Papers and Originals

Control of Pain in the Rheumatic Disorders*

F. DUDLEY HART,† M.D., F.R.C.P.

Brit. med. J., 1968, 3, 635–640

Summary: Pain may be attacked in the rheumatic diseases (1) centrally, with drugs ranging in efficiency from those which are potentially addictive and under the Dangerous Drugs Act (e.g., pethidine) and are therefore rarely used, down to simple analgesics such as paracetamol; (2) peripherally, by local action, whether it be by applications of heat or cold, by injections of local anaesthetics or anti-inflammatory agents, or by surgery; (3) peripherally, by anti-inflammatory non-analgesic agents taken systemically, such as the corticosteroids; and (4) peripherally, by anti-inflammatory-analgesic-antipyretic agents taken systemically, such as aspirin.

The exact sites of action of the pyrazoles, indomethacin, the anthranilic compounds, and other anti-inflammatory-analgesic-antipyretic drugs are as yet uncertain, but along with these methods of attacking the pain-producing areas help must also be given to the distressed mind behind the joints. Faith in the future, cheerfulness, freedom from depression, and the development of a philosophy to deal with the uncertainties of the disease are essential. It has been said that you don't have to be a doctor to treat uncomplicated lobar pneumonia: anybody with a bottle of penicillin in his hands holds the cure. It is the incurable diseases that are really worth treating, and that make demands on the physician. To quote Tuker: "My last word is this. Whoever has the care of a sorely stricken arthritic must encourage him to fulfil himself intellectually and spiritually, and to achieve—no matter what, but to achieve, so that he may nightly lay himself down on his bed of pain looking forward happily to the morrow's task, mind centred upon it, no matter what it is; sticking in stamps, research into anything you like, dabbling with pastel or water colours, writing chatty letters to friends. Anything at all, but let it be for him the most pressing thing of the day, and let him believe that you think it is. Help him and let him live, live fully."

This is perhaps the best analgesic of all.

Introduction

One who makes a study of the rheumatic diseases must make also a study of pain, for the essence of and the central theme throughout these disorders is pain, and few people suffer as much continuous or intermittent day-to-day pain as the arthritic sufferer. A great deal has been written about the virtues of pain. The late Reverend Dick Sheppard is reported to have said to Laurence Housman: "I like pain: it brings me nearer to my Master." But later, after more severe and more continuous pain, he wrote: "I do not love suffering, so you must not worry about me in that way. I dislike all that talk about how lovely it is to suffer. . . ."

A most gallant sufferer and one of the bravest men I have ever known wrote a long and moving thesis on what it is like to have rheumatoid arthritis: "I have the disease all over me: not one particle of me is untouched by it. As I sit here writing this piece I have a sharp pain in my right shoulder, in my right ear, in my right neck, in my right big toe, a bit of jabbing in my left neck and left jaw, and an ache in the scalp. If I were to move, I could at will set the rest of the orchestra on the go: it is just tuning up" (Tuker, 1958).

After over 20 years of working with this group of patients I am at the same time amazed and humbled when I see how many more saints than sinners emerge from their suffering, and I marvel at the fortitude with which these patients endure their daily unpleasant ration of pain. This is a point that only rarely emerges from a clinical trial or a report on the efficiency of some new form of treatment. Only the patient knows what he experiences. It is a pity we cannot measure it in units: one dolour, perhaps, for the amount of discomfort one can take for 10 minutes without reaching out for the next dose of aspirin. It is interesting to compare these sufferers, whose pains are due to no fault of their own, with the luetic patients with grossly deformed, ghastly looking Charcot joints who suffer little or no pain, as the nerves are destroyed as part of the disease process. They walk cheerfully into their old age with no discomfort whatsoever. If there is a moral here (which I doubt), it is that most of the crippling and dysfunction is not due to structural change, but simply and solely to pain. If I could give to the world one lasting present before I die, it would be a superb non-toxic analgesic which took pain and stiffness away and allowed normal function—a sort of heavenly aspirin or celestial codeine.

No group of sufferers have so much continuous day-to-day pain over such long periods as patients with chronic rheumatic complaints. This pain has to be controlled, for unrelieved pain breeds disuse and dysfunction, contractions and crippling, and few patients are so stoical as to need no analgesics on any occasion. The luetic sufferer with a grossly deranged and deformed Charcot joint can still get about and lead an active, though restricted life, for he has no pain. Pain in an acute joint lesion may perform a useful function by making the sufferer rest the affected member, but in a more chronic lesion it is more often essentially an evil thing, restricting function, inducing muscle wasting and crippling, and carrying with it many psychological overtones.

