



New York State
Office of Alcoholism & Substance Abuse Services
Addiction Services for Prevention, Treatment, Recovery

ADDICTION FYI YEARBOOK 2009 – Part I

This yearbook is a compilation of all the Addiction Medicine Briefs and FYI's sent out during the first part of the year (2009).

There will be at least one question asked per FYI and free CASAC credit can be earned by answering 75% or more of the questions correctly.

This yearbook contains the following FYI's:

1. Cigarettes and Menthol
2. Smoking Cessation and Adolescents
3. Holidays and Your Heart, Your Weight
4. Cocaine and the Heart
5. Holiday Food and Drug Interactions
6. Ketamine
7. Contaminated Cocaine
8. Skin Manifestations of Cocaine Use
9. Coronary Heart Disease and Passive Smoking
10. Wernicke's Encephalopathy - Korsakoff Syndrome
11. Infections and Immunity in Methamphetamine Dependent Users
12. Treatment of Alcohol Withdrawal Syndrome with Carbamazepine, Gabapentin and Nitrous Oxide
– Are they Effective?

Cigarettes and Menthol - Tobacco Companies are NOT our friends....Buyer

Tobacco companies learned early on that some people were choosing not to smoke as the smoke was harsh and caused throat and upper airway irritation. By adding menthol to cigarettes allowed for a cooling sensation in the mucosa and made it easier for the new smoker to accept. The tobacco companies knew that if they could make it less harsh and comfortable, more people would smoke and become addicted to cigarettes.

This fact is so well known to the tobacco companies that R. J. Reynolds has now begun to introduce the "Camel Crush". A "menthol-on-demand cigarette" that contains a small gelatin capsule in the filter that, when squeezed, turns a regular smoke into a menthol infused cigarette.

The tobacco companies know that newer smokers are more likely to continue with this deadly and costly addiction when the initial process is less harsh.

When it comes to cigarettes, beware...there is no safe cigarette and the tobacco companies know that. What is the impact on the newer smoker? One would imagine a less harsh cigarette could lead to an easier transition into dependence.



Menthol or not, cigarettes can be hard to quit. These tips are posted on the CDC's web site:

1. Set a date to quit smoking.
2. If you've tried to quit smoking before, think about what worked and what didn't.
3. Get rid of all your cigarettes and ashtrays at home, at work, and in your car.
4. Tell your family and friends that you're going to quit smoking. Ask for their support.
5. Ask your family and friends not to smoke around you or leave cigarettes out where you can see them.
6. Talk to a health care worker; ask them about quit-smoking medicines.
7. Get counseling to help you quit.
8. Sign up for a quit-smoking program at a local hospital or health center.

9. Try to distract yourself from urges to smoke. Talk to someone, go for a walk, or busy yourself with a task.
10. Change your routine when you first try to quit.
11. Do something to lower your stress. Options include exercise, reading, or a hot bath.
12. Plan something enjoyable to do every day.
13. Drink a lot of water and other fluids.
14. Keep trying. Smokers often try several times before they quit smoking for good. Hang in there; it's worth it.

Smoking Cessation in Adolescents

There have been no controlled trials for either nicotine replacement therapy or bupropion in adolescents. While the data in adults show benefits for both nicotine replacement and bupropion, nicotine patch therapy appears to decrease the amount of cigarettes smoked and withdrawal symptoms in adolescents, but effect on abstinence rates is unclear.

In a large open-label, non-placebo controlled trial, 101 adolescents aged 13-17 underwent six weeks of nicotine patch therapy with minimal behavioral therapy:

- Abstinence at six weeks was 10.9 percent; this decreased to 5 percent at 6 months.
- Average number of cigarettes per day decreased during the study from 18.2 to 1.8-2.5, but increased to 9.4 per day by six months.
- Expired CO levels correlated with reported number of cigarettes smoked; cotinine levels decreased in participants who quit smoking. (Smith TA, House RF Jr, Croghan IT, Gauvin TR, Colligan RC, Offord KP, Gomez-Dahl LC, Hurt RD. Nicotine patch therapy in adolescent smokers. *Pediatrics* 1996; 98:659-67.)

In a study by JH Price et al (*J Community Health*. 2007; 32(2):85-101), they examined pediatricians' use of nicotine replacement therapy (NRT) and the 5 A's counseling method (ask, advise, assess, assist, and arrange) with adolescent smokers. Using a mail survey, 203 randomly selected pediatricians (52 percent response rate) responded to a valid and reliable 37-item questionnaire regarding: perceptions of prescribing NRT, confidence in using NRT, perceived barriers to prescribing NRT, sources of information regarding NRT, and use of the 5 A's counseling method.

