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# the **S Q U A R E**

Healthcare **bulletin**

- ▣ **Burn Management**
- ▣ **Psoriatic Arthritis**
- ▣ **Guillain-Barre Syndrome**



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### Editorial



Dear Doctor,

We welcome you to this addition of "the SQUARE" healthcare bulletin!

As this is the first issue of 2015, we take this opportunity to offer our best wishes from the editorial team of "the SQUARE"! We present this bulletin in a new look this year!

In this issue we have presented a blend of topics. Firstly, we focused on "Burn Management". It is likely that burns are among the most common types of trauma occurring in any society. Even smaller burns may cause major morbidity, because the injury is very painful and may lead to disfiguring scar formation, primarily hypertrophic scarring. This article provides a basic overview of burn care. We have emphasized on "Psoriatic Arthritis", a type of arthritic inflammation that occurs in about 15 percent of patients who have a skin rash called psoriasis. This particular arthritis can affect any joint in the body, and symptoms vary from person to person. Research has shown that persistent inflammation from psoriatic arthritis can lead to joint damage. Fortunately, available treatments are effective for most people. Besides, in this issue, we have presented a feature on "Guillain-Barre Syndrome (GBS)", an acute, usually rapidly progressive but self-limited inflammatory polyneuropathy characterized by muscular weakness and mild distal sensory loss. Cause is thought to be autoimmune. This is currently the most frequent cause of acute flaccid paralysis worldwide and constitutes one of the serious emergencies in neurology. You will also find our regular feature "Test Yourself" and "Product Profile" in this issue.

We hope that you will find this issue both interesting and informative.

On behalf of the management of SQUARE we wish you all healthy, prosperous and long lives!

Thank you!



**Omar Akramur Rab**

MARCH 2015 VOL 22 NO.1

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**B**urn is a type of injury to flesh or skin caused by heat, electricity, chemicals, friction or radiation. Burns that affect only the superficial skin are known as superficial or first-degree burns. When damage penetrates into some of the underlying layers, it is a partial-thickness or second-degree burn. In a full-thickness or third-degree burn, the injury extends to all layers of the skin. A fourth-degree burn additionally involves injury to deeper tissues, such as muscle or bone.

The treatment required depends on the severity of the burn. Superficial burns may be managed with little more than simple pain relievers, while major burns may require prolonged treatment in specialized burn centers. Cooling with tap water may help relieve pain and decrease damage; however, prolonged exposure may result in low body temperature. Partial-thickness burns may require cleaning with soap and water, followed by dressings. It is not clear how to manage blisters, but it is probably reasonable to leave them intact. Full-thickness burns usually require surgical treatments, such as skin grafting. Extensive burns often require large amounts of intravenous fluid, because the subsequent inflammatory response causes significant capillary fluid leakage and edema. The most common complications of burns are infection and renal failure.

While large burns can be fatal, modern treatments developed since 1960 have significantly improved the outcomes, especially in children and young adults. The long-term outcome is primarily related to the size of burn and the age of the person affected.

### **Epidemiology**

As of 2004, 11 million burns required medical care worldwide and resulted in 300,000 deaths. This makes it the 4<sup>th</sup> leading cause of injuries after motor vehicle collisions, falls, and violence. About 90% of burns occur in the developing world. This has been attributed partly to overcrowding and an unsafe cooking situation. Overall, nearly 60% of fatal burns occur in Southeast Asia with a rate of 11.6 per 100,000.

In the developed world, adult males have twice the mortality as females from burns. This is probably due

to their higher risk occupations and greater risk-taking activities. In many countries in the developing world, however, females have twice the risk of males. This is often related to accidents in the kitchen or domestic violence. In children, deaths from burns occur at more than ten times the rate in the developing than the developed world. Overall, in children it is one of the top fifteen leading causes of death. From the 1980s to 2004, many countries have seen both a decrease in the rates of fatal burns and in burns generally.

### **Developed countries**

An estimated 500,000 burn injuries receive medical treatment yearly in the United States. They resulted in about 3,300 deaths in 2008. Most burns (70%) and deaths from burns occur in males. The highest incidence of fire burns occurs in those 18-35 years old, while the highest incidence of scalds occurs in children less than five years old and adults over 65. Electrical burns result in about 1,000 deaths per year. Lightning results in the death of about 60 people a year. In Europe, intentional burns occur most commonly in middle aged men.

### **Developing countries**

In India, about 700,000 to 800,000 people per year sustain significant burns, though very few are looked after in specialist burn units. The highest rates occur in women 16-35 years of age. Part of this high rate is related to unsafe kitchens and loose-fitting clothing typical to India. It is estimated that one-third of all burns in India are due to cloth-catching fire from open flames. Intentional burns are also a common cause and occur at high rates in young women, secondary to domestic violence and self-harm.

### **Pathophysiology**

At temperatures greater than 44 °C (111 °F), proteins begin losing their three-dimensional shape and start breaking down. This results in cell and tissue damage. Many of the direct health effects of a burn are secondary to disruption in the normal functioning of the skin. They include disruption of the skin's sensation, ability to prevent water loss through evaporation, and ability to control body temperature. Disruption of cell membranes causes cells to lose potassium to the spaces outside the cell and to take up water and sodium.

In large burns (over 30% of the total body surface area), there is a significant inflammatory response. This results in increased leakage of fluid from the capillaries, and subsequent tissue edema. This causes overall blood volume loss, with the remaining blood suffering significant plasma loss, making the blood more concentrated. Poor blood flow to organs such as the kidneys and gastrointestinal tract may result in renal failure and stomach ulcers.

Increased levels of catecholamines and cortisol can cause a hypermetabolic state that can last for years. This is associated with increased cardiac output, metabolism, a fast heart rate, and poor immune function.

### **Initial Evaluation and Resuscitation**

Before management of the burn wound, the patient should be properly and completely evaluated. Often, this is a brief effort, particularly in patients with small, uncomplicated wounds. In those with larger burns, evaluation of the wound is often of secondary importance. As described by the American College of Surgeons Committee on Trauma, evaluation of the burn patient is organized into a primary survey and secondary survey.

#### **Primary survey**

Burn patients should be systematically evaluated using the methodology of the American College of Surgeons Advanced Trauma Life Support course. This evaluation is described by the primary survey, with its emphasis on support of the airway, gas exchange, and circulatory stability. Evaluation of airways is an area of particular importance in burn patients. Early recognition of impending airway compromise, followed by prompt intubation, can be lifesaving. Obtain appropriate vascular access and place monitoring devices, then complete a systematic trauma survey, including indicated radiographs and laboratory studies.

#### **Secondary survey**

Burn patients should then undergo a burn-specific secondary survey, which should include a determination of the mechanism of injury, an evaluation for the presence or absence of inhalation injury and carbon monoxide intoxication, an examination for corneal burns, the consideration of

the possibility of abuse, and a detailed assessment of the burn wound.

Of particular importance is eliciting a detailed history upon first evaluation and transmitting this information with the patient to the next level of care. Inhalation injury is diagnosed based on a history of a closed-space exposure and soot in the nares and mouth. Carbon monoxide intoxication is probable in persons injured in structural fires, particularly if they are obtunded; carboxyhemoglobin levels can be misleading in those ventilated with oxygen. Persons with facial burns should undergo a careful examination of the cornea prior to the development of lid swelling that can compromise examination. After evaluation of the burn wound, begin fluid resuscitation and make decisions concerning outpatient or inpatient management or transfer to a burn center.

#### **Fluid resuscitation**

Burn patients demonstrate a graded capillary leak, which increases with injury size, delay in initiation of resuscitation and the presence of inhalation injury for the first 18-24 hours after injury. Because the changes are different in every patient, fluid resuscitation can only be loosely guided by formulas. The inherent inaccuracy of formulas requires continuous re-evaluation and adjustment of infusions based on resuscitation targets.

Most formulas recommend that all crystalloids should be isotonic during the first 24 hours, generally lactated Ringer's solution. In smaller children, whose gluconeogenic capacity is immature, hypoglycemia is a threat and Ringer's lactated solution with 5% dextrose should be added at a maintenance rate.

The modified Brooke or Parkland formulas are reasonable consensus formulas and are used to help determine the initial volume of infusion. Half of the total calculated 24-hour volume is administered in the first 8 hours post injury. Should the resuscitation be delayed, this volume is administered so that infusion is completed by the end of the eighth hour post injury. After 18-24 hours, capillary integrity generally returns and fluid administration should be decreased, following resuscitation endpoints. At this point, colloid administration is useful.

