

Chapter 1

What is Detox (and what it is not!)

This book was written originally as training manual for the physician assistants and nurse practitioners who worked and trained with me in an active inpatient detox center and as such assumes that you have a good understanding of basic medicine and pharmacology.

First off, I have to state that the subject of detox is acknowledgement of both the science of medicine and definitely the art of medicine. Why both? Because there is no other field of medicine that encompasses such an arena of possibilities (with the exception of emergency medicine) but which also requires you to deal be practiced in the art of dealing with difficult patients in ways that arrive at the best care, even when the patient frequently does not share that goal. Thus, inpatient detox is a combination of emergency medicine, internal medicine, pharmacology, detective work, psychiatry and the art of self-protection all rolled into one specialty.

To elaborate a bit, no other field of medicine requires you to deal with patients who frequently do not want to be there, do not want to tell you the truth (or may not even know the truth). Patients who may have acute, life-threatening conditions developing before your eyes and yet will shower you with obscenities, spit, and possibly vomitus, all the while trying to either hit you (and/or the staff working with you) simply to convince you to let them go.

And to add further frustration, you may have just seen this same patient the day or week before in the same situation and their attitude was the same then. For, unfortunately, the field of medical detox has a high ratio of what is known as frequent flyers, patients for whom there is little hope that they will stop their self-destructive behavior, despite your best efforts.

Yet despite all the hazards to the field, there is no disputing that someone knowledgeable has to do this work and that it does take a considerable knowledge base to be able to do it right ... thus this book was created.

Please note: I fully acknowledge that alcoholism is a genetic disease and that it is as unwanted by the patient as any fulminant disease. I plan to try my best to avoid the political or social aspects of alcoholism or drug usage and addiction in this book, as that subject is way beyond the scope of this book. Nor will I deal with the actual treatment of addictions, but will instead concentrate on getting the patient safely through the detox period, so that they can survive to be in a treatment program. Believe me that is complicated enough.

In this book I intend to concentrate on the inpatient detox, not outpatient or social detox, and more importantly, the whys of inpatient detox. (Which are significantly different than outpatient or social detox center protocols, which are used for more stable patients.) The reason for this is that while inpatient detox is not rocket science, it is, in fact, an ART. It is an art because every patient is different and your instincts and experience will definitely tailor

your responses to the patients. Thus, the whys should guide you in the best practice of these complicated patients so that you can deliver the best possible care.

What is difference? **(Between Inpatient and Outpatient Detox)**

Inpatient detox is frequently misunderstood; partly, because most clinicians do not want to deal with the intoxicated, uncooperative patient. Many health care practitioners and institutions do not take the detox patient seriously. They place them in minimal care settings and treat them with benzodiazepams and simply wait out their intoxicated period. Then, once they are “sober,” they release them back into the environment from which they came. Unfortunately, a certain percentage of these patients wind up developing complications and the institutions that admitted them end up spending huge sums of money when the more intensive of these patients wind up in intensive care.

In my personal experience and opinion, it should only be a very rare patient with very significant comorbidity who winds up in intensive care. All other patients can be treated in much lower care settings IF they are treated correctly and the paradigms are understood. This does NOT mean a social or outpatient detox situation, but rather an inpatient ward where full hospital resources are available, just not at the level of intensive care.

Of course most patients who present intoxicated do not need to be admitted to a detox center. The majority of patients can, in fact, be treated in a social detox setting at very low cost. These are the patients with no medical complications, who have not been taking drugs with suppressive properties regularly for any significant time, and who do not have significant medical co-morbidities. Both in terms of dollars and time, these patients are not best treated on an inpatient setting. Thus, a person who has simply had too much to drink can sleep it off, or can be watched in a non high-risk area or a non-hospital based social detox center. They surely do not need to be admitted to a hospital.

However, this brings me to a point that needs to be stated clearly: the art of detox is NOT sobering up patients. One of the barriers to this appropriate care is that, unfortunately, the average person and institution misunderstands even the term “detox.” They erroneously believe that detox is simply as the place to sober up “the drunks.”

Instead, inpatient detox needs to deal with patients with significant withdrawal symptoms and co-morbidity, like histories of (recent) past DT's, seizures, serious mental illness, serious medical problems or significant additional drug abuse. These co-morbidities impact the probability that the patient will have complications that, unless treated correctly early, will wind up costing the admitting institution significant dollars beyond the cost of simply drying that patient out. So, in fact, the purpose if an inpatient detox specialist is to minimize those costs by aggressively treating and preventing complications, thus minimizing both hospital lengths of stay and the relative costs of that stay by preventing admissions to the intensive care units.

