Methodic elaboration for practical lesson in

Dermatovenerology

for students of Medicine Faculty nr.2

Topic N2

Acne vulgaris. Rosacea. Viral infections of the skin.

ACNE VULGARIS

Acne vulgaris is the most common of all skin disorders. It is a chronic inflammatory process that affects the pilosebaceous unit in virtually every adolescent and in many adults and prepubertal children as well.

Etiology and Pathogenesis

It is crucial to understand the pathogenesis of acne, because effective therapy must be based on such an understanding.

Acne vulgaris evolves within the pilosebaceous unit via a multifactorial pathogenesis. The central pathogenic factors in acne are:

- Excessive sebum production secondary to androgen stimulation;
- Abnormal follicular keratinization resulting in follicular plugging;
- Proliferation of Propionibacterium acnes (P acnes), an anaerobic organism normally resident in the follicle;
- Inflammation following chemotaxis and the release of various proinflammatory mediators.

The increase in adrenal androgens during the prepubertal period triggers the enlargement of the sebaceous glands. These enlarged sebaceous glands produce increased amounts of sebum, which flows through the canal of the sebaceous follicle. This canal is lined with a keratinizing epithelium. In acne patients, there is increased production of the follicular corneocytes lining the follicle and retention of these corneocytes within the follicle. The abnormally desquamated corneocytes and the excess sebum build up within the follicle to form a microscopic, bulging mass. This enclosed, sebum-rich environment is ideal for the proliferation of P acnes, the anaerobic bacterium that produces chemotactic factors and recruits proinflammatory molecules involved in the inflammatory phase of acne. Staphylococcus epidermidis is the aerobic bacterium that usually forwards acne vulgaris progression. .

Acne Lesions

Lesions are confined to the face, shoulders, upper chest and back. The primary lesion of acne vulgaris is the microcomedo, the microscopic, bulging mass that results from a combination of hyperproliferative corneocytes and sebum and leads to follicular plugging.

- The closed comedo (whitehead) is the first visible acne lesion. It is a noninflammatory lesion that evolves from the microcomedo and appears as a white dot ranging from 0.1 to 3.0 mm in diameter.
- The open comedo (blackhead) is a 0.1- to 3.0-mm noninflammatory lesion that looks like a black dot. Many acne patients mistakenly think the black dot is dirt, but researchers now believe the dark color is caused by the blockage of light transmission through the occluded follicle.

Inflammatory acne lesions include papules, pustules, nodules, and cysts.

- A papule is a pink-to-red, raised, palpable lesion with no visible accumulation of fluid, which can range from 1 to 4 mm in diameter.

- A pustule is a raised accumulation of purulent material on the skin's surface, and is similar in size to the papule. Pustules are sometimes characterized as superficial or deep. In a superficial pustule there is a localized rupture of the epithelium near the skin surface, and in a deep pustule there is extensive destruction of the entire epithelium.
- A nodule is a tender, firm lesion that may persist for weeks.
- Cysts may be as large as several centimeters in diameter, and they may drain a creamy, yellowish material.

Darkly pigmented skin affected by acne tends to develop significant postinflammatory hyperpigmentation. This tendency has given rise to the suggestion that a new acne lesion should be designated - the acne hyperpigmented macule (AHM). The AHM can last for 4 months or longer, and is often the central complaint of acne patients with skin of color.

Depressed or hypertrophic scarring and post-inflammatory hyperpigmentation can follow. Conglobate is the name given to a severe form of acne with all of the above features as well as abscesses or cysts with intercommunicating sinuses that contain thick serosanguinous fluid or pus. On resolution, it leaves deeply pitted or hypertrophic scars, sometimes joined by keloidal bridges. Acne scars can be classified into three different types—atrophic, hypertrophic, or keloidal. Atrophic acne scars are by far the most common type. Although hyperpigmentation is usually transient, it can per- sist, particularly in those with an already dark skin.

Classification of Acne

There is no single standardized grading system for acne, but there are several useful methods used to classify the disease. Most simply, acne is described as mild, moderate, or severe. Identifying the most severe predominant lesion - comedones (comedonal acne), papules/pustules (papulopustular acne, nodules/cysts (nodulocystic acne) - is another method used to categorize the disease and help guide therapy.

Diagnosis of Acne

The diagnosis of acne is generally made on clinical grounds and is usually fairly straightforward, although some rarer variants such as acne excoriée, chloracne, and acne fulminans (see below) can be diagnostically challenging and may require a dermatology consultation.

Investigations

None are usually necessary. Cultures are occasionally needed to exclude a pyogenic infection, an anaerobic infection or Gram-negative folliculitis. Only a few laboratories routinely culture *P. acnes* and test its sensitivity to antibiotics.

Any acne, including infantile acne, that is associated with virilization needs investigation to exclude anandrogen-secreting tumour of the adrenals, ovaries or testes, and to rule out congenital adrenal hyperplasia caused by 21-hydroxylase deficiency. Tests should then include the measurement of plasma testosterone, sex hormone-

binding globulin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), dehydroepiandrosterone sulphate, andro- stenedione, 17-hydroxyprogesterone, urinary free cortisol and, depending on the results, ultrasound examination or computed tomography scan of the ovaries and adrenals. Female patients should not be taking the oral contraceptive pill when these hormone levels are measured. Congenital adrenal hyperplasia is associated with high levels of 17-hydroxyprogesterone, and androgen secreting tumours with high androgen levels. Polycystic ovarian syndrome is characterized by modestly elevated testosterone, androstenedione and dehydroepiandrosterone sulphate levels, a reduced sex hormone-binding level and a LH : FSH ratio of greater than 2.5 : 1. Pelvic ultrasound may reveal multiple small ovarian cysts, although some acne patients have ovarian cysts without biochemical evidence of the polycystic ovarian syndrome.