As a general rule, burns over less than 15% of the body surface area are not associated with an extensive capillary leak, and children with burns of this size can be treated with fluid administered at 150% of a calculated maintenance rate and close observation of their hydration status. Those who are able and willing to take fluid by mouth may be given fluid by mouth, with additional fluid administered intravenously at a maintenance rate.

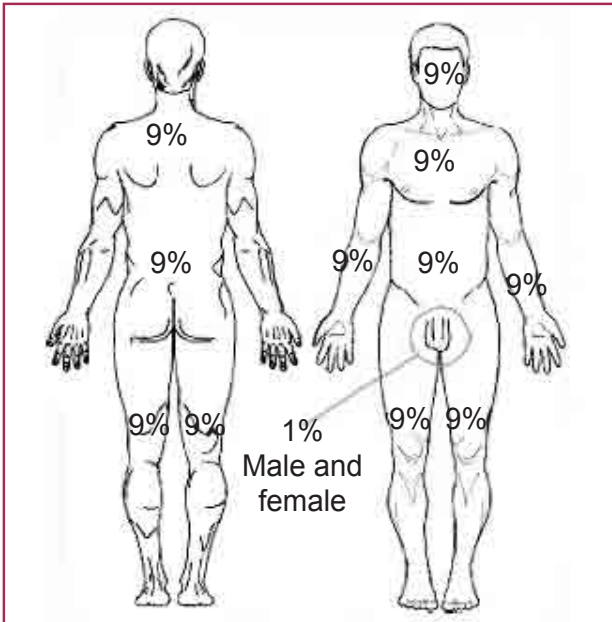


Figure : Wallace's "Rule of 9's" to assess burnt surface area

Pigmented urine is commonly seen in the setting of high-voltage or very deep thermal injury. This pigment should be cleared promptly to avoid renal failure. This can usually be achieved through the administration of additional crystalloid. The administration of bicarbonate may facilitate clearance of myoglobin by preventing its entry into the tubular cells. In rare circumstances, loop diuretics or mannitol can be useful, but this obscures urine output as a valid indicator of circulating volume.

Electrolyte levels should be carefully monitored and corrected. Cerebral edema and seizures can occur with severe hyponatremia, and rapid correction of hyponatremia may result in central pontine demyelinating lesions. Serum sodium, potassium, ionized calcium, phosphate and

magnesium levels should be monitored and kept within physiologic range. Ideally, enteral feeding is begun during resuscitation, except in patients with massive injuries or those who are under-resuscitated and less likely to tolerate tube feedings because of ileus secondary to splanchnic underperfusion.

### Assessment of Burnt Surface Area

- ❑ The "Rule of 9's" is commonly used to estimate the burnt surface area in adults.
- ❑ The body is divided into anatomical regions that represent 9% (or multiples of 9%) of the total body surface. The outstretched palm and fingers approximates to 1% of the body surface area.
- ❑ Morbidity and mortality rises with increasing burnt surface area. It also rises with increasing age so that even small burns may be fatal in elderly people.
- ❑ The 'Rule of 9's' method is too imprecise for estimating the burnt surface area in children because the infant or young child's head and lower extremities represent different proportions of surface area than in an adult.
- ❑ Burns greater than 15% in an adult, greater than 10% in a child, or any burn occurring in the very young or elderly are serious.

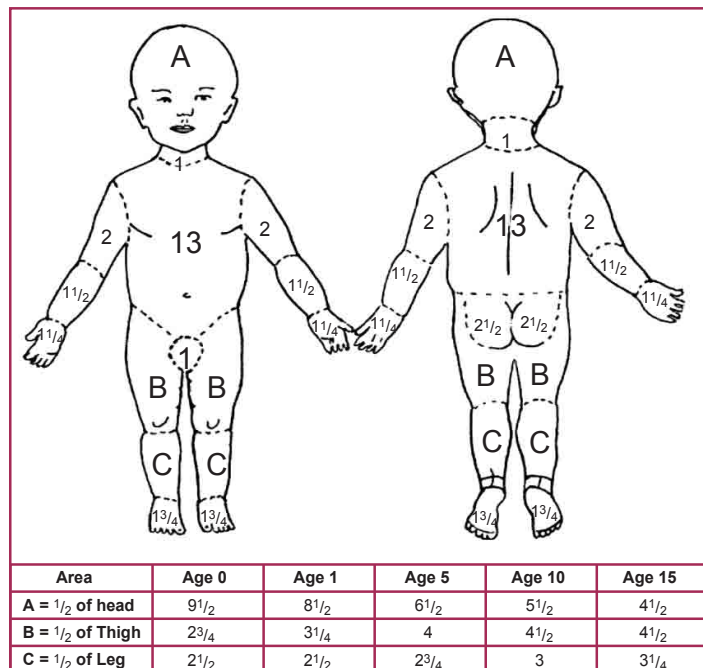


Figure : Lund and Browder chart to assess burnt surface area in children

## Depth of Burn

Burn depths are routinely underestimated during the initial examination. Devitalized tissue may appear viable for some time after injury, and often, some degree of progressive microvascular thrombosis is observed on the wound periphery. Consequently, the wound appearance changes over the days following injury. Serial examination of burn wounds can be very useful.

Burn depth is classified as first, second, third, or fourth degree, as follows:

- ❑ First-degree burns are usually red, dry, and painful. Burns initially termed first-degree are often actually superficial second-degree burns, with sloughing occurring the next day.



Figure : First-degree burn

- ❑ Second-degree burns are often red, wet, and very painful. Their depth, ability to heal, and propensity to form hypertrophic scars vary enormously.



Figure : Second-degree burn

- ❑ Third-degree burns are generally leathery in consistency, dry, insensate, and waxy. These wounds will not heal, except by contraction and limited epithelial migration, with resulting

hypertrophic and unstable cover. Burn blisters can overlie both second- and third-degree burns. The management of burn blisters remains controversial, yet intact blisters help greatly with pain control. Blister should be removed if infected.



Figure : Third-degree burn

- ❑ Fourth-degree burns involve underlying subcutaneous tissue, tendon or bone. Usually, even an experienced examiner has difficulty accurately determining burn depth during early examination. As a general rule, burn depth is underestimated upon initial examination.

## Indications for Hospitalization

- ❑ Greater than 15% burns in an adult
- ❑ Greater than 10% burns in a child
- ❑ Any burn in the very young, the elderly or the infirm
- ❑ Any full thickness burn
- ❑ Burns of special regions: face, hands, feet, perineum
- ❑ Circumferential burns
- ❑ Inhalation injury
- ❑ Associated trauma or significant pre-burn illness: e.g. diabetes, kidney disease

## Wound Care

### a. First aid :

- ❑ If the patient arrives at the health facility without first aid having been given, the burnt area should be thoroughly cooled with water to prevent further damage and all burnt clothing should be removed.

- ❑ If the burn area is limited, the burnt site should be immersed in cold water for 30 minutes to reduce pain and edema and to minimize tissue damage.



Figure : Burn dressing

- ❑ If the area of the burn is large, after it has been doused with cool water, clean wraps should be applied about the burnt area (or the whole patient) to prevent hypothermia.
- ❑ Hypothermia is a particular risk in young children.
- ❑ First 6 hours following injury are critical in the patients with severe burns; they must be transported to a hospital as soon as possible.

### b. Initial treatment :

- ❑ Initially, burns are sterile; should be focussed treatment on speedy healing and prevention of infection.
- ❑ In all cases, tetanus prophylaxis should be administered.
- ❑ Except in very small burns, adherent necrotic tissues should be debrided over the first several days.
- ❑ After debridement, the burn should be cleaned with 0.25% chlorhexidine solution, 0.1% cetrimide solution or another mild water-based antiseptic.
- ❑ Alcohol-based solutions should not used.
- ❑ Gentle scrubbing will remove the loose necrotic

tissue; a thin layer of antibiotic (silver sulfadiazine) should be applied thereafter.

- ❑ The burnt area should be dressed with petroleum gauze and dry gauze thick enough to prevent seepage to the outer layers.

### c. Daily treatment

- ❑ The dressing is needed to change daily or as often as necessary to prevent seepage through the dressing. On each dressing change any loose tissue should be removed.
- ❑ The wounds should be inspected for discoloration or hemorrhage, which indicate developing infection.
- ❑ Fever is not a useful sign as it may persist until the burn wound is closed.
- ❑ Cellulitis in the surrounding tissue is a better indicator of infection.
- ❑ Systemic antibiotics are needed in cases of haemolytic streptococcal wound infection or septicemia.
- ❑ *Pseudomonas aeruginosa* infection often results in septicemia and death.
- ❑ Topical antibiotic after each dressing.
- ❑ Silver sulfadiazine has limited eschar penetration and may cause neutropenia.
- ❑ Mafenide acetate is used without dressings. It penetrates eschar but causes acidosis.
- ❑ Burnt hands should be treated with special care to preserve function.
  - The hands should be covered with silver sulfadiazine and placed them in loose polythene gloves or bags secured at the wrist with a crepe bandage.
  - The hands should be elevated for the first 48 hours and then followed by hand exercise.
  - The gloves should be removed at least once a day to inspect the wound and apply antibiotic.
  - If skin grafting is necessary, treatment by a specialist is needed after healthy granulation tissue appears.

