# 4.7 Pharmacotherapeutics I & II

## SURGICAL PROPHYLAXIS

**Definition:**

Antibiotics administered before contamination of previously sterile tissues or fluids are considered prophylactic. The goal for prophylactic antibiotics is to prevent a surgical-site infection (SSI) from developing.

- Presumptive antibiotic therapy is administered when an infection is suspected but not yet proven. Therapeutic antibiotics are required for established infection.
- SSIs are classified as either incisional (such as cellulitis of the incision site) or involving an organ or space (such as with meningitis). Incisional SSIs may be superficial (skin or subcutaneous tissue) or deep (fascial and muscle layers). Both types, by definition, occur by postoperative day 30. This period extends to 1 year in the case of deep infection associated with prosthesis implantation.

**RISK FACTORS FOR SURGICAL WOUND INFECTION:**

- The traditional classification system developed by the National Research Council (NRC) stratifying surgical procedures by infection risk is reproduced in Table 48-1. The NRC wound classification for a specific procedure is determined intraoperatively and is the primary determinant of whether antibiotic prophylaxis is warranted.

- The Study on the Efficacy of Nosocomial Infection Control (SENIC) analyzed more than 100,000 surgery cases and identified abdominal operations, operations lasting more than 2 hours, contaminated or dirty procedures, and more than three underlying medical diagnoses as factors associated with an increased incidence of SSI. When the NRC classification described in Table 40-1 was stratified by the number of SENIC risk factors present, the infection rates varied by as much as a factor of 15 within the same operative category.
- The SENIC risk assessment technique has been modified to include the American Society of Anesthesiologists preoperative assessment score (Table

48-2). An American Society of Anesthesiologists score of 3 or above was associated with increased SSI risk.

**Microbiology:**

Bacteria involved in SSI are either acquired from the patient's normal flora (endogenous) or from contamination during the surgical procedure (exogenous).

• Loss of protective flora via antibiotics can upset the balance and allow pathogenic bacteria to proliferate and increase infectious risk.

• Normal flora can become pathogenic when translocated to a normally sterile tissue site or fluid during surgical procedures.

According to the National Nosocomial Infections Surveillance System, the five most common pathogens encountered in surgical wounds are Staphylococcus aureus, coagulase-negative staphylococci, Enterococci, Escherichia coli, and Pseudomonas aeruginosa.

• Impaired host defenses, vascular occlusive states, traumatized tissues, or presence of a foreign body greatly decrease the number of bacteria required to cause an SSI.

**Antibiotic issues:**

SCHEDULING ANTIBIOTIC ADMINISTRATION

• The following principles must be considered when providing antimicrobial surgical prophylaxis:

✓ Antimicrobials should be delivered to the surgical site prior to the initial incision. They should be administered with anesthesia, just prior to initial incision. Antibiotics should not be prescribed to be given "on-call to the OR."

✓ Bactericidal antibiotic tissue concentrations should be maintained throughout the surgical procedure

**ANTIMICROBIAL SELECTION:**

• The choice of the prophylactic antimicrobial depends on the type of surgical

procedure, most likely pathogenic organisms, safety and efficacy of the antimicrobial, current literature evidence supporting its use, and cost.
• Typically, gram-positive coverage is included in the choice of surgical prophylaxis, because organisms such as S. aureus and S. epidermidis are common skin flora.
• Parenteral antibiotic administration is favored because of its reliability in achieving suitable tissue concentrations.
• First-generation cephalosporins (particularly cefazolin) are the preferred choice, particularly for clean surgical procedures. Antianaerobic cephalosporins (such as cefoxitin or cefotetan) are appropriate choices when broad-spectrum anaerobic and gram-negative coverage is desired.
• Vancomycin may be considered for prophylactic therapy in surgical procedures involving implantation of a prosthetic device in which the rate of methicillin-resistant S. aureus (MRSA) is high. If the risk of MRSA is low and a β-lactam hypersensitivity exists, clindamycin can be used instead of cefazolin in order to limit vancomycin use.

**RECOMMENDATIONS FOR SPECIFIC TYPES OF SURGERIES:**

GASTRODUODENAL SURGERY:

• The risk of infection rises with conditions that increase gastric pH and subsequent bacterial overgrowth, such as obstruction, hemorrhage, malignancy, or acid-suppression therapy (clean-contaminated).
• A single dose of IV cefazolin will provide adequate prophylaxis for most cases. Oral ciprofloxacin may be used for patients with β-lactam hypersensitivity.
• Postoperative therapeutic antibiotics may be indicated if perforation is detected during surgery, depending on whether an established infection is present.

BILIARY TRACT SURGERY:

• Antibiotic prophylaxis has been proven beneficial for surgery involving the biliary tract.

• Most frequently encountered organisms include E. coli, Klebsiella, and Enterococci. Single-dose prophylaxis with cefazolin is currently recommended. Ciprofloxacin and levofloxacin are alternatives for patients with β-lactam hypersensitivity.
• For low-risk patients undergoing elective laparoscopic cholecystectomy, antibiotic prophylaxis is of no benefit and is not recommended.
• Some surgeons use presumptive antibiotics for cases of acute cholecystitis or cholangitis and defer surgery until the patient is afebrile, in an attempt to decrease infection rates further, but this practice is controversial.
• Detection of an active infection during surgery (gangrenous gallbladder, suppurative cholangitis) is an indication for therapeutic postoperative antibiotics.

COLORECTAL SURGERY:

• Anaerobes and gram-negative aerobes predominate in SSIs (see Table 48-4), although gram-positive aerobes are also important. Therefore, the risk of an SSI in the absence of an adequate prophylactic regimen is substantial.
• Reducing bacteria load with a thorough bowel preparation regimen (4 L of polyethylene glycol solution administered orally the day before surgery) is controversial, even though it is used by most surgeons.
• The combination of 1 g of neomycin and 1 g of erythromycin base given orally 19, 18, and 9 hours preoperatively is the most commonly used oral regimen in the United States.
• Whether perioperative parenteral antibiotics, in addition to the standard preoperative oral antibiotic regimen, will lower SSI rates further iscontroversial. Patients who cannot take oral medications should receive parenteral antibiotics.
• Postoperative antibiotics are unnecessary in the absence of any untoward events or findings during surgery.

APPENDECTOMY:

• A cephalosporin with antianaerobic activity such as cefoxitin or cefotetan is currently recommended as a first-line agent. Cefotetan may be superior for longer operations because of its longer duration of action.

