliac joint is used to test whether the joint is a source of low back pain, particularly when diffuse degenerative disease involving the lumbosacral spine is present. It is thought, by some clinicians, that local anesthetic injections of the joint may have some value in predicting response to intraarticular steroid injections.

Limitations. Because of the great interindividual variability in size and contour of sacroiliac joints,[122] and the inaccessibility of the joint line, it is probable that needles inserted without x-ray assistance usually fail to enter the joint space and are actually injections into the fibrous structures well outside the joint. If the procedure is done under fluoroscopic or CT control, the inferior extent of the joint can be identified and the joint space itself may be entered.[119,123] Without radiographic guidance, there is no means to confirm accurate delivery of local anesthetic. When imaging is used to document the intraarticular spread of injectate, intraarticular placement is found to be reliable.[119] It is not clear

whether intraarticular spread is necessary to achieve efficacy. Pain relief after injection may actually be related to infiltration of sacroiliac ligament or sacrospinalis muscle with anesthetic and give the incorrect impression that the joint is the pain source.

Studies. Follow-up of a series of 35 patients treated with sacroiliac joint injections (Reynolds AR, Abram SE: unpublished data, 1984) showed that 28 patients experienced transient relief with local anesthetic and were given injections of triamcinolone diacetate. Of the 20 patients followed long-term, 7 had persistent improvement in symptoms (relief of 75% of pain or better) at the end of 6 months. There are no prospective or controlled evaluations of the technique, and no data that indicate the sensitivity or specificity of sacroiliac injection as a means of diagnosing the joint as a source of pain.

Conclusion. Analgesia after sacroiliac injection with local anesthetic may be helpful to differentiate sacroiliac arthropathy from facet disease, myofascial pain, or disc disease, although this is unproved.

Facet Blockade

Rationale. The zygapophyseal (facet) joints are paired diarthrodial articulations between the posterior elements of adjacent vertebrae that determine the relative motions of the adjacent vertebrae. Rudimentary fibroadipose menisci and synovial folds cushion the superior and inferior poles of the lumbar zygapophyseal joints,[124] but, with age, these typically disappear, and the cartilage on the joint surfaces thins.[125]

The medial branch of the dorsal primary ramus of the spinal nerve supplies the facet joint and the supraspinous and interspinous ligaments. Of these, only the facet joint capsule is consistently found to be well innervated by nociceptive fibers that also penetrate the capsule and supply the synovial folds.[126] Each facet joint receives branches from the spinal nerves that exit the vertebral canal through the adjacent intervertebral foramen and from the foramen one segment above.[127,128]

Injection of hypertonic saline into or around the lumbar facet joint capsule produces pain in the back, buttocks, and proximal thigh.[129] Physiologic recordings in laboratory animals have documented mechanoreceptive sensory fields in facet joints.[130] Distension of normal cervical facet joint capsules produces unilateral pain referred to occipital and upper neck regions for the atlanto-occipital, atlanto-axial, and C2/3 joints and scapular pain from joint C6/7.[131,132] Substance P, a neuropeptide characteristic of nociceptive neurons, is found in facet capsule neurons,[133] which also supports the concept that the facet joints are a source of pain. Rotation and extension between two adjacent vertebrae increases facet stress, as does loss of disc height,[134] all of which may be stimuli for facet pain. Facet menisci are innervated by small myelinated nerves,[135] in which substance P is present[136] but rare.[137] An entrapment syndrome involving the facet menisci has been proposed,[124] but there is no clear evidence to implicate this in the production of back pain.

The site of origin of nonradicular back and neck pain almost always poses a diagnostic dilemma. In addition to the facet joints, other structures in the vertebral column are also richly innervated, such as the posterior and anterior longitudinal ligaments, annular ligament of the intervertebral disc, anterior dura mater, and the costovertebral joints.[138-140] Stimulation of these other vertebral elements by injection or during surgery in awake patients with local anesthesia evokes pain in the back, hip, and buttock indistinguishable from pain produced by facet irritation.[141-144] Pain can occur in the absence of changes on plane radiographs of the vertebral column. Computed tomographic imaging is more sensitive, but degenerative facet arthritis is also seen in 10% of asymptomatic patients,[145] making the benefit of imaging uncertain. Although the value of bone scan is unproved, a positive finding may support the diagnosis of facet arthropathy and may direct attention to a particular joint. Because there is no specific pathognemonic finding[146] or test, the clinical criteria for making the diagnosis of facet pain remain undefined. Therefore, diagnostic injections are often performed to help indicate the contribution of the facet.

Facet blockade is achieved either by injection of local anesthetic into the joint space or around the medial branch of the posterior primary rami of the spinal nerves that innervate the joint. After joint injection, the patient's pain can be attributed to the facet if: (1) the pain produced by needling is similar to the usual pain, (2) pain relief is noted in response to local anesthetic injection, and (3) sensory examination shows no evidence of segmental spinal nerve block.

Limitations. There is no physiologic means to test the adequacy of facet blocks. There is no cutaneous innervation of the nerves to the joints, so adequacy of the block cannot be confirmed by superficial examination after medial branch blockade. Provocative stimuli of the joint, such as mechanical or chemical irritation, could be repeated after intraarticular injection of medial

nerve block to check adequacy of denervation, but this has not been investigated.