Pain in the rheumatic diseases is a mixture of worry about the future, annoyance at being unable to lead a normal life, nausea and dyspepsia on occasion from the medicaments swallowed, rage at being told what to do by well-meaning friends, stiffness, weakness, and local and general pain, and with all this, not infrequently, a mental depression which may sometimes be severe and dominate the scene. Patients with an inflammatory arthropathy, such as rheumatoid arthritis, also frequently feel systemically ill, lose weight, and have fever and

* Based on a lecture given before the Willesden General Hospital Medical Society on 15 May 1968.

† Westminster Hospital, London S.W.1.

anorexia. For this extremely complicated, varied, and complex mixture of unpleasantness the word "pain" is most inadequate. And just as in the laboratory experimentally induced pain becomes agony as time passes without relief, so the very persistence of pain, its chronicity, multiplies and increases the discomfort and psychic overtones.

Nature of Pain

One might imagine that in this year of grace, 1968, we know far more about the basic nature of pain than did our fathers. Such hardly seems to be the case, though we are probably more conscious of our ignorance. As Graham Weddell (1966) said at the International Symposium on Pain at the Henry Ford Hospital, Detroit, in October 1964, it seems improbable that simple anatomical studies are going to be of much further help in the study of pain sensibility; they must be supplemented by histochemical and electrophysiological data before they can be subjected to interpretation. Kruger (1966), at the same conference, talking on the thalamic projection of pain, concluded that, although "pain" memories had been assumed to exist and that identifying the thalamic locus of such cells would clarify the basic problem of pain representation, an alternative view would be that pain is not a sensory modality, but a complex response related to a certain variety of sensory events. Kruger says: "The quest for 'pain' neurons at more peripheral levels has certainly been remarkably elusive. Is it possible that neurons uniquely responsive to noxious stimuli are non-existent?"

Whatever the pathways, Beecher (1966) observed that many years ago the point was made that in human suffering there are two major components, the original sensation, or primary phenomenon, and the psychological modification of it, the reaction or secondary phenomenon. The latter is a highly individual thing. The patient's mental reaction to the primary stimulus, his view of its seriousness and danger, may influence the clinical picture greatly. Clinical pain can therefore not be easily copied, and assessments of the effects of analgesics must in the final analysis be made on sufferers with disease rather than normal subjects given artificial painful stimuli; as Beecher says, this is the difference between real and contrived sensations.

A patient was admitted to the wards under my care two years ago in great distress. She had seen many specialists, and had had many investigations without a positive diagnosis being made. Over the previous 12 months her outstanding symptom was of severe intractable pain in the lower thorax which gave her no relief by day or night, and she was then receiving morphine or pethidine several times a day. There was such evident anxiety present that she was confidently reassured, and within a few days was needing only one or two doses of dihydrocodeine in the 24 hours, and was sleeping well without analgesics, merely removing her hearing-aid at night. Nevertheless, some months later a metastatic malignant lesion appeared at the site in question. The reaction to the painful stimulus was clearly the important thing here, as it so often is. Fear and uncertainty are not only magnifying, but distorting, glasses.

Severe injury in the heat of battle may be painless: in the blitz, a patient on admission to our hospital complained of no pain, though her leg was connected only by a flap of skin to the body. Beecher reported that in wounded soldiers in the last war about 25% needed medication to ease pain; 75% did not. In the civilian patients who had undergone usually less severe major surgery these figures were reversed. In the one group many distractions were present; in the other the patient was in a position where he anticipated and expected pain. I can myself personally vouch for the great relief and ease of discomfort that comes to one as the ambulance enters the hospital yard after one or two hours of uncertainty at the roadside. As a sense of security and relief flows in, anxiety and pains diminish markedly. All who have worked with placebos know how effective they can be, and how clinical trials of analgesic substances must be devoid of emotional content of any sort. Though the patient must be aware of, and agree to, take part in their trial, the exact time at which they are given should be unknown, not only to him, but to all taking part, otherwise this placebo effect, or its opposite—a nocebo response—may wreck results.

Painful Stimulus

Let us start at the trigger, the point of pain. The skin covering the whole body is sensitive to pain. According to Kellgren (1964) there are pain spots coinciding with special nerve endings which form a rich subepidermal plexus and ramify through all layers of the skin, a few penetrating as deep as the stratum granulosum, and this subepithelial plexus springs from the fine fibres of the peripheral nerves of the deeper structures. The subcutaneous deep fascia, periosteum, joint capsules, ligaments, and sheaths of nerves and blood vessels are highly sensitive, but muscle, synovia, and fat are less so, while articular cartilage and compact bone are apparently insensitive to pain, giving rise to a sensation of pressure only when artificially stimulated. From skin, muscle, and joints, the nerve impulse is carried through the peripheral nerves to the cord, leaving their cell station in the posterior root ganglia, entering the cord through the posterior roots, and ending by synapse in the substantia gelatinosa of the posterior horns (Kellgren, 1964). Pain nerves from blood vessels may follow a periarterial course at the periphery for some distance before joining the nerve trunks. Pain arising in the skin is well localized, but pain of deeper structures may be diffuse and poorly localized.