• Single-dose therapy with cefotetan is adequate. Intraoperative dosing of cefoxitin may be required if the procedure extends beyond 3 hours.
• Established intraabdominal infections require appropriate therapeutic postoperative antibiotics.

UROLOGIC PROCEDURES:

• As long as the urine is sterile preoperatively, the risk of SSI after urologic procedures is low, and the benefit of prophylactic antibiotics in this setting is controversial. E. coli is the most frequently encountered organism.
• Antibiotic prophylaxis is warranted in high-risk patients (e.g., prolonged indwelling catheterization, positive urine cultures, and neutropenia) undergoing transurethral, perineal, or suprapubic resection of the prostate, resection of bladder tumors, or cystoscopy.
• Specific recommendations are listed in Table 48-4.
• Urologic procedures requiring an abdominal approach such as a nephrectomy or cystectomy require prophylaxis appropriate for a clean-contaminated abdominal procedure.

CESAREAN SECTION:

• Antibiotics are efficacious to prevent SSIs for women undergoing cesarean section regardless of underlying risk factors.
• Cefazolin, 2 g IV, remains the drug of choice. Providing a broader spectrum by using cefoxitin against anaerobes or piperacillin for better coverage against Pseudomonas or enterococci, for example, does not lower postoperative infection rates any further in comparative studies.
• Antibiotics should be administered just after the umbilical cord is clamped, avoiding exposure of the infant to the drug

.
HYSTERECTOMY:

• Vaginal hysterectomies are associated with a high rate of postoperative infection when performed without the benefit of prophylactic antibiotics.
• A single preoperative dose of cefazolin or cefoxitin is recommended for vaginal hysterectomy. For patients with β-lactam hypersensitivity, a single

preoperative dose of metronidazole or doxycycline is effective.
• Abdominal hysterectomy SSI rates are correspondingly lower than vaginal hysterectomy rates. However, prophylactic antibiotics are still recommended regardless of underlying risk factors.
• Both cefazolin and antianaerobic cephalosporins (e.g., cefoxitin, cefotetan) have been studied extensively for abdominal hysterectomy. Single-dose cefotetan is superior to single-dose cefazolin. The antibiotic course should not exceed 24 hours in duration.

HEAD AND NECK SURGERY:

• Use of prophylactic antibiotics during head and neck surgery depends on the procedure type. Clean procedures, such as parotidectomy or a simple tooth extraction, are associated with low rates of SSI. Head and neck procedures involving an incision through a mucosal layer carry a high risk of SSI.
• Specific recommendations for prophylaxis are listed in Table 48-4.
• While typical doses of cefazolin are ineffective for anaerobic infections, the recommended 2-g dose produces concentrations high enough to be inhibitory to these organisms. A 24-hour duration has been used in most studies, but single-dose therapy may also be effective.
• For most head and neck cancer resections, 24 hours of clindamycin is appropriate.

CARDIAC SURGERY:

• Although most cardiac surgeries are technically clean procedures, prophylactic antibiotics have been shown to lower rates of SSI.
• The usual pathogens are skin flora (see Table 48-4) and, rarely, gram-negative enteric organisms.
• Risk factors for developing an SSI after cardiac surgery include obesity, renal insufficiency, connective tissue disease, reexploration for bleeding, and poorly timed administration of antibiotics.
• Cefazolin has been extensively studied and is currently considered the drug of choice. Patients weighing 80 kg should receive 2 g cefazolin rather than 1 g. Doses should be administered no earlier than 60 minutes before the first incision and no later than the beginning of induction of anesthesia.
• Extending antibiotic administration beyond 48 hours does not lower SSI rates.

• Vancomycin use may be justified in hospitals with a high incidence of SSI with MRSA or when sternal wounds are to be explored for possible mediastinitis.

NONCARDIAC VASCULAR SURGERY:

• Prophylactic antibiotics are beneficial, especially in procedures involving the abdominal aorta and the lower extremities.
• Twenty-four hours of prophylaxis with IV cefazolin is adequate. For patients with β-lactam allergy, 24 hours of oral ciprofloxacin is effective
.

ORTHOPEDIC SURGERY:

• Prophylactic antibiotics are beneficial in cases involving implantation of prosthetic material (pins, plates, artificial joints).
• The most likely pathogens mirror those of other clean procedures and include staphylococci and, infrequently, gram-negative aerobes. Cefazolin is the best-studied antibiotic and is thus the drug of choice. For hip fracture repairs and joint replacements, it should be administered for 24 hours. Vancomycin is not recommended unless a patient has a history of β-lactam hypersensitivity or the propensity for MRSA infection at the institution necessitates its use.

NEUROSURGERY

• The use of prophylactic antibiotics in neurosurgery is controversial.
• Single doses of cefazolin or, where required, vancomycin appear to lower SSI risk after craniotomy.

MINIMALLY INVASIVE AND LAPAROSCOPIC SURGERY

• The role of prophylactic antimicrobials depends on the type of procedure performed and preexisting risk factors for infection. There are insufficient clinical trials to provide general recommendations.

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# PHARMACOTHERAPEUTICS I&II

## OSTEOARTHRITIS

## Introduction:

Osteoarthritis (OA) is a type of joint disease that results from breakdown of joint cartilage and underlying bone. The most common symptoms are joint pain and stiffness. Usually the symptoms progress slowly over years. Initially they may only occur after exercise, but can become constant over time. Other symptoms may include joint swelling, decreased range of motion, and, when the back is affected, weakness or numbness of the arms and legs. The most commonly involved joints are the two near the ends of the fingers and the joint at the base of the thumbs; the knee and hip joints; and the joints of the neck and lower back. Joints on one side of the body are often more affected than those on the other. The symptoms can interfere with work and normal daily activities. Unlike some other types of arthritis, only the joints, not internal organs, are affected.

Causes include previous joint injury, abnormal joint or limb development, and inherited factors. Risk is greater in those who are overweight, have legs of different lengths, or have jobs that result in high levels of joint stress. Osteoarthritis is believed to be caused by mechanical stress on the joint and low grade inflammatory processes]. It develops as cartilage is lost and the underlying bone becomes affected. As pain may make it difficult to exercise, muscle loss may occur. ] Diagnosis is typically based on signs and symptoms, with medical imaging and other tests used to support or rule out other problems. In contrast to rheumatoid arthritis, in osteoarthritis the joints do not become hot or red.