The use of facet or medial branch injections for diagnosis relies on the assumption that facets are a source of pain. This premise is accepted by most authorities, although the frequency of this as the primary element producing a patient's pain is debated. Disc degeneration is present in all cases of lumbar facet disease evident by CT or magnetic resonance imaging.[147] Disc disease identified by discography was present in 64% of patients with a positive cervical medial branch test for facet joint disease.[148] Pathologic changes in facets are a common cause of injury to nerve roots,[149] and may irritate afferents on the posterolateral aspect of the disc. These other disease processes could, therefore, be the cause of pain in patients with incidental abnormalities of the facet, or at least contribute to a condition more complex than purely a facet origin of pain. Because there is no histopathologic or imaging standard,[150] the frequency of pain from the facet *per se* has been estimated only by relief in response to injections. This inevitably involves circular logic, but yields a positive indication of cervical facet etiology in unselected patients with posttraumatic neck pain of approximately 70% (range 63%–100%).[148,151–153] In subjects clinically suspected of having lumbar facet pain, confirmation by relief after injection ranges from 16% to 94%.[154–159] In a noncontrolled and nonblinded study of patients with chronic low back pain without radiculopathy, 25% of those assigned to receive medial branch nerve blockade of a randomly chosen joint had immediate relief, and 38% had relief after injection into the suspected joint.[160] These rates are similar to the frequency of placebo response. Total absence of pain after injection of local anesthetic into the lumbar facets is much less common, occurring in only approximately 7% of patients with back pain.[155,161] It is reasonable to conclude that, in many study groups, the facets are an origin of at least part of the patients' pain, but rarely the unique or major source.

Mechanical irritation of the joint capsule during facet injection may produce discomfort resembling the patient's typical pain. Because cervical[131,162] and lumbar[129,154,162,163] facet stimulation produces broadly overlapping areas of pain distribution, even into the distal extremity, this is not a strong indicator of pain origin. Patients in whom usual pain is recreated by facet stimulation are not necessarily the same patients in whom local anesthetic in the joint relieve pain,[156] and there is a poor correlation between pain provocation and relief from local anesthetic injection.[164] In one study,[159] 31% of patients with a positive response to pain provocation failed to have relief after anesthetic injection into that lumbar facet, and 40% that had relief from injection had not had typical pain during needle stimulation or distension of the facet capsule with contrast.

The specificity of facet denervation depends on limiting anesthetic spread to the target site—either the joint space or nerves to the joint. Detailed sensory and motor testing after these blocks has not been reported. The facet joints are not capacious. Rupture during intraarticular injection has been identified after injection of more than 1 ml into cervical facets[165] and after most lumbar injections,[158,166] and has been demonstrated in cadaver facet injections.[159] Because joint capsule rupture spills local anesthetic into neighboring tissues, pain relieved by facet injection could originate in other structures, such as muscle, periosteum, and ligaments. Passage of anesthetic into the epidural space or intervertebral foramen, which occurs routinely with capsule rupture,[158,166] could interrupt nociception from sensitive structures in the vertebral canal, such as anterior dura and posterior longitudinal ligament, or from any distal site by effects on afferent fibers in the spinal roots. Of patients with clinical indications of lumbar facet pain, 18% were found to have spondylolysis,[167] a defect in the vertebral arch due to chronic stress. With this condition, intraarticular facet injection is consistently followed by spread of solution into the epidural space and to adjacent and contralateral facets, and even laterally along a spinal nerve,[167] limiting specificity of the test.

Blockade of medial branches not only denervates the joints they supply but also the muscles, ligaments, and periosteum into which they ramify. Sources of pain in these alternative sites will be relieved by medial branch block. Fluid distribution during cervical medial branch block is variable, with the area of consistent coverage being a small subset of the area into which spread may be observed. Injectate, however, does not travel to anterior primary rami or to medial branches of adjacent posterior rami.[152] Because each medial branch supplies parts of two facets, complete denervation of one facet requires partial blockade of the facet above and below. Therefore, relief from the blocks cannot distinguish between pain originating at any of the three. Because medial nerve blockade more accurately simulates the effect of radiofrequency denervation than does intraarticular injection, it is the appropriate diagnostic test before that procedure.

Reproducibility of the test is not high. In one study,

facet injections in 176 patients with low back pain produced relief in 83 (47%), but a repeat injection was positive in only 26 (31%) of the 83.[168] This indicates either a strong placebo component or subtle technical difficulties that cannot be controlled. The authors of this study claim that the second injection determines which of the responders to the initial injections were true positives, and not placebos. This logic apparently dismisses another possible explanation that the two time-positive responders may have been placebo responders each time. Even when relief is found during repeated diagnostic injections, there is no feature of the patients' histories of physical examinations that correlate with a positive diagnosis by this more demanding criterion,[169] drawing the relevance of blocks into uncertainty.

Studies. Validation of the use of intraarticular and medial branch injections to document facet pain requires demonstration that: (1) the injections, as described, are effective in denervating the joint, and (2) such denervation can be used to distinguish between various sources of back pain. No means has been described to test the adequacy of facet denervation, so success rates have not been determined. Relief of pain in patients with presumed facet arthropathy is not a suitable test of physiologic blockade success. Because the diagnosis of a painful facet relies on injections for confirmation, evidence for either is circular. Inability to directly confirm that the block is successful and that the joint is denervated weakens the diagnostic use of facet and medial nerve injections.

Failure to enter the joint during attempted intraarticular injection has been reported in 16–38% of lumbar injections[155,170] and 44% of cervical facet injections.[153] To a degree, cervical medial branch block has been validated by comparison to intraarticular injection; all of seven patients who were relieved by blockade of the branches innervating a joint had relief after intraarticular injection of that joint on a different occasion, although as much as 2 ml of local anesthetic was injected into the joint.[156]

Because no standard to confirm facet pain is available for correlation with block findings, the ability of facet blocks to validly distinguish the source of back pain has not been established. In addition, the clinical usefulness of facet blocks is drawn into question by several findings. In general, a facet etiology is identified infrequently when small intraarticular injectate volumes are used.[45,159] This means that either larger (more than 1.5 ml) volumes are necessary for adequate intraarticular block, or, more likely, that large volume injections block pain from sources other than the facet. The only studies with control subjects also raise doubts. In one, local anesthetic resulted in relief in 54% of patients with back pain, but 43% of these responders also were relieved by injection of a randomly chosen uninvolved facet joint.[156] A controlled trial that examined improvement 1 h after injection found no difference in groups that had local anesthetic injected into the joints, outside the joints, or normal saline injected into the joints.[171] In a study in which researchers compared duration of analgesia after cervical medial branch blocks on two different occasions to determine a false positive rate, 27% either had a duration of analgesia longer for lidocaine than for bupivacaine or no analgesia at all on the second injection.[172] The only study that was controlled and blinded showed no difference in pain relief between intraarticular lidocaine or saline injection.[161]

