Athens Kidney Center
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and diagnose depression, start effective treatment and monitor for response to therapy, with a goal of reduced disability, reduced rates of completed suicides, remission of disease, prevention of future relapse and return to premorbid occupational/psychosocial functioning. To achieve those, depression should be actively sought, as some patients may not complain of a depressed mood: use a screening tool (there are several, such as the Beck Depression Inventory, Hamilton Depression Inventory, Quick Inventory, et cetera, but the 2 question PHQ-2 is as solid as any: "Have you lost interest or pleasure in things you used to love? Do you feel flat, down, depressed or hopeless?" 1 out of 2 should prompt a formal test); search for common medical presentations of depression (multiple medical visits, typically more than 5 visits per year; multiple and unexplained clinical symptoms; impaired work or family relationships; changes in interpersonal relationships; dampened affect or flat mood; poor adherence or follow-through with treatment recommendations; recent weight change; poor sleep routine; excessive fatigue; symptoms of irritable bowel syndrome; poor memory or other cognitive complaints such as trouble concentrating or making decisions) and focus on patients at high risk for depression (positive family or personal history of major depression or substance abuse; recent loss; chronic medical illness; stressful life events; traumatic events; major life changes; history of domestic abuse or violence). Depression should be characterized based on its evolution (gradual or abrupt onset), severity of symptoms, associated functional impairment, number/severity of past episodes, prior response to treatment, history of suicidality and past suicide attempts, underlying "stressors", past history of substance abuse/dependence, past history of mania or psychosis and history of injury/violence. The lifetime prevalence of suicide in patients hospitalized for suicidality is 8.6% but lifetime risk is 4% for depressed patients without hospitalization for suicidality. Therefore, always assess for suicidality: "Do you feel that life is worth living? Do you wish you were dead? Have you thought about ending your life? If so, have you thought about how you would do it? What keeps you from harming yourself?" Those who have tried suicide before or have a well planned strategy for suicide are more likely to eventually complete suicide. Suicides are most frequent in the first two weeks following hospital discharge or after introduction of anti-depressants (as energy recovery precedes mood resolution). Differential diagnosis of major depression include (a) dysthymic disorder; (b) adjustment disorder with depressed mood; (c); substance-induced mood disorder; (d) mood disorder due to a general medical condition; (e) bereavement. A comprehensive treatment plan for major depression should be focused on achieving remission, should be ideally collaborative, must include family and caregivers, and should provide for diagnosis, prognosis and treatment options (including duration of therapy, common side effects and expected benefits). Treatment should aim at complete freedom from depressive symptoms, prevention of relapse, monitoring for side-effects of treatment and drug toxicity, checking and documenting drug compliance, education and self-exploration of depression and its literature, encouraging appropriate physical activity and full discussion of treatment options (psychotherapy vs. pharmacology). The decision in choosing drug treatment over psychotherapy is influenced by severity of symptoms, presence of psychosocial stressors, presence of co-morbid medical conditions, chronicity of symptoms, patient preferences, cultural expectations and availability of resources. Psychotherapeutic options include cognitive behavioral therapy (CBT), interpersonal psychotherapy (IPT), short-term psychodynamic psychotherapy (STPP) and problem-solving therapy (PST), which are all efficacious. Psychotherapy is as effective as medications in mild-moderate depression, and there is some evidence to support lower relapse rates and better outcomes with psychotherapy. Medications are used in acute treatment phase, where focus is on attaining remission of symptoms, typically over 6-12 weeks) or as long as it takes to reach remission, which is defined as 2 months without major depressive signs or symptoms. Therapeutic compliance is more important than the specific drug selected for treatment. The patient should be reminded that drug side effects often precede therapeutic benefit, but typically recede over time; successful treatment often involves dosage adjustments and/or trial of a different medications; most patients will be on medications 6-12 months after an adequate response; patients may show some symptomatic response at 2 weeks after onset of treatment; medications should be continued as prescribed even after one feels better; and that premature discontinuation of treatment has been associated with a 77% increase in the risk of relapse/recurrence of symptoms. Selecting the specific agent should be tailored to patient/family history of response to previous drug; doctor's experience with specific drugs; patient's preferences; side effect profile of drug; relative safety of drug following overdose; drug availability and cost; drug-drug interactions; and positive or negative impact of drug on the co-morbid psychiatric/medical condition. The common options are SSRIs (long publication track record, relative tolerability of side effects and good overall safety profile [even in overdose] without common adverse reaction associated with TCAs [anticholinergic and sedative effects] but often associated with headache, nervousness, insomnia, nausea and sexual side effects); Tricyclic Antidepressants (effective but poor side effect profile, but secondary amine TCAs [selective NE reuptake inhibitors such as nortriptyline and desipramine] cause less orthostatic hypotension and sedation than the tertiary amines [inhibit reuptake of both NE and serotonin such as amitriptyline and imipramine] and must be monitored carefully in cardiac patients, being still the #1 cause of lethal suicide in the US); Atypical Antidepressants (including Bupropion [which has less sexual side effects, but associated with seizures and weight loss], Duloxetine [useful for fibromyalgia, DM neuropathy], Mirtazapine [useful for insomnia/agitation], Nefazadone [has risk of liver toxicity], Trazodone [may be used with SSRIs at bedtime for insomnia], Venlafaxine and Desvenlafaxine, Maprotiline). For treatment-resistant depression, consider other strategies such as augmentation strategies (for partial responders, such as atypical-SSRI combinations, thyroxine-antidepressant combinations, TCA-SSRI combination, Li-antidepressant drug combination, et cetera), antidepressant drug combinations (when each has a different mechanism of action), consider partial or full-hospitalization particularly if there are safety concerns, phototherapy with a seasonal specifier, and finally, electro-convulsive therapy.