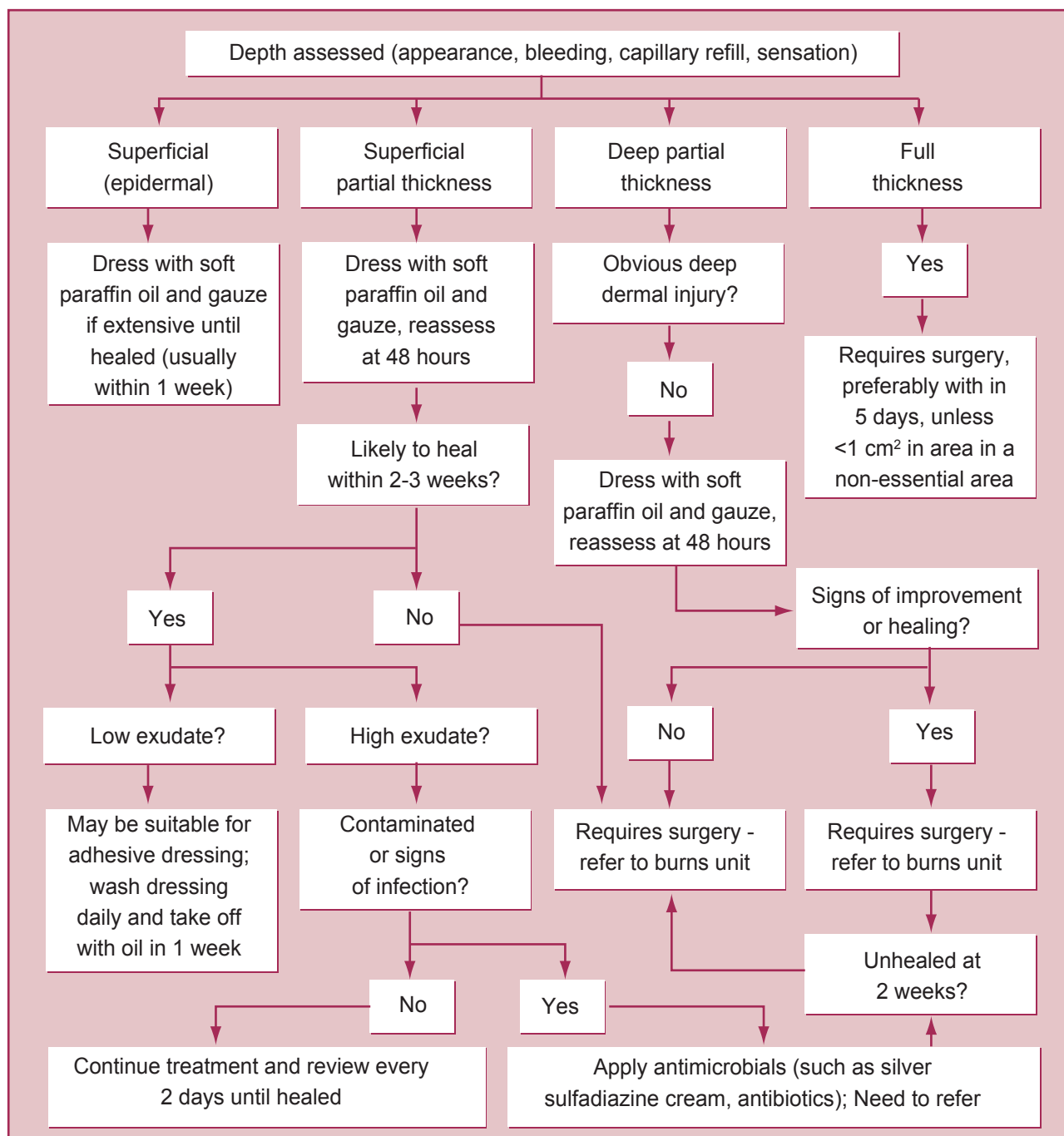


Figure : Algorithm of management of burn

## Surgery

Wounds requiring surgical closure with skin grafts or flaps (typically anything more than a small full thickness burn) should be dealt with as early as possible. Circumferential burns of the limbs or chest may need urgent surgical release of the skin, known as escharotomy. This is done to treat or prevent problems with distal circulation, or ventilation. It is uncertain if it is useful for neck or digit burns. Fasciotomies may be required for electrical burns.

## Complications

A number of complications may occur, with infections being the most common. Other potential complications include renal failure: pneumonia, cellulitis, urinary tract infections and respiratory failure. Risk factors for infection include: burns of more than 30% TBSA, full-thickness burns, extremes of age (young or old), or burns involving the legs or perineum. Pneumonia occurs particularly commonly in those with inhalation injuries.



Anemia secondary to full thickness burns of greater than 10% TBSA is common. Electrical burns may lead to compartment syndrome or rhabdomyolysis due to muscle breakdown. Blood clotting in the veins of the legs is estimated to occur in 6 to 25% of people. The hypermetabolic state that may persist for years after a major burn can result in a decrease in bone density and a loss of muscle mass. Keloids may form subsequent to a burn, particularly in those who are young and dark skinned.

Following a burn, children may have significant psychological trauma and experience post-traumatic stress disorder. Scarring may also result in a disturbance in body image. In the developing world, significant burns may result in social isolation, extreme poverty and child abandonment.

## Rehabilitation

The final phase of burn care is rehabilitation and reconstruction. As survival has improved, this field has evolved rapidly and becoming highly specialized. Therapy should begin in the critical care setting with giving priorities that include :

- ❑ Ranging
- ❑ Splinting and
- ❑ Antideformity positioning

Ranging is ideally performed twice daily with the therapist taking all joints through a passive range of motion. These activities help to prevent the occurrence of many common contractures. As the seriously burnt patient begins to recover, priorities should be focused on continuing passive ranging, increasing active ranging and strengthening, minimizing edema, pursuing activities of daily living, and preparing for work or play and school.

Important aspects of rehabilitation after discharge include ongoing and progressive ranging and strengthening, postoperative therapy after reconstructive operations and scar management. The most difficult hypertrophic scarring is seen in deep dermal burns that heal spontaneously in less than 3 weeks. Therapies should be focused to minimize hypertrophic scarring that began as soon as the burns are

well healed. Therapies also include scar massage, compression garments, topical silicone, steroid injections and management of pruritus.

If the patients participate in a coordinated multi-disciplinary burn aftercare program, most of them will be satisfying long-term outcomes.

## Summary

- ❑ Full thickness injuries have no regenerative elements left. Unless they are very small they will take weeks to heal and undergo severe contraction. They should be referred for surgery as early as possible.
- ❑ Deep dermal injuries are unlikely to heal within three weeks. The incidence of unsightly hypertrophic scarring rises from 33% to 78% if healing is delayed from three to six weeks. Therefore these injuries should also be excised and grafted within the first 5-10 days.
- ❑ Superficial wounds should heal by regeneration within two weeks. They should be cleaned, dressed, and reviewed on alternate days to optimise the wound healing environment. Any burn not healed within two weeks should be referred for assessment.

## References:

- ❑ Burn - Wikipedia
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- ❑ Medscape.com
- ❑ BMJ VOLUME 329 17 JULY 2004

**P**soriatic arthritis is a sero-negative arthritis. It can develop at any time, but it most commonly appears between the ages of 30 and 50. Genes, the immune system and environmental factors are all believed to play a role in the onset of the disease. Early recognition, diagnosis and treatment of psoriatic arthritis are critical to relieve pain and inflammation and help prevent progressive joint damage. Effective treatment for psoriatic arthritis can relieve pain, reduce swelling, help keep joints working properly and possibly prevent further joint damage. Research continues to show a link between psoriatic arthritis and several other serious health conditions such as cardiovascular disease, diabetes and depression.

