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INSIDE

Sweatin' with the Oldies

ABSTRACT & COMMENTARY

Synopsis: *Night sweats, day sweats, and hot flashes occur frequently in the elderly and are more closely associated with common ailments than serious illnesses.*

Source: Mold JW, et al. *Ann Fam Med*. 2004;2:391-397.

NIGHT SWEATS, DAY SWEATS, AND HOT FLASHES ARE COMMONLY reported symptoms in primary care. Mold and colleagues previously examined the prevalence of these symptoms in an adult population that included perimenopausal women.[1] Since hot flashes and night sweats are closely associated with menopause, they studied a population 64 years and older.

Physicians in the Oklahoma Physicians Resources/Research Network compiled lists of active, elderly patients, totaling close to 4000. After excluding patients who had died, were in nursing homes, were too confused to provide reliable information, had switched physicians, could not be reached by telephone, declined to participate, or could not understand telephone instructions, 799 were left to enroll. Four more were excluded because they did not respond to the night sweats question. The study population was 57% female, 88% white, and highly educated (59% with college or graduate degree). Cigarette use and excessive alcohol use were low (7.5% and 6.3%, respectively).

Night sweats, day sweats, and hot flashes were present in 10.3%, 8.7%, and 7.8%, respectively. Some participants reported more than one symptom; overall, 17.7% (140) had at least one symptom. In multivariate analysis ($P < 0.01$), night sweats were associated with age, fever, muscle cramps, visual problems, and numbness in hands and feet. Day sweats were associated with fever, restless legs, lightheadedness, and diabetes. Hot flashes were associated with nonwhite race, fever, nervous spells, and bone pain. In univariate analysis, there was no association with any of the three symptoms and autoimmune diseases, sarcoidosis, tuberculosis, chronic hepatitis, cancer, or thyroid disease. Individual symptoms were grouped into subgroups (for instance, impaired vision, impaired hearing, impaired smell, or numbness of hands or feet into "sensory deficit"). Subjects with night sweats, day sweats, or hot flashes were more likely to

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have a sensory deficit, bodily pain, visceral pain, or a mood disturbance than those without the three cardinal symptoms. They also scored lower on various quality-of-life scales.

COMMENT BY ALLAN J. WILKE, MD

One problem with this study is that 80% of the original group were excluded for one reason or another. Mold et al state that the study participants were younger, better educated, more likely male, and had better self-rated health than those people who were excluded. This raises the question of selection bias. Mold et al believe that, if anything, this would tend to underestimate the true prevalence of the primary symptoms. Another potential bias is that the illnesses were all self-reported and not confirmed by chart review.

The most striking finding is the lack of association with any of the "serious" illnesses (autoimmune diseases, TB, cancer, sarcoidosis, hyperthyroidism, etc.) that we were taught to look for. This is primarily the result of conducting the study in a primary care setting. This raises an interesting dilemma. If one of your elderly patients complains of night sweats, day sweats, or hot flashes, how far and in what direction do you take your investigation? While keeping in mind the classical, but rare, illnesses associated with these symptoms, you would do well to look for the other, more common, illnesses outlined above. ■

Reference

1. Mold JW, et al. *J Fam Pract.* 2002;51:452-456.

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Obesity—Is Surgery Finally Here for This Important CV Risk Factor?

ABSTRACT & COMMENTARY

Synopsis: *Effective weight loss was achieved in morbidly obese patients after undergoing bariatric surgery. A substantial majority of patients with diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea experienced complete resolution or improvement.*

Source: Buchwald H, et al. *JAMA*. 2004;292:1724-1737.

OBESITY IS A SIGNIFICANT RISK FACTOR IN AND OF itself for the development of coronary artery disease. The Metabolic Syndrome (MS) is a recently defined and rapidly evolving area of clinical and basic research and clinical care and is becoming an important public health issue which is of growing concern since is usually associated with obesity (ie, defined as a body mass index BMI of equal to or greater than 30) which affects approximately 1.7 billion individuals in the world. Of particular interest are the facts that the percentage of overweight adults is highest in the United States[1-4] and obesity among children is also on the rise, an alarming trend in view of the fact that early obesity is a strong predictor of later cardiovascular disease. The distribution of body fat may also play a role in the development of coronary heart disease, with abdominal obesity posing a substantially greater risk in both women and men. A waist circumference of 35 inches in women and

40 inches in men is an easily measured marker of increased coronary heart disease risk.