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SECOND OPINION

November 2011 *A monthly medical newsletter for the Athens medical community* Volume 2, #11

FROM THE EDITOR

This edition of Second Opinion is devoted to our annual CME offering- Medical Connections- which took place on October 22, 2011. Well attended, well organized, well advertised and well presented (only if I may say so myself), this yearly update owes a lot to the selfless service of Fred Young, MD, Dale Green, MD, Delena Montgomery, Jason Jones, and the rest of the hardworking CME crew at ARMC. Laboring in the vineyards of the 1% is often a thankless job, but we ought to pause and say a collective "Thank You" to those gentlemen and lady. Approximately a third of Athens physicians were present and accounted for; for the missing 67%, we present an abbreviated index of those proceedings. Now, no Athens doctor would have any earthly reason to occupy Prince Avenue- or anywhere else, for that matter.

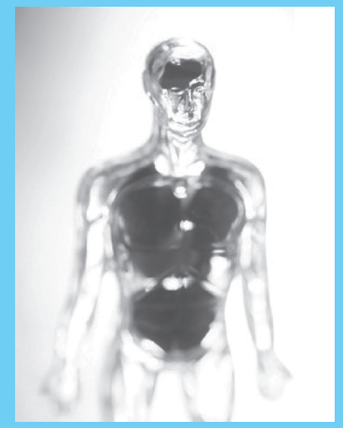
See you Friday lunch-time, at the CME lounge.