Long-term benefit may follow intraarticular zygapophyseal joint injection, especially if steroid is included. Steroid injected into the lumbar facet joints produces significant relief, outlasting the local anesthetic in 30–54% of groups of selected patients with back pain.[155,158,170,171] The use of local anesthetic injection to predict response to steroids is uncertain. The only blinded trial of facet steroid injection found that the completeness of response to local anesthetic did not predict the degree of steroid effect.[155] Another study found no benefit from cervical facet steroid injection, even though the same patients experienced complete relief from local anesthetic.[151] Steroid injection is probably appropriate during a diagnostic injection study because the additional risk of injecting the steroid after the needle is already in place is minimal.

Insufficient data are available with regard to the ability of facet blocks to predict the response to surgical or neuroablative therapy. Radiofrequency facet denervation failed to benefit 36% of patients who had excellent relief from intraarticular injection.[162] In another report,[173] the positive predictive value of relief after local anesthetic block of the lumbar medial branch of the posterior primary ramus was 0.45 in anticipating success from radiofrequency denervation (45% of block successes also were radiofrequency successes). Specificity and sensitivity cannot be determined because radiofrequency surgery was not performed if blocks provided less than moderate relief. Relief after facet injection has been examined as a prognostic indicator for response to posterolateral lumbosacral fusions,[174] but

block results did not accurately predict surgical outcome.

Conclusion. Injections intended to block afferents from facet joints have been found useful by a number of authors. However, the literature on the topic is from its relatively few advocates. Also, the inability to confirm success of a block and the lack of convincing evidence for efficacy and diagnostic specificity of these techniques dictates that findings should be interpreted cautiously.

Selective Spinal Nerve Injection

Rationale. In complicated patients with radiculopathy, the contribution of root inflammation to pain may not be certain, or the level of the pathology may be unclear. Imaging by CT or magnetic resonance and electrophysiologic evaluation by electromyography may be inconsistent or may not fit with clinical findings. Frequent positive findings in imaging of asymptomatic subjects[145,175] demonstrates the inability of abnormal anatomy to indicate a pain source. A further cause of confusion is the presence of pathology at multiple levels, because the origin of pain may be any one or a combination of sites, as is also true when upper lumbar pathology coexists with hip joint disease. Finally, evaluation is especially difficult after laminectomy, because imaging is impeded by scar tissue in the epidural space.

Injection of individual spinal nerves by a paravertebral approach (also termed foraminal injection, and mistakenly referred to as nerve root injection), usually at lumbar levels, has been used to elucidate the mechanism and source of pain in these unclear situations. The premise is that needle contact will identify the nerve that produces the patient's characteristic pain and that local anesthetic delivered to the pathogenic nerve will be uniquely analgesic. A test is considered positive for a given nerve if needle contact produces pain similar to the patient's usual pain, and if relief follows local anesthetic injection, including lack of pain during maneuvers that produced pain before the block, such as straight leg lift or walking. Advocates point out that selective spinal nerve block, as with facet injection, tests pain production mechanisms dynamically rather than simply displaying anatomic abnormalities that may or may not produce pain. Often, this method is used for surgical planning, such as determining the site of foraminotomy.

Limitations. Without radiographic guidance, diagnostic accuracy can be expected to suffer from inability to select the proper level and confirm needle placement at the intervertebral foramen.

The pain provocation portion of the spinal nerve injection test examines pain quality and distribution. Duplication of the typical quality of the pain as a criterion is supported by the demonstration that inflamed nerves are more sensitive to manipulation than normal nerves.[142] The distribution of the evoked sensation is less certain to be reliable. Because pain with the stimulation of different roots produces overlapping areas of radiation,[142] these patterns may not distinguish the involved root from adjacent ones.

Successful neural interruption must be confirmed by means other than pain relief before attributing relief to the block. However, it is not clear that anesthetizing a single spinal nerve should produce discernible peripheral sensory changes. Isolated monoradiculopathy is commonly associated with numbness, but this pathologic condition is probably more complex than just segmental nerve dysfunction, and probably includes changes in central connections.[176] In one study, selective spinal nerve injection reliably produced peripheral sensory changes in dermatome mapping studies, but 2 ml of anesthetic was injected, raising the question of spread to adjacent levels.[177] Because surgical division of a single root produces no loss of cutaneous sensation,[92] it remains uncertain whether cutaneous sensory monitoring can accurately indicate the presence or absence of selective spinal nerve block. No other methods of determining block success, such as thermography or somatosensory-evoked potentials, have been examined.

Pain relief with blockade of a spinal nerve cannot distinguish between pathology of the proximal nerve in the intervertebral foramen or pain transmitted from distal sites by that nerve. Tissue injury in the nerve's distribution and neuropathic pain alike would be relieved by a proximal block of a nerve. The ability of injection to block vertebral pain without blocking hip pain has not been demonstrated. The accuracy of spinal nerve block depends on limiting spread of anesthetic to the selected nerve alone. Flow into the intervertebral foramen and epidural space is commonly observed and definitely compromises this assumption.[178-180] Not only will this block pain transmitted by the sinuvertebral nerve from the dura, posterior longtitudinal ligament, and annular ligament of the disc, but any spread *via* the epidural space to other segmental levels could produce misleading results. For instance, injection of a normal S1 with spread to an inflamed L5 could produce relief, with the responsible nerve assumed to be S1. For this

reason, this test should not be used outside the context of thorough overall evaluation.