## Epidemiology

- ❑ Psoriatic arthritis is thought to occur in up to 1% of the general population but prevalence rates vary widely among studies.
- ❑ Since the late 20th century, the incidence of psoriatic arthritis appears to have been rising in men and women. Reasons for the increase are unknown; it may be related to a true change in incidence or to a greater overall awareness of the diagnosis by physicians.
- ❑ The number of diagnosed cases of psoriasis and psoriatic arthritis has risen dramatically in sub-Saharan Africa in association with the area's escalating epidemic of HIV infection.
- ❑ Race predilection in psoriatic arthritis has not been well studied. However, whites are known to be affected more commonly than are persons of other racial groups.
- ❑ Psoriatic arthritis characteristically develops in middle aged persons, but it can occur at almost any age. In the juvenile form, the age of onset is 9-11 years.
- ❑ The male-to-female ratio for psoriatic arthritis is 1:1, with the exception of some subsets of patients. Females, however, are more commonly affected with symmetrical polyarthritis resembling RA and the juvenile form. In contrast, the spondylitic form of psoriatic arthritis, which affects the axial spine, has a male-to-female ratio of 3:1.

## Etiopathogenesis

The etiology of psoriatic arthritis remains unknown, but much information has been gathered.

- ❑ Genetic factors play an important role in susceptibility to psoriasis and psoriatic arthritis; approximately 40% of patients with either of these conditions have a family history of them in first-degree relatives.
- ❑ Comparing psoriasis with psoriatic arthritis, it has been found that in psoriatic arthritis there is a stronger association with HLA-B alleles than with HLA-C alleles, while psoriasis (particularly early onset psoriasis) is associated with HLA-C.



Figure : Psoriasis of the knee

- ❑ Autoantibodies against nuclear antigens, cytokeratin, epidermal keratins and heat-shock proteins have been reported in persons with psoriatic arthritis, indicating that the disease has a humoral immune component.
- ❑ The pathologic process of skin and joint lesions in psoriatic arthritis is an inflammatory reaction, and evidence also indicates the presence of autoimmunity, perhaps mediated by complement activation. The inflammatory nature of the skin and joint lesions in psoriatic arthritis is demonstrated by synovial-lining cell hyperplasia and mononuclear infiltration, resembling the histopathologic changes of RA. However, synovial-lining hyperplasia is less, macrophages are fewer, and vascularity is greater in psoriatic arthritis than in RA synovium.
- ❑ The cytokine profile for psoriatic arthritis reflects a complex interplay between T cells and monocyte

macrophages. Type 1 helper T-cell cytokines (eg, TNF-alpha, IL-1 beta, IL-10) are more prevalent in psoriatic arthritis than in RA, suggesting that these 2 disorders may result from a different underlying mechanism.

- Dendritic cells have been found in the synovial fluid of patients with psoriatic arthritis and are reactive in the mixed leukocyte reaction; the inference is that the dendritic cells present an unknown antigen to CD4+ cells within the joints and skin of patients with psoriatic arthritis, leading to T-cell activation.



Figure : Sausage-shaped fingers in Psoriatic Arthritis

- Fibroblasts from the skin and synovia of patients with psoriatic arthritis have an increased proliferative activity and the capability to secrete increased amounts of IL-1, IL-6, and platelet-derived growth factors. Several studies suggest that cytokines secreted from activated T cells and other mononuclear proinflammatory cells induce proliferation and activation of synovial and epidermal fibroblasts.
- The temporal relationship between certain viral and bacterial infections and the development or exacerbation of psoriasis and psoriatic arthritis suggests a possible pathogenetic role for viruses and bacteria.
- Psoriasis and psoriatic arthritis have been reported to be associated with HIV infection and to be prevalent in some HIV-endemic areas. Although the prevalence of psoriasis in patients infected with HIV is similar to that in the general population, patients with HIV infection usually have more extensive erythrodermic psoriasis, and patients with psoriasis may present with

exacerbation of their skin disease after being infected with HIV.

- The theory of environmental factors playing a role in the etiology of psoriatic arthritis involves a process of superantigens reacting with autoantigens.

## Clinical Features

Psoriasis appears to precede the onset of psoriatic arthritis in 60-80% of patients. However, in as many as 15-20% of patients, arthritis appears before the psoriasis, in which case a family history of psoriasis may reveal a hereditary pattern. Occasionally, arthritis and psoriasis appear simultaneously.

- In some cases, patients may experience only stiffness and pain, with few objective findings. In a patient who presents with musculoskeletal symptoms without a history of psoriasis, the diagnosis can be suspected based on a family history of psoriasis and the pattern of arthritis. One third of patients may develop inflammatory ocular symptoms reminiscent of reactive arthritis
- Recognition of the patterns of joint involvement, as follow, is essential to the diagnosis of psoriatic arthritis: asymmetrical oligoarticular arthritis, symmetrical polyarthritis, distal interphalangeal arthropathy, arthritis mutilans, spondylitis with or without sacroiliitis.
- As in other spondyloarthropathies, the condition termed enthesopathy or enthesitis, reflecting inflammation at tendon or ligament insertions into bone, may be seen in psoriatic arthritis. Enthesopathy is observed more often at the attachment of the Achilles tendon and the plantar fascia to the calcaneus with the development of insertional spurs.
- Dactylitis with sausage digits occurs in as many as 35% of patients. Diagnosis is also suggested by asymmetrical joint involvement, dactylitis, the absence of RF, and DIP involvement in the absence of osteoarthritis. When localized to the foot or toe, the symptoms of psoriatic arthritis may be mistaken for gout.
- Skin lesion that are seen in the context of psoriatic arthritis include: scaly, erythematous plaques, guttate lesions, pustules, erythroderma.

- ❑ Nails are involved in 80% of patients with psoriatic arthritis but in only 20% of patients with uncomplicated psoriasis. The changes in the nails that support the diagnosis of psoriatic arthritis are: Beau lines, leukonychia, onycholysis, oil spots, subungual hyperkeratosis, splinter hemorrhages, spotted lunulae, transverse ridging, cracking of the free edge of the nail and Uniform nail pitting.
- ❑ Extra-articular features are observed less frequently in patients with psoriatic arthritis than in those with RA. In patients with psoriatic arthritis, synovitis has a predilection for the flexor tendon sheath, with sparing of the extensor tendon sheath; both tendon sheaths are commonly involved in persons with RA.
- ❑ Subcutaneous nodules are rare in patients with psoriatic arthritis.
- ❑ Ocular involvement may occur in 30% of patients with psoriatic arthritis, including conjunctivitis in 20% of patients and acute anterior uveitis in 7% of them. In patients with uveitis, 43% have sacroiliitis and 40% are HLA-B27-positive. Scleritis and keratoconjunctivitis sicca are rare. Possible ocular findings also include iritis.
- ❑ Inflammation of the aortic valve root, which may lead to insufficiency, has been described in patients with psoriatic arthritis and is similar to that observed more frequently in persons with ankylosing spondylitis or reactive arthritis. Occasionally, patients with psoriatic arthritis may develop secondary amyloidosis.

## Investigations

- ❑ An elevated ESR is found in approximately 40% of patients with psoriatic arthritis.
- ❑ Patients with psoriatic arthritis are typically

seronegative for RF, although RF is detected in 5-9% of patients.

- ❑ Antinuclear antibody titers in persons with psoriatic arthritis do not differ from those of age and sex-matched controls in 10-20% of patients with generalized skin disease, the serum uric acid concentration may be increased and, on occasion, may predispose patients to acute gouty arthritis.
- ❑ Serum IgA levels are increased in two thirds of patients with psoriatic arthritis and in one third of patients with psoriasis.



### Psoriatic arthritis associated with

- 1) abnormality in DIP joint of 1<sup>st</sup> and 2<sup>nd</sup> fingers
- 2) Early changes in DIP joint of 4<sup>th</sup> finger
- 3) Other changes: ankylosis in DIP joint of 5<sup>th</sup> finger

Figure : X-ray of Psoriatic Arthritis in hands

- ❑ The histopathology of psoriatic synovitis is similar to that observed in other inflammatory arthritides, with a notable lack of intrasynovial immunoglobulin and RF production and a greater propensity for fibrous ankylosis, osseous resorption, and heterotopic bone formation.
- ❑ X-ray features have helped to distinguish psoriatic arthritis from other causes of polyarthritis. Early bony erosions occur at the cartilaginous edge, and cartilage initially is preserved, with maintenance of a normal joint space. Juxta-articular osteopenia, which is a hallmark of RA, is minimal in persons with psoriatic arthritis. Asymmetrical erosive changes in the small joints of the hands and feet are typical of psoriatic arthritis and have a predilection (in decreasing order) for the DIP, PIP, MTP, MCP.

The pencil-in-cup deformity observed in the hands and feet of patients with severe joint disease usually affects the DIP joints but also may involve the proximal interphalangeal joints.