The rise in the prevalence of obesity is associated with dramatic increases in the prevalence of obesity co-morbidities such as type 2 diabetes (probably secondary primarily to insulin resistance), hyperlipidemia, and hypertension, all conditions which are associated with a significant increase in risk for the development of coronary artery disease.

The pharmaceutical industry, in partnership with the medical profession, has been very successful in developing the medications and techniques used to control the 3 important medical conditions (hypertension, dyslipidemia, and glucose intolerance) often found to be in patients with the MS. However, the fourth important feature, obesity also usually found in patients with the MS has been particularly difficult to control. The obesity problem is quite massive since by some estimates, as high as 66% of the US population is considered to be overweight and almost half of these individuals are defined as being obese. Unfortunately diet therapy with and without support organizations has proven to be relatively ineffective in treating obesity over the long term.[5,6] In 1991, the National Institutes of Health established guidelines for the surgical therapy (ie, bariatric surgery) of morbid obesity (ie, BMI equal to or greater than 40 or BMI equal to or greater than 35 in the presence of significant co morbidities).

The literature with respect to the outcomes after bariatric surgery is quite extensive but had not been previously reviewed systematically nor subjected to a meta-analysis. Buchwald and colleagues corrected this deficiency by performing a meta-analysis of all articles on bariatric surgery published in the English language between 1990 and 2003.[7] After reviewing 2738 citations, they extracted 136 studies which included a total of 22,094 patients of which 72.6% were women with a mean age of 39 years. Excess weight loss occurred in 47.5% of the patients who underwent gastric banding, in 61.6% of gastric bypass patients, in 68.2% of gastroplasty patients and in up to 70.1% of patients who were subjected to bilio-pancreatic diversion or duodenal switch; the mean percentage was 61.2% for all patients and procedures. Operative mortality ranged from 0.1-1.1%. Diabetes was completely resolved in 76.8% of patients and resolved or improved in 86.0%. Hyperlipidemia improved in 70% or more of patients. Hypertension was resolved in 61.7% of patients and resolved or improved in 78.5%. Obstructive sleep apnea was resolved in 85.7% of patients.

COMMENT BY HAROLD L. KARPMAN, MD

A large, prospective, observational study of 43,457 women with a 12 year follow-up demonstrated that weight loss of at least 9 kg was associated with a 53% reduction in all obesity-related deaths.[8] Spurred on by the failure of traditional diet methods to produce permanent weight loss, bariatric surgery has been extensively performed and carefully studied over the past 15 years. Based on the results of Buchwald's meta-analysis,[7] it is clear that the significant weight loss that occurs over the long-term in the majority of morbidly obese individuals after bariatric surgery reverses, eliminates, or significantly ameliorates diabetes, hypertension, hyperlipidemia and obstructive sleep apnea in the majority of the patients. The operative 30-day mortality rates are low and, even after accounting for the pain and anxiety of surgery, the inconveniences of dietary restrictions and exposure to possible surgical complications, the majority of patients have experienced an improved quality-of-life because of improved appearance, and improved social and economic opportunities.[9-14]

Until recently, obesity had never been categorized as an illness thus preventing Medicare from covering for treatments for obesity-related conditions. In July 2004, Tommy G. Thompson, secretary of the US Department of Health and Human Services, announced that Medicare would remove barriers to covering all services for the treatment of obesity if the available scientific and medical evidence demonstrated their effectiveness in improving health outcomes. Much of the government's attention to this problem will be focused on gathering evidence to justify payment for diet programs and behavior therapies and obviously, bariatric surgery will also be carefully evaluated to determine whether or not Medicare beneficiaries will be eligible for this aggressive approach for the treatment of obesity itself rather than simply for the treatment only of the consequences of obesity. Hopefully, the report by Buchwald[7] will help speed the evaluation process along.

