PSORIASIS

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General Comments:

1) Galen 2nd Century-but not real psoriasis
2) Willan-classic description 1801
3) Women=Men
4) 2nd to 4th decade, but any age, not rare in children
5) Caucasians > African Americans > American Indians, but East Africans = Caucasians (most African Americans came from West Africa)
6) clearly genes play a role and in 36% there is a family history, but is multifactorial, not simple genetic inheritance, and tends to occur earlier with each generation
7) may have asociated arthritis, and 60% of those patients have HLA-B27 and usually have nail changes

Biochemical Defect:

1) Hyperproliferation with increased turnover time? I was taught 36^0 turnover time, which is why they started MTX q12h for 36 hours, but that seems incorrect - it is just twice normal.
2) Disorder of keratinization?
3) Dermal disease? Destruction of dermal blood vessels with laser has improved psoriasis
4) Are all of the biochemical changes, like changes in cAMP and cGMP, a result of the psoriatic changes, or the cause?
5) Circulating factors? Is this why patients on dialysis sometimes improve?
6) Immune disease? Is this why cyclosporine, which affects the synthesis of interleukin 2 and T cell growth factor works? Is this why AIDS patients, whose HIV virus infects Langerhans cells get psoriasis? Is this why many topical therapies, which affects the Langerhans cells, work?
7) Neurologic: One interesting experiment in nature took place when a physician with psoriasis had a knee operation. After the operation, the skin around the knee was numb, and the psoriasis disappeared. when the sensory nerves regrew, the psoriasis reappeared.

Triggers:

1) Trauma, with the Koebner phenomenon
2) Infections, such as strep (we'll talk about this under tx)
3) Medications, such as Lithium, Beta blockers such as propanolol, indomethacin, antimalarials, iodides, penicillin, and all of the NSAID's which have an effect on prostaglandins blocking the cycloxygenase pathway and enhancing the lipoxygenase pathway
4) steroid withdrawal

Clinical:

1) Elbows, knees, scalp, umbilicus, cleft of the buttocks and of course inverse psoriasis that takes a more seborrheic pattern, with the axillae, v area of the chest and pubic area tending to be involved. Auspitz sign
2) Nails have pits, oil spots and dystrophy
3) Arthritis-usually DIP with psoriasis preceding arthritis 75% and concommitant 10%, occasionally asymmetric oligoarthritis

Variants:

1) Guttate-usually acute, look for strep, maybe even always tx for strep if tonsils are present, because strep can be present in tonsil even with a negative throat culture
2) Pustular-Von Zombusch in 1910, females 2x males, with ocular involvement possible
3) Pustular hand and feet-1/3 have arthritis. Is it true psoriasis?
4) Pustular disease of pregnancy-with hypercalcemia - is it psoriasis?
5) Exfoliative erythroderma - 16% - 24% may have psoriasis as the cause
6) Follicular psoriasis

Pathology:

1) Hyperkeratosis, parakeratosis, decreased granular layer, elongation of rete ridges and dermal papillae and Munro's abscesses filled with polys
2) THIS IS NOT DIAGNOSTIC! In all cases, the dx is psoriasiform!

DDX:

1) Parapsoriasis, PRP, Reiters, Lues, MF
2) Dermatophytes - KOH, Culture (Saboraud's vs DTM) - usually 1 nail is traumatic, 2 to 9 nails tinea and all 10 nails endogenous
3) Lichen Planus of the Nails

Therapy:

Topical:

1) Corticosteroids - fast response, fast recurrence after stopping tx. Mention tachyphylaxis, usual side effects, systemic absorption. Lack of fluoride molecule no guarantee of safety!!
2) Steroids + occlusion - even with class 1 (discuss classes) occlusion makes it more effective. Interestingly enough, occlusion itself is therapeutic! Hydration effect?
3) Intralesional steroids - rarely used today, but good for recalcitrant plaques
4) Tar therapy - crude coal tar useful esp. with UVB, the Goeckerman tx-but expensive! ... but patients often stay clear for months. Narrow band UVB, at 313 nanometers, is esp. effective, perhaps as effective as PUVA, of which we'll speak in a minute.
5) Heliotherapy - sun is a gift for psoriatics, and may be a reason it is so rare on the face. with heliotherapy, balneotherapy, such as at the Dead Sea. Perhaps the greater intensity of UVA in that area or the minerals in the water, or just relaxation or what? Many European insurance companies will pay for a trip to a psoriatic spa there as it is cheaper than hospitalization.
6) Anthralin - often called a tar because it is brown and smelly, it is a derivative of the bark of the Goa tree. Now that we know it penetrates psoriatic plaques within 30 minutes or so, we have ths SCAT technique. Some of the purified anthralins are fairly elegant and apply and wash off easily, such as Drithrocream and Micanol. Often patients are started on topical steroids in the morning and anthralin in the evening, until they're clear and then they're left on just the anthralin.
7) Capsaicin - the extremely useful red pepper derived anodyne has also been used to treat psoriasis, with the concept that it may help local neuropeptide disorders.
8) PUVA - psoralens have been around a long time and their effects were known in Egypt for 1000's of years. Combining either oral psoralens or topical psoralens or topical psoralens with UVA is easy, elegant and effective. Unfortunately, besides the total body sensitization, including the eyes, with the oral products, and the high frequency of burns associated with the topical, so called 'bath therapy´ all have a very high incidence of skin cancer, esp. Squamous Cell Ca, down the road.
9) Topical anti-cancer drugs, such as 5 fluorouracil, methotrexate and mechlorethamine tend to work but not well, indicating that either absorption is a problem or that simple increased cell turnover may not be the total cause of psoriasis.
10) Calcipotriol-it was noted that Vitamin D3, when used systemically, helped psoriatics, so an analogue, calcipotriol was developed and when used less than 100 grams a week, is both effective and safe. It seems to decrease

IL-8, which is a stimulator of keratinocyte growth, and increase IL-10, which inhibits T cell activation. Side effects are primarily irritation, and, like the SCAT therapy, is often used once a day, with a once a day application of a potent steroid, until the patient clears, and then they're left on the calciportiol.

11) Tazarotene-Vitamin A analogues proved to be useful orally - We'll talk about them in a minute, so various topical retinoids were tried, and tazarotene proved to be somewhat useful, though irritation tends to limit patient acceptance.

Oral therapy:

1) Arsenic-was once popular and indeed used for many diseases
2) Methotrexate-with the concept that psoriasis, like certain cancers, was characterized by a rapid turnover of cells, various anti-cancer drugs were tried in severe psoriatics. Aminopterin worked OK but was soon replaced by methotrexate, which is a commonly used therapy today. Besides the acute effects on the hematopoetic system, and the rare incidence of pneumonitis, liver damage is the almost constant concomitant of prolonged methotrexate usage. We almost always not only follow the LFT's but also get a liver bx after a total dosage of 1.5 grams, or even 1.0 grams if the patient is a 'high risk' patient. Alcohol and othe hepatotoxins, as well as many drugs, such as aspirin, sulfa drugs, probenecid, phenytoin, penicillin, etc are absolutely contraindicated for patients on MTX. Based on the now known to be erroneous concept that the epidermis 'turned over' in 36 hours, it was, and still is given usually every 12 hours for three treatments once a week, which seems to be safer than on a daily basis. Interestingly enough, the rheumatologists, who also use a lot of methotrexate, don't seem to see much liver damage in their patients, so there may be something about psoriatics that puts them at a higher risk.
3) Hydroxyurea - a ribonucleotide reductase inhibitor - works OK, but not great. It is fairly safe however.
4) Sulfasalazine - this is often used in patients with inflammatory bowel disease, but is occasionally dramatically useful in patients with psoriasis. We'll discuss this a bit later.
5) Retinoids: Etretinate is effective for plaque type and esp. pustular psoriasis, at a dosage of 0.25 to 0.5 mg/kg day. It is a teratogen and has a long $\frac{1}{2}$ life of about 168 days, making it unacceptable in most women of a child bearing age. As with all retinoids, dry skin, cheilitis, increased triglycerides and cholesterol are seen in almost all; patients. Acitretin is also effective and has a shorter $\frac{1}{2}$ life, of 2-4 days, though hepatotoxins may prolong its $\frac{1}{2}$ life. Isotretin, or 13 cis retinoic acid, the usual retinoid used for acne, isn't very effective in psoriasis but when seems quite effective when used with PUVA therapy. The combination of various retinoids and PUVA was first developed to try and decrease the amount of UVA given, and in that aspect, is useful-this combination is often called 'RePuva'.
6) Cyclosporin - Initially used as an immunosuppressive agent for transplant patients, it is a calmodulin antagonist in the phosphoinisitol pathway (what does this mean?), and inhibits phospholipase A2 with a concomitant decrease in arachidonic acid metabolites. It also inhibits polyamine synthesis. All in all, it suppresses the immune system dramatically but also works quite dramatically. side effects include hypertension and nephrotoxicity, with increased chances of lymphoma and skin cancer. Dermatologists often use a lower dose than transplant surgeons, and start at 5 mg/kg/day. Many drugs can raise the blood levels significantly, including grapefruit juicè!
7) FK 506 also called Tacrolimus, was developed in Japan and is also used orally for transplant patients. A topical form is now being investigated and at least in atopic patients, seems quite useful. I'm sure it will also be tried in psoriatic patients.

Other Therapies:

1) I believe that suppressing the immune

system, though it dramatically makes patients with a number of diseases look (and feel) better, is conceptually flawed and will be looked back on with the same feelings we now have for the older therapies of bleeding and purging. Suppressing the immune system is not a good thing, as we'll see in our talk on AIDS. Would you treat a child with arthritis from Lyme disease with Methotrexate or antibiotics? And yet, before they knew about Lyme disease, many of these children did get immunosuppressive drugs! Because patients genes are always the same during their lives, the fact that psoriasis can wax and wane indicates that other, external factors, play a role in psoriasis, and it is better to try and eliminate those external factors rather than suppress the reaction to them.

2) We know that infections like strep can initiate or worsen psoriasis in the at risk patients, so I routinely treat all acute psoriatics, or those with an acute guttate flare, with penicillin. If they have enlarged tonsils, as mentioned above they may still be harboring strep in them, despite penicillin tx, so I advise removal of the tonsils.
3) I routinely try, for my severe psoriatics, what I call "Cyclical round of anti's" , such as antibiotics, antivirals, antifungals, etc. Patients may get a month of ciprofloxin along with a famcyclovir, should this not work, then a month or so of metronidazole and a good anti-staph drug such as dicloxacillin. One of my favorites is Itraconazole, I've cleared up many patients with 'incurable eczema', on suppressive systemic corticosteroids, with itraconazole, but more about that too, later.
4) Another good concept is the 'anti-neutrophil' class of drugs. Many drugs make neutrophils go away and these include erythromycin, dapsone (which is fairly safe in G6PD+patients, used with cimetidine), colchicine and niacinamide, though avoid the long acting type, as it can be associated with liver damage.

In general, I initially use potent topical corticosteroids on psoriatic patients, with penicillin or other anti-strep drug for an acute flare. Once they're stable, I add in either calciptriol or the SCAT technique, and get them off the topical steroids as soon as possible. If these don't help control the patient I then start the 'cyclical round of antis' and only if these all fail do I entertain immunosuppressive techniques. Patients with serious acute flares, especially pustular, are of course a different case, as are pregnant patients. The fact that there are so many techniques indicates that there is no ideal technique! Though the famous Persian philosopher Occam suggested keeping things as simple as possible, in psoriasis it may not be that easy.