Pathology

Skin biopsies are rarely performed for the purpose of diagnosing acne. Histopathologic findings, however, mirror the pathogenic events described above. The key pathologic features of acne are follicular plugging and distention and perifollicular inflammation. Evolving acne lesions may show rupture of the follicle with an influx of lymphocytes, polymorphonuclear leukocytes, macrophages, and foreign-body giant cells. Late stages may reveal granuloma formation and/or scarring.

Differential Diagnosis

There are 2 diseases that are rather frequently confused with acne: rosacea (often called acne rosacea in the older literature) and perioral dermatitis. We will discuss rosacea in depth later, but it may be distinguished from acne by several features:

- Age: rosacea patients are generally older than are acne patients;
- Type of lesion: acne lesions are by definition follicular, while rosacea lesions are not; and
- Distribution pattern: rosacea usually affects primarily the central third of the face, while acne is generally more widespread on the face, neck, back, and chest.
- Perioral dermatitis is a difficult disorder to define because of variable clinical presentations. As the name implies, its distribution pattern is generally perioral, although occasionally it may be more widely distributed on the face. The disorder is seen most commonly in young adult women, but may affect both sexes and all ages. Clinically, it is characterized by a combination of eczematous and acneiform features. When eczematous features are absent, the disorder may be difficult to differentiate from acne, with the perioral pattern often the most useful clue.

Rarer conditions that may present with follicular papules and/or pustules (and occasionally dermatitis) are Demodex folliculitis and Pityrosporum folliculitis. Caused by mites and yeast-like organisms, respectively, these disorders can only be diagnosed by microscopic examination or therapeutic trials. Patients who are suspected of having

these conditions or who fail to respond to appropriate acne therapy should be referred for a dermatologic consultation.

Acne Treatment -- General Principles

Since acne is a chronic, emotionally stressful condition that may persist for years, patient education is extremely important. The treating physician must establish good communication with the patient (and, often, the patient's family). Patients and family must understand that treatment may last for years and that a change in treatment may need to be made from time to time. I try to stress that no 2 patients or treatment regimens are the same.

Treatment should be directed toward the known pathogenic factors involved in acne. These include follicular hyperproliferation, excess sebum, *P acnes,* and inflammation. The grade and severity of the acne help in determining which of the following treatments, alone or in combination, is most appropriate. When a topical or systemic antibiotic is used, it should be used in conjunction with benzoyl peroxide to reduce the emergence of resistance.

A good skin care regimen is very important. Patients must understand that acne is not caused by poor hygiene and that they cannot wash it away. Aggressive washing and the use of abrasive cleansers should be avoided. The best advice is to cleanse the face twice daily with tepid water and a mild soap or soap substitute. Warn your patients to avoid washcloths or to use them gently and to avoid picking and squeezing acne lesions.

Topical Acne Therapy

Topical therapy for acne can be divided into:

I. Topical antimicrobials/antibiotics:
   - Benzoyl Peroxide.(BP) is an antimicrobial that is very effective for killing P acnes. BP-containing products are available in a variety of formulations, including gels, creams, lotions, washes, and bar soaps, in a variety of concentrations (most often 2.5%, 5%, and 10%). Concentration should be adjusted to skin type and tolerance, since BP may cause skin irritation, erythema, and dryness.
   - Topical Antibiotics kill P acnes and also exhibit significant anti-inflammatory properties. Thus, while topical antibiotics do not have a major effect on comedo formation, they are active against inflammatory lesions such as papules and pustules. Because, like BP, these drugs do not have a major impact on comedo formation, they are most often used in combination with topical retinoids. The most widely prescribed topical antibiotics are clindamycin 1% and topical erythromycin 1.5% .They are originally available as hydroalcoholic solutions dispensed, hydrophilic gels and lotions.

2. Topical retinoids (TR), are the treatment of choice for comedonal acne and are definitely the most effective agents for clearing microcomedones. TR

seem to be especially effective in combination therapy with BP or topical antibiotics. Such combination therapy seems quite logical when one recalls the basic pathophysiology of acne, ie, a combination of comedo formation, proliferation of P acnes, and inflammation. Thus, the value of a regimen that combines antibiotics to kill P acnes and suppress inflammation with topical retinoids to resolve comedones and add additional anti-inflammatory effects is clear.
    - Tetinoin 0.025% gel and 0.05% cream.
    - Adapalene is available in 0.1% gel (Differin)
    - Tazarotene 0.1% gel (Tazorac),
3. Miscellaneous Topical Therapy. Older therapies still available include arious products containing sulfur, resorcinol, and salicylic acid (decrease follicular occlusion in acne vulgaris) These are generally less effective than the newer topical agents discussed above.
4. Azelaic acid (Azelex), a dicarboxylic acid available in a 20% cream with efficacy against inflammatory (and to a lesser degree, comedonal) lesions.