Studies. The frequency of successful spinal nerve blockade has not been determined. In no studies using spinal nerve block for diagnosis were cutaneous sensory changes examined. Satisfactory needle placement could not be achieved in 10% of patients at L4, 15% at L5, and 30% at S1.[178] In another report, 18% of tests failed because of pain that exceeded the patient's tolerance or failure to stimulate the desired root, most often at S1.[181]

In several retrospective studies, researchers investigated the ability of selective spinal nerve blocks to diagnose disease and predict surgical outcome. The positive predictive value (fraction of patients with injections that indicate radiculopathy in whom surgery confirmed radicular pathology at the level indicated by the test) ranged from 87% to 100%.[178,179,181,182] The negative predictive value (percent of patients with a negative injection test and confirmed at surgery to have normal nerve roots) is poorly studied, because few patients had surgery in the negative test groups; negative predictive values were 27% and 38% of the small number of patients operated on despite a negative test.[178,179] Only one prospective study has appeared, which showed a positive predictive value of 95% and an untested negative predictive value.[183] Sensitivity and specificity cannot be determined from these studies because of the unknown disease incidence in the complete group. In general, the accuracy of nerve blocks is better than imaging or electromyography.[178,183] No control subjects were used in these studies, and the use of cervical diagnostic spinal nerve injections has not been examined formally.

A recent retrospective report[180] attempted to predict surgical outcome by evaluating pain relief in response to steroid injection at the spinal nerve. Most patients were tested with selective spinal nerve blocks, but 20% received epidural injection, and patients whose pain was not relieved by local anesthetic were not included in the steroid test. All patients had surgery regardless of test outcome, so complete outcome data are available. False-positive rate (percent of failed surgery who had favorable response to injection) was 5%, and false-negative rate (percent of surgical successes who had no response to steroid) was 35%, indicating that patients unlikely to benefit from surgery can be identified reliably by failing to respond to steroid, but some who would benefit from surgery will be missed by this test. In patients with pain lasting longer than 1 yr, however, nearly all patients who would benefit from surgery were identified by their response to steroid (false-negative rate of 15%).

Studies repeatedly demonstrated that pain relief by paravertebral spinal nerve injection does not predict success by neuroablative surgery, either by dorsal rhizotomy[184,185] or dorsal root ganglionectomy.[186]

Conclusion. Spinal nerve injection is often used to plan decompressive surgery on complicated patients. However, the accuracy of this diagnostic information has not been proved by controlled and blinded studies. No role has been demonstrated for these blocks in evaluating patients for neuroablative procedures.

Greater Occipital Nerve Block

Rationale. The greater occipital nerve is the continuation of the medial branch of the posterior primary ramus of the C2 spinal nerve, which distributes cutaneous sensory fibers to the scalp as far rostral as the vertex. Several theories have proposed involvement of the C2 spinal and greater occipital nerves in production of headache. Initial analysis suggested that the origin of the spinal nerve or the posterior root ganglion may be pinched between the atlas and axis by extension and rotation.[187] Further research proved that this is mechanically unlikely.[188,189] A more popular theory invokes irritation of the greater occipital nerve as it penetrates muscle layers. The passage through the muscular portion of the semispinalis capitus is rarely restricted, but the aperture through the trapezius is by a nondistensible channel that typically deforms the nerve.[190] Entrapment here may be the origin of nerve irritation that initiates neuralgic pain.

Greater occipital neuralgia and cervical facet arthropathy are putative sources of cervicogenic headache, which is clinically distinguished from migraine and tension-type headaches by unilateral pain, symptoms and signs of neck involvement (ipsilateral neck, shoulder or arm pain; tenderness or postural pain in the neck; decreased range of neck motion), nonclustering moderate pain that throbs and spreads forward from the neck, and a history of head or neck trauma.[191,192] Transient elimination of pain by greater occipital nerve block is used as a key criterion in the evaluation of cervicogenic headache.[191]

Limitations. Selective blockade of the nerve at the proposed pathogenic site requires injection where it penetrates through the trapezius, but the site shows marked interindividual variability.[190,193] Effective block

is confirmed when anesthesia develops in the distribution of the nerve.

Cervicogenic headache is a poorly documented entity[194] with no consistent histopathologic or radiologic findings.[195] The typical lack of sensory deficit in the area of distribution of the greater occipital nerve does not support a neuropathic mechanism.[189] Alternatively, it is possible that pain radiating in the distribution of the greater occipital nerve represents converging deep somatic input from the lateral atlanto-axial joint, which is innervated by the C2 anterior ramus,[189] or from irritation of suboccipital muscles and periosteum, which has been shown to produce ascending headache.[196]

Because all the proposed pathophysiologies of cervicogenic headache are unproved, the meaning of blockade responses do not rest on a solid mechanistic base. Therefore, no defined process has been proved when relief follows greater occipital nerve block. Also, the therapeutic plan is not well defined after a favorable response to test injections. There are no data on the use of this block for treatment, and the surgical therapy for presumed greater occipital neuralgia has not been promising.[197,198] Favorable responses to radiofrequency lesions of the greater occipital nerve have been claimed.[199] Patients who had pain relief after bilateral greater occipital nerve block with 10–15 ml of local anesthetic on each side received heat lesions to the nerves during general anesthesia. Although good-to-excellent relief was reported in 85% of cases, neural interruption was not documented, and there were no control subjects.

Studies. No information is available regarding rates of successful greater occipital nerve blockade. The ability of the block to identify patients with disease is hampered by inexact definition of cervicogenic headache and no means of confirmation. Most studies, as well as the definition of the condition, come from a single group of authors. In one report,[200] patients clinically categorized as having migraine, cervicogenic, or tension-type headaches were tested with greater occipital and supraorbital nerve blocks, the latter as control subjects. Cervicogenic headache patients were most relieved by occipital injection. However, supraorbital block also produced relief (about half as much, and not selective for cervicogenic patients), and the two blocks relieved pain at the other poles of the head. Although this calls into question the basis of relief, a mechanism is offered in which sensory tracts converge on common upper cord and brain stem centers.[201] In another report,[192] the ability of greater occipital nerve block (confirmed successful by sensory examination) to provide relief was compared with selective blocks of cervical spinal nerves and the C2/3 facet in patients with symptoms of cervicogenic headache. The patterns of responses were thought to discriminate between various origins of pain, but analgesia, to some degree, followed most blocks.