But hold on! Bariatric surgery is not a slam dunk. Although the 30-day mortality rate is low, postoperative complications are not infrequent and, in fact, up to 20% of all patients undergoing bariatric surgery require ICU admission postoperatively. In addition, anastomotic leakage and infection, iron malabsorption (and secondary anemia), vitamin deficiencies with associated disabling neuropathy and other complications of surgery and/or of rapid weight loss can occur. Therefore, obviously, before considering bariatric surgery, patients should be carefully counseled and a psychiatric consultation should be obtained for many reasons but especially to determine the degree of the patient's motivation and commitment. For the motivated patient, the results of bariatric surgery appear to be quite spectacular resulting in significant excess weight loss in the majority of patients and in significant improvement in co-morbid illnesses (ie, diabetes, hypertension, and hyperlipidemia) which all have clearly

been demonstrated to have a significant potential to shorten life and produce symptomatic coronary artery disease. However, is again important to emphasize that for bariatric surgery to be successful, patients must be carefully selected and should be strongly motivated in order to reduce the inevitable incidence of surgical failure in achieving the anticipated weight loss goals. ■

References

1. Mokdad AH, et al. *JAMA.* 1999;282:1519-1522.
2. Update: Prevalence of overweight among children, adolescents and adults-United States 1988-1994. *MMWR Morb Mortal Wkly Rep*. 1997;46:199-202.
3. Kopelman PG. *Nature*. 2000;404:635-643.
4. Rosengren A, et al. *Eur Heart J.* 1999;20:269-277.
5. Manson JE, et al. *N Engl J Med*. 1990;322:882-889.
6. Roxrode KM, et al. *JAMA*. 1998;280:1843-1848.
7. Buchwald H, et al. *JAMA*. 2004;292:1724-1737.
8. Williamson DF, et al. *Am J Epidemiol*. 1995;141: 1128-1141.
9. Karlson J, et al. *Int J Obes Relat Metab Disor*. 1998;22:113-126.
10. Kral JG. *Int J Risk Safety Med*. 1995;7:111-120.
11. Rand CS, et al. *South Med J*. 1990;83:1390-1395.
12. van Gernert WG, et al. *Am J. Clin Nutr*. 1998;67: 197-201.
13. Dymek MP, et al. *Obes Surg*. 2001;21;32-39.
14. Waters GS, et al. *Am J Surg*. 1991;161:154-157.

A New Class of Drugs That Lowers HbA1C and Promotes Weight Loss in Type 2 Diabetes

ABSTRACT & COMMENTARY

Synopsis: *Exenatide (Extendin-4) significantly lowered HbA1C and caused weight loss in Type 2 diabetes patients.*

Source: Buse JB, et al. *Diabetes Care.* 2004;27:2628-2635.

Exenatide is an incretin mimetic. Incretins are gut peptide hormones which are activated by nutrient ingestion. Some peptide hormones, in particular glucagon-like peptide (GLP-1) have been noted to play a role in beta cell health. GLP-1 acts via GLP-1 receptors on beta cells to enhance proinsulin gene transcription and replenishes beta cell insulin stores.[1]

The objective of this study was to evaluate the ability of exenatide to improve glycemic control in patients with type 2 diabetes failing maximally effective doses of a sulfonylurea as monotherapy.

This was a blinded, placebo controlled, 30-week study. After a 4-week, single blind, placebo lead in period, 377 subjects were randomized (60% men, age 55 ± 11 years; BMI, mean of 33 $kg.m^2$; HbA1C, 8.6). At 4 weeks they were begun on 5 ug subcutaneous exenatide twice daily (before breakfast and dinner; arms A + B) or placebo. Subsequently subjects in arm B were escalated to 10 ug b.i.d. exenatide. All subjects continued sulfonylurea therapy.

At week 30, mean HbA1C changes from baseline were -0.86, -.46, and 0.12 for the 10 µg, 5 µg and placebo arms.

Of subjects with baseline HbA1C greater than 7% (n = 237) 41% (10 µg), 33% (5 µg), and 9% (placebo) achieved HbA1C less than 7%. Fasting plasma glucose concentrations decreased in the 10 µg arm compared with placebo. Subjects in the exenatide arms had a dose-dependent progressive weight loss with an end of study loss in the 10 µg arm of -1.6 kg. from baseline. The most frequent adverse events were generally mild or moderate and gastrointestinal in nature. No severe hypoglycemia was observed.

Buse and colleagues concluded that exenatide significantly reduced HbA1C in patients with type 2 diabetes failing maximal doses of a sulfonylurea. It was generally well tolerated and associated with weight loss.[4]

COMMENT BY RALPH R. HALL, MD, FACP

One of the important aspects of this study was a favorable decrease in the proinsulin to insulin ratio toward more physiological proportions. This is consistent with the findings that exenatide may favorably effect beta cell regeneration.