Systemic Acne Therapy

Severe acne or moderate acne that is not responsive to topical therapy may require systemic therapy. Such therapy may include oral antibiotics, oral isotretinoin, or hormonal therapy.

1. **Oral Antibiotics**
    a. Oxytetracycline and tetracycline. An average starting dosage for an adult is 500 mg twice daily, but up to 1.5 g/day may be needed in resistant cases. The antibiotic should not be used for less than 3 months and may be needed for 1–2 years, or even longer.
    b. *Minocycline* 50 mg twice daily or 100 mg once or twice daily.
    c. *Doxycycline*, 100 mg once or twice daily is a cheaper alternative to minocycline, but more frequently associated with phototoxic skin reactions. A new low-dose preparation (40 mg; Oracea, USA) is given once daily and inhibits acne by stopping inflammation in and around the pilosebaceous follicles without apparently affecting the bacterial flora of the vagina or elsewhere.
    d. *Erythromycin (*dosage as for oxytetracycline) is the next antibiotic of choice but is preferable to tetracyclines in women who might become pregnant. Its major drawbacks are nausea and the widespread development of resistant *Proprionibacteria,* which leads to therapeutic failure.
    e. Azitromicin alternative 3 days consecently
2. **Oral isotretinoin** (13-cis-retinoic acid) is a systemic retinoid that is highly effective in the treatment of severe, recalcitrant acne vulgaris. It is routinely given for 4-6 months only, in a dosage of 0.5 –1 mg/kg body weight/day; young men with truncal acne usually require the higher dosage.

3. **Hormonal**
    a. Co-cyprindiol, a combined antiandrogen–oestrogen treatment (Dianette: 2 mg cyproterone acetate and 0.035 mg ethinylestradiol), is available in many countries and may help persistent acne in women.
    b. Ethinyl estradiol 35 μg/norgestimate (Ortho Tri-Cyclen) and ethinylestradiol 20 –35 μg/norethindrone acetate (Estrostep) have been approved for use in acne in the USA.
    c. Spironolactone blocks the androgen receptor, and reduces sebum production. It may be added to the OCP after 3 months if there has been an inadequate response. The usual dosage is 25–100 mg/day with food.
4. **Physical**
    a. Treatment with various lasers, in particular the pulsed dye 585 nm laser, has been tried. While results show some benefit, there are no data on long-term outcomes, or trials comparing lasers with other acne treatments.
    b. Peeling procedures and epidermabrasion with gritty soaps peel off more of the stratum corneum than they open comedones, and are not generally recommended,

ROZACEA

Rosacea affects the face of adults, usually women. Although its peak incidence is in the thirties and forties, it can also be seen in the young or old. It may coexist with acne but is distinct from it. Rosacea develops gradually. Many patients, unaware that they suffer from a treatable skin condition, assume that the intermittent facial flushing, papules, and pustules are adult acne, sun or wind burn, or normal effects of aging. Correct diagnosis and early treatment of rosacea are important because, if left untreated, rosacea can progress to irreversible disfigurement and vision loss.

Clinical features

Rosacea is a vascular disorder of distinct, predictable symptoms that follows a remarkably homogenous clinical course. Rosacea generally involves the cheeks, nose, chin, and forehead, with a predilection for the nose in men. There are four acknowledged general stages of rosacea.

1. Stage I can be described as pre-rosacea. This stage is characterized by frequent blushing, especially in those who have a family history of rosacea. Blushing as a symptom of rosacea can start in childhood, although the typical age of onset for rosacea is 30 to 60 years. There might be increased frequency of facial flushing or complaints of burning, redness, and stinging when using common skin care products or antiacne therapies.
2. The second stage of rosacea is vascular. At this point in the disease progression, transitory erythema of midfacial areas, as well as slight telangiectasias, become apparent.
3. In the third stage of rosacea, the facial redness becomes deeper and permanent. Telangiectasias increase, and papules and pustules begin to

develop. During this stage, ocular changes, such as conjunctivitis and blepharitis, can develop. Edema can develop in the region above the nasolabial folds.

4. In the fourth stage, there is continued and increased skin and ocular inflammation. Ocular inflammation can progress to keratitis and result in loss of vision. Multiple telangiectasias can be found in the paranasal region. It is at this point that fibroplasia and sebaceous hyperplasia of the skin produces the nasal enlargement known as rhinophyma.

Several skin conditions share some clinical features with rosacea. Acne vulgaris causes comedones, papules, pustules, and localized inflammatory nodules but not the generalized erythema, telangiectasias, and other vascular features of rosacea. Seborrheic dermatitis, perioral dermatitis, and the malar rash of lupus can all cause mild erythema, but these conditions will not produce the characteristic flushing, telangiectasias, papules, and pustules of rosacea.

Sarcoidosis can closely mimic rosacea by producing red papules on the face, but the disease will usually manifest itself in other organs as well. In addition, a biopsy will show sarcoid granulomas.