Beze Adogu, MD, Ph.D, FACP

CHRONIC WOUND MANAGEMENT

by: Dan Cojanu, MD

A chronic wound is an "acute wound with an unresolved impediment". Such a wound has failed to proceed through an orderly and timely reparative process designed to reproduce both anatomic and functional integrity at the site of injury. Chronic wounds afflict 6.5 million people in the United States; an estimated 2% of the general population will experience a chronic wound sometime in their lives. There is an increased burden of chronic wounds due to: (a) an aging population, (b) increased prevalence in obesity and type 2 diabetes mellitus, (c) expanded trauma-care utilization amongst war veterans, (d) increasing health care costs. We spend an estimated $25 billion annually on chronic wound therapy, a huge drain on the Medicare (health) budget, and is associated with reduced productivity and diminished quality of life. The types of chronic wounds are: (a) Pressure Ulcers, with 2.5 million sufferers in the US at a cost of $11 billion yearly (cost of treating a single full-thickness pressure ulcer is estimated at $70,000 in direct and indirect costs), mostly found amongst the frail, infirm, bedridden or neuropathic (unresponsive to pain); (b) Diabetic Ulcers, a consequence of microvascular disease in sufferers, of which there are 23 million diabetics in the US, a quarter of who will develop a diabetic foot ulcer at some point (at a cost of $9 billion/year for foot ulcer treatment alone), leading to limb amputation in 12% of foot ulcers (cost of amputations related to diabetes mellitus is $3 billion/year) and 50% of amputees will develop another ulcer within 5 years post-amputation; (c) Venous Ulcers have an annual prevalence of 600,000 in the US (accounting for 70-90% of lower extremity ulceration at an annual cost of $2.5-3.5 billion) and cost approximately $9,600 to treat 1 solitary venous ulcer, whilst a third of cases experience four or more episodes of ulcer recurrence after initial treatment (with 2 million workdays lost each year at a cost of $2 billion annually in lost wages). Instruction in the science and care of wounds is vestigial in most medical schools: physiology of tissue injury occupies (on average) 0.5 and 0.2 hours in the first and second years of medical school, and none in the third and forth years. As TK Hunt remarked: "Problem wounds are a problem because they fail to do what we expect- they fail to heal after adequate surgical and antibiotic treatment." In the words of William Hoff , "A chronic wound is an acute wound with an impediment- the impediment may be the treating physician." Ambroise Paré, a barber-surgeon with the French Army at the Battle of Turin, on depleting his standard 16th century fare of boiling oil was the first to experiment with a mixture of egg yolk, turpentine and oil of roses in treating gunpowder-inflicted body injuries. In his words, "I dressed the wound, and God healed him". Now, we better understand how God works: wound healing proceeds via an overlapping pattern of events which include (a) hemostasis, (b) inflammation, (c) proliferation, and (d) remodeling. Each phase is orchestrated by interactive molecular signals, chiefly cytokines, which mediate both tissue inflammation and healing. Following injury, a clot is formed, then rapid platelet activation at the injury site with release of platelet cell factors such as cytokines and growth factors. A fibrin matrix provides a scaffold for mediator cells, including neutrophils, monocytes, fibroblasts and endothelial cells, and within 1 week of trauma, inflammation is full-blown encompassing a process of vasodilation, neutrophil/macrophage influx, release of (inflammatory) mediators such as prostaglandins, histamine, interleukins, TNF-alpha and MMP. Cytokines are released by nucleated cells as modulators of immune or reparative processes and controllers of cell growth, cell differentiation, intermediary metabolism and intracellular protein synthesis. Cytokines include chemokines, lymphokines, monokines, interleukins, colony-stimulating factors and interferons. Cellular proliferation on the other hand involves epithelialization, angiogenesis and formation of provisional matrix, which predominant cells are fibroblasts (stimulated by PDGF, EGF), endothelial cells (stimulated by VEGF to begin forming new capillary tubes) and fibroblasts. Provisional matrix is composed of collagen type 3, glycosaminoglycans and fibronectin, later transforming into type 1 collagen in order to increase tensile strength. Epithelialization involves detachment of basilar keratinocytes, cell migration, cell proliferation, differentiation, and the formation of new epithelium which is characterized by having fewer basal cells, lacking rete pegs, and showing increased susceptibility to malignant transformation. Maturation and remodeling begin when the wound is closed, and only end when scar tissue is reformed, lasting up to 2