Xu et al achieved enhanced replication and neogenesis of beta cells in rats using extendin-4.[2] Bonner-Weir noted in a presentation that Xu found that in partially pancreatectomized rats, after removal of 90% of the pancreas, extendin-4 ameliorated hyperglycemia. A 40% increase in beta cell mass was observed as well as increased replication and neogensis.[3]

DeFronzo et al, in a study similar to that of Busse et al, using patients who were on metformin and given exenatide found similar improvements in HbA1C and weight loss.[4]

Nausea occurred in a number of patients early in these studies but decreased with time and was not associated with a large number of patient withdrawals from the study. Nausea did not appear to be the reason for

weight loss since patients who did not experience nausea experienced similar weight loss.

The exenatide glucose lowering effect appears to be attributed to an effect on daytime postprandial glycemia because the glucose lowering effect on fasting plasma glucose was modest compared to the reduction in HbA1C.

Incretin hormones enhance insulin secretion, reduce glucagon secretion, inhibit gastric emptying, and improve satiety. They also appear to stimulate beta cell replication and neogenesis resulting in increasing beta cell mass. Incretin memetic hormones such as exenatide are promising additions to our current treatment of type 2 diabetes. ■

References

1. Stoffers DA, et al. *Dibetes*. 2000;49:741-748.
2. Xu G, et al. *Diabetes*. 1999;48:2270-2276.
3. Bonner-Weir S. (Symposium): Resurecting Beta Cell Function, Amer Assoc Clin Endo 13th Annual Meeting 2004.
4. DeFronzo R, et al. (Abstract) America Diabetes Assoc. 64th Annual session, 2004 (6-LB, late breaking abstracts).

Resolution of Hepatitis C Infection

ABSTRACT & COMMENTARY

Synopsis: *Studies on HCV infection resolution show that PBMC HCV-RNA may remain, despite clearance of the virus from plasma.*

Source: Wawrzynowicz-Syczewska M, et al. Natural History of Acute Symptomatic Hepatitis Type C. *Infection.* 2004;32: 138-143.

HEPATITIS C INFECTION IS USUALLY ASYMPTOMATIC, but with insidious progression. This paper from Poland features the outcomes of a series of patients with acute hepatitis C in order to determine the resolution or progression of disease. In the 10-year period from 1988-1998, 159 patients were recognized with acute HCV, 77 of which were eventually enrolled into the study. In 46, an incubation period could be determined. Past hepatitis B infection was detected in 19. Of the 77 patients, 23 (30%) became spontaneously negative for serum HCV-RNA and had no elevation of ALT. All but 3 of these patients were still anti-HCV antibody positive. Of the 30% who were negative for routine HCV viral load analysis, 2 had positive HCV in peripheral blood mononuclear cell (PBMC) assay.

Comparison of HCV-RNA(+) and HCV-RNA(-), by univariate analysis, revealed that HCV clearance was associated with higher hepatic enzymes and a history of alcohol abuse. Multiple other analysis showed the same associations.

There were 45 liver biopsies available for review. None showed severe inflammation. Clinically silent cirrhosis was present in 19%. Mild or minimal forms of chronic hepatitis was the common finding. Factors that were associated statistically with advanced liver histologic findings included male gender, heavy alcohol consumption, increased iron stores measured as serum ferritin (particularly with levels > 115 ng/mL), and older age at time of exposure.

■ **COMMENT BY JOSEPH F. JOHN Jr, MD**

This study is unusual because Wawrzynowicz-Syczewska and colleagues found a number of patients with a history of acute HCV, the median time after acute infection being 8 years. A unique aspect of the study was the use of HCV detection in PBMCs, an approach that showed patients with negative viral loads , done by routine testing, may still have detectable HCV using PBMC analysis. This finding suggests that perhaps more rigorous searches for latent HCV infection, possibly using PBMC assays, will have implications for future antiviral chemotherapy.

Ironically, the more icteric the initial episode, the more likely the spontaneous resolution. Wawrzynowicz-Syczewska et al emphasize this finding, suggesting that early lymphocyte stimulation allows a better cell-mediated response to infection.

The issue of fibrosis/cirrhosis is more confusing. In this study, about 20% of patients had histologic evidence of cirrhosis. Recall that the findings of inflammation were so minimal that the progression of the disease to fibrosis/cirrhosis involves other factors, Wawrzynowicz-Syczewska would argue, more than the inflammatory response. ■

Pharmacology Update

Histrelin Implant (Vantas)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

THE FDA HAS APPROVED A LONG-ACTING IMPLANT FOR the palliative treatment of prostate cancer. The implant is a sterile non-biodegradable (hydrophilic polymer), diffusion-controlled reservoir delivery system that releases the histrelin for 12 months. Histrelin is a pep-

tide agonist of luteinizing hormone-release hormone (LHRH). The product is marketed by Vantas Pharma as Vantas. This implant joins another 12-month LHRH agonist implant, leuprolide acetate (Viadur).