Results:

- 44 percent of pediatricians did not feel competent in helping adolescents quit smoking cigarettes.
 - The low level of perceived competence in helping adolescents quit smoking may be due to how few pediatricians identified medical school as a major source of information on helping adolescents stop smoking.
- Less than one-fifth (17 percent) were currently prescribing NRT.
- 48 percent perceived NRT to be safe for adolescent use but a majority (53 percent) rated themselves as not confident in their ability to use NRT.
- Those who prescribed NRT used transdermal patches (81 percent), nicotine gum (53 percent), or bupropion (44 percent).
- Pediatricians based their decisions on using NRT on whether: the adolescent showed openness to quitting (78 percent), the adolescent requested NRT (72 percent), and if the adolescent had a health problem exacerbated by smoking (56 percent).
- Helping adolescents quit smoking by incorporating five components (the 5 A's) into their tobacco cessation guidance, the vast majority of family physicians and pediatricians screen adolescents for smoking but are much less likely to intervene by assisting them in quitting.

Implications for Practice

- Pediatricians should regularly address the subject of smoking with their patients.
- Pediatricians need to have a system in place in which they can identify on the patient chart whether the patient is a smoker.
- Pediatricians should spend at least three minutes exploring how they can assist the youth in reducing or eliminating tobacco use. Research has shown that minimal counseling (as few as three minutes) regarding cigarette smoking was associated with a 13 percent quit rate.
- For adolescents addicted to nicotine, they may need assistance in quitting by using NRT products.
- Pediatricians may need to seek out, for themselves and their staff, training in the 5A's and NRT therapy to feel sufficiently competent in applying these interventions with adolescent smokers.
- Peer support may be a useful adjunct to treatment.

Ref: Kaplan CP, Perez-Stable EJ, Fuentes-Afflick E, et al. (2004) Smoking cessation counseling with young patients: the practices of family physicians and pediatricians. Arch Pediatr Adolesc Med 158:83-90.

Holidays: Your Heart and Your Weight

Strike a balance between celebration and health.

Is it true that more alcohol is consumed over vacations? Is drug use also increased? Can this use affect the heart?

Students who vacationed with friends during spring break dramatically increased their alcohol use. In contrast, students who stayed home or vacationed with parents during spring break were at low risk for excessive alcohol use according to research done by Grekin et al (*J Stud Alcohol Drugs*.2007; 68(5):681-8). Their findings highlight the need for targeted drinking interventions geared specifically toward students taking trips with friends and for further research into both personal and environmental variables that predict increases in drinking during spring break.

Studies about drug use and holidays are scant, however, there was a study done in Australia on the effects of backpacking holidays on alcohol, tobacco and drug use. (Bellis et al *BMC Public Health*. 2007; 7:1) found that the use of alcohol and other drugs by backpackers visiting Australia was common with use of illicit drugs being substantially higher than in peers of the same age in their home country. Individuals showed a significant increase in frequency of alcohol consumption in Australia compared to their behavior in their home country with the proportion drinking five or more times per week rising from 20.7% to 40.3%. The study noted that relatively few individuals were recruited into drug use (3.0%, cannabis; 2.7% ecstasy; 0.7%, methamphetamine). However, over half of the sample (55.0%) used at least one illicit drug when backpacking. Risk factors for illicit drug use while backpacking included being a regular club goer, being male, being based in Sydney, travelling without a partner or spouse, having been in Australia more than four weeks, Australia being the only destination on their vacation and drinking or smoking 5 or more days a week.

Holidays are good times, but they can also be a time that impacts your cardiac system greatly. One specific disorder related to alcohol and the holidays is "Holiday Heart Syndrome". It has long been recognized that alcohol consumed in large quantities for many years can induce an alcoholic cardiomyopathy, whereby the muscle of the heart is damaged and the heart does not function in a normal manner.

In 1978, Ettinger et al conducted a study evaluating 32 separate episodes of irregular heart rates in 24 patients. These patients consumed alcohol heavily and regularly; in addition, they took part in a weekend or holiday drinking binge immediately prior to evaluation. Based on the results of this study, the term *holiday heart syndrome* was coined. It was defined as an acute cardiac rhythm and/or conduction disturbance, most commonly supraventricular tachyarrhythmia, associated with heavy ethanol consumption in a person **without other clinical evidence of heart disease**. Typically, this resolved rapidly with spontaneous recovery during subsequent abstinence from alcohol use.