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years in duration and associated with reduced tissue cellularity, decreased vascularity, ultimately achieving about 80% of the tensile strength of original tissue. There is a constant balance between collagen synthesis and lysis, with full maturation of collagen fibers attained through intramolecular and intermolecular cross-linking. Therefore, healing wounds are characterized as having low levels of bacterial contamination, low titers of inflammatory cytokines, low levels of tissue/cellular proteases, an intact functional matrix, high mitogenic activity with mitotically competent cells in situ. Conversely, chronic wounds have high levels of bacterial contaminants (present as biofilms), as well as high titers of inflammatory cytokines, proteases and reactive oxygen species (ROS), as well as degraded non-functional matrix and low mitogenic activity. Identifiable impediments to wound healing include protein-calorie malnutrition, poor tissue perfusion, secondary infection, associated neuropathy, edema, application of topical medications, presence of underlying malignancy, advanced age (which affects angiogenesis and cellular healing, and often associated with a higher prevalence of dessication and dryness), presence of necrotic/devitalized tissue, acute or chronic illness (especially neuromuscular or cardio-pulmonary disease, collagen-vascular disorders and immunocompromise), medications/dressings (especially corticosteroids, cytotoxics, nicotine, and several topicals such as Dakins solution, Betadine, and all dressings- as the injunction "wet to dry" actually means repetitive tissue trauma which does not create a moist wound environment). To help develop a practical concept of wound pathology, we need a common language: the TIME concept of Tissue (nonviable or deficient tissue can physically impede the migration of cells across the wound bed and also act as a focus for secondary infection), Infection (perpetuates a cycle of repeated insult and injury which must be corrected for cellular migration to proceed), Moisture (moisture imbalance either in excess or deficient in wound desiccation can both delay healing; a desiccated wound bed will physically impede cellular migration and wound contraction), Edge (the wound's edge which is is a migrating epithelial ridge is a visible sign of wound healing, whilst a non-migrating edge indicates that both patient and wound must be reassessed). In conclusion, effective wound management lies in a combination of 3 approaches: treat the underlying medical problems, adequately prepare the wound bed (by tissue debridement, removal of bio-burden, management of exudate and maintenance of a moist wound environment) and address any patient centered concerns.

CHRONIC KIDNEY DISEASE

by: Beze Adogu, MD, PhD

Chronic kidney disease (CKD) is defined as any structural or functional abnormality of kidneys lasting over 3 months in duration regardless of GFR. Clinical clues that suggest chronicity include: prior historical documentation, relative normalcy of other components of electrolyte panel (suggesting metabolic adaptation), symptomatic tolerance for severe azotemia, absence of oliguria/anuria, presence of chronic anemia, structural evidence of bilateral renal atrophy, stigmata of ectopic calcification (including annular calcification or band keratopathy) or renal osteodystrophy or secondary hyperparathyroidism, presence of otherwise unexplained peripheral neuropathy. CKD is common: over 10 million Americans have lost 50% or more of their kidney function (Jones et al, Am J Kid Dis, 1998) and the ESRD population has enlarged in part because of wider acceptance of dialysis/transplant as therapeutic options, improved survival of prevalent ESRD patients , a fast-increasing CKD population driven by an aging population, survival from ICU-based acute kidney failure and the epidemic of diabetes/obesity. Therefore, increased incidence of ESRD has outpaced increased incidence in CKD by 70% (Hsu et al, Ann Intern Med, 