Pathophysiology

The cause is still unknown. Rosacea is often seen in those who flush easily in response to warmth, spicy food, alcohol or embarrassment. Psychological abnormalities, including neuroticism and depression, are more often secondary to the skin condition than their cause. No pharmacological defect has been found that explains these flushing attacks. However, the warmer skin that results may make normal bacteria behave differently, setting off papules, pustules and other inflammation. Sebum excretion rate and skin microbiology are normal. A pathogenic role for the hair follicle mite, *Demodex folliculorum,* or for *Helicobacter pylori* infection of the gastric mucosa has not been proved. Triggers that cause episodes of flushing and blushing play a part in the development of rosacea. Exposure to temperature extremes can cause the face to become flushed as well as strenuous exercise, heat from sunlight, severe sunburn, stress, anxiety, cold wind, and moving to a warm or hot environment from a cold one such as heated shops and offices during the winter. There are also some food and drinks that can trigger flushing, including alcohol, food and beverages containing caffeine (especially, hot tea and coffee), foods high in histamines and spicy food. Foods high in histamine (red wine, aged cheeses, yogurt, beer, cured pork products such as bacon, etc.) can even cause persistent facial flushing in those individuals without rosacea due to a separate condition, histamine intolerance. Certain medications and topical irritants can quickly trigger rosacea. Some acne and wrinkle treatments that have been reported to cause rosacea include microdermabrasion and chemical peels, as well as high dosages of isotretinoin, benzoyl peroxide, and tretinoin. *Steroid induced rosacea* is the term given to rosacea caused by the long term use of topical or nasal steroids oinments. These steroids are often prescribed for seborrheic dermatitis. Dosage should be slowly decreased and not immediately stopped to avoid a flare up.

Although the exact pathogenesis of rosacea is unknown, the pathologic process is well described. The erythema of rosacea is caused by dilation of the superficial vasculature of the face. It is thought that atrophy of the papillary dermis provides for easier visualization of the dermal capillaries. Edema can develop as a result of the increased blood flow in the superficial vasculature. This edema might contribute to the late-stage fibroplasia and rhinophyma. It has been suggested that Helicobacter pylori infection is a cause of rosacea. H. pylori, originally implicated as the cause of gastric ulcers, has more recently been associated with urticaria, Henoch-Schonlein purpura, and Sjödogren syndrome. Thus the role of H. pylori in rosacea remains uncertain, and the cause of rosacea remains elusive.

Differential diagnosis

Acne has already been mentioned. Rosacea differs from it by its background of erythema and telangiectases, and by the absence of comedones. The distribution of the lesions is different too, as rosacea affects the central face but not the trunk. Also rosacea usually appears after adolescence. Sun-damaged skin with or without acne cosmetica causes most diagnostic difficulty. Remember, rosacea affects primarily the central, less mobile parts of the face, whereas sun damage and acne cosmetica are more generalized over the face. Seborrhoeic eczema, perioral dermatitis systemic lupus erythematosus and photodermatitis should be considered but do not show the papulopustules of rosacea.

Treatment

The most important first step in the treatment of rosacea is the avoidance of triggers. Triggers are both exposures and situations that can cause a flare-up of the flushing and skin changes in rosacea. Principal among these is sun exposure. Rosacea patients must be advised always to apply a nonirritating facial sun block when outdoors. Stress, through autonomic activation, can also increase the flushing. Alcohol consumption, while not a cause in itself, can aggravate this condition through peripheral vasodilation. Spicy foods can also aggravate the symptoms of rosacea through autonomic stimulation. Finally, care must be taken to use only those facial cleansers, lotions, and cosmetics that are nonirritating, hypoallergenic, and noncomedogenic.

Rosacea should be treated at its earliest manifestations to mitigate progression to the stages of edema and irreversible fibrosis. Antibiotics have traditionally been considered the first line of therapy, although their success is considered to be primarily due to anti-inflammatory effects rather than antimicrobial ones.

- Oral antibiotics:
    - Tetracycline is the primary oral antibiotic prescribed for rosacea therapy, at a dosage of 1.0 to 1.5 g/d divided into 2 to 4 daily doses.
    - Minocycline at 100 mg two times a day is an acceptable alternative.
    - Doxycycline is another acceptable alternative, although the monohydrate formulation, in a dosage of 100 mg once daily, is more

consistently effective and has fewer gastrointestinal side effects than the hyclate form.
    - Clarithromycin, 250 mg to 500 mg twice daily, has been found to be as effective as doxycycline but with a more benign side effect profile.
- Topical metronidazole, which is effective for stage I and stage II rosacea and avoids the toxicity of systemic treatment, is considered first-line therapy. Metronidazole is available in a twice-daily application of 0.75% cream or gel and in a newer once-daily 1.0% formulation.
- Azelaic acid is a naturally occurring, dicarboxylic acid possessing antibacterial activity. It is available as a 20% cream and is generally used as an alternative treatment for acne vulgaris.
- Topical retinoic acid has been shown to have a beneficial effect on the vascular component of rosacea. (0.05% retinaldehyde cream for 6 months)
- Topical vitamin C preparations have recently been studied in the reduction of the erythema of rosacea. Daily use of an over-the-counter cosmetic 5.0% vitamin C (L-ascorbic acid) preparation was used in an observer-blinded and placebo-controlled study.

HERPES SIMPLEX

Two different virus types (HSV-1 and HSV-2) that can be distinguished in the laboratory cause herpes simplex virus (HSV) infections. HSV-1 is generally associated with oral infections and HSV-2 with genital infections. HSV-1 genital infections and HSV-2 oral infections are becoming more common, possibly as a result of oral-genital sexual contact.

