INTRODUCTION: THE GRAYING OF AMERICA
For the first time in our history, medical advances in the 20th century have made it possible that more than 10% of some national populations are over the age of 65. This has been referred to as the “graying of America” in the United States and has stimulated interest in the consequences of aging and the care of the elderly. The branch of medicine dealing with medical problems and care of the elderly is called “geriatrics”. The more broadly based scientific discipline that deals with all aspects of aging (social, biological, psychological, etc.) is called “gerontology”.

We commonly, or intuitively, know that each day animals are born, grow, mature, then begin to lose some of their capabilities to function “normally”, then finally they die. This chronology and the onset of aging is specific to each species; for example, the dog is old at about 12 years, rodents at 2 or 3 years, a horse at 15 to 20 years and a human at about 60 to 90. It appears that there is an organizational plan within each species. An interesting phenomena related to aging is the Hayflick phenomenon, named after the American biologist who first described it. It is related to factors within the cell of a species that determine its capacity to multiply, the exhaustion of that capacity and its relation to life span. For example, cells removed from an organism and allowed to grow in tissue culture will divide only a certain number of times and then die. In humans, there are about 50 divisions, about 25 in the chicken and about 14 to 28 in the mouse; but the Galapagos tortoise undergoes 90 to 125 doublings. If the normal explanted human cells have undergone about 40 divisions and then frozen and thawed, they will only undergo about 10 additional divisions; again related back to the number unique to the species.

The loss of capabilities of an individual during aging is progressive, irreversible and universal for all members of a specific species and is termed “aging”. From the outward appearance, it is very evident in humans as a decline in height, muscle shrinkage, thinning and graying of hair and wrinkling of skin. Internally, it is more significant as there is a progressive loss of cells in the brain, kidneys and other vital organs. There is less competence in these cells and tissues and this is reflected in functional declines by the individual. It appears that nerve cells from the brain to

GOALS AND OBJECTIVES
Goal: To provide supportive information to assist pharmacists in more effectively counseling geriatric patients and in advocating the rational treatment of arthritis.
Objectives: After reading and studying this article, the participant should be able to:
1. discuss the characteristics of the aging patient.
2. define the various types of arthritis.
3. describe the various approaches to treating the different types of arthritis.
4. consult with healthcare professionals in the management of arthritis, and the compounding of patient-specific medications.
the spinal cord diminish and those that remain conduct impulses at a slower rate so that reaction time is slowed; also, memory shows a decline.

There is much biological variability in the aging process; some individuals appear “old” at age 50 and others are quite active even at age 80 or 90. Generally, the longer-lived individuals show a later onset of the aging process and a slower progression in the rate of aging than “normal”. There also appears to be a genetic factor involved as long life seems to run in families. Disuse of bodily organ systems appears to accelerate their deterioration. This is quite obvious with muscle and bone but it also is true of memory and thinking. Consequently, it is important to exercise both the body and the mind throughout life and not settle into a “passive” lifestyle. Another interesting phenomenon is that nonsmoking can increase one’s life expectancy by about four years.

PHYSIOLOGICAL CHANGES IN THE ELDERLY

As one ages, there is a multitude of changes that occur in almost every system in the body. These changes include increased adipose tissue of 14-30% by age 70, decreased lean body weight, decreased total body water and plasma volume and decreased thickness of the skin. Also included are the loss of teeth, decreased salivation, decreased GI motility, neurological changes including decreased neurons, brain weight and volume, decreased cognitive skills and increased reaction to positive or negative stimuli. Decreased estrogen can lead to osteoporosis, decreased glucose tolerance and atrophy of the thyroid gland also occurs. Hepatic changes include decreased liver size, decreased hepatic blood flow and decreased albumin with serious disease or poor nutrition. In the kidney, there is a decrease in the glomeruli by 30-40% by age 80, decreased creatinine clearance without a decrease in serum creatinine, decreased renal blood flow, decreased renin and a decreased concentrating ability. There can also be visual and auditory problems, decreased respiratory function, decreased active transport, decreased first-pass metabolism and increased gastric pH.