Therefore, we will not consider admission to the inpatient detox ward simply based on the amount of alcohol or illicit substance in the blood (with the exception of alcohol poisoning, a subject we will deal with specifically in a later chapter), but rather based on the dangers that occur when such a patient is withdrawing or coming down from alcohol or other depressant substances. Patients without such co-morbid conditions are best managed in social or outpatient detox settings because it is vastly less expensive to the bill payer and also less restrictive to the patient.

In fact, in earlier years, as high as five to ten percent of people who went into full-blown delirium tremens (DTs) wound up with Wernicke- Korsakoff syndrome or died despite subsequent treatment. Today such deaths are rare, not only because we have better treatment but mostly because clinicians, for the most part, recognize the symptoms of a patient beginning to get into trouble and stop the progression before they reach DTs. However, of patients who do develop DTs, five percent will die, mostly due to cardiac arrhythmias and/or aspiration.

Additionally, it is well known that there is a very high preponderance of psychiatric problems in patients with chronic alcoholism and/or drug use/abuse. (As both primary and/or secondary problems.) From organic depression to schizophrenia, to drug-induced mood disorders and psychosis, alcohol makes all these conditions worse and the conditions make the use of alcohol (and drugs) more likely and the effects of drinking and using worse.

So this book will deal with the withdrawal process and the dangers it presents from the point of view of being treated in an inpatient detox center by the detox specialist. As you will see, those dangers are very real and, in fact, are multifocal. Believe me, I couldn't possibly cover them all! Therefore, I have concentrated on the more common concerns.

An important note on viewpoint. This book is written from the viewpoint of someone who works on an inpatient detox unit daily and is not meant as an academic text. It is instead a review of articles and material already published and pearls of personal experience, not new material, but instead a compendium of such material.

Please note that while I applaud the science of medicine and believe we must practice science based medicine there is a difference in both approach and viewpoint between the practice of treating the patient who wants to be there and wants to participate in getting better and those who can not or will not do so.

Much of what I have included is based on experience, personal opinion, and knowledge gained over the years. Therefore, my opinions should be taken as such and questioned and researched so that you can benefit from the continual improvement of the science of medicine in addition to this material.

Why Specialized Detox units?

People who practice medicine rarely like to bring up the cost of a service, especially as a criteria, because we have been trained that our goal is (and should be) to provide the best care we can and use what should be done as the criteria instead of looking at the cost of a service as the criteria for how something should (or if it should) be done.

Unfortunately, alcohol and drug addiction is an area that impacts greatly on the economics of the whole medical system and there are no clear, precise answers on how to deal with this situation.

Furthermore, the disease process is so disabling that, in many cases, the patient doesn't have the capability to produce an income for themselves, let alone have the resources to pay for their treatment. Therefore, frequently the cost of alcoholism and drug detoxification is frequently born by the state and county governments.

Additionally, these departments have a fixed (and chronically strapped) budget so that cost becomes a huge factor in how they would prefer that patients be treated.

Now there are no clear studies I have found that would delineate what percentage of patients presenting to the local detox center require medical detoxification. (Meaning they have to be transferred to the local medial center.) But it is clear that these patients do cause a huge cost and drain on the financial resources of those who pay for these services.

So while the cost per patient per day is low in the local non-medical detox center, the cost of the patient who is admitted to intensive care is one of the higher possible costs and quickly brings the overall cost of detox far higher than it should be.

Even for those who are admitted to a hospital based detox ward, the length of stay is also extremely variable, averaging from three to ten days, depending on the severity of the patient, the drugs they have been using, their medical comorbidity and the intensity and route of their usage. Please note that this discussion, of length of stay, refers to the detoxification of patients, NOT treatment of their addiction, which is a completely different subject.

There is good news, however, the fact is that with good detox treatment the overall length of stay of patients with even high blood alcohol levels and with many co-morbid medical conditions can be managed on a NON-intensive care unit. Experience has shown that the average length of stay of such units is between three and four days, which is lower than the average length of stay in the average non-detox unit.

This, of course, directly decreases the costs of the detox and can, in fact, improve morbidity and mortality rates and long-term complication rates. Which is good for both patients and the institutions paying for such care.

This, of course requires an excellent understanding of the pathophysiology of detoxification and the complications of such. But the point is that such units and specialist are good for both patient care and for those paying the costs of the detox.

That is what this book is all about.