Conclusion. The anatomy of the greater occipital nerve is well defined and the block easily confirmed, but the diagnostic meaning of a favorable response is clouded by the lack of pathophysiologic understanding of cervicogenic headache.

Selective Sympathetic Blockade

Rationale. Sympathetic efferent activity is a suspected pathogenic component in a number of conditions. In some, such as hyperhidrosis, the participation of sympathetic fibers is well documented. In other diseases, such as sudden sensory-neural hearing loss, peripheral vascular disease, dysrhythmia from long-QT syndrome, central pain,[16] pain after plexus injury, and trigeminal or postherpetic neuralgia,[202] the diagnosis is clear but the role of sympathetic activity is uncertain and controversial. Finally, in a large category of poorly defined pain states that are grouped under the terms reflex sympathetic dystrophy or causalgia, a sympathetic contribution is suspected because blood flow and trophic changes are evident, but the pathophysiology is largely obscure. In these settings, selective interruption of sympathetic neural traffic to the involved area may provide diagnostic insight and guide future therapy. If blockade relieves pain, indicated therapies might include further local anesthetic blocks, systemic treatment with sympathetically active drugs (*e.g.*, clonidine and prazosin), or destructive therapy with neurolytic injection or surgery. Failure of relief after sympathetic blockade would argue against the use of these treatments.

Limitations. Sympathetic denervation in the area of disease is evident by sudomotor, vasomotor, and ocular changes. Many measures have been used to judge the efficacy of sympathetic blockade, although none has become an accepted standard. Horner's syndrome is easily observed but documents only blockade of sympathetic fibers to the head. Skin resistance (sympathogalvanic) response[203,204] and pulse amplitude changes[205] are difficult to quantify. Microneurography[203] is direct but invasive and requires elaborate equipment and expertise, as does laser skin blood flow measurement.[206] Sweat testing[207] is cumbersome, time consuming, and

not well accepted by patients, and, therefore, not widely used. Most common is the measurement of skin temperature by thermography or contact thermometry. A temperature increase of 1.0–3.0° C is typically used[208,209] as a threshold to confirm the onset of sympathetic blockade, but the method is ineffective if skin is warm at the outset of a block.

Although local anesthetic blockade of sympathetic activity to the extremities produces vasodilatation, vasoconstriction follows segmental block of sympathetic fibers to the trunk,[37] possibly by blockade of sympathetic vasodilator fibers.[210] Skin temperature in pathologic conditions is controlled by a balance between sympathetic vasoconstriction from norepinephrine release and vasodilatation from release of vasoactive peptides from C nociceptors during antidromic activity.[211] Temperature change in the field of a blocked peripheral nerve will depend on the relative contribution of these opposing systems. From the available information, it is apparent that completeness of sympathetic block may depend on the monitored parameter chosen.

The cervical trunk may be blocked independent of the stellate ganglion or fibers to the brachial plexus, so occurrence of ptosis, meiosis, facial anhydrosis, conjunctival hyperemia, or nasal stuffiness does not assure sympathetic block of fibers to the arm. Stellate, thoracic, or lumbar sympathetic injections that produce no measurable evidence of sympathetic blockade cannot reveal disease pathophysiology, regardless of the response of pain.

Stellate ganglion injection may fail to produce sympathetic denervation for several reasons. Alternative routes allow sympathetic fibers to reach peripheral sites without transit through the stellate ganglion. These include passage in the nerves of Kuntz from the second and third intercostal nerves to the brachial plexus,[212,213] distribution *via* the carotid, subclavian, and vertebral arteries,[214–216] and by directly entering the peripheral nerves after synapses outside the sympathetic chain in intermediate ganglia located in spinal nerves.[217] Sympathetic fibers can probably also bypass the sympathetic chain in the sinuvertebral nerve of Luschka.[218] The principal reason for failure of injection to produce stellate ganglion blockade is lack of delivery of anesthetic to the ganglion. Whereas the ganglion resides at the lower edge of the head of the first rib,[219] solution injected at cervical levels passes anterior into the mediastinum.[220,221]

At lumbar levels, multiple pathways of sympathetic fibers include collateral chains[79,222] and crossover of fibers from the contralateral chain.[223–225] These alternative pathways may allow persistent sympathetic innervation to reach the lower extremities despite a properly performed lumbar sympathetic block. Confusion can also result if local anesthetic solution is conveyed to the epidural space through the fibrous tunnel along the waist of the vertebral body. The resulting undesired somatic blockade could produce analgesia that is then attributed to a sympathetic mechanism.

The diagnostic usefulness of sympathetic blockade depends on the ability to selectively interfere with sympathetic activity and maintain continuity of somatic pathways. Solution injected into the paravertebral space readily enters the epidural space.[226] The only study that examined detailed somatic sensory changes after sympathetic blocks found that nociceptive block without anesthesia was common.[34] A subtle somatic block with analgesia but intact sense of touch would create the impression of analgesia from sympathetic blockade if altered pain sensation is not specifically identified.

Blocks of the paravertebral sympathetic chain inevitably interrupt visceral afferent signals as well as efferent sympathetic activity.[104] This could create a false conclusion with regard to the source and mechanism of pain. For instance, a stellate ganglion block will stop arm pain from myocardial ischemia but could be credited with identifying a sympathetically dependent pain process.