- ❑ Computed tomography (CT) scanning and MRI may be useful for detecting early signs of joint synovitis. MRI is particularly sensitive for detecting sacroiliitic synovitis, enthesitis, and erosions; it can also be used with gadolinium to increase sensitivity. MRI may show inflammation in the small joints of the hands, involving the collateral ligaments and soft tissues around the joint capsule, a finding not found in persons with RA.
- ❑ Ultrasonography has a somewhat undefined, but emerging, role in the diagnosis and management of psoriatic arthritis, including the differentiation of synovitis and enthesitis, accurate and objective monitoring of disease activity, and accurate delivery of local therapy.

### Management

The treatment of psoriatic arthritis is directed at controlling the inflammatory process. Psoriasis of skin, when present, must be treated simultaneously.

### EULAR recommendations

The European League Against Rheumatism (EULAR) developed 10 treatment recommendations, 5 overarching principles, and a research agenda for psoriatic arthritis. The recommendations are as follows:

- ❑ NSAIDs can be administered for the relief of musculoskeletal signs and symptoms.
- ❑ Treatment with disease-modifying anti-rheumatic drugs (DMARDs) should be considered at an early stage for patients with active disease.
- ❑ If a patient with active psoriatic arthritis also has clinically relevant psoriasis, preference should be given to treatment with methotrexate or other disease-modifying drugs that are also effective against psoriasis
- ❑ Adjunctive treatment with local corticosteroid injections should be considered; cautious use of systemic steroids, if administered at the lowest effective dose, can also be considered.

- ❑ If active psoriatic arthritis fails to adequately respond to one or more DMARDs, TNF inhibitor therapy should be employed
- ❑ TNF-inhibitor therapy should also be considered if a patient with active enthesitis and/or dactylitis does not show sufficient response to NSAIDs or local steroid injections
- ❑ TNF-inhibitor therapy should be considered if a patient has active, predominantly axial disease that does not respond sufficiently to NSAIDs
- ❑ Exceptional use of TNF-inhibitor therapy may be considered if a very active patient is disease-modifying-treatment naïve
- ❑ If a TNF inhibitor produces an inadequate response, consideration should be given to replacing it with another TNF inhibitor
- ❑ If adjustments are made in a patient's therapy, then co-morbidities, safety concerns and other considerations beyond the psoriatic arthritis itself should be factored into the change

### Pharmacotherapy

Medical treatment regimens include the use of NSAIDs and DMARDs.

DMARDs include methotrexate, sulfasalazine, cyclosporine, and leflunomide, as well as biologic agents (eg, anti-TNF medications, IL-12 or IL-23 antibodies).

In September 2013, the FDA and the European Union approved ustekinumab, an interleukin-12/23 inhibitor, for the treatment of active psoriatic arthritis in adults who have not responded adequately to previous treatment with non-biologic DMARDs. The drug was already approved in Europe and the United States for treatment of moderate to severe psoriatic plaques in adults. In the same month, the FDA also approved the TNF inhibitor certolizumab for the treatment of active psoriatic arthritis in adults.

Apremilast, was approved in March 2014 by the FDA for treatment of active psoriatic arthritis. It is a phosphodiesterase-4 (PDE4) inhibitor that is specific for cAMP, resulting in increased intracellular cAMP levels.

In patients with severe skin inflammation, medications such as methotrexate, retinoic acid derivatives, and psoralen plus ultraviolet (UV) light should be considered. These agents have been shown to work on skin and joint manifestations.

Intra-articular injection of entheses or single inflamed joints with corticosteroids may be particularly effective in some patients.

In a study completed by the Psoriatic Arthritis Study Group, patients with psoriasis and psoriatic arthritis who were receiving stable doses of methotrexate were found to benefit from the addition of 1 or more courses of intramuscular alefacept, a T-cell inhibitor via a human lymphocyte function-associated antigen 3 (LFA-3) Fc fusion protein that blocks the interaction between CD2 on T cells and LFA-3 on antigen-presenting cells. Further benefit in psoriatic arthritis was apparent after a second course of alefacept, and no additional toxicity was observed.

Sulfasalazine and cyclosporine are 2 second-line DMARDs that have received particular attention in the management of psoriatic arthritis.

Cyclosporine appears to be an effective agent for the treatment of psoriasis and psoriatic arthritis. The major concern with this drug is its toxicity, especially its nephrotoxicity, and hypertension.

Combination therapy (eg, methotrexate / sulfasalazine, methotrexate / cyclosporine) may be more efficacious in some patients.

Antimalarials, particularly hydroxychloroquine, are usually avoided in patients with psoriasis for fear of precipitating exfoliative dermatitis or exacerbating psoriasis.

Systemic corticosteroids are usually avoided because of possible rebound of the skin disease upon withdrawal.

## Physical Therapy

The rehabilitation treatment program for patients with psoriatic arthritis should be individualized and should be started early in the disease process. Such a program should consider the use of the following:

- ❑ Rest
- ❑ Heat and cold therapy for pain
- ❑ Orthotics
- ❑ Vocational re-adjustments

## Synovectomy and Arthroplasty

Currently, no prospective studies are addressing surgical intervention in patients with psoriatic arthritis. Patients in severe pain or with significant contractures may be referred for possible surgical intervention. Treatment should be aimed at pain relief or increasing the patient's function.

Arthroscopic synovectomy has been effective in treating severe, chronic, monoarticular synovitis.

Joint replacement is occasionally necessary. Hip and knee joint replacements have been successful, for the most part, in patients with psoriatic arthritis. Arthrodesis and arthroplasty have also been used on joints, such as the proximal interphalangeal joint of the thumb. The wrist often spontaneously fuses, and this may relieve the patient's pain without surgical intervention.

For arthritis mutilans, surgical intervention is usually directed toward salvage of the hand. Combinations of arthrodesis, arthroplasty, and bone grafts to lengthen the digits may be used.

## Prognosis

Although psoriatic arthritis was originally thought to be relatively mild, as many as 40% of patients may develop erosive and deforming arthritis. Of patients observed in a large outpatient psoriatic arthritis clinic, 7% required musculoskeletal surgery.

## Reference:

- ❑ [emedicine.medscape.com](http://emedicine.medscape.com)

**G**uillain-Barre Syndrome (GBS) may be described as a collection of clinical syndromes that manifests as an acute inflammatory polyradiculoneuropathy with resultant weakness and diminished reflexes. Since poliomyelitis has nearly been eliminated, the Guillain-Barre Syndrome is currently the most frequent cause of acute flaccid paralysis worldwide and constitutes one of the serious emergencies in neurology. Though it is said that the Guillain-Barre Syndrome has a favorable prognosis, up to 20% of patients remain severely disabled and death occurs in approximately 5% cases.

### Epidemiology

- ❑ In 1859, Landry published a report on 10 patients with an ascending paralysis
- ❑ GBS has been reported throughout the international community; no racial preponderance exists
- ❑ GBS has a male-to-female ratio of 1.5:1; male preponderance is especially seen in older patients
- ❑ It may occur in all age groups

### Etiology

GBS is considered to be a post-infectious, immune-mediated disease targeting peripheral nerves. Up to two-thirds of patients report an antecedent bacterial or viral respiratory or gastrointestinal illness prior to the onset of neurological symptoms. Administrations of certain vaccinations and other systemic illnesses have also been associated with GBS.

- ❑ In several clinical studies, *Campylobacter jejuni* was the most commonly isolated pathogen in GBS; serological studies in a Dutch GBS trial identified 32% of patients with a recent infection, while studies in northern China documented infection rates as high as 60%; *Campylobacter jejuni* infections can also have a subclinical course, resulting in patients with no reported infectious symptoms prior to the development of GBS.
- ❑ Cytomegalovirus (CMV) infections are the second most commonly reported infections preceding GBS, with CMV being the most common viral trigger of GBS. The aforementioned Dutch GBS

study found CMV to be present in 13% of patients

- ❑ Epstein-Barr virus (EBV), *Mycoplasma pneumoniae*, varicella-zoster virus (VZV) and human immunodeficiency virus (HIV) are less frequently identified infectious agents in GBS patients; infections with *Haemophilus influenzae*, *Borrelia burgdorferi*, para-influenza virus type 1, influenza A virus, influenza B virus, adenovirus, and herpes simplex virus have been demonstrated in patients with GBS, but not more frequently than in controls.
- ❑ Vaccinations have been linked to GBS by temporal association; in most cases no definite causal relation has been established between vaccines and GBS (with the exception of rabies vaccine prepared from infected brain tissue and the 1976 mass immunization against a new H1N1 swine flu); large studies have failed to establish any statistically significant causal relationship between administration of the measles vaccine and GBS
- ❑ No definite cause-effect relationships have been established among drugs and GBS; a study indicated that antibiotic therapy with fluoroquinolones also is associated with the development of GBS; case reports exist in the setting of tumor necrosis factor antagonist agents used in rheumatoid arthritis and also in streptokinase, isotretinoin, danazol, captopril, gold and heroin; In a case-controlled study, patients with GBS reported more frequent penicillin and anti-motility drug use and less frequent oral contraceptive use
- ❑ Surgery, trauma, pregnancy, systemic lupus erythematosus, sarcoidosis, lymphoma and snakebite have been reported as possible triggers of GBS, but these associations remain mostly anecdotal.