Treatment includes exercise, decreasing joint stress such as by rest or use of a cane, support groups, and pain medications.] Weight loss may help in those who are overweight. Pain medications may include paracetamol (acetaminophen) as well as NSAIDs such as naproxen or ibuprofen. Long-term opioid use is not recommended due to lack of information on benefits as well as risks of addiction and other side effects. Joint replacement surgery may be an option if there is ongoing disability despite other treatments. An artificial joint typically lasts 10 to 15 years.

Osteoarthritis is the most common form of arthritis, affecting about 237 million people, or 3.3% of the world's population. In the United States, 30 to 53 million people are affected, and in Australia, about 1.9 million people are affected. It becomes more common as people become older. Among those over 60 years old, about 10% of males and 18% of females are affected. Osteoarthritis is the cause of about 2% of years lived with disability.

**Signs and symptoms:**

The main symptom is pain, causing loss of ability and often stiffness. The pain is typically made worse by prolonged activity and relieved by rest. Stiffness is most common in the morning, and typically lasts less than thirty minutes after beginning daily activities, but may return after periods of inactivity. Osteoarthritis can cause a crackling noise (called "crepitus") when the affected joint is moved, especially shoulder and knee joint. A person may also complain of joint locking and joint instability. These symptoms would affect their

daily activities due to pain and stiffness. Some people report increased pain associated with cold temperature, high humidity, or a drop in barometric pressure, but studies have had mixed results.

Osteoarthritis commonly affects the hands, feet, spine, and the large weight-bearing joints, such as the hips and knees, although in theory, any joint in the body can be affected. As osteoarthritis progresses, movement patterns (such as gait), are typically affected. Osteoarthritis is the most common cause of a joint effusion of the knee.

In smaller joints, such as at the fingers, hard bony enlargements, called Heberden's nodes (on the distal interphalangeal joints) or Bouchard's nodes (on the proximal interphalangeal joints), may form, and though they are not necessarily painful, they do limit the movement of the fingers significantly. Osteoarthritis of the toes may be a factor causing formation of bunions, rendering them red or swollen.

**Causes:**

Damage from mechanical stress with insufficient self repair by joints is believed to be the primary cause of osteoarthritis. Sources of this stress may include misalignments of bones caused by congenital or pathogenic causes; mechanical injury; excess body weight; loss of strength in the muscles supporting a joint; and impairment of peripheral nerves, leading to sudden or uncoordinated movements. However exercise, including running in the absence of injury, has not been found to increase the risk of knee osteoarthritis. Nor has cracking one's knuckles been found to play a role.
Primary:

The development of osteoarthritis is correlated with a history of previous joint injury and with obesity, especially with respect to knees.Changes in sex hormone levels may play a role in the development of osteoarthritis, as it is more prevalent among post-menopausal women than among men of the same age.] Conflicting evidence exists for the differences in hip and knee osteoarthritis in African American and Caucasians.

Occupational:

Occupational disease and Occupational injury
Increased risk of developing knee and hip osteoarthritis was found among those who work with manual handling (e.g. lifting), have physically demanding work, walk at work, and have climbing tasks at work (e.g. climb stairs or ladders). NWith hip osteoarthritis in particular, increased risk of development over time was found among those who work in bent or twisted positions. For knee osteoarthritis in particular, increased risk was found among those who work in a kneeling or squatting position, experience heavy lifting in combination with a kneeling or squatting posture, and work standing up.Women and men have similar occupational risks for the development of osteoarthritis.

Secondary:

This type of osteoarthritis is caused by other factors but the resulting pathology is the same as for primary osteoarthritis:

- Alkaptonuria
- Congenital disorders of joints

- Diabetes doubles the risk of having a joint replacement due to osteoarthritis and people with diabetes have joint replacements at a younger age than those without diabetes.
- Ehlers-Danlos syndrome
- Hemochromatosis and Wilson's disease
- Inflammatory diseases (such as Perthes' disease), (Lyme disease), and all chronic forms of arthritis (e.g., costochondritis, gout, and rheumatoid arthritis). In gout, uric acid crystals cause the cartilage to degenerate at a faster pace.
- Injury to joints or ligaments (such as the ACL), as a result of an accident or orthopedic operations.
- Ligamentous deterioration or instability may be a factor.
- Marfan syndrome
- Obesity
- Joint infection

**Pathophysiology:**

While osteoarthritis is a degenerative joint disease that may cause gross cartilage loss and morphological damage to other joint tissues, more subtle biochemical changes occur in the earliest stages of osteoarthritis progression. The water content of healthy cartilage is finely balanced by compressive force driving water out and hydrostatic and osmotic pressure drawing water in. Collagen fibres exert the compressive force, whereas the Gibbs–Donnan effect and cartilage proteoglycans create osmotic pressure which tends to draw water in.

However, during onset of osteoarthritis, the collagen matrix becomes more disorganized and there is a decrease in proteoglycan content within cartilage. The breakdown of collagen fibers results in a net

increase in water content. This increase occurs because whilst there is an overall loss of proteoglycans (and thus a decreased osmotic pull), it is outweighed by a loss of collagen. Without the protective effects of the proteoglycans, the collagen fibers of the cartilage can become susceptible to degradation and thus exacerbate the degeneration. Inflammation of the synovium (joint cavity lining) and the surrounding joint capsule can also occur, though often mild (compared to the synovial inflammation that occurs in rheumatoid arthritis). This can happen as breakdown products from the cartilage are released into the synovial space, and the cells lining the joint attempt to remove them.[citation needed]

Other structures within the joint can also be affected.] The ligaments within the joint become thickened and fibrotic and the menisci can become damaged and wear away. Menisci can be completely absent by the time a person undergoes a joint replacement. New bone outgrowths, called "spurs" or osteophytes, can form on the margins of the joints, possibly in an attempt to improve the congruence of the articular cartilage surfaces in the absence of the menisci. The subchondral bone volume increases and becomes less mineralized (hypomineralization). All these changes can cause problems functioning. The pain in an osteoarthritic joint has been related to thickened synovium and to subchondral bone lesions.

**Diagnosis:**

Synovial fluid examinations.

Diagnosis is made with reasonable certainty based on history and clinical examination.] X-rays may confirm the diagnosis. The typical changes seen on X-ray include: joint space narrowing, subchondral sclerosis (increased bone formation around the joint), subchondral cyst formation, and osteophytes. Plain films may not correlate with the

findings on physical examination or with the degree of pain.] Usually other imaging techniques are not necessary to clinically diagnose osteoarthritis.