A fundamental limitation of diagnostic sympathetic blockade is a lack of understanding about the role of the sympathetic nervous system in pain production.[227,228] Evidence now indicates that excessive sympathetic activity is almost certainly not the explanation of pain.[229–232] The enigmatic pathophysiology and ambiguous definitions of reflex sympathetic dystrophy and other painful conditions in which the sympathetic nervous system plays a putative role frustrate the interpretation and application of findings from blocks.[233]

Studies. Rates of success in actually interrupting sympathetic activity after injections intended for that purpose is incompletely known. After cervical paratracheal injection, Warrick[234] observed that very few patients had warming of the hand. Carron and Litwiller[208] reported that a 3 ml injection increased hand temperature 1.5° C in all of more than 700 blocks. Using 15 ml of an equal mix of 1% lidocaine and 0.5% bupivacaine, Ready *et al.*[235] had 100% success in producing Horner's syndrome, but 75% success in warming the ipsilateral hand by 1° C. Malmqvist *et al.*[236] observed an 87% success rate in producing Horner's syndrome, but 26 (48%) of 54 subjects with initial ipsilateral hand temperature

of ≤32° C failed to warm to ≥34° C within 20 min. Only 11.5% of their blocks met 5 criteria of success, those being Horner's syndrome, increased hand temperature, ≥50% increase in skin blood flow, increased skin resistance (to ≥113% of baseline), and abolished skin resistance response. In 100 consecutive C6 anterior tubercle blocks,[209] 84% resulted in Horner's syndrome, indicative of at least some blockade of sympathetic fibers to the head. Only 60% caused the ipsilateral hand to warm by 1.5° C or more, and because the contralateral hand frequently warmed also, in only 27% did the ipsilateral hand warm by 1.5° C more than the contralateral hand. From these studies, it is apparent that blockade of sympathetic innervation to the upper extremity is a variable result of stellate ganglion injections. There is little difference in the adequacy of sympathetic blockade by paravertebral injection at C7 level compared with C6.[221,236,237] Injection through a needle placed at the head of the first rib requires CT guidance but assures successful blockade.[238]

There are no studies of the success rates for lumbar sympathetic block except by Hatangdi and Boas (using phenol),[239] who reported success in increasing the skin temperature > 1° C in 61–68% of patients.

Diagnostic sympathetic blocks are most often used to evaluate painful conditions. There is no histopathologic or serologic standard to confirm a sympathetic contribution to pain production, so there have been few studies that measured the ability of blockade to accurately diagnose a sympathetic role. The available reports raise doubt as to whether analgesia after sympathetic blockade indicates a sympathetic contribution to pain. The degree of sympathetic dysfunction does not correlate with the response of pain to sympathetic blockade,[16,240] and the timing of changes in pain does not necessarily match the onset of manifestations of sympathetic block. When sympathetic activity is measured with microelectrode neurography in limbs with pain relieved by local anesthetic sympathetic block, sympathetic efferent traffic is normal.[229] Response of pain to sympathetic blockade does not predict levels of norepinephrine and its metabolite in the venous effluent from limbs with features of reflex sympathetic dystrophy.[232] In fact, venous plasma catecholamine levels are less on the painful side than on the nonaffected side. These findings make less plausible the belief that sympathetic block analgesia identifies regional sympathetic hyperactivity. The important question of whether the response to sympathetic blockade guides therapy toward a better outcome has not been addressed formally.

Conclusion. Confusion surrounds many aspects of care for patients in whom pain or other dysfunction is suspected to be based in the sympathetic nervous system. Response to a block, therefore, offers an apparently concrete diagnostic insight. Considerations enumerated above, however, suggest that the diagnostic value of sympathetic blockade has been overestimated. Appropriate use calls for care in documenting the desired physiologic response and restraint in interpretation of the results. There should be caution to avoid the circular logic of defining sympathetically maintained pain as conditions improved by sympathetic blocks, and the blocks defined as successful if they relieve a pain assumed to be sympathetically maintained.

Intravenous Regional Sympathetic Block

Rationale. Intravenous regional (IVR) injection of both guanethidine[241] and bretylium[242] have been used therapeutically in patients with sympathetically maintained pain. Both drugs inhibit release of norepinephrine from nerve terminals, and guanethidine depletes tissues of norepinephrine. The patient's response during the postblock period should be an indicator of the extent to which pain is sympathetically mediated.

Limitations. Guanethidine often causes severe burning pain in patients with allodynia,[243,244] perhaps due to norepinephrine released with the onset of guanethidine action. Itching, piloerection, edema, or engorgement of the tissues in the injected area also may occur. There have been no comparisons of diagnostic suitability of guanethidine *versus* bretylium IVR blockade.

The ischemic block produced by the tourniquet may have a profound and selective effect on conduction in Aβ and Aδ fibers,[47] and thereby produce analgesia independent of sympathetic interruption. There have been no comparisons of block with guanethidine or bretyllium or *versus* with saline alone. A more profound or more prolonged response to the procedure done with the active drug would then indicate a sympathetic component to the pain.

Guanethidine has been demonstrated to affect central nervous system levels of serotonin and to have anticholinergic effects.‡ Local anesthetic effects are not reported, and local anesthetic IVR blockade has produced only brief relief of pain in patients who had prolonged relief after IVR guanethidine.[243]

Studies. Intravenous regional guanethidine predict-

‡ Furst CI: The biochemistry of guanethidine. Advances in Drug Research 1967; 4:133–61.

ably eliminates allodynia but has no effects on other sensory function.[243,245] Increased peripheral temperature and blood flow follows IVR guanethidine but not IVR saline. Vasodilatation may be delayed by hours after cuff deflation, and complete blockade of vascular control is rare.[243] There is no temporal relation between pain relief and manifestations of sympathetic blockade. This may be due to a vasodilatory action of guanethidine independent of effects on norepinephrine release.[246]

Bonelli *et al.*[247] found that IVR guanethidine was more effective in patients who exhibited dystrophic changes associated with reflex sympathetic dystrophy. Loh and Nathan[16] found that IVR guanethidine and local anesthetic sympathetic chain injections had identical effects on pain in 9 of 10 painful limbs. There is a high correlation between relief of pain from intravenous phentolamine and from IVR guanethidine.[248] These cross comparisons support the notion that each is producing analgesia by a common sympatholytic mechanism.