Those who have injected a tennis elbow or an acutely painful rheumatoid elbow will often be surprised that not only the pain at the affected spot is eased, but also pain up and down the arm from shoulder to wrist. Such local anaesthesia will —temporarily at least—abolish pain, but if a local tender spot is referred from a site elsewhere, although tenderness is removed, pain and restriction of movement persist. Few pains in rheumatology are based on a simple peripheral pain spot, and even a so-called "tennis elbow," due usually to a forceful backhand shot causing injury to attachments of the common tendon of origin of the forearm extensors, may be productive of secondary overtones. Nevertheless, local therapy may help in easing pain: injections of hydrocortisone or a suitable analogue or a local anaesthetic agent, local heat, or counter-irritation. The agonizing pain of a swollen, distended bursa is rapidly relieved by incision and evacuation of some of its contents; the same intense pain of tissues under tension also occurs in gout, an early whitlow, or a "hot Heberden's node" in its early acute inflammatory red state. Though this node is a manifestation of osteoarthrosis, essentially a degenerative condition, it may start as an acutely painful condition in the terminal interphalangeal joint, which the patient may attack herself with a needle in an effort to ease the tension and relieve the pain. In the average rheumatic sufferer, however, whether osteoarthritic, rheumatoid, or spondylitic, pain points are multiple and most lie deeper, and local attacks on pain peripherally constitutes only a small part of the therapeutic programme.

Pain Threshold

It is of interest that although much attention has been paid to placebo reactors in clinical assessment of drugs given to relieve pain and great efforts have been made to pick two groups of patients with similar extent and acuity of disease to receive drug and placebo, little had been done to assess the pain threshold in such patients. We have attending the unit some patients who are singularly uncomplaining, and who

have very high thresholds to artificial painful stimuli. The two most outstanding ones are both deeply religious, and have a complete faith in the Almighty and His medical servant, the physician in charge of their case. One with severe unremitting rheumatoid arthritis of seven years' duration hobbled into the clinic, having never missed a day's work at her telephone exchange. She made no complaint of pain, only difficulty in getting about. Three years later she was wheeled into the clinic, still making no complaint of pain, and was found to have fractures of necks of both femora and of one arm. She was not a hysteric and was mentally normal, though not highly intelligent, and her pain threshold was higher than that of anybody then working in the clinic, as judged by Hollander's test (Hollander, 1939).

Singularly little work has been done on this question of pain threshold in the rheumatic diseases, though for many years we have used Libman's sign in the clinic (Libman, 1934). This is a rough measure of individual pain threshold: firm pressure in the normal subject to the mastoid being painless, to the styloid process painful. Though a very crude method, it is occasionally useful in separating the normal average from the hyposensitive subject.

In 1954 Keele reported the use of a pressure algometer, applied to the forehead, which correlated closely with other methods such as the forearm ischaemic method of Lewis (1942), and the method of Hollander (1939), where pain is produced by tightening a blood-pressure cuff applied round a small nutmeg grater above the elbow. More recently Keele (1968), using the pressure algometer, was able to divide patients with coronary thromboses into high, normal, and low threshold categories: severity, extent, and duration of pain and morphine requirements were all found to be diminished with raising of the pain threshold. We have used Hollander's method in the past, and are now carrying out a study with Keele's algometer. It has for some time seemed clear to us that relapses with increase of pain in rheumatoid arthritis may be true, due to increased activity of the disease, or false, due to altered mood arising from depression or other factors of psychogenic nature. Studies of pain threshold might well prove informative here.

Morning Stiffness

Immobility in bed at night is characteristically and typically followed by increased swelling, tenderness, pain, and stiffness in the joints in the morning in active rheumatoid disease. The early morning is usually the worst time in the 24 hours for the rheumatoid sufferer. Morning stiffness and pain may also be marked in lumbar disc disease, and pain is common in cervical disc disorders, the early morning after rising being the most painful period in the 24 hours. In giant-cell arteritis morning stiffness and pain in shoulder and hip girdles may be very pronounced. In patients with ankylosing spondylitis the mornings are also usually the worst time for pain and stiffness, the tissues in both diseases "gelling" in the night.

Swelling of fingers has been shown to be more pronounced in the mornings in rheumatoid arthritis (Boardman and Hart, 1967), and many spondylitics voluntarily rise in the night once or several times to prevent the morning stiffness, which may last anything from an hour to half the day. To prevent it, corticosteroids may be given by mouth on retiring, or indomethacin by mouth or by suppository. We have found the indomethacin 100-mg. suppository to be more efficient in this respect than the 250-mg. suppositories of phenylbutazone or oxyphenbutazone. Holt and Hawkins (1965) found that indomethacin suppositories give satisfactory blood levels, and there may be less likelihood of dyspepsia with their use, though, as with phenylbutazone suppositories, it may still occur. The duration of therapeutic action of aspirin and most of its substitutes taken on retiring is too short to have much effect in the early morning, though phenylbutazone and oxyphenbutazone, because of their prolonged action, may, taken orally day by day, exert a beneficial action through the night.