The most common rhythm disorder is atrial fibrillation, which usually converts to normal sinus rhythm (normal beating of the heart) within 24 hours. The clinical course is benign, and specific therapy is usually not indicated. Interestingly, even modest alcohol intake can be identified as a trigger in some patients with paroxysmal (intermittent) atrial fibrillation. Several mechanisms are theorized to be responsible for the occurrence of this irregular heart rate caused by alcohol. The possible etiologies include an increased secretion of epinephrine and norepinephrine, a rise in the level of plasma free fatty acids, and an indirect effect through acetaldehyde, the primary metabolite of alcohol.

Recently, similar reports indicated that recreational use of marijuana may have similar effects.

What about your weight and the holiday season?

Hull et al (*Nutr J* 2006; 5:29) stated that “more people than ever are considered obese and the resulting health problems are evident. These facts highlight the need for identification of critical time periods for weight gain”. They investigated the changes that occur in weight during the Thanksgiving holiday break in college students. 94 college students were recruited and a significant ($P < 0.05$) increase in body weight was found between pre (72.1 kg) and post (72.6 kg) Thanksgiving holiday. When gender and class standing were looked at, a significant ($P < 0.05$) increase in body weight was observed between the pre and post Thanksgiving holiday in males (0.6 kg), females (0.4 kg) and graduate students (0.8 kg). When participants were classified as normal or as overweight/obese, a significant 1.0 kg BW gain was found ($P < 0.05$) in the overweight/obese group compared to a non significant 0.2 kg gain in the normal group. Thus, **data indicated that participants gained a significant amount of body weight (0.5 kg) during the Thanksgiving holiday**. While an increase in body weight of half a kilogram may not be cause for alarm, the increase could have potential long-term health consequences if participants retained this weight gain throughout the year.

Yanovski et al (*N Engl J Med* 2000; 342(12):861-7) stated that “it is commonly asserted that the average American gains 5 lb (2.3 kg) or more over the holiday period between Thanksgiving and New Year's Day”. They set out to get an actual holiday-related weight variation in a sample of 195 adults. The results showed that the mean weight increased significantly during the holiday period (gain, 0.37 \pm 1.52 kg; $P < 0.001$), but not during the preholiday period or the post-holiday period. The average holiday weight gain was less than commonly asserted but this gain was not reversed during the spring or summer months: **the net 0.48-kg weight gain in the fall and winter was there to stay**.

Cocaine and the Heart

- Cocaine accounts for more than 100,000 emergency department visits in the U.S. each year, with chest pain being one of the most common complaints seen in 40 percent of cocaine-related emergency room visits.
- Long-term regular cocaine abuse impairs cardiac left ventricular function in African-Americans, according to research by Dr. Shenghan Lai and colleagues (American Journal of Cardiology 97(7):1085-1088, 2006).
 - Magnetic resonance imaging of heart muscle contractions disclosed lower pumping efficiency in areas of the left ventricular wall.
 - **The findings suggest that prolonged exposure to the drug may cause sub-clinical impairment that increases risk for cardiac events.**
- Acute cocaine abuse has previously been associated with several cardiac complications, including driving up the blood pressure, increased heart rate, and increased contractility. It also has vasoconstrictive (vessel narrowing) effects on the coronary arteries and is associated with increased platelet activation and clotting. Arrhythmia, ruptured aorta, heart attack and sudden death have all been seen after cocaine use.
- While the full pathological effects of cocaine are unknown, researchers believe a cocaine induced heart attack appears to occur soon after cocaine use, usually within the first few hours; although other studies suggest that, particularly in chronic users, ischemia or lack of oxygen to the tissues can occur many hours or even days after cocaine use.
- Echocardiograms, EKG's and serum creatine kinase values may show abnormal results because of cocaine use, so that these usual means of diagnosing a heart attack cannot be relied upon; cardiac biomarkers such as troponin can help diagnose cocaine associated heart attacks.
- Benzodiazepines should be considered an initial treatment among patients with cocaine associated heart attacks because they can relieve the chest pain and improve the blood pressure and heart rate. Nitroglycerin can also be effective to relieve chest pain and reduce blood pressure. Beta blockers may cause increased coronary narrowing (vasoconstriction) and should be avoided in cocaine associated heart attacks.

Holiday Food and Drug Interactions - Hazardous to your Health

Over the holiday season many people eat larger amounts of food and drink more than usual. There are many opportunities to try new foods. No matter the holiday, one constant is that food rules. This change in diet can have harmful effects and adverse reactions if the person is also taking medications. Approximately 91 million Americans are currently taking prescription medications. This number does not take into account over-the-counter medication use. This change in diet is perceived as a limited event, but it can have a significant impact on health.