No studies have specifically examined the diagnostic value of IVR sympathetic block in identifying patients who will have long-term therapeutic benefit from systemic or regional sympatholytic measures.

Conclusion. The response to intravenous regional guanethidine or bretyllium may help confirm a sympathetic component of a given patient's pain, particularly if the response has been compared with an IVR placebo procedure. Information obtained from the procedure should be evaluated together with clinical findings and response to other diagnostic interventions, such as paravertebral sympathetic blocks or the phentolamine test.

Differential Neuraxial Block

Rationale. The classic approach to differential neuraxial analgesia was described by McCollum and Stephen in 1964[249] and subsequently modified.[250,251] The intent is to provide diagnostic information for patients with lower extremity or lower trunk pain. Initially, a placebo is injected, followed by a local anesthetic solution capable of selectively blocking sympathetic efferents. If no relief is achieved, a concentration capable of producing sensory blockade is injected, and followed, in the absence of pain relief, by a solution that will block motor fibers as well. By observing changes in pain during the different phases of the block, the pain origin can be distinguished as psychogenic, sympathetic, nociceptive (sensory based), or central.

A subarachnoid site of injection has been used most extensively. A major drawback to the differential spinal block is the prolonged time required to perform and assess the individual steps. In a modified technique,[252] a placebo (saline) injection is followed by 100 mg procaine injected intrathecally. Pain relief after these injections and relief during gradual resolution of neural blockade are noted. An epidural technique also has been used in a fashion similar to the subarachnoid method.[253] After a placebo injection of saline, 0.25% lidocaine is injected to block sympathetic fibers, then 0.5% lidocaine to block sensation as well, and, finally, 1% lidocaine to produce surgical anesthesia.

A preliminary report suggested the use of opioid instead of local anesthetic as the analgesic agent,[253] arguing that opioid effects are more specific and don't provide a cue of numbness or warmth to trigger placebo or psychogenic responses. After placebo injections, 1 μg/kg fentanyl in 5 ml normal saline is injected through an epidural catheter. Analgesia indicates a predominantly nociceptive mechanism of pain instead of a predominantly psychologic one, as does reversal of the analgesia by intravenous injection of 0.4 mg naloxone unobserved by the subject. These methods have not been compared formally with the classic approach.

Limitations. There are a number of possible drawbacks to the traditional technique of differential spinal blockage. Early descriptions of the technique report that either pain fibers or sympathetic fibers may be blocked first,[254] and that the injected solutions may fail to provide the desired block.[250,255] The entire premise of the ability to achieve a steady state block of certain fiber types while sparing others in the desired order is flawed. Lack of obvious sensory changes does not assure that neural processing has not been altered, and a dense block adequate for surgery does not indicate an absence of afferent sensory traffic or efferent sympathetic impulses. Neurophysiologic study of awake humans and analysis of conduction in various laboratory preparations consistently point to the impossibility of complete block of one fiber type without at least partial block of others.

Further considerations erode the theoretic plausibility of diagnostic differential blockade. When nociceptive afferent fibers are active, as may occur with spontaneous discharge arising from an injured peripheral nerve or from persistent discharge of a nociceptor by a noxious stimulus, they may be subject to use-dependent block and be more affected by low concentrations of anesthetic than normal afferents that are quiescent. In addition, subblocking concentrations of local anesthetics are capable of reducing the maximum firing rates of axons.[45] Because pain induced by nociceptor activa-

tion is proportional to firing frequency, a modest reduction in the firing frequency could result in diminished pain. In both instances, although evidence of sensory block is not detected by sensory testing, pain relief from blockade of nociceptor fibers may be achieved, and pain relief may be mistakenly attributed to sympathetic blockade. Whereas the one-shot technique has the advantage of not depending on achieving a critical concentration of anesthetic in the cerebrospinal fluid, it does depend on the premise that A and C fibers recover function before B fibers, which is probably incorrect.

Even if a true differential block of sympathetic fibers were documented, there are a number of potential causes for uninterpretable responses or misinterpretation: (1) patients who fail to obtain relief from subarachnoid 0.5% or 1% procaine may actually experience an increase in activity of some spinal cord neurons because of blockade of certain afferent or spinal cord pathways. For instance, A fibers, including Aβ fibers, may be blocked by a concentration of anesthetic that spares C fibers,[42] reducing the inhibitory effect of large afferent activity on dorsal horn neurons; (2) intrathecal local anesthetic may block descending inhibitory fibers lying superficially in the dorsolateral funiculus,[22] again producing disinhibition; (3) pain returning after pinprick sensation does not necessarily imply a sympathetic mechanism. Prolonged pain relief has been described after local anesthetic blocks in conditions other than sympathetic dystrophy.[31] Such prolonged effects may relate to changes in central processing. The temporary reduction in sensory input may allow sensitized dorsal horn neurons to return to more normal function, and it may take considerable time before noxious inputs can reestablish spinal cord sensitization; (4) there is no way to assess pain in any position other than lateral recumbent, ruling out any diagnostic benefit for patients whose pain improves when lying down or is activity dependent; and (5) anatomic consideration makes a uniform progression of block from sympathetic to sensory unlikely. Specifically, complete block of roots caudal to L2 will provide sensory interruption but leave sympathetic fibers unaffected,[256] because all white rami communicantes exit the cord between T1 and L2.