Spasm

Spasm is a word often used in medicine, and even more often abused, for nothing is easier than to explain transient symptoms by postulating a temporary contraction of skeletal or arterial muscle. Much of this so-called spasm is a sudden voluntary muscular contraction to anticipate or prevent pain, or it may be a true hyperreactive stretch reflex. True muscle spasm, nevertheless, may accompany severe deep pain of more than temporary duration (Lewis and Kellgren, 1939). For instance, 6% saline injected into muscles of the trunk produces segmental pain and rigidity of the appropriate segment, possibly as a result of a spinal reflex. In the limb segmental musculature is more widely distributed, with the result that muscle spasm appears as widespread fine fasciculation, demonstrable by electromyography, though less readily clinically. It has been suggested (Simons *et al.*, 1943) that this reflex motor activity may lead to local muscle fatigue and to secondary pain arising in the muscles themselves, and this theory was often used in wards and clinics to explain pains arising around painful joints and apparently in the muscles serving these joints. The bulk of evidence, however, is in favour of the painful joint being the culprit, for if effectively relieved by local therapy pain in the surrounding muscles is also relieved at the same time, the so-called "spasm-pain" being referred from the affected joint. I have on two occasions seen localized spasm and rigidity of one rectus muscle, that is, unilateral boarding of the abdomen; in one case it was due to infection, and in the other to haemorrhage, muscle rigidity rapidly resolving on evacuation of blood or pus from the rectus sheath.

Drugs

The drugs available for the relief of pain in the rheumatic disorders fall into the following categories:

(1) Simple analgesics without demonstrable anti-inflammatory action (for example, paracetamol; codeine; dihydrocodeine; dextropropoxyphene.

(2) Analgesics with anti-inflammatory and antipyretic action (for example, acetylsalicylic acid; the pyrazoles, phenylbutazone and oxyphenbutazone; the anthranilic compounds, mefenamic and flufenamic acids; indomethacin).

(3) Analgesics potentially addictive and therefore rarely used (for example, dipipanone; pethidine; morphine). Pentazocine is unusual in being apparently not addictive.

(4) Anti-inflammatory agents without analgesic properties (for example, the corticosteroids and corticotrophin).

(5) Psychotropic agents which, by altering mood, help to ease pain: antidepressants (for example, imipramine; amitriptyline; protriptyline; monoamine oxidase inhibitors (for example, iproniazid, isocarboxazid, tranylcypromine; phenelzine, etc.); tranquillizers and sedatives (for example, chlordiazepoxide; barbiturates; meprobamate; diazepam); stimulants (for example, amphetamine; methyl and dexamphetamine, usually given with amylobarbitone).

(6) Long-term anti-inflammatory agents, the action of which is not understood (for example, gold salts; chloroquine).

(7) Agents possibly acting on lysosomes (for example, colchicine).

(8) Immunosuppressive agents (for example, chlorambucil; azathioprine, still in the experimental phase as regards treatment of the rheumatic disorders, and potentially dangerous).

(9) Agents which, by improving general health, may raise the pain threshold (for example, iron; blood transfusions; vitamins).

It is clear that with such a large part of the *British Pharmacopoeia* available and potentially helpful the prescriber's part is not a simple one. The basis of therapy lies essentially and usually in groups 1 and 2; group 4, the corticosteroids, are extremely useful, but must be used in conservative dosage (7

mg. of prednisone or less daily for continual therapy), for the bad reputation they have earned in the last 18 years has been largely due to prolonged overdosage. Preparations containing two or more drugs, very popular in the past, still continue to be popular; in a recent *MIMS* 67 out of 101 analgesics listed were of this nature. Only rarely do such mixtures have any great advantage over single substances. Most aspirin compounds still contain phenacetin, for instance, which, on present evidence, is both toxic and unnecessary. If more than one drug is necessary for the rheumatic sufferer, as it often is, in most cases they are best prescribed individually in the minimal effective dosage. Drug therapy in the rheumatic disorders should be like climbing a ladder: one starts at the bottom and goes up only as far as is absolutely necessary.