Some examples of how foods and drugs can interact include:

- Food can speed up or slow down the action of a medication.
- Food can impair absorption of vitamins and minerals in the body.
- Drugs can stimulate or suppress the appetite.
- Drugs may alter how nutrients are used in the body.
- Herbs may interact with anesthesia, beta-blockers and anticoagulants.
- Food can slow the absorption of some medicines throughout the body.
 - Meals high in carbohydrates can adversely affect the absorption rate of some medications.
- Some medications need food to help with absorption for the body's use.

Alcohol-Drug Interactions: Although not technically a food, alcohol is often grouped with foods when considering interactions with medications. The National Institute of Alcohol Abuse and Alcoholism estimates that 25 percent of emergency room admissions may have alcohol-drug interactions as a component of the underlying problem. The elderly are especially at risk for this type of interaction since they consume more than 30 percent of all prescription medications consumed in the United States today. The risk for alcohol abuse is also significant in the elderly population.

Alcohol intensifies the effect of some medications, such as sedatives or pain medicines. Some medications increase the effects of alcohol causing dizziness, drowsiness, inability to control balance or walk properly. Alcohol can exhaust enzymes needed to metabolize the medication, thereby increasing the level of the medication.

Many physical signs may be attributed to an adverse drug reaction. These include:

- fatigue
- constipation or diarrhea
- confusion
- incontinence
- frequent falls
- depression

- weakness or tremors
- excess drowsiness or dizziness
- agitation or anxiety
- decreased sexual behavior

Some common food and drug interactions:

- **Zoloft® and Alcohol:** Consuming alcohol when taking certain medications could potentially lead to decreased drug effectiveness and an increase in side effects. In rare cases, the combination of alcohol and drugs produce a life-threatening reaction. Alcohol will have an effect on most medications that work in the central nervous system. Drinking alcohol while using a Serotonin Selective Reuptake Inhibitor (i.e., Zoloft®, sertraline HCl) could impair mental and motor skills; using alcohol when on a medication that treats insomnia could result in increased sedation.
- **MAOIs and Gravy:** Food can decrease or increase the effects of a drug or cause dangerous side effects. For example, eating tyramine rich foods (i.e., spinach, grapes, packaged gravy, aged cheese) while on a Monoamine Oxidase (MAO) Inhibitor (i.e., Parnate®, tranycypromine sulfate) can increase blood pressure and cause a serious and potentially life-threatening hypertensive crisis. And using Lipitor®, Atorvastin calcium in conjunction with grapefruit juice can lead to muscle pain and weakness.
- **Pepto-Bismol and Prescription Drugs:** Anything from antacids to cold and flu medications can lead to adverse effects when combined with prescription drugs. These over-the-counter remedies can also decrease the effectiveness of prescription medication.
- **Cipro:** an antibiotic prescribed to treat bacterial infections, as well as other antibiotics in its class, can bind with dairy products, preventing proper absorption.
- **Sular:** a high blood pressure medication, shouldn't be taken with high-fat foods because the interaction increases the amount of the drug in the bloodstream, increasing the side effects.
- **Over-the-counter drugs:** Tylenol, Midol and cough and cold products, which all contain acetaminophen, can cause liver damage when combined with large amounts of alcohol.
- **Grapefruit juice:** provides many nutrients, including vitamin C, potassium and lycopene. But chemicals in grapefruit juice and grapefruit pulp interfere with the enzymes that break down various drugs in the digestive system — including certain calcium channel blockers and cholesterol-lowering drugs. The result can be excessively high levels of these drugs in the blood and an increased risk of potentially serious side effects. Pomelos and Seville oranges, a type of bitter orange often used to make marmalade and compotes, may have a similar effect. Juices from oranges and other citrus fruits do not interact with medications in the same way. Citrus fruits are good sources of many nutrients, and should be included regularly in a healthy diet.

A sampling of drugs known to have potentially serious interactions with grapefruit products:

| Drug name | Type of drug |
|---|---|
| Amiodarone (Cordarone) | A drug used to treat and prevent abnormal heart rhythms (arrhythmias) |
| Buspirone (BuSpar), sertraline (Zoloft) | Antidepressants |
| Carbamazepine (Carbatrol, Tegretol) | An anti-seizure medication |
| Cyclosporine (Neoral, Sandimmune), tacrolimus (Prograf) | Immunosuppressant drugs |
| Felodipine (Plendil), nifedipine (Procardia), nimodipine (Nimotop), nisoldipine (Sular) | Calcium channel blockers used to treat high blood pressure |
| Saquinavir | An HIV medication |
| Simvastatin (Zocor), lovastatin (Mevacor), atorvastatin (Lipitor) | Statins used to treat high cholesterol |