In 1990, the American College of Rheumatology, using data from a multi-center study, developed a set of criteria for the diagnosis of hand osteoarthritis based on hard tissue enlargement and swelling of certain joints. These criteria were found to be 92% sensitive and 98% specific for hand osteoarthritis versus other entities such as rheumatoid arthritis and spondyloarthropathies.

**Classifications:**

A number of classification systems are used for gradation of osteoarthritis:

- WOMAC scale, taking into account pain, stiffness and functional limitation.
- Kellgren-Lawrence grading scale for osteoarthritis of the knee. It uses only projectional radiography features.
- Tönnis classification for osteoarthritis of the hip joint, also using only projectional radiography features.
- Knee injury and Osteoarthritis Outcome Score (KOOS) and Hip disability and Osteoarthritis Outcome Score (HOOS) surveys.
- Osteoarthritis can be classified into either primary or secondary depending on whether or not there is an identifiable underlying cause.

X-ray of erosive osteoarthritis of the fingers, also zooming in on two joints with the typical "gull-wing" appearance.

Both primary generalized nodal osteoarthritis and erosive osteoarthritis (EOA, also called inflammatory osteoarthritis) are subsets of primary osteoarthritis. EOA is a much less common, and more aggressive inflammatory form of osteoarthritis which often affects the distal interphalangeal joints of the hand and has characteristic articular erosive changes on x-ray.

Osteoarthritis can be classified by the joint affected:

- Hand:
  Trapeziometacarpal osteoarthritis
- Wrist (wrist osteoarthritis)
- Vertebral column (spondylosis)
  Facet joint arthrosis
- Hip osteoarthritis
- Knee osteoarthritis

**Management:**

Lifestyle modification (such as weight loss and exercise) and pain medications are the mainstays of treatment. Acetaminophen (also known as paracetamol) is recommended first line with NSAIDs being used as add on therapy only if pain relief is not sufficient.] Medications that alter the course of the disease have not been found as of 2018. Recommendations include modification of risk factors through targeted interventions including 1) obesity and overweight, 2) physical activity, 3) dietary exposures, 4) comorbidity, 5) biomechanical factors, 6) occupational factors.

Lifestyle changes:

For overweight people, weight loss may be an important factor. Patient education has been shown to be helpful in the self-management of arthritis. It decreases pain, improves function, reduces stiffness and fatigue, and reduces medical usage. Patient education can provide on average 20% more pain relief when compared to NSAIDs alone.

Physical measures:

Moderate exercise may be beneficial with respect to pain and function in those with osteoarthritis of the knee and hip. These exercises should occur at least three times per week. While some evidence supports certain physical therapies, evidence for a combined program is limited. Providing clear advice, making exercises enjoyable, and reassuring people about the importance of doing exercises may lead to greater benefit and more participation. Limited evidence suggests that supervised exercise therapy may improve exercise adherence. There is not enough evidence to determine the effectiveness of massage therapy. The evidence for manual therapy is inconclusive. Functional, gait, and balance training have been recommended to address impairments of position sense, balance, and strength in individuals with lower extremity arthritis as these can contribute to a higher rate of falls in older individuals.For people with hand osteoarthritis, exercises may provide small benefits for improving hand function, reducing pain, and relieving finger joint stiffness.

Lateral wedge insoles and neutral insoles do not appear to be useful in osteoarthritis of the knee. Knee braces may help but their usefulness has also been disputed.For pain management heat can be used to relieve stiffness, and cold can relieve muscle spasms and pain. Among people with hip and knee osteoarthritis, exercise in water

may reduce pain and disability, and increase quality of life in the short term. Also therapeutic exercise programs such as aerobics and walking reduce pain and improve physical functioning for up to 6 months after the end of the program for people with knee osteoarthritis.

**Medications:**

- **By mouth:**

The pain medication paracetamol (acetaminophen) is the first line treatment for osteoarthritis.Pain relief does not differ according to dosage. However, a 2015 review found acetaminophen to only have a small short term benefit with some laboratory concerns of liver inflammation.For mild to moderate symptoms effectiveness of acetaminophen is similar to non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen, though for more severe symptoms NSAIDs may be more effective. NSAIDs are associated with greater side effects such as gastrointestinal bleeding.

Another class of NSAIDs, COX-2 selective inhibitors (such as celecoxib) are equally effective when compared to nonselective NSAIDs, and have lower rates of adverse gastrointestinal effects, but higher rates of cardiovascular disease such as myocardial infarction. They are also more expensive than non-specific NSAIDs. Benefits and risks vary in individuals and need consideration when making treatment decisions, and further unbiased research comparing NSAIDS and COX-2 selective inhibitors is needed.] NSAIDS applied

topically are effective for a small number of people. The COX-2 selective inhibitor rofecoxib was removed from the market in 2004, as cardiovascular events were associated with long term use.

Failure to achieve desired pain relief in osteoarthritis after 2 weeks should trigger reassessment of dosage and pain medication. Opioids by mouth, including both weak opioids such as tramadol and stronger opioids, are also often prescribed. Their appropriateness is uncertain, and opioids are often recommended only when first line therapies have failed or are contraindicated. This is due to their small benefit and relatively large risk of side effects.The use of tramadol likely does not improve pain or physical function and likely increases the incidence of adverse side effects. Oral steroids are not recommended in the treatment of osteoarthritis.]

Use of the antibiotic doxycycline orally for treating osteoarthritis is not associated with clinical improvements in function or joint pain. Any small benefit related to the potential for doxycycline therapy to address the narrowing of the joint space is not clear, and any benefit is outweighed by the potential harm from side effects.

**Topical:**

There are several NSAIDs available for topical use, including diclofenac. A Cochrane review from 2016 concluded that reasonably reliable evidence is available only for use of topical diclofenac and ketoprofen in people aged over 40 years with painful knee arthritis. Transdermal opioid pain medications are not typically recommended in the treatment of osteoarthritis.The use of topical capsaicin to treat osteoarthritis is controversial, as some reviews found benefit while others did not.

**Joint injection :**

Steroids

Joint injection of glucocorticoids (such as hydrocortisone) leads to short term pain relief that may last between a few weeks and a few months.]

Hyaluronic acid :

Injections of hyaluronic acid have not produced improvement compared to placebo for knee arthritis, but did increase risk of further pain. In ankle osteoarthritis, evidence is unclear.