### Pathophysiology

GBS is a post-infectious immune-mediated disease. Cellular immune mechanism plays an important role in its development. Many of the identified infectious agents are thought to induce production of antibodies that cross-react with specific gangliosides (four types: GM1, GD1a, GT1a, and GQ1b) and

glycolipids that are distributed throughout the myelin in the peripheral nervous system (molecular mimicry).

The pathophysiological mechanism of an antecedent illness and of GBS can be typified by *Campylobacter jejuni* infections. Immune responses directed against lipopolysaccharide antigens in the capsule of *Campylobacter jejuni* result in antibodies that cross-react with ganglioside GM1 in myelin, resulting in immunological damage to the peripheral nervous system.

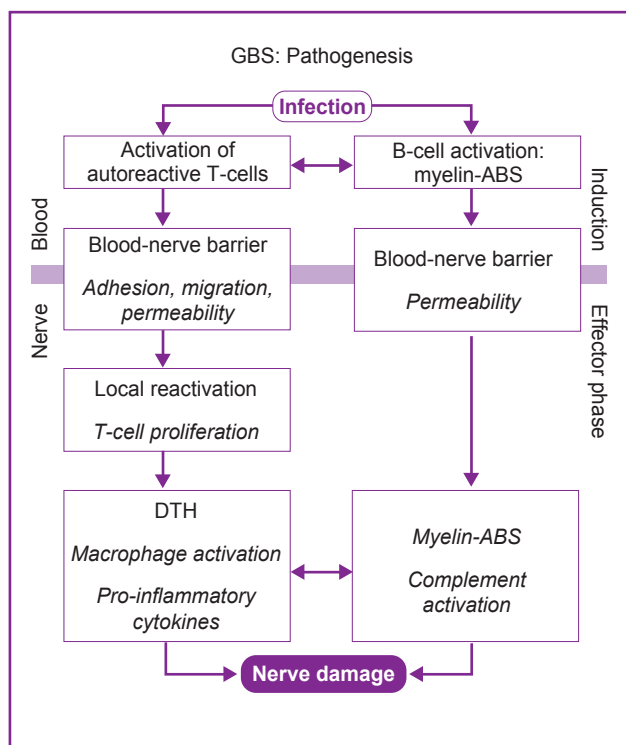


Figure : Pathogenesis of GBS

The classic pathological findings are inflammatory infiltrates consisting mainly of T cells and macrophages. There are also areas of demyelination, often associated with signs of secondary axonal degeneration. Pathological changes can be detected in the spinal roots, as well as in the large and small motor and sensory nerves. There is evidence of early complement activation, which is based on antibody binding to the outer surface of the Schwann cell and deposition of activated complement components. Macrophage invasion is observed within 1 week after complement-mediated myelin damage occurs.

## Variants of Guillain-Barre Syndrome

Several variants of GBS have been recognized. These disorders share similar patterns of evolution, symptom overlap, and probable immune-mediated pathogenesis. Recovery from them varies.

### ❑ Acute inflammatory demyelinating polyneuropathy :

The acute inflammatory demyelinating polyneuropathy (AIDP) subtype is the most commonly identified form in the Europe, North America and the developed world (up to 90% of cases). It is generally preceded by a bacterial or viral infection. Nearly 40% of patients with AIDP are seropositive for *Campylobacter jejuni*. Lymphocytic infiltration and macrophage-mediated peripheral nerve demyelination is the cardinal pathological feature. Symptoms generally resolve with remyelination.

### ❑ Acute motor axonal neuropathy:

The acute motor axonal neuropathy (AMAN) subtype is a purely motor disorder that is more prevalent in pediatric age groups. AMAN is generally characterized by rapidly progressive symmetrical ascending weakness and ensuing respiratory failure. Nearly 70-75% of patients with AMAN are seropositive for *Campylobacter jejuni*. Patients typically have high titers of antibodies to gangliosides (GM1, GD1a, GD1b). Inflammation of the spinal anterior root may lead to disruption of the blood-CNS barrier. Biopsies show Wallerian-like degeneration without significant lymphocytic inflammation. Prognosis is often quite favorable. Recovery is rapid in many cases but severely disabled patients with AMAN may show improvement over a period of years. One third of patients with AMAN may actually be hyperreflexic (significantly associated with the presence of anti-GM1 antibodies).

### ❑ Acute motor-sensory axonal neuropathy :

Acute motor-sensory axonal neuropathy (AMSAN) is a severe acute illness differing from AMAN in that it also affects sensory nerves and roots. Patients are typically adults. AMSAN often presents as rapid and severe motor and sensory dysfunction. Marked muscle wasting is characteristic, and recovery is poorer than it is from electrophysiologically similar cases of AMAN.



As with AMAN, AMSAN is often associated with preceding *Campylobacter jejuni* diarrhea. Pathological findings show severe axonal degeneration of motor and sensory nerve fibers with little demyelination. AMAN and AMSAN occur mainly in northern China, Japan, and Mexico, making up only 5-10% percent of GBS cases in the United States.

#### ❑ **Miller-Fisher syndrome :**

Miller-Fisher syndrome (MFS) appears to be more common among patients with the GBS who live in eastern Asia than among those who live in other parts of the world. It is observed in about 5% of all cases of GBS. Miller-Fisher syndrome classically presents as a triad of ataxia, areflexia and ophthalmoplegia. Acute onset of external ophthalmoplegia is a cardinal feature. Ataxia tends to be out of proportion to the degree of sensory loss. Patients may also have mild limb weakness, ptosis, facial palsy or bulbar palsy. Patients have reduced or absent sensory nerve action potentials and absent tibial H reflex.

Most patients with the Miller Fisher syndrome have evidence of infection 1 to 3 weeks before the development of ophthalmoplegia or ataxia; in one study, 20% of patients had *Campylobacter jejuni* infection and 8% had *Haemophilus influenzae* infection.

Anti-GQ1b antibodies are prominent in MFS, and have a relatively high specificity and sensitivity for the disease. Dense concentrations of GQ1b ganglioside are found in the oculomotor, trochlear, and abducens nerves, which may explain the relationship between anti-GQ1b antibodies and ophthalmoplegia. Patients with acute oropharyngeal palsy carry anti-GQ1b/GT1a IgG antibodies. The disease peaks at a median of 1 week, and improvement often starts at a median of 2 weeks. Recovery from ataxia and recovery from ophthalmoplegia take a median of 1 and 3 months, respectively. By 6 months after the onset of neurologic symptoms, most patients have recovered from ataxia and ophthalmoplegia.

#### ❑ **Acute panautonomic neuropathy :**

Acute panautonomic neuropathy, the rarest GBS

variant, involves the sympathetic and parasympathetic nervous systems. Patients have severe postural hypotension, bowel and bladder retention, anhidrosis, decreased salivation and lacrimation and pupillary abnormalities. Cardiovascular involvement is common and dysrhythmias are a significant source of mortality. Significant motor or sensory involvement is lacking. Recovery is gradual and often incomplete.

#### ❑ **Pure sensory GBS :**

A pure sensory variant of GBS has been described in the literature. It is typified by a rapid onset of sensory loss, sensory ataxia, and areflexia in a symmetrical and widespread pattern. Lumbar puncture studies show albuminocytologic dissociation in the CSF and results from electromyography (EMG) show characteristic signs of a demyelinating process in the peripheral nerves. The prognosis in pure GBS is generally good. Immunotherapies, such as plasma exchange and the administration of IVIGs, can be tried in patients with severe disease or slow recovery.

#### ❑ **Other variants :**

The pharyngeal-cervical-brachial variant of GBS is distinguished by isolated facial, oropharyngeal, cervical, and upper limb weakness without lower limb involvement. There can be combinations of any of the above subtypes, and virtually any combination of nerve injury. There are likely mild cases that cause temporary symptoms, improve spontaneously, and never get definitively diagnosed. Other unusual clinical variants with restricted patterns of weakness are observed only in rare cases.