Herpes simplex virus infections have two phases: the primary infection, after which the virus becomes established in a nerve ganglion; and the secondary phase, characterized by recurrent disease at the same site.

The rate of recurrence varies with virus type and anatomic site. Genital recurrences are nearly 6 times more frequent than oral-labial recurrences. Genital HSV-2 infections recur more often than genital HSV-1 infections. Oral-labial HSV-1 infections recur more often than HSV-2 infections.

Infections can occur anywhere on the skin. Infection in one area does not protect the patient from subsequent infection at a different site. Lesions are intraepidermal and usually heal without scarring.

Primary infection. Many primary infections are asymptomatic and can be detected only by an elevated IgG antibody titer. Like most virus infections, the severity of disease increases with age. Respiratory droplets may spread the virus, by direct contact with an active lesion, or by virus-containing fluid such as saliva or cervical secretions in patients with no evidence of active disease.

Symptoms occur from 3 to 7 or more days after contact. Tenderness, pain, mild paresthesias, or burning occur prior to the onset of lesions at the site of inoculation.

Localized pain, tender lymphadenopathy, headache, generalized aching, and fever are characteristic prodromal symptoms. Some patients have no prodromal symptoms.

Grouped vesicles on an erythematous base appear and subsequently erode. The vesicles in primary herpes simplex are more numerous and scattered than in the recurrent infection. The vesicles of herpes simplex are uniform in size in contrast to the vesicles seen in herpes zoster that vary in size. Mucous membrane lesions accumulate exudate, where-as skin lesions form a crust. Lesions last for 2 to 6 weeks unless secondarily infected and heal without scarring.

During this primary infection, the virus enters the nerve endings in the skin directly below the lesions and ascends through peripheral nerves to the dorsal root ganglia, where it apparently remains in a latent stage.

Recurrent infection. Local skin trauma, (e.g., ultraviolet light exposure, chapping, abrasion) or systemic changes (e.g., menses, fatigue, fever) reactivate the virus, which then travels down the peripheral nerves to the site of initial infection and causes the characteristic focal, recurrent infection. Recurrent infection is not inevitable. Many individuals have a rise in antibody titer and never experience recurrence. The prodromal symptoms, lasting 2 to 24 hours, resemble those of the primary infection. Within 12 hours, a group of lesions evolves rapidly from an erythematousis base to form papules and then vesicles. The dome-shaped, tense vesicles rapidly umbilical. In 2 to 4 days, they rupture forming aphthaelike erosions in the mouth and vaginal area or erosions covered by crusts on the lips and skin. Crusts are shed in approximately 8 days to reveal a pink, reepithelialized surface.

In contrast to the primary infection, systemic symptoms and lymphadenopathy are rare unless there is secondary infection.

The frequency of recurrence varies with anatomic site and virus type. The frequency of recurrence of HSV-2 genital herpes is higher than HSV-1 oral-labial infection. HSV-1 oral infections recur more often than genital HSV-1 infections. HSV-2 genital infections recur 6 times more frequently than HSV-1 genital infections. The frequency of recurrence is lowest for oral-labial HSB-2 infections.

Distribution

I. Oral-labial herpes simplex.
- **Primary infection.** Gingivostomatitis and pharingitis in children between 1 and 5 years.
- **Recurrent infection.** Herpes labialis.

II. Cutaneous herpes simplex.
- Herpes simplex may appear on any skin surface.

III. Genital Herpes simplex (herpes progenitalis) (penis, vulva, rectum, cervix, pubic area).

Complications

1. Herpes encephalitis or meningitis can occur without any cutaneous clues.
2. Disseminated herpes simplex: widespread vesicles may be part of a severe illness in newborns, debilitated children or immunosuppressed adults.
3. Eczema herpeticum: patients with atopic eczema are particularly susceptible to widespread cutaneous herpes simplex infections. Those looking after patients with atopic eczema should stay away if they have cold sores.
4. Herpes simplex can cause recurrent dendritic ulcers leading to corneal scarring.

Investigations

None are usually needed. Doubts over the diagnosis can be dispelled by culturing the virus from vesicle fluid. Antibody titres rise with primary, but not with recurrent infections.

Treatment.

'Old-fashioned' remedies suffice for occasional mild recurrent attacks; sunblock may cut down their frequency. Dabbing with surgical spirit is helpful, and secondary bacterial infection can be reduced by topical bacitracin, mupirocin, anilini solutions, framycetin or fusidic acid. Aciclovir cream, applied five or six times a day for the first 4 days of the episode, may cut down the length of attacks. More effective still is oral aciclovir 200 mg five times daily for 5 days, although this is usually reserved for those with widespread or systemic involvement. Famciclovir and valaciclovir are metabolized by the body into aciclovir and are as effective as aciclovir, having the additional advantage of better absorbtion and fewer doses per day. Recurrences in the immunocompromised can usually be prevented by long-term treatment at a lower dosage. Sometimes when we have acyclovir-resistant herpes simplex virus (HSV) and varicella zoster virus (VZV) we may use foscarnet that inhibits the replication, at least in vitro, of multiple herpes family viruses, hepatitis B virus, and the human immunodeficiency virus.