Platelet rich plasma:

The effectiveness of injections of platelet-rich plasma is unclear; there are suggestions that such injections improve function but not pain, and are associated with increased risk.A Cochrane review of studies involving PRP found the evidence to be insufficient.

**Surgery:**

Joint replacement:

If the impact of symptoms of osteoarthritis on quality of life is significant and more conservative management is ineffective, joint replacement surgery or resurfacing may be recommended. Evidence supports joint replacement for both knees and hips as it is both

clinically effective and cost-effective. For people who have shoulder osteoarthritis and do not respond to medications, surgical options include a shoulder hemiarthroplasty (replacing a part of the joint), and total shoulder arthroplasty (replacing the joint).

Biological joint replacement involves replacing the diseased tissues with new ones. This can either be from the person (autograft) or from a donor (allograft).People undergoing a joint transplant (osteochondral allograft) do not need to take immunosuppressants as bone and cartilage tissues have limited immune responses. Autologous articular cartilage transfer from a non-weight-bearing area to the damaged area, called osteochondral autograft transfer system (OATS), is one possible procedure that is being studied. When the missing cartilage is a focal defect, autologous chondrocyte implantation is also an option.

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# PSORIASIS

## DEFINITION:

- Psoriasis is a common chronic inflammatory disease characterized by recurrent exacerbations and remissions of thickened, erythematous, and scaling plaques.

## PATHOPHYSIOLOGY:

- Cell-mediated immune mechanisms play a central role in psoriasis. Cutaneous inflammatory T-cell–mediated immune activation requires two Tcell signals mediated via cell–cell interactions by surface proteins and antigen-presenting cells such as dendritic cells or macrophages. The first signal is the interaction of the T-cell receptor with antigen presented by antigen-presenting cells. The second signal (called costimulation) is mediated through various surface interactions.
- Once T cells are activated, they migrate from lymph nodes and the bloodstream into skin and secrete various cytokines (e.g., interferon, interleukin 2 [IL-2]) that induce the pathologic changes of psoriasis. Local keratinocytes and neutrophils are induced to produce other cytokines, such as tumor necrosis factor (TNF- IL-8, and others. As a result of pathogenic T-cell production and activation, psoriatic epidermal cells proliferate at a rate sevenfold faster than normal epidermal cells. Epidermal proliferation is also elevated in apparently normal skin of psoriatic patients.
- There is a significant genetic component in psoriasis. Studies of histocompatibility antigens in psoriatic patients indicate a number of significant associations, especially with HLA-Cw6, where the relative likelihood for developing psoriasis is 9 to 15 times normal. Climate, stress, alcohol, smoking, infection, trauma, and drugs may aggravate psoriasis. Warm seasons and sunlight improve psoriasis in 80% of patients, whereas 90% of patients worsen in cold weather. Psoriatic lesions may develop at the site of injury (e.g., rubbing, venipuncture, bites, surgery) on normal-appearing skin (Koebner response). Lithium carbonate, β-adrenergic blockers, some antimalarials, nonsteroidal antiinflammatory drugs, and tetracyclines have been reported to exacerbate psoriasis.

## CLINICAL PRESENTATION:

- Psoriatic lesions are relatively asymptomatic, but about 25% of patients complain of pruritus.
- Lesions are characterized by sharply demarcated, erythematous papules and plaques often covered with silver-white fine scales. Initial lesions are usually small papules that enlarge over time and coalesce into plaques. If the fine scale is removed, a salmon-pink lesion is exposed, perhaps with punctate bleeding from prominent dermal capillaries (Auspitz sign).
- Scalp psoriasis ranges from diffuse scaling on an erythematous scalp to thickened plaques with exudation, microabscesses, and fissures. Trunk, back, arm, and leg lesions may be generalized, scattered, discrete, droplike lesions or large plaques. Palms, soles, face, and genitalia may also be involved. Affected nails are often pitted and associated with subungual keratotic material. Yellowing under the nail plate may be seen.

- Psoriatic arthritis is a distinct clinical entity in which both psoriatic lesions and inflammatory arthritis-like symptoms occur. Distal interphalangeal joints and adjacent nails are most commonly involved, but knees, elbows, wrists, and ankles may also be affected.

**DIAGNOSIS:**

- The diagnosis is based on physical examination findings of the characteristic lesions of psoriasis.
- The medical history of a patient with psoriasis should include information about the onset and duration of lesions, family history of psoriasis, presence of exacerbating factors, previous history of antipsoriatic treatment (if any) along with efficacy and adverse effect data, exposure to chemicals and toxins, and allergies (food, drugs, and environmental).
- Skin biopsy of lesional skin is useful in confirming the diagnosis.

**TREATMENT:**

NONPHARMACOLOGIC THERAPY

- **Emollients (moisturizers)** hydrate the stratum corneum and minimize water evaporation. They may enhance desquamation, eliminate scaling, and decrease pruritus. The lotions, creams, or ointments often need to be applied up to four times a day to achieve a beneficial response. Adverse effects include folliculitis and allergic or irritant contact dermatitis.
- **Balneotherapy** (and **climatotherapy**) involves bathing in waters containing certain salts, often combined with natural sun exposure. The salts in certain waters (e.g., the Dead Sea) reduce activated T cells in skin and may be remittive for psoriasis.

PHARMACOLOGICAL THERAPY: **TOPICAL PHARMACOTHERAPY**

**Corticosteroids**

- **Topical corticosteroids** (Table 16-1) may halt synthesis and mitosis of DNA in epidermal cells and appear to inhibit phospholipase A, lowering the amounts of arachidonic acid, prostaglandins, and leukotrienes in the skin. These effects, coupled with local vasoconstriction, reduce erythema, pruritus, and scaling. As antipsoriatic agents, they are best used adjunctively with a product that specifically functions to normalize epidermal hyperproliferation.
- Low-potency products (e.g., hydrocortisone 1%) have a weak antiinflammatory effect and are safest for long-term application, for use on the face and intertriginous areas, for use with occlusion, and for use in infants and young children.
- Medium-potency products are used in moderate inflammatory dermatoses. They may be used on the face and intertriginous areas for a limited time.
- High-potency preparations are used primarily as alternatives to systemic corticosteroids when local therapy is feasible.
- Very high potency products may be used for thick, chronic psoriatic lesions but for only short periods of time and on relatively small surface areas.
- Ointments are the most effective formulations for psoriasis because they have an occlusive oily phase that conveys a hydrating effect and enhances penetration of the corticosteroid into the dermis. They are not suited for use in the axilla, groin, or other

intertriginous areas where maceration and folliculitis may develop secondary to the occlusive effect. Creams are more cosmetically desirable for some patients. They may be used in intertriginous areas even though their lower oil content makesthem more drying than ointments.