### **Clinical Presentation**

- ❑ The typical patient with Guillain-Barre Syndrome (GBS) presents 2-4 weeks following a relatively benign respiratory or gastrointestinal illness in most cases. Initial complaints are finger dysesthesia and proximal muscle weakness of the lower extremities; the weakness may progress over hours to days in ascending order to involve the arms, truncal muscles, cranial nerves, and muscles of respiration; variants of GBS may present as pure motor dysfunction or acute dysautonomia

- ❑ **Weakness** : The classic clinical picture of weakness is ascending and symmetrical in nature. The lower limbs are usually involved before the upper limbs. Proximal muscles may be involved earlier than the more distal ones. Trunk, bulbar and respiratory muscles can be affected as well. Severity may range from mild weakness to complete tetraplegia with ventilatory failure.
  - ❑ **Cranial nerve involvement** : Cranial nerve involvement is observed in 45-75% of patients with GBS. Cranial nerves III-VII and IX-XII may be affected. Common complaints include facial droop (may mimic Bell's palsy), ophthalmoplegia, pupillary disturbances. The Miller-Fisher variant of GBS is unique in that this subtype begins with cranial nerve deficits.
  - ❑ **Sensory changes** : Most patients complain of paresthesias, numbness, or similar sensory changes. Sensory symptoms often precede the weakness. Paresthesias generally begin in the toes and fingertips, progressing upward but generally not extending beyond the wrists or ankles. Loss of vibration, proprioception, touch, and pain distally may be present. Sensory symptoms are usually mild. In most cases, objective findings of sensory loss tend to be minimal and variable.
  - ❑ **Pain** : In a prospective, longitudinal study of pain in patients with GBS, 89% of patients reported pain that was attributable to GBS at some time during their illness. On initial presentation, almost 50% of patients described the pain as severe and distressing. The mechanism of pain is uncertain and may be a product of several factors. Pain can result from direct nerve injury or from the paralysis and prolonged immobilization. Dysesthesias frequently are described as burning, tingling, or shock-like sensations and are often more prevalent in the lower extremities than in the upper extremities.
  - ❑ **Autonomic changes** : Tachycardia, bradycardia, facial flushing, paroxysmal hypertension, orthostatic hypotension, anhidrosis and/or diaphoresis.
  - ❑ **Respiratory involvement** : About 40% of patients present with respiratory or oropharyngeal weakness. Typical complaints include dyspnea on exertion, shortness of breath, difficulty swallowing, slurring of speech etc. Ventilatory failure with required respiratory support occurs in up to one third of patients at some time during the course of their disease.
  - ❑ Recovery usually begins 2-4 weeks after cessation of disease progression ceases; the mean time to clinical recovery is 200 days.
- Some patients with atypical presentation, incomplete weakness, and some inconsistencies in their physical examination are frequently diagnosed as having a psychological reaction or hysteria, and the diagnosis is very difficult. They are frequently sent home from the emergency department and then return with persistent or progressive symptoms hours to days later.

### Differential Diagnoses

Clinical conditions mimicking Guillain-Barre Syndrome include acute myelopathy (from compression, transverse myelitis, vascular injury), chronic inflammatory demyelinating polyneuropathy, conversion disorder, human immunodeficiency virus infection, peripheral neuropathy, neurotoxic fish or shellfish poisoning, paraneoplastic neuropathy, poliomyelitis, spinal cord compression, toxic neuropathies (arsenic, thallium, organophosphates, lead), vitamin deficiency (eg, vitamin B-12, folate, thiamine), bilateral lacunar strokes, acute cerebellar ataxia syndromes, posterior fossa structural lesion, multiple sclerosis etc.

### Investigations

Guillain-Barre Syndrome (GBS) is generally diagnosed on clinical grounds. Basic laboratory studies, such as complete blood count, metabolic panels are normal and of limited value. They are often ordered to exclude other diagnoses and to better assess functional status and prognosis. The ordering of specific tests should be guided by the patient's history and presentation. Electromyography and nerve conduction studies can be very helpful in the diagnosis.

### A. To detect the evidence of neuronal involvement :

- Nerve Conduction Studies (NCS) :

Nerve conduction abnormalities have become more prominent during the initial weeks of the disease even if patients clinical status is improving. It may be very helpful in the prognostic evaluation of patients with suspected GBS. Abnormalities in NCS that are consistent with demyelination are sensitive and represent specific findings for classic GBS. Signs of demyelination can include nerve conduction slowing, prolongation of the distal latencies, prolongation or absence of the F-waves, conduction block or dispersion of responses. Changes on NCS should be present in at least 2 nerves in regions that are not typical for those associated with compressive mononeuropathies. In the axonal variant of the disease, absent or markedly reduced distal compound muscle action potential (CMAP) is observed on NCS. On needle examination, profuse and early denervation potentials (fibrillations) also support the conclusion that there has been axonal injury.

- Electromyography (EMG) :

EMG studies carried out in patients of the GBS group showed demyelinating type of polyneuropathy with reduced voluntary motor unit recruitment. Some patients also showed axonal type of polyneuropathy showing denervation pattern.

- Lumber puncture :

Most, but not all, patients with GBS have an elevated CSF protein level (>400 mg/L), with normal CSF cell counts (albuminocytological dissociation). Elevated or rising protein levels on serial lumbar punctures and 10 or fewer mononuclear cells/mm<sup>3</sup> strongly support the diagnosis. A normal CSF protein level does not rule out GBS, however, as the level may remain normal in 10% of patients. CSF protein may not rise until 1-2 weeks after the onset of weakness. Normal CSF cell counts may not be a feature of GBS in HIV-infected patients. CSF pleocytosis is well recognized in HIV-associated GBS.

- Pulmonary Function Tests :

Maximal inspiratory pressures, vital capacity, maximal expiratory pressures are measurements of

neuromuscular function and predict diaphragmatic and abdominal muscle strength. Frequent evaluations of these parameters should be performed at bedside to monitor respiratory status and the need for ventilatory assistance. Forced vital capacity (FVC) is also very helpful in guiding disposition and therapy. Patients with an FVC of less than 15-20 mL/kg, maximum inspiratory pressure of less than 30 cm water, or a maximum expiratory pressure of less than 40 cm water generally progress to require prophylactic intubation and mechanical ventilation. Respiratory assistance should also be considered when there is a decrease in oxygen saturation (arterial partial pressure of oxygen < 70 mm Hg). Negative inspiratory force (NIF) is a relatively easy bedside test to measure respiratory muscle function and can easily be performed every half hour to hour in difficult cases. Normal is usually greater than 60 cm water. If the NIF is dropping or nears 20 cm water, respiratory support needs to be available.

- Magnetic Resonance Imaging :

MRI is sensitive, but nonspecific, for diagnosis. However, it can reveal nerve root enhancement and may be an effective diagnostic adjunct. Spinal nerve root enhancement with Gadolinium is a nonspecific feature seen in inflammatory conditions and is caused by disruption of the blood-nerve barrier. Selective anterior nerve root enhancement appears to be strongly suggestive of GBS, with the cauda equina nerve roots being enhanced in 83% of patients.

- Histology :

Lymphocyte and macrophage infiltration is observed on microscopic examination of peripheral nerves, with macrophage influx believed to be responsible for the multifocal demyelination seen in GBS. Cellular infiltrates are scattered throughout the cranial nerves, nerve roots, dorsal root ganglia and peripheral nerves. A variable degree of Wallerian degeneration also can be observed with severe inflammatory changes.

- Others :

Muscle biopsy may help to distinguish GBS from a primary myopathy in unclear cases. Many different abnormalities may be seen on electrocardiography

(ECG), including second and third-degree atrioventricular (AV) blocks, T-wave abnormalities, ST depression, QRS widening and various rhythm disturbances.

## **B. To exclude differential diagnoses :**

Some other investigations may be required in difficult conditions, such as: thyroid panel, rheumatology profiles, vitamin B-12, folic acid, Hb A1C, liver function tests, serum electrolytes and calcium, creatinine phosphokinase, erythrocyte sedimentation rate (ESR), serum protein electrophoresis, heavy metal screening,

## **C. To detect evidence of recent infectious disease :**

Serologic studies are of limited value in the diagnosis of GBS. Assays for antibodies to the following infectious agents may be considered:

- ❑ *Campylobacter jejuni*
- ❑ Cytomegalovirus
- ❑ Epstein-Barr virus
- ❑ Herpes simplex virus
- ❑ Human Immunodeficiency Virus
- ❑ *Mycoplasma pneumoniae*

Serum autoantibodies are not measured routinely in the work-up of GBS, but results may be helpful in patients with a questionable diagnosis or a variant of GBS.