What you should remember about food-drug interactions:

- Read the prescription label on the container. If you do not understand something, or think you need more information, ask your physician or pharmacist.
- Read directions, warnings, and interaction precautions printed on all medication labels and package inserts. Even over-the-counter medications can cause problems.
- Take medication with a full glass of water.
- Do not stir medication into your food or take capsules apart (unless directed by your physician). This may change the way the drug works.
- Do not take vitamin pills at the same time you take medication - vitamins and minerals can interact with some drugs.
- Do not mix medications into hot drinks, because the heat from the drink may destroy the effectiveness of the drug.
- Never take medications with alcoholic drinks.
- Be sure to tell your physician and pharmacist about all medications you are taking, both prescription and non-prescription.

Ketamine

Ketamine, one of the dissociative anesthetics may be a possible treatment for depression. What we know about ketamine:

- Ketamine was developed by Parke-Davis in 1962 as part of an effort to find a safer anesthetic alternative to phencyclidine (PCP) which caused hallucinations and seizures.
- Street names include jet, super acid, Special K, green and K.
- Ketamine comes in a clear liquid and a white or off-white powder form.

How is Ketamine used?

- Ketamine is a tranquilizer most commonly used on animals.
- The powder form can be used for injection when dissolved
- The liquid form can be injected, consumed in drinks, or added to smokable materials.
- Use of the drug can cause delirium, amnesia, depression, and long-term memory and cognitive difficulties.
- The incidence of recreational ketamine use increased especially in the context of raves and other parties (club drug).

Medical uses and research

- Since it suppresses breathing much less than most other available anesthetics, ketamine is still used in human medicine as an anesthetic; however, due to the severe hallucinations caused by ketamine, there are better anesthetics.
- There is ongoing research in France, the Netherlands, Russia, and the U.S. into the drug's usefulness in pain therapy, depression suppression, and for the treatment of alcoholism and opiate dependence.
- Researchers, who have published in the Archives of General Psychiatry (02/08) studied the effect of ketamine on the brain by using brain scans. Past studies found that the drug improved symptoms among depressed individuals.
- The NIH report of August 2006 noted that: "People with treatment-resistant depression experienced symptom relief in as little as two hours with a single intravenous dose of ketamine. Some participants in this study, who previously had tried an average of six medications without relief, continued to show benefits over the next seven days after just a single dose of the experimental treatment, according to researchers conducting the study at the National Institutes of Health's National Institute of Mental Health."
 - "Used in very low doses, the medication is important for research, but is unlikely to become a widely used clinical treatment for depression because of potential side effects, including hallucinations and euphoria, at higher doses. However, scientists say this research could point the way toward development of a new class of faster and longer acting medications. None of the patients in this study, all of whom received a low dose,

had serious side effects. Study results were published in the August 2006 issue of the *Archives of General Psychiatry*.”

- “Ketamine blocks the *N*-methyl-D-aspartic acid (NMDA) receptor. Previous studies have shown that agents that block the NMDA receptor reduce depression-like behaviors in animals. NMDA receptors are critical for receiving the signals of glutamate, a brain chemical that enhances the electrical flow among brain cells that is required for normal function. Studies indicate that dysregulation in glutamate could be among the causes of depression. Scientists think the reason current antidepressant medications take weeks to work is that they act on targets close to the beginning of a series of biochemical reactions that regulate mood. The medications’ effects then have to trickle down through the rest of the reactions, which takes time. Scientists theorize that ketamine skips much of this route because its target, the NMDA receptor, is closer to the end of the series of reactions in question.”

Caution: Ketamine abuse can lead to destruction of lower urinary tract

Chu et al in *BJUI* (2008) describe a syndrome of cystitis and contracted bladder associated with ketamine abuse. Their syndrome included:

- Urinary frequency
- Dysuria (painful urination)
- Urinary urgency
- Incontinence
- Painful hematuria (blood in the urine)
- Epithelial inflammation of the bladder
- Hydronephrosis (dilation of the pelvis and calices of the kidney – area where the ureter joins the kidney – resulting from obstruction of the flow of urine)
- Mild renal insufficiency

The underlying pathophysiologic mechanism is unknown. It appears that the lower urinary tract is affected much more commonly than the upper tract (kidneys, pelvis, calices). One theory is that a ketamine metabolite is responsible and it has a much longer contact time in the bladder than in the upper urinary tract. Thus, there is a direct toxic effect.