- Topical corticosteroids are applied two to four times daily during longterm therapy.
- Adverse effects include local tissue atrophy, skin degeneration, and striae. If detected early, these effects may be reversible with discontinuation. Thinning of the epidermis may result in visibly distended capillaries (telangiectasias) and purpura. Acneiform eruptions and masking of symptoms of bacterial or fungal skin infections have been reported. Systemic consequences include risk of suppression of the hypothalamic-pituitary-adrenal axis, hyperglycemia, and development of cushingoid features. Tachyphylaxis and rebound flare of psoriasis after abrupt cessation of therapy can also occur.

**Calcipotriene**

- (Dovonex) is a synthetic vitamin D analog used for mild to moderate plaque psoriasis. Improvement is usually seen within 2 weeks of treatment, and approximately 70% of patients demonstrate marked improvement after 8 weeks. Adverse effects occur in about 10% of patients and include lesional and perilesional burning and stinging. Calcipotriene 0.005% cream, ointmen, or solution is applied one or two times a day (no more than 100 g/wk).
- Calcitriol and tacalcitol are other vitamin D derivatives that have been studied for treatment of psoriasis.

**Tazarotene**

- (Tazorac) is a synthetic retinoid that is hydrolyzed to its active metabolite, tazarotenic acid, which modulates keratinocyte proliferation and differentiation. It is available as a 0.05% or 0.1% gel and cream and is applied once daily (usually in the evening) for mild to moderate plaque psoriasis. Adverse effects are dose- and frequency related and include mild to moderate pruritus, burning, stinging, and erythema. Application of the gel to eczematous skin or to more than 20% of body surface area is not recommended because this may lead to extensive systemic absorption.Tazarotene is often used with topical corticosteroids to decrease local adverse effects and increase efficacy.

**SYSTEMIC PHARMACOTHERAPY:**

**Cyclosporine** demonstrates immunosuppressive activity by inhibiting the first phase of T-cell activation. It also inhibits release of inflammatory mediators from mast cells, basophils, and polymorphonuclear cells. It is used in the treatment of both cutaneous and arthritis manifestations of severe psoriasis.The usual dose is between 2.5 and 5 mg/kg/day given in two divided doses.Adverse effects include nephrotoxicity, hypertension, hypomagnesemia, hyperkalemia, alterations in liver function tests, elevations of serum lipids, GI intolerance, paresthesias, hypertrichosis, and gingival hyperplasia. Cumulative treatment for more than 2 years may increase the risk of malignancy, including skin cancers and lymphoproliferative disorders.

**Methotrexate**, an antimetabolite, is indicated for moderate to severe psoriasis. It is particularly beneficial for psoriatic arthritis. It is also indicated for patients refractory to topical or UV therapy. Methotrexate can be administered orally, subcutaneously, or intramuscularly. The starting dose is 7.5 to 15 mg per week, increased incrementally by 2.5 mg every 2 to 4 weeks until response; maximal doses are approximately 25 mg/wk. Adverse effects include nausea, vomiting, mucosal ulceration, stomatitis, malaise, headache, macrocytic anemia, and hepatic and pulmonary toxicity. Nausea and macrocytic anemia can be ameliorated by giving oral folic acid 1 to 5 mg/day. Methotrexate should be avoided in patients with active infections and in those with liver disease. It is contraindicated in pregnancy because it is teratogenic.

**REFERENCE:**

Barbara Wells, Joseph DiPiro, Terry Schwinghammer, Cecily DiPiro - Pharmacotherapy Handbook-McGraw-Hill Medical (2008)

# PHARM. D 4TH YEAR:

## 4.1 PHARMACOTHERAPEUTICS III

## 5.PAIN MANAGEMENT INCLUDING PAIN PATHWAYS, NEURALGIAS, HEADACHES.

### INTRODUCTION:

Pain Management is a medical approach that draws on disciplines in science and alternative healing to study the prevention, diagnosis, and treatment of pain. Pain management programs can employ massage therapy, analgesic medications, physical therapy, and epidural steroid injections, among others to treat back pain.

### Pain Management for Specific Types of Pain

- Acute pain: non-opioids, weak opioids, opioids, non-pharmacological treatments such as ice or bioelectric therapy.
- Chronic pain: non-opioids, weak opioids, opioids, antidepressants, capsaicin cream, non-pharmacological treatments such as bioelectric therapy, radiation therapy.

### The General Pain Pathway

Within the pain pathway there are 3 orders of neurons which carry action potentials signalling pain.

- First order neurons – These are pseudounipolar neurons which have cells bodies within the dorsal root ganglion. They have one axon which splits into two branches, a peripheral branch (which extends towards the peripheries) and a central branch (which extends centrally into spinal cord/brainstem).
- Second order neurons – The cell bodies of these neurons are found in the Rexed laminae of the spinal cord, or in the nuclei of the cranial nerves within the brain stem. These neurons then decussate in the anterior white commissure and ascend cranially in the spinothalamic tract to the ventral posterolateral (VPL) nucleus of the thalamus.
- Third order neurons – The cell bodies of third order neurons lie within the VPL of the thalamus. They project via the posterior limb of the internal capsule to terminate in the ipsilateral postcentral gyrus (primary somatosensory cortex). The postcentral gyrus is somatotopically organised. Therefore, pain signals initiated in the hand will terminate in the area of the cortex dedicated to represent sensations of the hand.

## ACTIVATION OF FIRST ORDER NEURONS

### Nociceptors

Some first order neurons have specialist receptors called nociceptors which are activated through various noxious stimuli. Nociceptors exists at the free nerve endings of the primary afferent neuron.

Since nociceptors are free nerve endings this means they are unencapsulated cutaneous receptors. This is opposed to encapsulated cutaneous receptors (e.g. Merkel's discs) which detect other sensory modalities such as vibration and stretching of skin.

Similar to other sensory modalities, each nociceptor has its own receptive field. This means one nociceptor will transduce the signal of pain when a particular region is skin is stimulated. The size of receptive fields vary throughout the body and there is often overlap with neighbouring fields.

Areas such as the fingertips have smaller receptive fields than areas such as the forearm. In addition, they have a larger density of free nerve endings within this receptive field. This difference is important as it allows for greater acuity in detecting a sensory stimulus.