Chapter 2

The need for Excellent Exams

One of the biggest problem you will face as a detox specialist is the mind set of those who deal intermittently with the chronic alcoholic and drug abuser. The problem is not the patient themselves but instead those, including the medical professionals, who deal with these patients. The typical detox patient is less than ideal: they are frequently (and definitely) less than cooperative and generally cannot pay for the medical or supportive care they require. As a result, many people and facilities will provide the absolute basic, essential requirements and then transfer them out as fast as they can.

While I can understand this from an economic viewpoint, it leaves the patient in a tenuous situation at best. Additionally, and unfortunately, due to the fact that these patients usually have a history of being seen repeatedly for the same condition, the providers who see them tend to rely on past history to make their assessments rather than do the work of obtaining a new data set. Thus, they do a less than a thorough exam of the obnoxious patient, who has now presented for the third or fourth time this month for same condition.

Blame cannot be placed totally on the care facilities. Because these patients are not only generally uncooperative and unappreciative to begin with, they do not understand the need to repeat assessments, which, from their standpoint have already been done. Therefore, such patients frequently resist attempts to do an adequate assessment or garner complete histories of how they came to be brought to the evaluation center. Sometimes these patients resist to the point of being physically violent. Even requests to assess can set off physical violence in some patients.

Unfortunately this is a recipe for a disaster that is only waiting to happen.

The final ingredient in this recipe is that these patients frequently experience blackouts and thus frequently truly do not know what has happened to them. Real-life experience has taught me that patients can leave detox, resume drinking, and in less than a single day get into fights, fall or sustain very significant physical trauma and yet not even be aware of it or may minimize the importance of such.

Such patients may present with developing head injuries, ruptured spleens and significant fractures that are not picked up, even though they may have been evaluated by EMT ambulances, an emergency room, or trauma center only hours before they were brought to the detox center. Unfortunately I have seen all of these exact situations.

In a nut-shell, it comes down to the fact that EVERY patient who presents to a medical detox facility NEEDS have a NEW physical assessment EVERY time they present. Regardless if they just left your facility or an ER an hour ago, the ONLY way you can tell that they have not

sustained a serious injury from the time they left to the time they present is to do a good examination YOURSELF!

It is true that you do not have to repeat a lengthy history of data that does not change (past military history, age they started drinking, past DWI's, social history, etc.). It is imperative that you update any clinically relevant data that is prone to change - especially trauma and surgical and medical diagnosis. Also include what history you know, including police reports, so as to allow other staff and other shifts to be able to assess changes in the patient as they begin their detox.

Particular care and interest has to be placed on any new or significant contusions, deformities, or neurological findings. Remember that the patient may not want to, or even be able, to tell you the truth of what happened, let alone any details. The reason they will give is for personal or even legal reasons. (Patients may believe they will have legal problem from telling you the truth, regardless of what you tell them.)

In addition, EVERY patient who presents needs to have at least a basic laboratory exam of basic parameters to include electrolytes, kidney function, magnesium, levels of any anti-seizure medications they were on, and a CBC.

The obvious reason why all patients need a new work up on presentation is simply that it is good medicine. Doing so gives you both a present evaluation and a good base line with which to compare changes. If the patient begins to deteriorate, then you have something solid to compare the new finding with. This makes your decisions of what to do considerably easier.

I can tell you from experience that over time you WILL run into situations where it was your base line exam that gives you the clue to what is happening and, thus, what to do about it. Don't handicap yourself or the patient by doing a limited exam.

Sometimes you will get patients who attempt to refuse to cooperate with any exam at all. Over time you will learn ways of verbally convincing them that it is in their best interest to at least let you do a "partial exam." Even if you are not able to do a good exam, you will be able to get the basics - including lungs, heart, baseline neurological, abdominal exam, condition of their extremities and laboratory exam in very short order. Then, once they are more cognicent, you can go back and complete your exam.

You will find that this is not only good medicine, but that it will also give you data to allow you to discover, and thus treat, medical problems before they become crises. This will make both you and your patient's lives easier. It is worth the effort to insist on the practice of good medicine. It also makes your costs go down.

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Chapter 3

Understanding the Withdrawal process

Simple Withdrawal versus Hallucinosiis versus DT's

There is a great disparity between how patients in withdrawal are treated depending on the location they are treated and the specialty of the clinician treating the withdrawal process. This directly causes a significant difference in the treatment outcomes and the cost of the process.