Contaminated Cocaine

It has been reported by the Departments of Health in New Mexico, Canada and Delaware that there have been several cases of agranulocytosis (*uh-gran-yuh-loh-sahy-toh-sis*) following the use of cocaine. This condition leaves patients unable to fight off infections.

The unusual condition can be fatal because it compromises the immune system. It appears that the condition could be related to using cocaine that is contaminated with levamisole. The U.S. Department of Justice reported that between January and April 2008, levamisole found in tested cocaine had increased from 9 percent to 19 percent.

Levamisole is a cancer (antineoplastic) medication used in cancer treatment. It is also widely used in veterinary medicine in the de-worming of many animals. Serious side effects have been reported with the use of levamisole including: allergic reactions (difficulty breathing; closing of the throat; swelling of the lips, tongue, or face; or hives); decreased bone marrow function or blood problems (fever or chills; or signs of infection); nervous system problems (confusion or loss of consciousness, extreme fatigue, memory loss, muscle weakness, numbness or tingling; seizure, speech disturbances); and others.

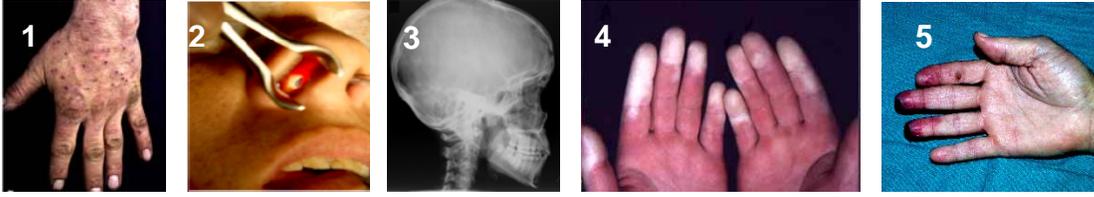
People who use cocaine and experience one or more of the following should see a doctor and inform them of their cocaine use:

- Persistent or recurrent fever and chills
- Worsening swollen glands
- Painful sores in the mouth or around the anus
- Frequent, persistent or worsening skin infections
- Pneumonia
- Worsening or persistent sore throat
- Thrush - a white coating of the mouth, tongue, or throat
- Other unusual infection

Skin Manifestations of Cocaine Use

Cocaine affects many systems of the body, including the skin (Brewer et al., Journal of the American Academy of Dermatology, 2008):

- Acute multifocal skin necrosis - pathologic death of skin cells
- Acute generalized exanthematous pustulosis - eruption of small elevations of skin containing pus
- Subcutaneous fat necrosis of the newborn - pathologic death of fat cells
- Cutaneous fibrosis - fibrous tissue formation in the skin
- Blackened hyperkeratotic palms ("crack hands") - horny layer of the skin is blackened
- Chronic skin ulcers
- Scleroderma - disease where there is thickening of the skin caused by swelling and thickening of the fibrous layer
- Cocaine - related bullous disease - blebs or enlarged air spaces in the lung
- Delusional parasitosis - significant itching and excoriations from scratching (see picture #1 below)
- Nasal septum perforation (see picture #2 below)
- Palatal perforation - hole in the palate
- Pott puffy tumor - osteomyelitis of the frontal sinus (see picture #3 below) - inflammation of the bone marrow and adjacent bone and cartilage
- Dental caries - tooth decay
- Gingival recession - gums recede
- Oral blisters
- Pseudovasculitis - false inflammation of the blood vessels
- Urticarial vasculitis - hive formation
- Stevens-Johnson syndrome - a life-threatening condition affecting the skin in which cell death causes the epidermis to separate from the dermal layer of the skin
- Midline destructive granulomas - nodules that destroy the underlying tissue
- Churg-Strauss vasculitis - an extremely rare disease that results from inflammation and which causes injury to organ systems.
- Raynaud phenomenon - Rare disorders that affects blood vessels. These disorders are marked by brief episodes of vasospasm (narrowing of the blood vessels - see picture #4 below)
- Necrotizing granulomatous vasculitis - destruction of the vascular system by granuloma
- Schonlein-Henoch vasculitis - A systemic vasculitis that causes the blood vessels in the skin to become inflamed, causing red spots. When the blood vessels in the skin get inflamed, they can bleed, causing a rash that is called purpura.
- Palpable purpura - hemorrhage into the skin that can be raised and thus felt
- Necrotizing vasculitis - blood vessels are destroyed
- Buerger's disease - Thromboangiitis Obliterans - an inflammatory disease of the small and medium sized arteries and veins of the extremities (see picture #5 below)



Brewer et al., Journal of the American Academy of Dermatology, 2008

Coronary Heart Disease and Passive Smoking

American Heart month is February and during this time, the health industry tries to raise and promote awareness and the benefits of staying fit through exercise and good nutrition. As part of a health plan for everyone, passive smoking must be taken into account.