One problem with drug therapy in the elderly is that their pharmacokinetics and pharmacodynamics are different than those in the median-age adult. Due to the generally slower rate of drug metabolism, inappropriate drug therapy in the elderly can cause symptoms that may be misinterpreted as disease symptoms, especially dizziness and falling. Inappropriate therapy can also cause impaired quality of life, hospitalization and even death. The general tendency is to overmedicate the elderly.

DISEASES/DISORDERS AFFECTING THE ELDERLY

Diseases affecting the elderly include hearing loss, atherosclerosis, Alzheimer’s, polymyalgia rheumatica, fibromyalgia, giant cell arteritis, crystal arthropathies (such as gout), falls, fractures, osteoporosis, insomnia, depression, dementia, urinary incontinence, benign prostate hypertrophy, urinary tract infections, constipation, GI bleeding, cardiovascular disease, stroke and diabetes. In geriatric medicine, the goal is to eliminate or minimize the disease processes that prevent us from living to the natural end of one’s life. Two processes affecting large numbers of geriatric patients are Alzheimer’s disease and rheumatologic problems.

Alzheimer’s disease symptoms were formerly dismissed as consequences of aging but in the 1980s, it was recognized as the most common cause of intellectual deterioration in the elderly and the middle-aged. Its cause is related to the death of nerve cells in the cerebral cortex and generally causes speech disturbances, disorientation and severe short-term memory loss; these lead to progressive loss of mental faculties although the individual remains physically healthy. Two characteristic abnormalities in the cellular structure of the brain tissue include neuritic plaques and neurofibrillary tangles; victims also have a deficiency of the neurotransmitter acetylcholine. Also, Alzheimer’s may be related to a virus, abnormal concentrations of aluminum, a hereditary involvement and/or Down’s syndrome.

Approximately 80% of the population have at least one rheumatologic complaint by their 60’s. These conditions may affect mobility, quality of life and may limit an individual’s ability to live independently. Included in the rheumatologic disease are polymyalgia rheumatica (a syndrome characterized by pain and morning stiffness in the neck, shoulder girdle and pelvic girdle), fibromyalgia (characterized by chronic diffuse muscle pain), giant cell arteritis (temporal arteritis, a vasculitis that involves the aorta and its proximal branches, crystal arthropathies (gout, pseudo-gout, caused by intra-articular deposits of monosodium urate and calcium pyrophosphate in joints) and degenerative joint diseases, including arthritis. Due to the extensive numbers of patients suffering from arthritis, the remainder of this issue will deal specifically with patients suffering from arthritic disease.

ARTHITIS

A 1998 study estimated that 40 million Americans had some form of arthritis; this number is expected to grow to almost 60 million within the next 20 years. Pharmacists are often the first point of contact for patients complaining of painful or stiff joints. They frequently are seeking non-prescription products for self-treatment. What can be recommended for self-treatment and what recommendations can be made to health care practitioners for the patients they treat? First of all, there is currently no cure for arthritis. However, there are products that can be recommended to alleviate many of the painful symptoms associated with the disease. Let’s start by looking at the different types of arthritis.
There are four common types of arthritis as follows: Osteoarthritis, also called wear and tear arthritis, primarily occurs as a natural part of the aging process and affects an estimated 20 million Americans. Rheumatoid arthritis occurs mostly in women and is a very serious, often crippling, form of the disease, affecting some 2.5 million Americans. Ankylosing spondylitis often occurs in young men aged 15 to 40 and can result in a “frozen” spine. Also, a type of arthritis can follow an injury and result in conditions such as tennis elbow and lower back pain.

Osteoarthritis begins when the cartilage covering the ends of bones at the joints becomes rough and patchy. These rough spots progress to the growth of tiny bone spurs initiating a chain reaction of irritation of the muscles, tendons then inflammation followed by pain.