Neuraxial opioid block may be ineffective in relieving pain that is nonetheless nonpsychogenic, especially neuropathic and visceral pain or incident pain with movement.[257,258] Also, systemic naloxone is not likely to completely reverse the analgesic effects of neuraxial opioids.[259]

Studies. There have been no outcome studies to support claims that differential spinal block leads to selection of more effective treatment. Specifically, there are no data that document higher success rates from repeated sympathetic blocks among patients who experienced relief after 0.25% procaine compared with patients who exhibit other responses. Sanders *et al.*[260] examined the relation between the presence of psychopathology and the incidence of inappropriate responses to differential spinal. They concluded that psychopathology was no more likely among inappropriate responders.

Conclusion. The ability of differential neuraxial blocks to diagnose various categories of pain generation is unproved. Basic considerations probably make it an unachievable goal.

Systemic Phentolamine

Rationale. Phentolamine is an α1 adrenergic blocking agent administered intravenously to determine whether a patient's pain is sympathetically mediated. It has the diagnostic advantage over local anesthetic sympathetic blocks because it does not interrupt afferent traffic from visceral or somatic structures. Sudomotor function is mediated by cholinergic transmission and, therefore, is not affected by adrenergic blockade, but sudomotor activity does not play an important role in pain generation.[261] It would seem logical that analgesia in response to intravenous phentolamine would predict a beneficial response to intermittent or continuous local anesthetic sympathetic blocks or to oral or transdermal sympatholytic drugs.

If phentolamine produces evidence of sympathetic block such as nasal congestion, hypotension, or skin warming, absence of concurrent pain relief is thought to disprove a sympathetic contribution. If a placebo produces no analgesia but phentolamine does, with appearance of an increase in skin temperature coincident with pain relief, a sympathetic role is suspected. Complications include predictable nasal stuffiness and occasional sinus tachycardia, premature ventricular contractions, dizziness, or wheezing.[262] The safety of reduced doses of phentolamine has been confirmed in children.[248] Subjects with advanced cardiovascular disease such as heart block, unstable angina, or congestive heart failure are considered unsuitable for the test. Doses of approximately 0.5 mg/kg are used, and whenever substantial relief of pain is obtained or significant hypotension occurs, the test is terminated.[248,263]

Limitations. Phentolamine has been shown to have local anesthetic properties,[264,265] which raises the question of whether relief could be by pharmacologic mechanisms other than sympathetic interruption. The degree

of sympathetic blockade by phentolamine infusion is unclear, because larger doses and more rapid administration produce greater increase in extremity blood flow and temperature, and sympathetic responses persist even after the largest doses examined.[266] As with other tests of sympathetic function, a fundamental limitation is the ambiguous role of sympathetic function in pain. The role of $\alpha 1$ receptors is uncertain.[233] Even though a patient experiences relief from intravenous phentolamine, oral sympathetic blocking drugs may be ineffective because side effects, particularly orthostatic hypotension, may preclude intense blockade comparable with the potent effect of intravenous phentolamine.

Studies. Raja *et al.*[263] administered intravenous phentolamine and, on another occasion, local anesthetic sympathetic blocks to 20 patients with suspected sympathetically maintained pain. Comparisons of the maximum pain relief from the two procedures yielded a high correlation. Patients generally experienced relief of both spontaneous and evoked pain (allodynia). Only two patients had relief from saline, an extraordinarily low incidence of placebo response. Arner[248] found that 33% of 48 patients tested with intravenous phentolamine experienced relief of pain. All of the patients who had relief with phentolamine experienced a reduction in pain with intravenous regional guanethidine, whereas only 1 of 12 patients who failed the phentolamine test had relief from guanethidine. Overall, they found a false-positive rate of 0% and a false-negative rate of 32% if guanethidine relief is assumed to indicate presence of disease (sympathetically maintained pain).

Shir *et al.*[262] found relief from phentolamine infusion in 25% of patients with pain and with clinical evidence of a sympathetic contribution. The low response rates in this and the study by Arner[248] are at or below typical placebo response rates. Several authors[67,68] caution that placebo responses may require 15–60 min to become evident. If adequate time is allowed, placebo either has the same frequency of analgesia as phentolamine administration,[68] or placebo analgesia is observed in all subjects,[67] making the phentolamine test impossible to interpret. No studies have determined whether the response to intravenous phentolamine predicts the therapeutic efficacy of local anesthetic sympathetic blocks or systemic sympathetic blocking agents.

Studies typically report administration of phentolamine to a predetermined dose rather than until a physiologic effect (nasal congestion, hypotension, skin warming) is achieved. Without such a physiologic endpoint, it is not possible to distinguish inadequate phentolamine dose from a lack of $\alpha 1$ receptor involvement in the pain generation.

Conclusion. Response to intravenous phentolamine appears to correlate well with responses to local anesthetic paravertebral sympathetic blocks and guanethidine intravenous regional sympathetic blocks. It is not clear, however, that either of these are an acceptable standard of pure and complete sympathetic interruption. Response to phentolamine should be considered in conjunction with clinical findings and other diagnostic tests. Considered alone, it may not be very sensitive or specific. The ability of the phentolamine response to predict outcome of therapy with sympatholytic treatments has not been tested. It is not clear how using a phentolamine trial would improve on simply a trial of oral sympatholytic therapy.

Summary

On the basis of the published material reviewed above, we conclude that there are many limitations that weaken the theoretic basis for neural blockade as a diagnostic or prognostic tool. In addition, these procedures in general lack thorough documentation of clinical usefulness. Reasonable employment of diagnostic neural blockade, therefore, requires not only care in technique and confirmation of effects, but also caution in interpretation and application of the results. This critical evaluation needs to be tempered, however, by two further observations. Experienced and observant clinicians have found these procedures may, on certain occasions, provide information that is helpful in guiding subsequent therapy, so we should not be in haste to dismiss the accumulated judgment of practitioners. Finally, the confusion and complexity that typifies diagnosis in chronic pain may justify the selective use of diagnostic blocks that make anatomic and physiologic sense, even if their validity is incompletely proved.

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