Antibodies to self-antigens (GM1, GQ1b) are observed in the sera of 60-70% of patients with GBS during the acute phase, with gangliosides being the major target antigens.

Specific antibodies found in association with GBS include the following:

- ❑ Antibodies to GM1 : Frequently found in the sera of patients with the acute motor axonal neuropathy (AMAN) or acute demyelinating polyradiculoneuropathy (AIDP) variants of GBS
- ❑ Anti-GM1 antibodies : Elevated titers are closely associated antecedent *Campylobacter jejuni* infections
- ❑ Anti-GQ1b antibodies : Found in patients with

GBS with ophthalmoplegia, including patients with the Miller-Fisher variant

Other antibodies to different major and minor gangliosides also have been found in GBS patients.

## **Treatment**

Patients who are diagnosed with GBS should be admitted to a hospital for close monitoring until it has been determined that the course of the disease has reached a plateau or undergone reversal. Continued progression may result in a neuromuscular emergency with profound paralysis, respiratory insufficiency, and/or autonomic dysfunction with cardiovascular complications.

Approximately one third of patients require admission to an ICU, primarily because of respiratory failure. After medical stabilization, patients can be treated on a general medical/neurologic floor, but continued vigilance remains important in preventing respiratory, cardiovascular, and other medical complications. Patients with persistent functional impairments may need to be transferred to an in patient rehabilitation unit.

Early recognition and treatment of GBS also may be important in the long-term prognosis, especially in the patient with poor clinical prognostic signs, such as older age, a rapidly progressing course, and antecedent diarrhea.

Immunomodulatory treatment has been used to hasten recovery. Intravenous immunoglobulin (IVIG) and plasma exchange have proved equally effective. Corticosteroids (oral and intravenous) have not been found to have a clinical benefit in GBS. Consequently, this class of drugs is not currently employed in treatment of the syndrome.

Continued care is needed to minimize problems related to immobility, neurogenic bowel and bladder, and pain. Early involvement of allied health staff is recommended.

## **References:**

- ❑ [www.nejm.org](http://www.nejm.org)
- ❑ [emedicine.medscape.com](http://emedicine.medscape.com)

## Test Yourself - 36

### Correct Answers :

1. d   2. b   3. c   4. c   5. c   6. a

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## Test Yourself - 37

### 1. The followings are true for "Psoriatic Arthritis" except :

- It develops in persons aged 35-55 years.
- There is a stronger association with HLA-C alleles than with HLA-B alleles in psoriatic arthritis.
- It has been reported to be associated with HIV infection.
- Nails are involved in 80% of patients with psoriatic arthritis.

### 2. All the followings are correct for "Burn Management" except :

- The most common complications of burns are infection and renal failure.
- At temperatures greater than 44° C, proteins lose their three-dimensional shape and start breaking down.
- In third-degree burn the injury extends to deeper tissue including muscle and bone.
- The burn patients demonstrate a graded capillary leak, which increases with injury size.

### 3. All the below are true for "Guillain-Barré Syndrome" except :

- CMV infections are the most commonly reported infections preceding GBS.
- The AIDP subtype is the most commonly identified form in the Europe, North America and the developed world.
- The typical patient with GBS presents 2-4 weeks following a relatively benign respiratory or GI illness in most cases.
- Cranial nerve involvement is observed in 45-75% of patients with GBS.

### 4. All the followings are correct for "Burn Management" except :

- The "Rule of 9's" is commonly used to estimate the burnt surface area in adults.
- Burns greater than 15% in adult, greater than 10% in a child are serious.
- In all cases tetanus prophylaxis should be administered.
- The first 12 hours following injury are critical.

### 5. The followings are right for "Psoriatic Arthritis" except :

- Serum IgA levels are increased in two thirds of patients with psoriatic arthritis.
- Treatment with DMARDs should be considered at an early stage for patient with active diseases.
- Apremilast was approved by the FDA in March 2013 for treatment of active psoriatic arthritis.
- As many as 40% of the patients may develop erosive and deforming arthritis.

### 6. All the followings are correct for "Guillain-Barré Syndrome" except :

- GBS is generally diagnosed on clinical grounds.
- All patients with GBS have an elevated CSF protein level.
- Antibodies to self-antigens are observed in the sera of 60-70% of patients.
- Antibodies to GM1, frequently found in the sera of patients with AMAN or AIDP variants.

Soon our officials will be visiting you with a token of our appreciation

## Compositon

**Clopirox™** Cream : Each gram cream contains Ciclopirox Olamine USP 10mg.

## Phamacology

Ciclopirox Olamine is a synthetic broad spectrum antifungal agent that inhibits the growth of pathogenic dermatophytes, yeasts and *Malassezia furfur*. Ciclopirox Olamine exhibits fungicidal activity in-vitro against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, *Microsporum canis* and *Candida albicans*. The mode of action of Ciclopirox Olamine was studied mainly in *Candida albicans*. It is presumed that Ciclopirox Olamine mediated growth inhibition or death of fungal cells is primarily caused by in-vitro cellular depletion of some essential substrates and/or ions and that such effects are brought about through blockage of their uptake from the medium. In addition to its broad spectrum of antifungal action, Ciclopirox also exerts antibacterial activity against many gram-positive and gram-negative bacteria. The anti-inflammatory effects of Ciclopirox have been demonstrated in human polymorphonuclear cells, where Ciclopirox has inhibited the synthesis of prostaglandin and leukotriene. Ciclopirox can also exhibit its anti-inflammatory effects by inhibiting the formation of 5-lipoxygenase and cyclooxygenase.

## Indication

**Clopirox™** cream is indicated for the topical treatment of the following dermal infections: Tinea pedis, Tinea cruris and Tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum* and *Microsporum canis*, candidiasis (moniliasis) due to *Candida albicans* and Tinea (pityriasis) versicolor due to *Malassezia furfur*. **Clopirox™** Cream is also highly effective against some gram-negative & some gram-positive bacteria. Owing to its anti-inflammatory effects, Ciclopirox Olamine alone is sufficient to treat mild to moderate inflammatory fungal infections.

## Dosage and Administration

**Clopirox™** cream should be gently massaged onto the affected and surrounding skin areas twice daily for four weeks. Clinical improvement with relief of

pruritus and other symptoms usually occurs within the first week of treatment. If a patient shows no clinical improvement after four weeks of treatment with **Clopirox™** cream, the diagnosis should be redetermined. Patients with Tinea versicolor usually exhibit clinical and mycological clearing after two weeks of treatment.

## Contraindication

Ciclopirox Olamine cream is contraindicated in individuals who have shown hypersensitivity to any of its components.

## Adverse Reactions

Ciclopirox Olamine cream is well-tolerated with a low incidence of adverse reactions reported in clinical trials.

## Precaution

Ciclopirox Olamine cream is not for ophthalmic use.

## Use in Pregnancy

Pregnancy category B.

## Use in Nursing Mother

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Ciclopirox Olamine cream is administered to nursing women.

## Use in Children

Safety and effectiveness in children below the age of 10 years have not been established.

## Storage

Store in a cool and dry place at 20°C to 25°C, protected from light. Keep out of the reach of children.

## How Supplied

**Clopirox™** cream : Each pack has an aluminum tube containing 10 gm cream.

# Ace<sup>®</sup>

Paracetamol BP 500 mg tablet

**Disintegrates...  
...within 30 seconds!**

Special formulation ensures



**Faster Disintegration**



**Faster Dissolution**



**Faster Absorption**



**Faster Action**

## Bisocor<sup>®</sup>

Bisoprolol Fumarate USP Tablet

2.5 mg

5 mg

10 mg

## The most selective $\beta_1$ - blocker

- The most selective  $\beta_1$ -blocker for Asthmatic Hypertensive Patients
- No effect on glucose metabolism in diabetic patients
- No effect on lipid profile over long-term use
- No negative effect on sexual function

Since 1958



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# Burna™

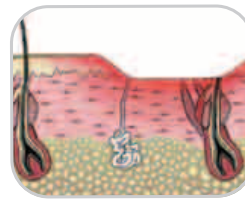
Silver Sulfadiazine USP 1%

## Treats burn wounds effectively



- Ensures broad antimicrobial spectrum
- Prevents infections successfully
- Heals burn wounds effectively
- Provides excellent cure rate

**Dose:** The cream should be applied once or twice daily to a thickness of approximately 1.5 mm in the burn areas. The area should be covered with cream at all times until satisfactory healing occurs.



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*We care for skin™*



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