Some forms of arthritis appear to run in families; in fact, genetic markers have been found in the white blood cells of those with rheumatoid arthritis and ankylosing spondylitis. In rheumatoid arthritis, the immune systems begins to attack the body itself. This results in tissue inflammation and can be a primary cause of damage, mostly to joints. This inflammation causes heat and swelling and the synovium may be destroyed.

Osteoarthritis is the most common arthropathy in geriatric practice. It is responsible for about 70% of all total knee and 60% of all total hip replacements. These procedures reduce the risk of disability and indirect economic costs to patients and society. As our population continues to age, the costs will escalate since preventive and medical interventions are not yet available. Technically, this generalized osteoarthritis is also defined as a polyarticular illness in a predictable distribution of involvement, including the DIP joints (Heberden’s nodes), PIP joints (Bouchard nodes), the base of the thumb (first CMC joint), the knees, cervical lumbar spines, and the first MTP joint. It is most common in women, frequently occurring in a pattern of finger and varus medial or patellofemoral knee osteoarthritis. Also, a rapidly destructive arthropathy of the hip is mostly a unilateral arthritis that occurs predominantly in older women. These patients may have osteoarthritis in other joints such as the shoulder or knee that may deteriorate along with a progressive femoral head collapse and resorption of the hip.

Pain associated with arthritis is usually initially use-related. Later, rest or night pain appears in the progression of the disease. Patients also experience stiffness and tenderness.

There is at this time no cure for arthritis but it sometimes just goes into remission. The goals of treatment are to relieve pain and to maintain or improve function. No current interventions are known to actually change the natural history of symptomatic disease. The nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used to treat the symptoms of arthritis. There is, however, much concern that the use of the NSAIDs is excessive and often leads to side effects, including gastric ulcer and perforation; a means of minimizing these side effects is discussed later. For oral administration, it has been recommended that ibuprofen may be the safest and piroxicam the most hazardous NSAID.

One recent study implicated the NSAIDs in 3% of all hospitalizations among the elderly in England; this was due either to GI toxicity or for heart and renal problems aggravated by the NSAIDs. If oral NSAID therapy is implemented, it should be monitored and periodically reassessed. Also, an alternate route, such as topical NSAID therapy, should be considered. The major risk with NSAIDS has been upper GI toxicity in the elderly, especially gastric ulcer in elderly women resulting in higher rates of bleeding perforation and death from peptic ulcer disease.

Acetaminophen in a dose of 2600 to 4000 mg daily is approximately equivalent to ibuprofen in doses of 1200 to 2400 mg or naprosyn 750 mg per day. The dose of acetaminophen should not exceed 4000 mg daily in otherwise healthy patients; the dose should be halved in patients with mild liver disease and should not be used in patients with advanced liver disease or alcoholism since hepatotoxicity may be potentiated. The COX-2 inhibitors such as Celebrex (celecoxib) and Vioxx (rofecoxib) are also increasingly used and may not have the serious GI side effects associated with the NSAIDs.

Capsaicin cream is often used to treat the symptoms of osteoarthritis in joints; its mechanism of action is thought to be by depletion of substance P (a key molecule in the transmission of pain signals from the body to the spinal cord and eventually the brain) in nerve fibers. It is more effective if continuously used on a daily schedule. Capsaicin is the active enzyme found in hot chili peppers of the genus Capsicum Oital). Various creams, lotions and gels can be compounded. Generally, immediately after application, capsaicin causes burning; however, some individuals eventually develop a tolerance to this burning irritation. It is used in strengths up to 0.25%.

Methyl salicylate and other topical rubefacients are commonly used by patients purchasing them as nonprescription drugs.

Corticosteroid intra-articular injections are used but often do not provide lasting relief. Dexamethasone sodium phosphate is being increasingly administered using iontophoresis, which is the forced movement of drugs using a small electric current through the skin into the inflamed area using a small iontophoric device.