Rheumatoid Arthritis

Rheumatoid arthritis is the disorder par excellence where all secondary pain factors come into play. Many affected areas discharge repeated pain stimuli from several joints, and, in addition, systemic illness and psychological overtones add to and complicate the picture. The treatment of this difficult and prolonged disorder makes more demands on the physician than almost any other condition. Not only must appropriate analgesics be supplied, but also trust, some affection, sympathy, and understanding, all of which help to relieve the patient's "pain." Drugs on the D.D.A. list should rarely, if ever, be used, for the risks of addiction in such cases are very real; but, of the others, the popular ones are acetylsalicylic acid in some form, paracetamol, codeine or dihydrocodeine bitartrate, aspirin-phenacetin tablets (phenacetin is very rarely prescribed alone), dihydrocodeine, phenylbutazone, and oxyphenbutazone, and, more recently, dextropropoxyphene, mefenamic and flufenamic acids, and indomethacin.

The choice from these depends on effect and tolerance in the individual case, but usually aspirin in some form is used first, usually four- to six-hourly in doses of 0.6–1 g. (10–15 gr.). Boardman and I (Boardman and Hart, 1967) have shown that daily doses up to 2–3 g. have an analgesic action, but that larger doses are necessary to produce blood and tissue levels which have a measurable anti-inflammatory effect on the fingers of rheumatoid sufferers. Only if aspirin fails or produces toxic effects are other substances tried. Whatever programme of rest, exercise, and physiotherapy is used, whether gold salts, antimalarials, or surgery, the vast majority of patients will need analgesics occasionally or, usually, regularly. From interviews with five patients, each of whom had had rheumatoid arthritis for more than 30 years uninterruptedly, of all of the many therapeutic agents used over these years aspirin was placed first, usually in soluble form. This was the agent which had over the years given them most relief with least side-effects. Though salicylates usually cause slight blood loss in the stools if given repeatedly, this is not usually accompanied by dyspepsia, and only occasionally are they productive of severe anaemia.

Phenacetin is much less popular now than it was, and in our opinion should be deleted from compound analgesic tablets, as Reckitts have recently done with their soluble effervescent compound codeine tablets (Codis). We removed it at Westminster Hospital, and increased the aspirin and codeine, in 1955, and this modified tab. codein. co. remains very popular with the patients. The case against phenacetin as an agent toxic to the kidney may be incomplete, as phenacetin is never given alone but always in combination with other drugs, but in all probability it is the agent responsible for necrosis of the renal papilla and damage to the renal parenchyma. Apart from this toxic effect, sulphaemoglobinaemia and methaemoglobinaemia are also real and well-proved complications.

Exacerbation of rheumatoid arthritis may be triggered off by a number of factors: changes in or stopping treatment, infection, overexertion, or trauma. Such acute episodes may be polyarthritic or confined to one or two joints; if the latter, trauma or local infection may be responsible, and any ugly, swollen, hot joint should be aspirated lest it be due to a pyarthrosis, for rheumatoid joints are easily infected and pyaemia, particularly with the *Staphylococcus aureus*, is not uncommon. General exacerbation of the disease is best treated by bed rest, higher dosage of analgesics, and perhaps by a short course of injections of corticotrophin, preferably as an inpatient. This may bring the disease under control more rapidly than most agents, and dosage may be gradually reduced and discontinued after 10 to 20 days; though rebound may occur, the previous therapy may subsequently often be adequate to control the disease.

Corticosteroids may be used, but conservative dosage under 7 mg. of prednisone or its equivalent is unlikely to be sufficient, and high dosage will produce adrenal suppression and in time other unwanted effects if dosage cannot soon be reduced. For acute pain the addition of tinct. opii 7½–20 minims (0.5–1.3 ml.) to 10–20 g. (0.65 to 1.3 g.) of aspirin in a freshly made mixture is very useful, but aspirin in this form soon deteriorates and may quickly become a powerful gastric irritant. A similar paracetamol-cum-opio mixture containing 1.5–2 g. of paracetamol does not have this drawback. Substances under the D.D.A. are best avoided, though dipipanone or the compound dipipanone plus cyclizine hydrochloride (Diconal) may be useful taken rarely and not repeatedly. Injections of dihydrocodeine bitartrate 50–100 mg. may be useful if there is vomiting or nausea, and suppositories of indomethacin or phenylbutazone or oxyphenbutazone may be helpful under these circumstances: the former in my experience are the more effective.

Osteoarthrosis

Pain may be caused by a number of different mechanisms in osteoarthrosis. The rapidly developing "hot Heberden" node is an inflammatory process, the red, inflamed area being tense and distended. The condition subsides over a period, usually of several weeks, and is gradually replaced by the usual degenerative changes in the terminal interphalangeal joints of the fingers. Pain arising from the distal interphalangeal joints is notoriously difficult to treat, hot water or wax or cold compresses usually having little effect, and sometimes aggravating the condition. Analgesics are only partly helpful, and sedatives and hypnotics such as barbiturates, or a combination of both, may prove as useful. Osteoarthrosis in neck, hip, knee, and lumbar spine all call for different approaches—rest, immobility, exercises, passive movements, traction—according to the site and type of pain. Happily, most osteoarthrotic pains abate, even occasionally in hip and knee, though in these sites pains are usually persistent and unremitting.