HERPES ZOSTER.

Herpes zoster, or shingles, a cutaneous viral infection generally involving the skin of a single dermatome, occurs during the lifetime of 10% to 20% of all persons. People of all ages are affected; it occurs regularly in young individuals, but the incidence increases with age. There is increased incidence of zoster in normal children who acquire chicken pox when younger than 2 months. Patients with zoster are not more likely to have an underlying malignancy. Zoster may be the earliest clinical sign of the development of the acquired immunodeficiency syndrome in high-risk individuals.

Zoster rezults from reactivation of varicella virus that entered the cutaneous nerves during an earlier episode of chicken pox. Traveled to the dorsal root ganglia, and remained in a latent form. Age, immunosupressive drugs, lymphoma, fatigue, emotional upsets, and radiation therapy have been implicated in reactivating the virus, which

subsequently travels back down the sensory nerve infecting the skin. Some patients, particularly children with herpes zoster, have no history of chicken pox. They may have acquired chicken pox by the transplacentral route. Although reported, herpes zoster acquired by direct contact with a patient having active varicella or zoster is rare. Following contact with such patients, infections are more inclined to result from reactivation of latent infection.

Clinical manifestation. Preeruptiv pain, itching, orburning, generally localized to the dermatome, precedes the eruption by 4 to 5 days. Preeruptive tenderness or hypersthezia throughout the dermatome is a useful predictive sign. Prodromal syndrome may be absent, particularly in children.

Eruptive phase. Although generally limited to the skin of a single dermatome, the eruption may involve one or two adjacent dermatomes (ophthalmic, maxillary, mandibullary, **thoracic**, sacral zoster). Possibly because chicken pox is centripetal, the thoracic region is affected in two thirds of herpes zoster cases. An attack of herpes zoster does not confer lasting immunity, and it is not abnormal to have two or three epizodes in a lifetime. Occasionally, a few vesicles appear across the medline. The eruption begins with red, swollen plaques of various sizes and spreads to involve part or all of dermatome.

The vesicles arise in clusters from the erythematous base and become cloudy with purulent fluid by day 3 or 4. The vesicles vary in size, in contrast to the cluster of uniformly sizes vesicles noted in herpes simplex. Successive crops continue to appear for 7 days. Vesicles either umbilical or rupture before forming a crust, which falls off in 2 to 3 weeks. The elderly or debilitated patients may have a prolonged and difficult course.

For them, the eruption is typically more extensive and inflammatory, occasionally resulting in hemorrhage blisters, skin necrosis, secondary bacterial infection, or extensive scarring, which is sometimes hypertrophic or keloidal.

Complications.

1. Postherpetic neuralgia. Pain is the major cause of morbidity in zoster. There is an increasing incidence and duration of pain with age. Pain can persist in a dermatome for months or years after the lesions have disappeared. The pain is often severe, intractable, and exhausting. Postherpetic neuralgia is more common and persists longer in cases of trigeminal nerve involvement. The mechanism of pain has not been explained.
2. Dissemination in-patients with cancer, Hodgkin’s disease etc.
3. Motor paresis.
4. Necrosis, infection, and scarring.
5. Encephallitis.
6. Secondary impetiginization
7. Hearing injury and eyes involvement
8. Hypertrophic and keloid scars

Differential diagnosis.

Occasionally, before the rash has appeared, the initial pain is taken for an emergency such as acute appendicitis or myocardial infarction. An early painful red plaque may suggest cellulitis until other plaques in the dermatome appear or until vesicles develop on their tops. Otherwise, the dermatomal distribution and the pain allow zoster to be distinguished easily from herpes simplex, eczema and impetigo.

Laboratory diagnostic (herpes simplex, herpes zoster).

1. Culture of vesicle fluid.
2. Electron microscopy
3. Tzanck smear.
4. Histopathology.
5. Serology: herpes simplex IgG and IgM serum antibodies. Normal titers are less than 1:5 for IgG and IgM. The presence of IgM or a fourfold or greater rise in IgG titer indicates recent infection. The presence of IgG indicates past exposure.
6. Complement-fixation titers.
7. Direct immunofluorescence
8. Vesicular-fluid immunofluorescent antibody stains.

Treatment.

1. Acyclovir 800 mg 5 times a day for 7 days. (Valacyclovir 1000 mg 3 times a day for 7 days; Famcyclovir 500 mg 3 times a day for 7 days).
2. Topical therapy. Burow's solution or cool tap water.
3. Oral steroids. Steroid recipients report more complications.
4. Sympathetic blocks with 0,25% bupivacaine.
5. Analgesics.
6. Systemic carbamazepine, gabapentin or amitriptyline, or 4 weeks of topical capsaicin cream despite the burning sensation it sometimes causes, may be worthwhile for estalished post-herpetic neuralgia.

WARTS

Warts are benign epidermal neoplasms. Different viruses cause different types of warts. At least 60 distinct types of human papilloma virus (HPV) have been identified by their DNA composition (warts - common: 1, 2, 4, 7; warts – flat: 3, 10; plantar: 1, 2, 4).

Warts commonly occur in children and young adults, but may appear at any age. Warts transmitted simply by touch; it is not unusual to see warts on adjacent toes. Warts commonly appear at sites of trauma, on the hands, in periungual regions from nail biting, and on plantar surfaces.