2004). The epidemic of type 2 diabetes mellitus fuels the epidemic of CKD (Hostetter et al, NEJM 2001) but resources are relatively fixed: though ESRD population doubles q 10 years, kidney allograft supply for transplantation is fixed at about 13,000 q year. The cost of ESRD is ~30 billion dollars q year and the crude annual mortality of ESRD is 22%, That combination makes CKD a public health crisis, and management should include public awareness, better risk profiling (and channeling of resources), early diagnosis (which will require better diagnostic markers to be developed), aggressive cardiovascular management and specific kidney-directed treatment. The evolution of CKD can be modeled as a triphasic development: (a) risk factors (small at birth, ethnicity, small kidney size, advanced age, CKD amongst first-degree relatives, previous acute kidney failure); (b) initiation factors (chronic hypertension, diabetes mellitus, obstructive uropathy, prolonged ischemia/hypovolemia, genetic diseases (such as polycystic kidney disease), sepsis/pyelonephritis, vasculitis, glomerulonephritis, drug toxicity/allergies); (c) progression factors such as proteinuria, uncontrolled HTN, continued nephrotoxin exposure, chronic anemia, hyperlipidemia, smoking and metabolic acidosis. The clinical stages of CKD include stage 1 (albuminuria plus normal GFR ≥90 ml/min which afflicts 1.8% of adult US population), stage 2 (albuminuria plus GFR 60-89 which afflicts 3.2% of population), stage 3 (GFR 30-59 afflicting 7.7% of population), stage 4 (GFR 15-29 afflicting 0.35% of population), stage 5 (GFR <15 ml/min afflicting 2.4% of adult population). To effectively manage CKD, all physicians should identify patients at "high risk" for CKD, check annual UA and BMP where necessary, remember that there is no direct correlation b/w severity and symptoms of uremia, recall that compensation to CKD by adaptive hyperfiltration is a double-edged sword which leads to relentless (irreversible) renal decline after loss of >50% of initial kidney function, and that CKD is more likely to result in death than lead to ESRD (which makes CKD a CAD-equivalent) as well as bearing a risk of higher mortality, increased cancer risk and increased infection risk. The nephrologist should confirm the presence of renal insufficiency and estimate its severity, establish a reliable baseline function, identify the probable cause of CKD, propose safe & effective treatment whilst tracking the clinical course of CKD and its response to treatment. Treatment should incorporate (a) adequate HTN control, MDRD study by S Klahr et al, NEJM 1994/(MRFIT study by Klag et al, NEJM 1996; (b) reduction in proteinuria to <0.5 gram/day (MDRD study); (c) use of an RAAS antagonist either ACE inhibitor or angiotensin receptor blocker but probably not both (REIN trial by Ruggenenti et al, Lancet 1997) (d) Reduction in dietary salt intake (Heeg et al, Kidney International 1989); (e) correction/prevention of hypokalemia (Ray et al, Kidney International 1993); (f) reduction in aldosteronic drive (Brown et al, Kidney International 2000, Chrysostomou et al, NEJM 2001); (g) treatment of dyslipidemia (Keane et al, Kidney International 1994/Colhoun et al, Diabetologia 2001); (h) stop smoking (Remuzzi et al, Am J Kidney Dis, 1999); (i) avoid exposure to nephrotoxins, including NSAIDs, contrast dyes, et cetera; (j) treat incident anemia (Kuriyama et al, Nephron 1997); (k) monitor and correct Ca x P product; (l) monitor and correct hypervolemia (Hebert et al, JASNephrol, 2000); other factors of unclear prognostic import include estrogen beneficience, low protein diet, avoidance of hyperinsulinemia and the homocysteine paradox. CKD management should identify reversible exacerbators of CKD such as cardiac Failure/ prolonged hypotension, malignant hypertension, renal vein thrombosis, urologic obstruction, sepsis syndrome, hyperuricemia/tumor lysis syndrome, hypercalcemia, heavy metal toxicity and iatrogenic misadventure (typically from contrast dye, allergens and nephrotoxins/NSAIDs).