Efforts to break pain cycles by neurectomy, sympathectomy, and nerve blocks have been usually unrewarding, and in many cases bone surgery offers the only hope of pain relief. Of the usual analgesics, indomethacin and the pyrazoles are often helpful, as may be any of the other analgesic agents, but relief is usually only partial. Overuse and underuse in bad positions may aggravate osteoarthritic hips; for instance, walking or standing overlong on hard pavements or sitting for prolonged periods with legs in right-angled flexion. The one hip movement which is maintained fully without major discomfort is flexion; where all other movements are completely lost, this remains because the patient performs this one hip movement repeatedly throughout the day in sitting and standing. In Indian patients' hips the range of movement is usually greater because of the more complete range of movement performed in the day.

Adequate analgesia may help maintain function by allowing greater mobility and more effective exercises. As in rheumatoid arthritis, psychotropic drugs may be helpful in certain cases.

Pain of Arteritis

The severe, sheep-cell agglutination test positive, rheumatoid sufferer with advanced disease may start to complain of aches and pains of a new order in areas away from joints, in abdomen and thorax as well as in the extremities, unrelated in time and severity to his many articular pains. Such pains may be thought occasionally to be due to ischaemic heart disease, appendicitis, pelvic infection, or a variety of other causes. Their origin is in the arteritic changes that are a part of advanced rheumatoid disease; they are difficult to treat, and carry a bad prognosis. Other polyarteritic manifestations, such as gangrene of the extremities, are obvious from the start, but low-grade or acute thoracic or abdominal pains are less easy to diagnose. Neuropathic features carry their own particular blend of discomfort—a cocktail of numbness, discomfort, and odd sensations that are different from, and are added to, the background of articular pains.

The arteritis seen in older patients of giant-cell type gives a characteristic severe temporal headache in classical cases of temporal arteritis, but the marked stiffness, worse in the mornings, and pains in shoulder and pelvic girdle areas are often misdiagnosed in those cases where temporal vessels are spared. The markedly raised sedimentation rate, often over 70 mm. in one hour (Westergren), is a pointer to the correct diagnosis. Arteritic lesions in polyarteritis nodosa and disseminated lupus erythematosus may cause lesions in any system, and in their early stages respond, as do most inflammatory arteritic lesions, better to an effective anti-inflammatory drug such as the corticosteroids than to anything else. It is not without interest that anti-inflammatory drugs help greatly in most of the rheumatic disorders, and most of the drugs which have analgesic properties have also an antiphlogistic action. The oldest of them, aspirin, has been shown to act peripherally, and not centrally as we were taught as medical students (Lim, 1966).

Ankylosing Spondylitis

In this condition, as noted above, the morning stiffness which makes life miserable for so many rheumatoid sufferers is present, usually in marked degree. It is immobility in ankylosing spondylitis that produces aggravation of stiffness and pain, and the basis of therapy is therefore a programme of active exercises and relief of pain by drugs, so that a more active life can be led with greater freedom of spinal and hip movements. Aspirin is sufficient in mild cases, but, for many, indomethacin, oxyphenbutazone, or phenylbutazone is necessary, indomethacin also proving useful taken in suppository form at night to relieve morning stiffness. Orthodox therapy before the war lay in immobilizing the patients in plaster casts and jackets to achieve a good spinal position, overlooking the fact that function is more important than posture. Such therapy, by increasing stiffness in hip and spine, often produced crippling, and the lucky spondylitics in those days were those who were not correctly diagnosed, and were therefore not "correctly" treated.

A dangerous misdiagnosis was that of tuberculosis of bone and joint, for the two conditions may resemble each other quite closely in spine, hip, and other joints, the lytic lesion in spondylitis being mistaken for a tuberculous erosion. Immobility, useful in the one, is disaster in the other (Hart, 1968). Immobility of chest wall similarly leads to reduced respiratory function (Hart, Emerson, and Gregg, 1963), and an active, energetic, preferably outdoor life is better for these sufferers than one spent bent over desk or drawing-board, not only as regards spinal but also respiratory function: regular playing of the bagpipes helped one of my patients. Breathing exercises, though admirable, are less effective than the overbreathing of an energetic job. Effective pain relief, by increasing function, is therefore sound therapy, and phenylbutazone and oxyphenbutazone by their even, prolonged action over the 24 hours are very useful drugs. Indomethacin is also useful and has less danger of causing a blood dyscrasia. Any of the other analgesics may also be effective in different cases. Local deep *x*-ray therapy to the spine, the treatment of choice just after the war, has gone out of fashion because of the dangers of induction of leukaemia, but it does frequently relieve symptoms effectively (Hart, 1961), though only occasionally for periods of more than a year.