Indications

Histrelin implant is indicated in the palliative treatment of advanced prostate cancer.[1]

Dosage

One implant is inserted for 12 months. The optimal site is approximately half way between the shoulder and elbow in the crease between the bicep and triceps. The implant delivers 50-60 µg daily.[1]

Potential Advantages

The implant provides continuous LHRH therapy over 12 months independent of the patient's compliance. The non-biodegradable implant allows it to be removed if necessary because of adverse events or intolerance.

Potential Disadvantages

The implant extruded through the incision site in 8/171 patients in the clinical trials.[1]

Comments

Histrelin implant maintains castrated testosterone levels (50 ng/dL) from week 4 to at least week 52. The mean serum testosterone level was 15 ng/dL at week 4 and 14.3 ng/dL at week 52. Serum prostate specific antigen decreased from baseline to normal range in 93% of patients. A spike in testosterone level occurred on day 2 and decreased to below baseline levels by week 2.[1] A transient spike in testosterone levels early in treatment is common with other LHRH antagonists as well. Patients may also experience worsening of symptoms, and onset of new symptoms. These may include bone pain, neuropathy, hematuria, or urethral or bladder outlet obstruction.[1] Antiandrogen therapy (eg, flutamide) may be used to prevent or attenuate this transient or flare phenomena.[2,3] About 14% of patients experienced local or insertion site reactions.[1] Histrelin implant is a hydrophilic polymer cartridge while the leuprolide acetate implant is a nonbiodegradable osmotically driven delivery system. There are currently no published comparative studies although the safety and efficacy of leuprolide appear to be similar.[3] The cost of the histrelin implant was not available at the time of this review. As a point of reference, the wholesale cost of the leuprolide implant is $4547.

Clinical Implications

LHRH agonists (eg, leuprolide, goserelin, histrelin) are important treatment option for advanced prostate cancer. It is, however, more expensive than orchiectomy. Both leuprolide and histrelin implant provide drug delivery for 12 months. Prospective studies are ongoing to assess the relative merits of intermittent versus continuous androgen blockage.[4] ■

References

1. Vantas Product Information. Valera Pharmaceuticals, Inc. October 2004.
2. Chertin B, et al. *J Urol*. 2000;163:838-844.
3. Fowler JE, et al *J Urol*. 2000;164:730-734.
4. Lablaw DA, et al. *J Clin Oncol*. 2004;22:2927-2941.

CME Questions

24. The metabolic syndrome is usually found in patients who are afflicted with:

a. hyperthyroidism.
b. indigestion and gastritis.
c. obesity.
d. hypothyroidism.

25. Bariatric surgery for obesity:

a. is dangerous and should not be recommended at this time.
b. results in long-term weight reduction in the majority of patients.
c. is associated with an unacceptably high 30-day postoperative mortality rate.
d. improves hyperlipidemia and hypertension but has no effect upon diabetes.

26. The US Department of Health and Human Services:

a. has always considered obesity to be an illness.
b. considers bariatric surgery to be experimental in nature.
c. endorses weight reduction diet programs and behavior therapies.
d. is currently in the process of gathering scientific and medical evidence to determine if surgical procedures to relieve morbid obesity should be reimbursable.

27. Obesity:

a. is a significant cardiovascular risk factor in and of itself.
b. affects almost 50% of the US population.
c. is not a childhood problem in the US.
d. is not an important feature of the metabolic syndrome.

28. In patients with night sweats, day sweats, or hot flashes, there is one associated symptom common to all 3. It is:

a. fever.
b. muscle cramps.
c. numbness in hands and feet.
d. diabetes.
e. nervous spells.

29. Which of the following statements is *false*?

a. Exenatide's effect appears to be primarily on postprandial glycemia.

b. Weight loss experienced by patients taking exenatide is probably due to the nausea experienced by some patients.
c. Exenatide may promote beta cell regeneration.
d. Exenatide inhibits gastric emptying.

Answers: 24 (c); 25 (b); 26 (d); 27 (a); 28 (a); 29 (b).

Attention Readers . . .