PEARLS IN SKIN CANCER MANAGEMENT

by: Ross Campbell, MD

There are over 3 million new cases of skin cancer per year in the US; 1 out of 5 Americans are destined to develop skin cancer, which is still the most common form of cancer in the country. Most are basal cell cancers and squamous cell cancers, with basal cell cancer (BCC) being 4-5x more common than squamous cell cancer (SCC) except within defined demographic groups (immunosuppressed, African-Americans, post-PUVA treatment). In addition, there are 67,000 new cases of melanoma each year, and someone dies in the US from malignant melanoma every hour. It is thought that the increase in skin cancer rates are attributable to our sun exposure habits, the depletion of protective ozone layer depletion (allowing an estimated 5% increased penetration of UV-B radiation to earth), effects of ionizing and other radiation (X-rays), chemical contaminants (such as arsenic and coal tars), presence of Marjolin's ulcers, infection with oncogenic viruses (especially HPV 16), immunocompromise (illustrated by development of skin cancer in 10-45% of solid organ transplant recipients, with SCC being 2-3x more common than BCC) and prevalence of inherited diseases that increase cancer susceptibility (xeroderma pigmentosum, albinism, basal cell nevus syndrome, etc). Basal cell cancer is commonly found in older folks, presenting as lesions on sun-exposed areas of face and scalp, ears, neck, extremities and trunk. Initial lesions are often followed by other lesions within 5 years. Subtypes of BCC are nodulo-ulcerative (most common), pigmented, morpheaform and superficial/multicentric (often misdiagnosed as eczema or psoriasis). BCCs are usually slowly progressive, enlarging over months/years with bleeding, ulceration or invasiveness, ultimately destroying underlying tissue such as muscle, bone and cartilage. Squamous cell cancer (SCC) arises from sun-damaged skin, usually actinic keratoses, anywhere on the body including lips, mouth, anogenital area and sun-exposed skin. Lesions on lips or dorsa of hands are very likely to be SCC rather than BCC. Metastatic SCC is more likely in recurrent disease, lesions >2 cm in diameter or 4 mm in depth, lesions with perineural invasion or at mucosal/peri-auricular sites, lesions in Marjolin's ulcers or lesions in the immunocompromised. Keratoacanthoma show initial rapid growth, often as an exophytic nodule with central keratin-filled crater, and then remains stable for months or spontaneously resolves or slowly progresses thereafter. Subtypes of SCC include invasive SCC, Bowen's disease and squamous cell carcinoma in-situ (which presents as thin, erythematous, scaling plaques that often progress into or coincide with concurrent invasive SCC, often misdiagnosed as psoriasis or eczema initially). The treatment of BCC and SCC include (a) electrodesiccation & curettage (EDC) where serial scraping and burning of lesion ultimately exposes a healthy base, but cure rate is dependent on clinical experience and there is an absence of "margin control" (i.e. pathologic confirmation of complete tumor removal) in what is essentially a "blind procedure"; (b) cryotherapy with liquid nitrogen which also lacks "margin control", and though used in treating malignancies, is probably best reserved for benign or premalignant lesion removal; (c) radiation therapy is effective in selected cases either as primary (especially in those unable to tolerate surgery) or adjuvant treatment (with surgery) but requires multiple treatments over 1-2 months, and tumor may recur in a more aggressive form or second malignancies present in irradiated skin; (d) surgical excision is performed with 3-5 mm "safety margins" around cancer (giving 89% cure rate), often accomplished by making ellipse and closing in linear fashion, though larger lesions may require flaps or grafts; (e) Mohs micrographic surgery has both the highest cure rate (97% - 99%) and best spares healthy tissue (as entire surgical margin is microscopically evaluated), now regarded as "standard therapy" for lesions in critical locations (cosmetic or functional reasons) or recurrent cancers or cancers with ill-defined margins, bulk (> 2 cm) or features of aggressiveness.