Gout

The agony of acute gout is usually a stage beyond that of the pain experienced in the other arthropathies. It matches the pain of a fracture recently enclosed in a too tight plaster. It is caused by acute inflammation in tissues which cannot readily expand, and is one of the most severe pains which can be experienced. A patient of mine who had an attack of gout following an acute coronary occlusion told me that it was the more severe of the two. This is usually "straight" or primary pain. The sufferer knows what it is, knows he is not going to die of it, and has no particular fears of complications, but it is a severe, agonizing pain just the same. Rapidity of pain relief is therefore important, and in our unit we place indomethacin first in efficiency (Boardman and Hart, 1965), phenylbutazone or oxyphenbutazone second, and colchicine third. Phenylbutazone may be given effectively by intramuscular injection (250 mg.), and colchicine may be given intravenously with great effect, though it is not without danger, and should not be repeated within eight hours. Death has occurred under such circumstances. Corticosteroids or corticotrophin are usually no more effective, but may be necessary in resistant cases. It is amazing how often sulphinpyrazone, probenecid, or allopurinol is mistakenly used in general practice for the control of an acute attack; these drugs have, of course, no effect on the acute, painful process, and are likely to precipitate further acute episodes when started de novo.

Bursitis

The pain of acute bursitis is often misdiagnosed, for it is often referred away from the primary site, or it may arise from bursae the existence of which the clinician has forgotten. Bywaters (1965) has referred to the large number of bursae—around 156—in the body. These can all become inflamed either locally or as part of a generalized rheumatoid arthritis, where they add considerably to the signs and symptoms of this disorder. There are, for instance, small bursae between the metatarsal heads, beneath the insertions of the psoas, and, according to Monro (1788, 1799), 18 in the hand, 6 around the elbow, 8 around the knee, and 14 around the hip—a total, as stated above, of 78 on each side of the body. They may become distended with viscous paste-like material, and sometimes with pus, and incision and evacuation may give immediate relief. When they are part of a rheumatoid process, aspiration (if possible) and installation of a locally acting corticosteroid may help, as in knee (semimembranosis) and shoulder (subacromial). Rheumatoid disease affects also tendons and synovial sheaths, and these form very characteristic and diagnostic swellings, one of the commonest being the involvement of the extensor sheaths on the backs of the hands. These are, however, rarely painful. It is the lesser-known and deeper bursae which may cause diagnostic difficulty. Injection of a local anaesthetic into the painful area may give relief if accurately sited.

Compression (Entrapment) Neuropathy

Until a few years ago the typical painful paraesthesiae of median nerve carpal-tunnel compression was attributed to a number of causes. Now, even if part of some other disease process such as amyloidosis with multiple myelomatosis, or

rheumatoid arthritis, surgical division of the transverse carpal ligament usually gives rapid and complete relief. Other compression neuropathies may occur, as of the ulnar nerve by the arcuate ligament below the elbow (Osborne, 1957), in the feet, and elsewhere. The subject is discussed in some detail by Thompson and Kopell (1959) and by Kopell, Thompson, and Postel (1962). Treatment lies in the localization of the compression and surgical release of the compressed nerve.

REFERENCES

Beecher, H. K. (1966). In *Pain*, edited by R. S. Knighton and P. R. Dumke, p. 221. London.
Boardman, P. L., and Hart, F. D. (1965). *Practitioner*, **194**, 560.
Boardman, P. L., and Hart, F. D. (1967). *Brit. med. J.*, **4**, 264.
Bywaters, E. G. L. (1965). *Ann. rheum. Dis.*, **24**, 215.
Hart, F. D. (1961). *Clin. Radiol.*, **12**, 130.
Hart, F. D. (1968). *Lancet*, **1**, 740.
Hart, F. D., Emerson, P. A., and Gregg, I. (1963). *Ann. rheum. Dis.*, **22**, 11.
Hollander, E. (1939). *J. Lab. clin. Med.*, **24**, 537.
Holt, L. P. J., and Hawkins, C. F. (1965). *Brit. med. J.*, **1**, 1354.
Keele, K. D. (1954). *Lancet*, **1**, 636.
Keele, K. D. (1968). *Brit. med. J.*, **1**, 670.
Kellgren, J. H. (1964). In *Textbook of the Rheumatic Diseases*, 3rd ed., p. 14, edited by W. S. C. Copeman. Edinburgh and London.
Kopell, H. P., Thompson, W. A. L., and Postel, A. H. (1962). *New Engl. J. Med.*, **266**, 16.
Kruger, L. (1966). In *Pain*, edited by R. S. Knighton and P. R. Dumke, p. 67. London.
Lewis, T. (1942). *Pain*, p. 97. New York.
Lewis, T., and Kellgren, J. H. (1939). *Clin. Sci.*, **4**, 47.
Libman, E. (1934). *J. Amer. med. Ass.*, **102**, 335.
Lim, R. K. S. (1966). In *Pain*, edited by R. S. Knighton and P. R. Dumke, p. 117. London.
Monro, A., secundus (1788). *A Description of all the Bursae Mucosae of the Human Body*. Edinburgh.
Monro, A., secundus (1799). *Abbildungen und Beschreibungen der Schleimsäcke des Menschlichen Körpers*, edited by J. C. Rosenmüller. Leipzig.
Osborne, G. V. (1957). *J. Bone Jt Surg.*, **39B**, 782.
Simons, D. J., May, E., Goodell, H., and Wolff, H. G. (1943). *Ass. Res. nerv. Dis. Proc.*, **23**, 228.
Thompson, W. A. L., and Kopell, H. P. (1959). *New Engl. J. Med.*, **260**, 1261
Tuker, Sir Francis (1958). Personal communication.
Weddell, G. (1966). In *Pain*, edited by R. S. Knighton and P. R. Dumke, p 3. London.