This is because many specialties treat the symptoms of the detoxing patient without treating the underlying cause of the symptoms. Unfortunately, this places the patient at increased risk despite the fact that the patient looks better outwardly. To prevent this situation, it is absolutely essential that you understand the reasons why the symptoms occur. So please bear with me a minute as I delve into anatomy and physiology.

The dangers of detox come partly from hyperactivity of the brain including a part called the reticular activating system (RAS). The RAS is a part of the brain that regulates how much activity goes on in the brain as a whole. The rest of the hyperactivity, while not yet completely understood, seems to come from the sudden decrease in suppressor chemicals that normally inhibit over-activity of the brain.

A good analogy is that depressants act like a brake on that part of the brain, slowing the function down. However, the brain adjusts overall brain activity (with time) to fight this slowing effect and pushes back against the drug causing the slowing. The longer the brake is applied, the stronger and more effective the brain becomes at pushing back. However, if that brake is suddenly removed, then there is nothing to keep the brain from having too much stimulation and the brain goes into hyper-drive.

Think of a car driving down the road with a governor that tried to keep a constant speed. If you apply the brake, then the governor tries to give the car more gas to speed it back up to the set speed. If you suddenly remove the brake, then the car will surge ahead, possibly fast enough for it to lose control and crash.

In fact, the physiology is that alcohol alters neurotransmission in the brain, particularly affecting the inhibitory neurotransmitter γ -aminobutyrate A (GABA-A). Alcohol allows more chloride to enter the neuron, making the neuronal cell membranes less likely to depolarize. This makes GABA far more effective. Because of this potentiation effect, long-term intake of alcohol causes an adaptive decrease in the amount of GABA produced. This is directly dependent upon the amount of alcohol consumed, liver status, and the length of time that alcohol has been consumed. When alcohol consumption is suddenly stopped, ethanol is no longer available to enhance GABA, so the inhibitory function is greatly reduced.

However, when there is an abrupt cessation of alcohol intake, a rebound stimulatory effect is produced, resulting in adrenergic hypersensitivity of the limbic system and brain stem. This

leads to irritability, which can be expressed as aggressive behavior, tremors, seizures, and possibly even frank DTs.

The reason for this irritability is that GABA usually inhibits other neurotransmitters, which are now functionally present in excess. These neurotransmitters, (particularly the catecholamines; norepinephrine and dopamine) produce stimulatory effects, which are essentially the opposite effects of alcohol. The functional excess of dopamine produces hyperactivity, tremors, hallucinations, delusions, and seizures. Other withdrawal signs include hand tremors, increased temperature, clouding of consciousness, nervousness, increased heart rate, insomnia, and increased blood pressure.

Thus, the treatment goal of detox is to control the entire GABA system and brain stem, not simply treat the myriad of physical symptoms that appear peripherally as the brain races too fast. Thus, if you treat the peripheral symptoms; elevated pulse and blood pressure, etc. with medications, but do not address the functional decrease in GABA, you have done nothing to treat the real cause (the rebound of the inhibitory centers of the brain) and the person is at a high risk of having seizures, and developing DTs.

Additionally, from the simile of the governor on the car, you can also see that drugs that do not affect the RAS or GABA system do not pose a direct threat of detox problems. Thus cocaine is not, in itself, a drug that can cause hyper-stimulation problems with detox. Note the cautious way I worded that statement. This is because cocaine can worsen psychiatric disorders and the psychiatric disorders may require hospitalization, but the person is not in physical danger from the withdrawal process of cocaine itself even though they may have significant problems from the intoxication. The same is true of amphetamines.

The same is also true for opiates, because while they do sedate the patient somewhat, they do not suppress the RAS or GABA except in large doses where they cause respiratory depression. Thus opiates do not cause seizures or DTs on withdrawal. Note they do cause other physical symptoms.

Also note that sudden withdrawal of all anti-seizure medications, or high dose benzodiazepines, pose much the same risk as withdrawal from alcohol, for many of the same reasons.

Essential Definitions

One thing that is imperative if one is to be able to treat detoxing patients correctly is to understand the conditions and the terms that are appropriate.

It is very common for the patient who is withdrawing from alcohol or other depressants to have tremors. However, tremors are NOT DTs. Hand tremors can be from withdrawal, benign essential (or familial) tremors or even deliberate attempts of the patient to get medications. Tongue tremors are far more accurate, harder to fake and are very accurate indicators of the state of RAS activation.