Individual variations in cell-mediated immunity may explain differences in severity and duration (AIDS, lymphomas, atopic eczema).

Warts: the primary lesion. Viral warts are tumors initiated by a viral infection of keratinocytes. The cells proliferate to form a mass but the mass remains confined to the epidermis. There are no 'roots' penetrating into the dermis.

1. **Common warts.** Common warts begin ass smooth, flesh-colored, non inflammatory papules and evolve into dome-shaped, gray-brown, hyperkeratotic growths with black dots on the surface, they may have long asymptomatic evolution. The black dots, which are thrombosed capillaries, are a useful diagnostic sign and may be exposed by paring the hyperkeratotic surface with a 15 surgical blade. The first sign is a smooth skin-coloured papule, often more easily felt than seen. As the lesion enlarges, its irregular hyperkeratotic surface and vertical shouders give it the classic 'warty' appearance. Common warts usually occur on the hands but are also often on the face and genitals. They are more often multiple than single. Pain is rare. Generally, the warts to become so numerous that they become confluent and obscure large areas of normal skin. The histopathological changes specific for common warts are acanthosis, papillomatosis and hyperkeratosis.**Treatment.** Topical salicylic acid preparations, liquid nitrogen, or very light electrocautery are the best methods for initial therapy The technique for application of salicylic acid is described in the treatment section for plantar warts.
2. **Flat warts** Flat warts are pink, light brown, or light yellow, and are slightly elevated, flat-topped papules that vary in size from 0,1 to 0,3 cm. There may be only a few, but generally they are numerous. Typical sites of involvement are the forehead, about the mouth, the backs of the hands, and shaved areas such as the beard area in men and the lower legs in women. A line of flat warts may appear as a result of scratching these sites. Flat warts are epidermal, solid, nitidous papules which involved dorsal surfaces of the hands, scalp and face. **Treatment.** Flat warts present a special therapeutic problem. Their duration may lengthy and they may be very resistant to treatment. In addition, they are generally located in cosmetically important areas where aggressive, scarring procedures are to be avoided. Treatment may be started with tretinoin cream 0,025%, 0,05%, or 0,1%, applied at bedtime over the entire involved area. The frequency of application is subsequently adjusted in order to produce a fine scaling with mild erythema. Treatment may be required for weeks or months and often is not effective. Freezing individual lesions with liquid nitrogen or exercising a very light touch with the electrocautery needle may be performed for patients who are concerned with cosmetic appearance and desire quick results. Treatment with 5-fluoroucill cream applied once or twice a day for 3 to 5 weeks may produce dramatic clearing of flat warts; it is worth the attempt if other measures fail. Persistent hyperpigmentation may occur following 5-fluorouracill use. This result may be minimized by applying the individual lesions with a cotton-tipped applicator. Warts may reappear in skin inflamed by 5-fluorouracill.

3. **Plantar warts.** Patients may refer to warts on any surface as plantar warts. Plantar warts frequently occur at points of maximum pressure, such as over the heads of the metatarsal bones or on the heels. A thick, painful callus forms in response to pressure and the foot is repositioned while walking. This may result in distortion of posture and pain in other parts of the foot, leg, or back. A little wart can cause a lot of trouble. Warts may appear anywhere on the plantar surface. A cluster of many warts that appears to fuse is referred to as a *mosaic wart.* **Treatment.** Plantar warts do not require therapy as long as they are painless. Although their number may increase, it is sometimes best simply to explain the natural history of the virus infection and for resolution rather than subject the patient to a long treatment program. Minimal discomfort can be relieved by periodically removing the callus with a blade or pumice stone. Painful warts must be treated. A technique that does not cause scarring should be used; scars on the soles of the feet may be painful and a lasting source of discomfort. Keratolytic therapy (salicylic acid).
    1. Keratolitic therapy (40% salicylic acid plasters for 24-48 ore).
    2. Blunt disection.
    3. Chemotherapy (Bichloracetic acid).
    4. Formalin 4% for 30 min.
    5. Cryosurgery.
    6. Contact immunotherapy (DNCB).
    7. Intralesional bleomycin sulfate.
4. **Plane warts** These smooth flat-topped papules are most common on the face and brow, on the backs of the hands and on the shaven legs of women. Usually skin-coloured or light brown, they become inflamed as a result of an immunological reaction, just before they resolve spontaneously. Lesions are multiple, painless and, like common warts, are sometimes arranged along a scratch line.
5. **Anogenital warts** *(condyloma acuminata)* Papillomatous cauliflower-like lesions, with a moist macerated vascular surface, can appear anywhere in this area usualy anogenital. They may coalesce to form huge fungat- ing plagues causing discomfort and irritation. The vaginal and anorectal mucosae may be affected. The presence of anogenital warts in children raises the spectre of sexual abuse, but is usually caused by autoinoculation from common warts elsewhere.

Course

Warts resolve spontaneously in the healthy as the immune response overcomes the infection. This happens within 6 months in some 30% of patients, and within 2years in 65%. Such spontaneous resolution, sometimes heralded by a punctate blackening caused by capillary thrombosis leaves no trace. Mosaic warts are notoriously slow to resolve and often resist all treatments. Warts persist and spread in immunocompromised patients (e.g. those on immunosuppressive therapy or with lymphoreticular disease). Seventy per cent

of renal allograft recipients will have warts 5 years after transplantation.