The size of cortical representation in the somatosensory cortex of a particular body part is also related to the size of the receptive fields in that body part. For example, because the fingertips have small receptive fields, and thus a greater degree of sensory acuity, they have a larger cortical representation.

Nociceptors can be found in the skin, muscle, joints, bone and organs (other than the brain) and can fire in response to a number of different stimuli. Three types of nociceptors exist:

- Mechanical nociceptors – detects sharp, pricking pain
- Thermal and mechano-thermal nociceptors – detects sensations which elicit pain which is slow and burning, or cold and sharp in nature
- Polymodal nociceptors – detects mechanical, thermal and chemical stimuli

### Transmission to the Spinal Cord

Signals from mechanical, thermal and mechano-thermal nociceptors are transmitted to the dorsal horn of the spinal cord predominantly by Aδ fibres. These myelinated fibres have a low threshold for firing and the fast conduction speed means they are responsible for transmitting the first pain felt.

In addition, Aδ fibres permit for the localisation of pain and form the afferent pathway for the reflexes elicited by pain. Aδ fibres predominantly terminate in Rexed laminae I where they mainly release the neurotransmitter glutamate.

Polymodal nociceptors transmit their signals into the dorsal horn through C fibres. C fibres are unmyelinated and a slow conduction speed. For this reason, C fibres are responsible for the secondary pain we feel which is often dull, deep and throbbing in nature. These fibres typically have large receptive fields and therefore lead to poor localisation of pain.

Compared to Aδ fibres, C fibres have a high threshold for firing. However, noxious stimuli can cause sensitisation of C fibres and reduce their threshold for firing. C fibres predominately terminate in Rexed laminae I and II and release the neurotransmitter substance P. Other neurotransmitters are released by primary afferent neurons terminating within the spinal cord such as aspartate and vasoactive peptide.

A variety of factors are released upon tissue damage which lead to the activation of nociceptors. These include:

- Arachidonic acid
- Potassium
- 5-HT
- Histamine
- Bradykinin
- Lactic acid
- ATP

## DESCENDING MODULATION OF PAIN

Within the central nervous system there are three types of opioid receptors which regulate neurotransmission of pain signals. These receptors are called mu, delta and kappa opioid receptors.

They are all G protein coupled receptors and their activation leads to a reduction in neurotransmitter release and cell hyperpolarisation, reducing cell excitability. Exogenous opioids, such as morphine, provide excellent analgesia by acting on these receptors. Likewise, our body contains endogenous opioids which can modulate pain physiologically. There are three types of endogenous opioids:

- B-endorphins – which predominately binds to mu opioid receptors
- Dynorphins – which predominately bind to kappa opioid receptors
- Enkephalins – which predominately bind to delta opioid receptors

Opioids can regulate pain on a number of levels, both within the spinal cord, brain stem and cortex. Within the spinal cord both dynorphins and enkephalins can act to reduce the transmission of pain signals in the dorsal horn. This is because the pre-synaptic ends of second order neurons have opioid receptors within the membrane. In addition, the post-synaptic end of first order neurons contain opioid receptors.

When endogenous opioids act on these receptors it reduces neurotransmitter release

from the first order neuron, and causes hyper polarization of the second order neuron. Together, this reduces the firing of action potentials in the second order neuron, blocking the transmission of pain signals.

## NEURALGIA:

Neuralgia is a stabbing, burning, and often severe pain due to an irritated or damaged nerve. The nerve may be anywhere in the body, and the damage may be caused by several things, including.

- aging
- diseases such as diabetes or multiple sclerosis
- an infection, such as shingles

Treatment for the pain of neuralgia depends on the cause.

### Types of neuralgia

Postherpetic neuralgia

This type of neuralgia occurs as a complication of shingles and may be anywhere on the body. Shingles is a viral infection characterized by a painful rash and blisters. Neuralgia can occur wherever the outbreak of shingles was. The pain can be mild or severe and persistent or intermittent. It can also last for months or years. In some cases, the pain may occur before the rash. It will always occur along the path of a nerve, so it's usually isolated to one side of the body.

Trigeminal neuralgia

This type of neuralgia is associated with pain from the trigeminal nerve, which travels from the brain and branches to different parts of the face. The pain can be caused by a blood vessel pressing down on the nerve where it meets with the brainsterr. It can also be caused by multiple sclerosis, injury to the nerve, or other causes.

Trigeminal neuralgia causes severe, recurrent pain in the face, usually on one side. It's most common in people who are older than 50 years.

Glossopharyngeal neuralgia

Pain from the glossopharyngeal nerve, which is in the throat, is not very common. This type of neuralgia produces pain in the neck and throat.

**Causes of neuralgia**

The cause of some types of nerve pain is not completely understood. You may feel nerve pain from damage or injury to a nerve, pressure on a nerve, or changes in the way the nerves function. The cause may also be unknown.

Infection

An infection can affect your nerves. For example, the cause of postherpetic neuralgia is shingles, an infection caused by the chickenpox virus. The likelihood of having this infection increases with age. An infection in a specific part of the body may also affect a nearby nerve. For example, if you have an infection in a tooth, it may affect the nerve and cause pain.

Multiple sclerosis

Multiple sclerosis (MS) is a disease caused by the deterioration of myelin, the covering of nerves. Trigeminal neuralgia may occur in someone with MS.

Pressure on nerves

Pressure or compression of nerves may cause neuralgia. The pressure may come from:

- bone

- ligament
- blood vessel
- tumor

The pressure of a swollen blood vessel is a common cause of trigeminal neuralgia.

Diabetes

Many people with diabetes have problems with their nerves, including neuralgia. The excess glucose in the bloodstream may damage nerves. This damage is most common in the hands, arms, feet, and legs.

## TREATMENT OF NEURALGIA

If your doctor can pinpoint the cause of your neuralgia, your treatment will focus on treating the underlying cause. If the cause is not found, treatment will focus on relieving your pain.

Potential treatments may include.

- surgery to relieve the pressure on the nerve
- better control of blood sugar levels in people with diabetes-caused neuralgia
- physical therapy
- nerve block, which is an injection directed at a particular nerve or nerve group and that is intended to "turn off" pain signals and reduce inflammation
- medications to relieve the pain

Medications prescribed may include.