Use of Capillary Blood in Measurement of Arterial Po_2

J. MACINTYRE,* M.B., CH.B. ; J. N. NORMAN,† M.D., PH.D., F.R.C.S. ; GEORGE SMITH,‡ M.D., CH.M., D.SC., F.R.C.S.

Brit. med. J., 1968, **3**, 640–643

Summary: In this study we investigated the possibility of obtaining accurate values of arterial Po_2 from specimens of capillary blood stored in glass capillary tubes and measured in an oxygen microelectrode. It has been shown that Po_2 measurements made on the Radiometer oxygen microelectrode are as accurate as those made on the macroelectrode and that the storage of blood is as satisfactory in glass capillary tubes as in glass syringes. The important feature in obtaining accurate values for arterial Po_2 is the choice of the capillary bed and its method of preparation for sampling. If the ear lobe is massaged with thurfyl nicotinate (Trafuril) it is possible to obtain values of Po_2 from the capillary blood which are in close agreement with arterial Po_2 in normal, hyperoxic, and shocked vasoconstricted patients.

Introduction

There is an increased awareness of the need to monitor the blood oxygen tension when efficient systems of oxygen administration are used in the management of severely ill patients suffering from a variety of anoxic conditions. It is of considerable importance to maintain adequate tissue oxygenation in states of stagnant anoxia until the underlying pathology is corrected, and where hyperbaric oxygen techniques are used frequent arterial Po_2 measurement is needed if oxygen poisoning is to be avoided (Norman and Smith, 1967). Capillary blood specimens can now be used for a variety of biochemical measurements, and with the recent advent of the oxygen microelectrode it should be possible to use specimens of capillary blood as an index of arterial oxygen tension. This would facilitate the management of patients receiving oxygen at normal and increased atmospheric pressures and may prove invaluable in paediatric practice, where repeated arterial samples are less easily obtained. Initial attempts to correlate capillary blood Po_2 and arterial Po_2 proved unsatisfactory, however, and this study was devised to assess the errors inherent in making such measurements.

Various electrode systems have been used to measure blood oxygen tension (Staub, 1961 ; Elridge and Fretwell, 1965 ; Johnstone, 1966 ; Moran, Kettel, and Cugell, 1966 ; Rhodes and Moser, 1966). Considerable errors can, however, be made if care is not taken in calibration of the electrode (Moran *et al.*, 1966 ; Rhodes and Moser, 1966 ; Adams and Morgan-Hughes, 1967), in the sampling of blood (Nunn, 1962 ; Johnstone, 1966), and if allowance is not made for time lapse between sampling and measurement (Nunn, 1962 ; Elridge and Fretwell, 1965 ; Lenfant and Aucutt, 1965 ; Johnstone, 1966). In practice the latter may be the most important source of error if the measurements are made in a laboratory situated at some distance from the patient.

It seemed desirable to evaluate (1) the accuracy of the oxygen microelectrode in the measurement of Po_2 of blood contained within glass capillary tubes as compared with that of the macroelectrode in the measurement of blood contained within glass syringes ; (2) the rate of decline of Po_2 of blood stored in glass capillary tubes, glass syringes, and plastic syringes, and to observe the effect of time, temperature, and initial oxygen tension on these three storage methods ; and (3) the importance of the capillary sampling site and the mode of preparation of the capillary bed previous to sampling in different states of peripheral perfusion.

Methods

The oxygen electrodes used were the Radiometer microelectrode (Radiometer Ref. E5046) and the Radiometer macroelectrode (Radiometer Ref. E5021). The electrodes were calibrated with nitrogen, air, and oxygen which had been warmed and humidified by passage through sintered glass humidifiers immersed in a thermostated water-bath maintained thermostatically at 37° C. The use of gases allowed the calibration

* Research Fellow in Surgery, University of Aberdeen.
† Lecturer in Surgical Science, University of Aberdeen.
‡ Regius Professor of Surgery, University of Aberdeen.