- There is evidence that passive cigarette smoking is a risk factor for coronary heart disease and this evidence has existed for more than 20 years (Surgeon General Report of 1986, 2006).
- Some research puts the risk at an increase of 30 percent over those individuals with no exposure.
- Lightwood et al in the *Am J Prev Med* (2009) estimate that 25 percent or more of the US population aged 35 to 84 years old are exposed to cigarette smoke either at home, in the workplace or both.
- Serum cotinine levels (metabolite of nicotine) show that substantial passive smoking and resulting coronary heart disease occurs in people with no self report of exposure.
- How does this risk occur?
 - Even as little as 30 minutes of passive smoking exposure rapidly impairs the vascular (blood vessels) endothelial (vessel walls) function in coronary arteries. This impairment of function is thought to be due to oxidative stress on the wall.
 - Passive smoking exposure has also been found to cause a decrease in high density lipoprotein cholesterol (good cholesterol) and an increase in blood viscosity (which can lead to clot formation in the coronary arteries).
- Passive smoking accounts for 15,200 to 75,100 coronary heart disease deaths per year in the United States.
- Passive smoking accounts for 1.2 - 6.0 billion dollars being spent on coronary heart disease treatment in the United States per year.
- Smoking bans have been effective and exposure to passive smoke has been reduced by 25 - 40 percent over the last 8 to 10 years.

Smoking cessation clearly benefits the smoker and the non-smoker (passive smoker).

Wernicke's Encephalopathy - Korsakoff Syndrome

There are many causes of traumatic brain injury and dementia. Not all cases are caused by a blow to the head. In the United Kingdom, where this research was conducted, it is estimated that between 10 and 24% of all cases of dementia are alcohol related. The mechanisms of alcohol related brain damage include:

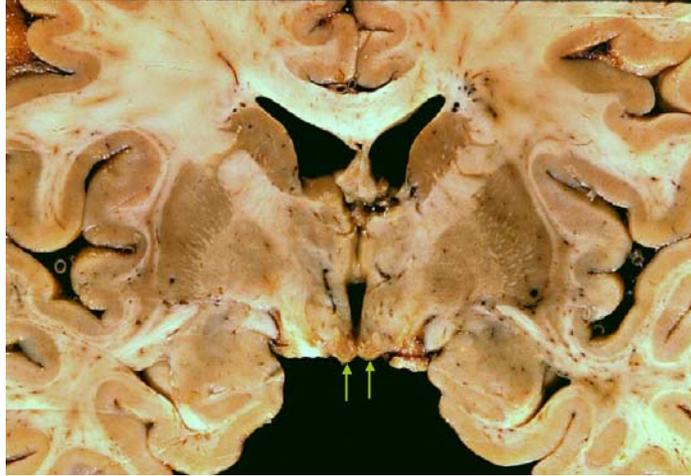
- Direct neurotoxin effects of alcohol
- Direct neurotoxin effects of Acetaldehyde (an alcohol metabolite)
- Thiamine depletion
- Metabolic factors associated with intoxication
- Metabolic factors associated with withdrawal
- Cerebrovascular disease
- Hepatic encephalopathy (a neuropsychiatric condition that occurs as a consequence of acute or chronic liver disease)
- Head injury related to alcohol use

Wernicke's encephalopathy is an acute neuropsychiatric reaction to thiamine deficiency. It is characterized by confusion, ataxia, nystagmus (rhythmical oscillation of the eyeballs) and ophthalmoplegia (lateral gaze paralysis). Only 20% of patients with Wernicke's are identified before death. Wernicke's encephalopathy is a medical emergency and leads to death in up to 20% of cases or goes onto Korsakoff's syndrome in 85% of the survivors. Up to 25% of the Korsakoff group will require long-term institutionalization.

Treatment of Wernicke's is high dose parental thiamine. The ocular signs recover in days to weeks after the treatment. The ataxia responds in the first week but can take 1-2 months to resolve. Acute confusion improves in the first 1 – 2 days but can take months to totally clear.

The Korsakoff syndrome includes confusion in a setting of the patient being totally awake with severely impaired conversation. The patient has impaired current and short- term memory loss and tends to invent recollections (confabulation) during conversation. The onset of Korsakoff syndrome is after a Wernicke event but can be insidious.