- Antidepressants such as amitriptyline or nortriptyline, which are effective in treating nerve pain
- Antiseizure medications such as carbamazepine, which is effective for trigeminal neuralgia
- short-term narcotic pain medications, such as codeine
- topical creams with capsaicin

## HEAD ACHES:

Headaches are one of the most common medical complaints; most people experience them at some point in their life. They can affect anyone regardless of age, race, and gender. The World Health Organization (WHO) reports that almost half of all adults worldwide will experience a headache in any given year. A headache can be a sign of stress or emotional distress, or it can result from a medical disorder, such as migraine or high blood pressure, anxiety, or depression. It can lead to other problems. People with chronic migraine headaches, for example, may find it hard to attend work regularly.

The International Headache Society (IHS) categorize headaches as primary, when they are not caused by another condition, or secondary, when there is a further underlying cause.

### Primary headaches

Primary headaches are stand-alone illnesses caused directly by the overactivity of, or problems with, structures in the head that are pain-sensitive.

This includes the blood vessels, muscles, and nerves of the head and neck. They may also result from changes in chemical activity in the brain.

Common primary headaches include migraines, cluster headaches, and tension headaches.

**Secondary headaches**

Secondary headaches are symptoms that happen when another condition stimulates the pain-sensitive nerves of the head. In other words, the headache symptoms can be attributed to another cause.

A wide range of different factors can cause secondary headaches.

These include:

- alcohol-induced hangover
- brain tumor
- blood clots
- bleeding in or around the brain
- "brain freeze," or ice-cream headaches
- carbon monoxide poisoning
- concussion
- dehydration
- glaucoma
- teeth-grinding at night

- influenza
- overuse of pain medication, known as rebound headaches
- panic attacks
- stroke

As headaches can be a symptom of a serious condition, it is important to seek medical advice if they become more severe, regular, or persistent.

For example, if a headache is more painful and disruptive than previous headaches, worsens, or fails to improve with medication or is accompanied by other symptoms such as confusion, fever, sensory changes, and stiffness in the neck, a doctor should be contacted immediately.

## TYPES

There are different types of headache.

### Tension headaches

Tension headaches are the most common form of primary headache. Such headaches normally begin slowly and gradually in the middle of the day.

The person can feel:

- as if they have a tight band around the head
- a constant, dull ache on both sides
- pain spread to or from the neck

Tension-type headaches can be either episodic or chronic. Episodic attacks are usually

a few hours in duration, but it can last for several days. Chronic headaches occur for 15 or more days a month for a period of at least 3 months.

## Migraines

A migraine headache may cause a pulsating, throbbing pain usually only on one side of the head. The aching may be accompanied by:

- blurred vision
- light-headedness
- nausea
- sensory disturbances known as auras

Migraine is the second most common form of primary headache and can have a significant impact on the life of an individual. According to the WHO, migraine is the sixth highest cause of days lost due to disability worldwide. A migraine can last from a few hours to between 2 and 3 days.

## Rebound headaches

Rebound or medication-overuse headaches stem from an excessive use of medication to treat headache symptoms. They are the most common cause of secondary headaches. They usually begin early in the day and persist throughout the day. They may improve with pain medication, but worsen when its effects wear off.

Along with the headache itself, rebound headaches can cause:

- neck pain
- restlessness

- a feeling of nasal congestion
- reduced sleep quality

Rebound headaches can cause a range of symptoms, and the pain can be different each day.

**Cluster headaches**

Cluster headaches usually last between 15 minutes and 3 hours, and they occur suddenly once per day up to eight times per day for a period of weeks to months. In between clusters, there may be no headache symptoms, and this headache-free period can last months to years.

The pain caused by cluster headaches is.

- one-sided
- severe
- often described as sharp or burning
- typically located in or around one eye

The affected area may become red and swollen, the eyelid may droop, and the nasal passage on the affected side may become stuffy and runny.

**Thunderclap headaches**

These are sudden, severe headaches that are often described as the "worst headache of my life." They reach maximum intensity in less than one minute and last longer than 5 minutes.

A thunderclap headache is often secondary to life-threatening conditions, such as intra-

cerebral hemorrhage, cerebral venous thrombosis, ruptured or unruptured aneurysms, reversible cerebral vasoconstriction syndrome (RVS), meningitis, and pituitary apoplexy.

People who experience these sudden, severe headaches should seek medical evaluation immediately.

## SYMPTOMS

Headaches can radiate across the head from a central point or have a vise-like quality. They can be sharp, throbbing or dull, appear gradually or suddenly. They can last from less than an hour up to several days.

The symptoms of a headache depend to some extent on what type of headache it is.

Tension headache: There may be general, mild to moderate pain that can feel like a band around the head. They tend to affect both sides of the head.

Migraine headache: There is often a severe throbbing pain in one part of the head, often the front or the side. There may be nausea and vomiting, and the person may feel especially sensitive to light or noise.

Cluster headaches: These can cause intense pain, often around one eye. They usually happen around a particular time of year, possibly over a period of 1 to 2 months.

## TREATMENT

The most common ways of treating headaches are rest and pain relief medication.

Generic pain relief medication is available over the counter (OTC), or doctors can prescribe preventative medication, such as tricyclic antidepressants, serotonin receptor agonists, anti-epileptic drugs, and beta-blockers.

It is important to follow the doctor's advice because overusing pain relief medication can lead to rebound headaches. The treatment of rebound headaches involves the reducing or stopping pain relief medication. In extreme cases, a short hospital stay may be needed to manage withdrawal safely and effectively.

## ALTERNATIVE TREATMENTS

Several alternative forms of treatment for headaches are available, but it is important to consult a doctor before making any major changes or beginning any alternative forms of treatment.

Alternative approaches include:

- acupuncture
- cognitive behavior therapy
- herbal and nutritional health products
- hypnosis
- meditation

Research has not provided evidence to confirm that all these methods work.

Sometimes, a headache may result from a deficiency of a particular nutrient or nutrients, especially magnesium and certain B vitamins. Nutrient deficiencies can be due to a poor quality diet, underlying malabsorption issues, or other medical conditions.

## HOME REMEDIES

A number of steps can be taken to reduce the risk of headaches and to ease the pain if

they do occur:

1. Apply a heat pack or ice pack to your head or neck, but avoid extreme temperatures.
2. Avoid stressors, where possible, and develop healthy coping strategies for unavoidable stress.
3. Eat regular meals, taking care to maintain stable blood sugar.

A hot shower can help, although in one rare condition hot water exposure can trigger headaches. Exercising regularly and getting enough rest and regular sleep contributes to overall health and stress reduction.