Also, gold compounds have been used. In badly damaged joints, surgical replacement with artificial joints is indicated. Researchers are looking for drugs that can stop the inflam-
A drug to prevent arthritis when the exact cause is not known. Other treatment modalities include weight loss; an 11.2 pound weight loss over ten years led to a 50% reduction in the risk of developing knee arthritis symptoms. In addition to weight loss, walking, exercise and a proper diet are important. It is also good to explain to the patient the difference between osteoarthritis and the more disabling rheumatoid disease. This will help to relieve their anxiety and improve their outlook on life. Rehabilitation is important to maintain and restore the patient’s ability to function independently.

Rheumatoid arthritis (an autoimmune disease) is quite different from osteoarthritis. The inflammation is first associated with the synovial membrane lining the joint. However, as the disease progresses, the diseased tissue produces collagenase and other enzymes that break down cartilage. In treating rheumatoid arthritis, NSAIDs are often first used but if they do not reduce the pain and swelling after two to four months, disease-modifying antirheumatic drugs are prescribed, including gold salts, hydroxychloroquine, sulfasalazine, methotrexate and etanercept.

**ALTERNATIVE MEDICINES**

Alternative medications commonly used include glucosamine sulfate, chondroitin sulfate, S-adenosylmethionine, fish oil, gamma linolenic acid, green tea and Type II collagen. Some of these natural medications are effective; some more so than others. As is the case with all medications, not all of them work in all patients. Many of the alternative medications are prescribed in various combinations by physicians for compounding by pharmacists. There are numerous dietary recommendations for low fat, vegetarian or near-vegetarian diets.

**COMPOUNDED MEDICATIONS FOR ARTHRITIS**

Many patients and health-care practitioners are unaware of the wide variety of medications that can be compounded for treating arthritis. Many compounded prescriptions are designed to be alternate routes of administration of commonly used drugs. For example, the orally administered NSAIDs can cause gastrointestinal distress which can lead to serious consequences; as an example, NSAID related GI distress causes approximately 20,000 deaths and over 100,000 hospitalizations annually in the United States. Also, it is estimated that 8 to 10% of kidney failures annually in the U.S. are caused by the use of these drugs. However, the NSAIDs can be administered topically and be just as effective while minimizing the potentially disastrous effects associated with oral administration of this class of drugs.

**COMPOUNDED FORMULATIONS FOR ARTHRITIS**

**Solution Examples:**

<table>
<thead>
<tr>
<th>Rx</th>
<th>Indomethacin 4% Topical Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indomethacin</td>
<td>4 g</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>5 mL</td>
</tr>
<tr>
<td>Hydroxypropyl cellulose</td>
<td>200 mg</td>
</tr>
<tr>
<td>Sodium lauryl sulfate</td>
<td>100 mg</td>
</tr>
<tr>
<td>Purified water</td>
<td>10 mL</td>
</tr>
<tr>
<td>Alcohol, 95%</td>
<td>qs 100 mL</td>
</tr>
</tbody>
</table>

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Mix the propylene glycol, sodium lauryl sulfate and purified water together.
4. Disperse the indomethacin in about 80 mL of the alcohol.
5. Add the aqueous phase to the indomethacin dispersion and mix well.
6. Add the hydroxypropyl cellulose and mix well.
7. Add sufficient alcohol to volume and mix well.
8. Package and label.

<table>
<thead>
<tr>
<th>Rx</th>
<th>Dexamethasone Sodium Phosphate 1 mg/mL for Iontophoresis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone sodium phosphate</td>
<td>100 mg</td>
</tr>
<tr>
<td>Sterile water for injection</td>
<td>qs 100 mL</td>
</tr>
</tbody>
</table>

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh the dexamethasone sodium phosphate.
3. Place in a suitable graduate and add sufficient sterile water for injection to volume.
4. Mix well and pass through a 0.2-micron sterile filter into a sterile container.
5. Package and label.