American Health Consultants is happy to announce that we are opening up our *Primary Care Reports* author process to our readers. A biweekly newsletter with approximately 5000 readers, each issue is a fully referenced, peer-reviewed monograph. Monographs range from 25-35 Microsoft Word document, double-spaced pages. Each article is thoroughly peer reviewed by colleagues and physicians specializing in the topic being covered. Once the idea for an article has been approved, deadlines and other details will be arranged. Authors will be compensated upon publication.

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By Louis Kuritzky, MD

Incidence of Diabetes in Middle-Aged Men is Related to Sleep Disturbances

THE CONSEQUENCES OF SLEEP DEPRIvation, as measured in otherwise healthy men, include elevations of sympathetic activity, increased levels of cortisol, and altered glucose metabolism. Although sleep abnormalities such as sleep apnea have been associated with cardiovascular risk, less information is available to describe the association of sleep disturbances and diabetes.

Study subjects comprised male participants in the Malmo Preventive Project (n = 22,444) originally enrolled from 1974 to 1984, and then followed for a mean of 15 years. Sleep disturbances were solicited by querying: "Do you have difficulties in falling asleep?" and, "Do you generally use sleeping pills more than 3 times a week?"

At baseline, 9.3% of subjects answered affirmatively to one of the sleep disturbance questions (Group 1); 2.4% answered affirmatively to both questions (Group 2). At followup, the percentage of individuals who ultimately developed diabetes was statistically significantly greater in Group 1 vs control (15.3% vs 9.1%, $P < 0.005$) and Group 2 vs control. (4.6% vs 2.3%, $P < 0.034$).

These data support the concept that sleep disturbance is linked not only with vascular pathology, but with long-term likelihood of the development of diabetes. ■

Nillson PM, et al. Diabetes Care. 2004; 27(10):2464-2469.

Renal Dysfunction and Cardiovascular Outcomes after Myocardial Infarction

ALTHOUGH MARKED ALTERATION IN renal function can be anticipated to compromise lifespan, whether less substantial decrements in renal function are associated with adverse outcomes, particularly cardiovascular, is not well defined. Renal failure doubles the risk of mortal myocardial infarction when compared with MI in the general population without kidney disease.

VALIANT (Valsartan in Acute Myocardial Infarction Trial) studied adults (n = 14,527) with a recent MI complicated by CHF, excluding those with a baseline creatinine > 2.5. Subjects were randomized to valsartan, captopril, or both and followed for a mean of 2 years.

One third of subjects met National Kidney Foundation guidelines for chronic kidney disease (GFR < 60 mL/min). As soon as the GFR fell to 80 mL/min or less, every GFR reduction of 10 units was associated with a 10% increase hazard for death and nonfatal cardiovascular events.

Although overt renal insufficiency often prompts clinician intervention, these data support more vigilance for even mild-moderate decline in GFR. Relying upon simple elevation of creatinine to identify persons at risk may not be sufficient. Clinicians are encouraged to calculate a GFR for at-risk persons. ■

Anavekar NG, et al. N Engl J Med. 2004;351:1285-1295.

Topical Treatments for Psoriasis

THE PREVALENCE OF PSORIASIS (PSR) in the US adult population is as high as 3%, usually beginning during adolescence. Although there is no available cure for PSR, most patients can enjoy disease control with topical agents, phototherapy, or systemic treatment.

Initial treatment of PSR is dictated by severity and degree of surface area involvement. In persons with less than 5% total body surface involvement, topical treatments (steroids, vitamin D analogs, coal tar, retinoids, and anthralin) are all considered appropriate and effective. More severe disease, which will generally require specialist consultation, is treated with UV B light, psoralen plus UV A light, oral retinoids, or methotrexate (especially if PSR is coincident with psoriatic arthritis). The most commonly used topicals are steroids and calcipotriene. Generally, steroids have been found to be superior to calcipotriene ointment, but combining therapies has been found more efficacious than either therapy alone.

Anthralin and tazarotene (a topical retinoid) also are effective for treatment of PSR. Because the administration of these two medications is more complex and associated with adverse local effects, they are more likely to be utilized in specialty settings. Coal tar topically has been shown to be statistically significantly effective, but cosmetic disadvantages limit its use to patients who have failed or been in tolerant of other agents. ■

Mikhail M, Scheinfeld N. Adv Stud Med. 2004;4(8):420-429.

In Future Issues:

Hepatitis C and Infection Risk