Diagnosis

Human papillomaviruses are confirmed by biopsy or molecular and biochemical tests.

Complications

1. Some plantar warts are very painful.
2. Epidermodysplasia verruciformis is a rare inherited disorder in which there is a universal wart infection, usually with HPV of unusual types. An impairment of cell-mediated immunity is commonly found and ensuing carcinomatous change frequently occurs.
3. Malignant change is otherwise rare, although infection with HPV types 16 and 18 predisposes to cervical carcinoma. HPV infections in immunocompromised patients (e.g. renal allograft recipients) have also been linked with skin cancer, especially on lightexposed areas.

Differential diagnosis

Most warts are easily recognized. The following must be ruled out.

1. *Molluscum contagiosum* are smooth, domeshaped and pearly, with central umbilication.
2. *Plantar corns* are found on pressure areas; there is no capillary bleeding on paring. They have a central keratotic core and are painful.
3. *Granuloma annulare* lesions have a smooth surface, as the lesions are dermal, and their outline is often annular.
4. *Condyloma lata* are seen in syphilis. They are rare but should not be confused with condyloma acuminata (warts). The lesions are flatter, greyer and less well defined. If in doubt, look for other signs of secondary syphilis and carry out serological tests.
5. *Amelanotic melanomas, squamous cell carcinomas and other epithelial malignancies* can present as verrucose nodules – those in patients over the age of 40 years should be examined with special care.

MOLLUSCUM CONTAGIOSUM

Cause

This common pox virus infection can be spread by direct contact (e.g. sexually or by sharing a towel at the swimming bath).

Presentation and course

The incubation period ranges from 2 to 6 weeks. Often, several members of one family are affected. Individual lesions are shiny, white or pink, and hemispherical; they grow slowly up to 0.5 cm in diameter. A central punctum, which may contain a cheesy

core, gives the lesions their characteristic umbilicated look.

On close inspection, a mosaic appearance may be seen. Multiple lesions are common and their distribution depends on the mode of infection. Atopic individuals and the immunocompromised are prone to especially extensive infections, spread by scratching and the use of topical steroids.

Untreated lesions usually clear in 6 – 9 months, often after a brief local inflammation. Large solitary lesions may take longer. Some leave depressed scars.

Clinical manifestations.

Molluscum contagiosum is a virus infection of the skin characterized by discrete, 2- to 5- mm, slightly umbilicated, flesh-colored, dome-shaped papules. It spreads by autoinoculation, by scratching, or by touching a lesion. The areas most commonly involved are the face, trunk, axillae, extremities in children, and the pubic and genital areas in adults. Lesions are frequently grouped; there may be few or many covering a wide area. Unilike warts, the palms and soles are not involved. It is not uncommon to see erythema and scaling at the periphery of a single or several lesions. This may be the result of inflammation from scratching or may be a hypersensitivity reaction. Lesions spread to inflamed skin, such as areas of atopic dermatitis. The individual lesion begins as a smooth, dome-shaped, white-to-flesh colored papule. With time, the center becomes solf and umbilicated. Most lesions are self-limiting and clear spontaneously in 6 to 9 months; however, they may last much longer. Genital molluscum contagiosum may be a manifestation of sexual abuse in children.

Diagnosis. Rapid confirmation can be made by removing a small lesion with a curette and placing it with a drop of potassium hydroxide between two microscope slides. The infected cells are dark, round, and disperse easily with slight pressure, whereas normal epithelial cells are flat, rectangular and tend to remain stuck together in sheets. Virions streaming out of the amorphous mass can be seen if Sedi-stain, a supravital stain used to stain urine sediments, is used. Toluidine blue gives the same result. Viral inclusions are easily seen in a fixed and stained biopsy specimen.

Complications

Eczematous patches often appear around mollusca. Traumatized or overtreated lesions may become secondarily infected.

Differential diagnosis

Inflamed lesions can simulate a boil. Large solitary lesions in adults can be confused with a keratoanthoma, an intradermal naevus or even a cystic basal cell carcinoma. Confusion with warts should not arise as these have a rough surface and no central pore.

Investigations

None are usually needed, but the diagnosis can be confirmed by looking under the microscope for large swollen epidermal cells, easily seen in unstained preparations of

debris expressed from a lesion. Extensive mollusa of the beard area may suggest need for HIV testing.

Treatment

Many simple destructive measures cause inflammation and then resolution. They include squeezing out the lesions with forceps, piercing them with an orange stick (preferably without phenol) and curettage. Liquid nitrogen, wart paints and topical imiquimod may also be helpful.

These measures are fine for adults, but young children dislike them and as mollusca are selflimiting, doing nothing is often the best option. Sometimes a local anaesthetic cream (EMLA) under polythene occlusion for an hour, will help children to tolerate more attacking treatment. Sparse eyelid lesions can be left alone but patients with numerous lesions may need to be referred to an ophthalmologist for curettage. Common sense measures help to limit spread within the family

Treatment.

1. Curettage.
2. Cryosurgery.
3. Tretinoin cream or gel.
4. Salicylic acid.
5. Cantharidin.
6. Laser therapy.