**Topical Gel (Pluronic-Lecithin Organogel) Examples:**

<table>
<thead>
<tr>
<th>Rx</th>
<th>Capsaicin 0.075%, Ketamine Hydrochloride 2% and Ketoprofen 10% in PLO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsaicin</td>
<td>75 mg</td>
</tr>
<tr>
<td>Ketamine hydrochloride</td>
<td>2 g</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>10 g</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>10 mL</td>
</tr>
<tr>
<td>Lecithin/isopropyl palmitate</td>
<td>22 mL</td>
</tr>
<tr>
<td>Pluronic F-127 30% gel</td>
<td>qs 100 mL</td>
</tr>
</tbody>
</table>

Note: The lecithin:isopropyl palmitate solution can be prepared by mixing 0.2 g sorbic acid, 50 g of soy lecithin and 50 g of isopropyl palmitate. The Pluronic F-127 solution can be prepared by mixing 0.2 g sorbic acid, 30 g of Pluronic F-127 and sufficient purified water to make 100 mL.

1. Calculate the required quantity of each ingredient for the total quantity to be prepared.
2. Accurately weigh/measure each ingredient.
3. Combine the capsaicin, ketamine hydrochloride and ketoprofen powders
4. Add sufficient propylene glycol to form a smooth paste.
5. Add the lecithin:isopropyl palmitate solution and mix well.
6. Add sufficient Pluronic F-127 gel to volume and mix well.
7. Package and label.

Note: In this formulation, some active ingredients can easily be omitted and others added as needed.

**Topical Ointment Example:**

<table>
<thead>
<tr>
<th>Rx</th>
<th>Capsicum 5% Ointment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsicum</td>
<td>5 g</td>
</tr>
<tr>
<td>Aquabase™</td>
<td>95 g</td>
</tr>
</tbody>
</table>

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh each ingredient.
3. Make a paste by incorporating a small quantity of the Aquabase into the capsicum.
4. Slowly incorporate the remaining Aquabase into the paste geometrically.
5. Mix until uniform.
6. Package and label.

**Medication Stick Example:**

**Topical Alcoholic Gel Example:**

<table>
<thead>
<tr>
<th>Rx</th>
<th>Piroxicam 1% Alcoholic Gel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piroxicam</td>
<td>1 g</td>
</tr>
<tr>
<td>Hydroxypropyl cellulose</td>
<td>1.75 g</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>5 mL</td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td>2 mL</td>
</tr>
<tr>
<td>70% Isopropyl alcohol qs</td>
<td>100 mL</td>
</tr>
</tbody>
</table>

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Add the hydroxypropyl cellulose powder to about 91 mL of 70% isopropyl alcohol and mix until a clear gel results.
4. Place the piroxicam powder in a mortar and add the propylene glycol and mix well.
5. Add the polysorbate 80 and mix well.
6. Incorporate the gel vehicle into the piroxicam mixture geometrically and mix until uniform.
7. Add sufficient 70% isopropyl alcohol to volume and mix well.
8. Package and label.

**Topical Cream Example:**

<table>
<thead>
<tr>
<th>Rx</th>
<th>Capsaicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsaicin</td>
<td>50 mg</td>
</tr>
<tr>
<td>Methyl salicylate</td>
<td>25 g</td>
</tr>
<tr>
<td>Menthol</td>
<td>2 g</td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td>5 mL</td>
</tr>
<tr>
<td>Dermabase™ qs</td>
<td>100 g</td>
</tr>
</tbody>
</table>

1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh/measure each ingredient.
3. Dissolve the menthol in the methyl salicylate.
4. Mix the capsaicin with the polysorbate 80.
5. Mix the two liquids from steps 3 and 4 together.
6. Slowly incorporate the resulting mixture into the Dermabase.
7. Package and label.

**REFERENCES**


**SUGGESTED READING**