FATTY LIVER DISEASE

by: Bradley Shepherd, MD

Fatty liver encompasses (a) hepatic steatosis, with or without inflammation/ fibrosis and (b) steatohepatitis (steatosis with hepatic inflammation). The 2 most common causes are alcohol-induced liver damage and so-called non-alcoholic fatty liver disease (NAFLD). Other etiologies include: TPN (parenteral nutrition), Wilson's disease, acute fatty liver of pregnancy, Reye's syndrome, medication-induced fatty liver (commonly from Amiodarone, steroids, Tamoxifen and HAART treatment in AIDS), rapid weight loss, and of course, "idiopathic" fatty liver. Some component of NAFLD may coexist with other etiologies of liver disease. The cause of NAFLD is unknown, but its presence strongly correlates with metabolic syndrome; about 69-100% of patients are obese, most being 10-40% above ideal body weight (IBW); 34-75% have type 2 diabetes mellitus; 20-80% are hyperlipidemic. Based on NHANES data, it is estimated that 6.4 million US adults may have NAFLD, which is more common in women (70-80%), shows ethnic bias (most common in Hispanics, least common in Blacks, which may partially but not completely be based on ethnic prevalence of obesity), and autopsy data suggest that 18.5% of obese patients have NAFLD. NAFLD may be associated with excessive alcohol consumption, use of specific drugs (listed above), recent changes in weight (gain or loss), and is supported by findings of (a) metabolic syndrome, (b) elevated transaminases in 90% of cases with ALT >>AST, (c) negative evaluation for other etiologies of fatty liver (notably viral hepatitis [HCV Ab, HAV Ab, HBV sAg/sAb/cAb], autoimmune liver disease [ANA, F-actin anti-smooth muscle antibody], iron overload, Wilson's disease, alpha-1 antitrypsin deficiency, celiac disease) and (d) characteristic changes on liver CT scan or ultrasound. In most cases, symptoms are vague and non-specific and jaundice is uncommon. Clinical course of NAFLD is variable and unpredictable; a study of 103 patients with serial liver biopsies showed that fibrosis progressed in 37%, was stable in 34%, and actually regressed in 29% of cases, which might suggest that NAFLD runs a more benign course than alcoholic liver disease. For comparison, alcoholic liver disease progresses to cirrhosis in 40-50% of cases but only in 10-20% of cases of NAFLD. There is better survival for NAFLD vs. alcoholic fatty liver, with 10 year survival rates of 60% vs 15 % (L. A. Adams et al, J Hepatology 2005; 42:132). The 3 major predictors of progressive fibrosis are type 2 diabetes mellitus, higher BMI, and presence of fibrosis on initial liver biopsy (C.A. Matteoni et al, Gastroenterol 1999;116:1413). A vexing question in management is deciding who needs liver biopsy: biopsy is the only way to confirm NAFLD, helps determine disease severity, and allows prognostication. Biopsy should not be done if it will not influence treatment. The major predictors of liver fibrosis are older age (>45 years), obesity, AST/ALT ratio >1, and presence of type 2 diabetes mellitus. Remember that severe/terminasl NAFLD can coexist with normal ALT levels. The cause of NAFLD is unknown, but research suggests the contribution of both insulin resistance and oxidative stress; insulin resistance leads to increased circulating insulin levels, and high portal vein levels of insulin/glucose may promote esterification of free fatty acids and g-3-p to form triglycerides in the liver, as hyperinsulinemia also blocks hepatic hydrolysis of triglycerides. Apo B-100, the rate limiting step in triglyceride/FFA export from hepatocytes is decreased in the presence of circulating insulin. The treatment of NAFLD includes sustained weight loss (using diet [1200-1500 kcals/day and 25% fat intake], medical therapies or bariatric surgery) with a goal of 10% ideal body weight in first 6 months. The benefits include normalization of liver tests, improvement in insulin resistance phenotype (and diabetes management), normalized lipid levels and better CV health. Specifically, a low calorie diet for up to 1 year combined with exercise has been shown to improve liver transaminases and improve noninvasive markers of steatosis (Clark et al, J Clin Gastroenterol 2006;40:S39-43) and a ketogenic diet improved steatosis and inflammation after 6 months, based on repeat biopsy (Tendler et al, Digestive Dis Sci 2007;52:589-93). The data on usefulness of vitamin E (probably unsafe for long-term use), thiazolidinediones (may reversibly improve liver fibrosis scores but aggravates weight gain in short-term, and biochemical changes relapse on drug discontinuance), metformin (well-tolerated and may improve liver fibrosis), ursodeoxycholic acid, HMG co-A reductase inhibitors (statins) and pentoxifylline are still incomplete. The role of surgical weight loss has garnered more support; of 18 patients with NAFLD and BMI >40 who underwent Roux-en-Y gastric bypass surgery, there was a reported mean loss of 60% of excess weight, liver steatosis disappeared in 84%, and hepatic fibrosis disappeared in 75% at two years post-surgery. However, surgery may worsen hepatic injury as a consequence of rapid weight loss, and questions about long-term safety post-surgery have been raised.

TREATING DEPRESSION

by: Shelley Nuss, MD

The 3 most common causes of long-term disability in the US are arthritis/back problems, heart diseases/stroke and major depression. Depression is a medical illness, not a character defect; treatment is universally effective; recovery is the rule, not the exception. Depression is common (16.6% of population will experience depression in lifetime, and 9% of adult population are depressed with 5% meeting definition of major depression), treatable (50% of diagnosed patients in primary care setting are treated, and 30% of the treated show substantial improvement at 12 months) and often undiagnosed (only 33-50% of depressed patients are detected by their primary doctors) or untreated (perhaps because 80% of depressed patients have another significant medical problem). Under-recognition and under-treatment are even worse in the elderly: depression is not a "normal" consequence of aging. Primary care doctors therefore detect less than 50% of those presenting with depressive symptoms, yet 75% of all depression is actually first diagnosed in the primary care setting. Depression costs our economy 386.6 million days of work loss per year from associated disability. Depression is more common amongst the very sick: 40% following stroke, 23-60% following cancer diagnosis, 33% after an acute MI, 15% in diabetics. The primary doctor has to detect