It is known that thiamine depletion affects at least 6 neurotransmitter systems including GABA. The neuropathy that can be seen with these disorders include neuronal loss, micro-hemorrhages, and gliosis (overgrowth of glial cells – the parenchyma of the brain) in the paraventricular and periaqueductal grey matter. Mammillary body (pair of small round bodies, located on the undersurface of the brain, that form part of the limbic system) pathology is seen in all Wernicke cases (note the normal mammillary bodies in the top picture and abnormal ones showing small hemorrhages due to thiamine deficiency in the bottom picture). There can also be seen variable degrees of cortical atrophy, especially of the frontal lobes.



Source: Kopelman et al Alcohol and Alcoholism Jan 2009 pp 1- 7

Infection and Immunity in Methamphetamine Dependent Users

- 15% of methamphetamine dependent users were hepatitis C positive (Gonzales et al., *Journal of Substance Abuse Treatment*, 2006 Vol. 31, 195-202)
 - 44% of the infections were in injection users
- Assessment of hepatitis A and B in methamphetamine dependent users:
 - 14% were positive for a past hepatitis A infection
 - 13% were positive for a past hepatitis B infection
 - 6% were positive for co-infection of B and C
 - 0.7% tested positive for acute hepatitis A and B
 - Injection users were more likely to have positive hepatitis A and B test results compared to non-injection users.
 - 27.4% tested positive for hepatitis A
 - 23.6% tested positive for hepatitis B
 - 16.3% tested positive for co-infection of hepatitis B and C
- It is important to note that hepatitis A in the face of B and C can lead to increased morbidity and mortality and that hepatitis B and C can result in an increase in hepatocellular carcinoma (liver cancer). (Hagan and Des Jarlais, *Mount Sinai Journal of Medicine*, 2000, Vol.67, 423-428)
- Methamphetamine inhibits innate immunity in host cells, thereby facilitating HCV replication in human hepatocytes (liver cells).
- Methamphetamine inhibited natural intracellular interferon alpha expression in human hepatocytes, which was associated with increased HCV replication.
- Methamphetamine also compromised the anti-HCV effect of recombinant interferon alpha as used for hepatitis C treatment.
- Treatment for methamphetamine dependence appears to be associated with significant reductions in HIV risky behavior (sexual and injection practices).
- Longer treatment retention and treatment completion were significantly related to greater reductions

Conclusion:

Adding assessments of hepatitis status to health care venues may result in heightened awareness of risk factors and early prevention and treatment opportunities, ultimately resulting in improvements in reducing the spread of hepatitis infections among all illicit drug using populations.

Treatment of Alcohol Withdrawal Syndrome with Carbamazepine, Gabapentin and Nitrous Oxide – Are they Effective?

A review of the treatment of alcohol withdrawal syndrome using carbamazepine, gabapentin and nitrous oxide can be found in the *American Journal of Health Systems Pharmacology's* June 2008 edition written by Prince and Turpin.

The conclusions of the review are:

Carbamazepine: This may be a useful agent for the treatment of alcohol withdrawal, particularly in the outpatient setting. The authors noted that additional trials are needed, since the trials that were reviewed had a very small sample size and included patients that did not use illicit substances. Also, in the trials that were evaluated, the carbamazepine was compared to benzodiazepines given in a fixed dose schedule as opposed to a preferable symptom-triggered protocol. Carbamazepine is also limited by its adverse effects which include: vertigo, pruritus, nausea and vomiting. High dose carbamazepine was associated with rash, diplopia, syncope, and ataxia. Drug interactions are not uncommon with its use. If it is used in seven day protocols, one does not have to worry about the liver or hematologic adverse effects.

Conclusion of the authors: Routine use of carbamazepine for alcohol withdrawal syndrome **should not be advocated** until additional trials have compared it to symptom-triggered benzodiazepine therapy.

Gabapentin: It is noted that gabapentin is similar in structure to the neurotransmitter GABA and it may help in its release. One trial found gabapentin not superior to placebo. It may be useful in mild withdrawal according to one study.

Conclusion of the authors: Routine use of gabapentin for alcohol withdrawal syndrome **cannot be recommended** until additional, well-designed, controlled **clinical trials are run**.

Nitrous Oxide: The authors felt that the clinical trials using nitrous oxide have been generally poor. One study used benzodiazepines and nitrous oxide so that no difference in efficacy was shown. Also, nitrous oxide requires the use of appropriate delivery apparatus as it is a gas. Training and equipment are needed which makes its use in alcohol withdrawal very limited.

Conclusion of the authors: Nitrous oxide **should not be used** in the treatment of alcohol withdrawal because sound clinical trials are lacking and its administration requires additional training and specialized devices.