When a person starts having activation of the GABA-A system, the first signs will be elevation of peripheral systems; temperature, pulse and blood pressure. Again as noted above, treating these symptoms will only mask the changes that are occurring in the brain. As further activation occurs, the patient will start seeing things out of the corner of their eyes.

Alcoholic Hallucinosis

Is the first stage of impending DTs and can be differentiated from DTs by the fact that the patient still has an intact sensorium. Usually patients report seeing spots or objects that look like dots or snow flakes, hearing things like radios playing music or the television being on (when there is no radio or television there), or classically, the feeling that bugs are crawling on them (this is called formication). The sensorium, however, will still remain clear. Rapid pulse rate and elevated blood pressure are symptoms of withdrawal and are not in themselves diagnostic of DTs.

Delerium tremens (DT's)

The definition of delirium tremens (DTs) is a disorder involving sudden and severe mental changes or neurologic changes (including possibly seizures). In DTs, the patient's sensorium will not be clear and they will develop a delirium and lose all orientation. As this progresses, the patient's temperature may also climb even further which can increase the risk of seizures and increase mental status changes.

WHY SOME PATIENTS DEVELOP WITHDRAWAL COMPLICATIONS AND OTHERS DO NOT

It is VERY important to note that the level of activation of the GABA-A system depends on the patient's tolerance to alcohol and thus the level of depression they had produced of the GABA-A system before they slowed down or stopped their drinking.

It is important to note that tolerance to alcohol develops because of adaptation to the chronic use of alcohol based on the quantity and length of time that they were drinking. It is not directly related to the acute level of alcohol in their system. Therefore, it is not uncommon (but not impossible) for patients who have been drinking excessive amounts for considerable time to experience alcoholic hallucinosis or even frank DTs while they still have significantly high blood alcohol levels.

From personal experience I have had (a limited number of) patients who would come into the detox center with blood alcohol levels that were in the mid to upper .400's and would still go

into frank DTs symptoms by the time blood alcohol levels dropped to the lower .300's or upper .200's if they were not receiving medications.

Many other patients can experience alcoholic hallucinosis with blood alcohol levels that are high enough to intoxicate non long-term drinkers. It is the tolerance to alcohol (the quantity of alcohol per 24 hour period), their liver status (which determines how fast they break down alcohol), the length of time they have been drinking (duration), PLUS whether they have ever previously experienced hallucinosis, DTs or seizures (regardless of cause) that determines the risk for the patient.

Finally, patients who develop too great of an activation of the GABA-A system are at risk for the full spectrum of seizures even if they have never had a seizure before.

Be aware, though, that co-factors like the use of other depressants, anti-seizure or anti-psychotic medications, or history of significant head injuries greatly increases the risk of seizures and thus requires a slower and more cautious detox.

TREATMENT (theory)

Since the real treatment of withdrawal of a depressant substance is to prevent or control rebound of the GABA-A system, then substances that affect this system are the best to use. The benchmark of these drugs is the benzodiazepine class of medications.

Unfortunately, the use of benzodiazepines in themselves are not enough to cover the entire GABA-A system and thus patients can still experience significant withdrawal symptoms even on moderate doses of benzodiazepines.

NOTE: Benzodiazepams only stimulate some of the GABA receptors of the brain.

Another problem is the fact that once started, benzodiazepine levels have to be maintained and decreased slowly. Experience has taught me that once the patient starts experiencing alcoholic hallucinosis, it takes significantly longer to complete the withdrawal process and risks of complications to the patient are significantly higher.

Thus the use of the longer acting benzodiazepines, in patients who can tolerate them, produces superior control of the hyper-activation of the GABA-A system than the use of the shorter half-life benzodiazepines do. Superior control of the GABA-A system can also be accomplished by the use of multiple, simultaneous medications rather than the use of a single medication, regardless of the dose. Therefore, aggressive treatment will use a combination of medications to treat the widest possible range spectrum of the GABA-A system.

OTHER CONSIDERATIONS

If the patient is not in DTs, ALL major psychotropic medications (typical and atypical), in general, should be stopped if possible. This is due to a combination of potentially lowering seizure thresholds and also due to changing the activity levels of the cytochrome P450A system of the liver, which is responsible for the breakdown of many other medications that the patient may take. Buspirone, especially, should not be given during detox as it dramatically lowers seizure thresholds.

Also, particular attention needs to be paid to the quantity of nicotine being used (both smoking and chewing). Note that both increases and decreases of nicotine can dramatically change how the liver processes other medications, especially during the detox period (directly affecting cytochrome P450A system).

Finally the history taken on admission should, if possible, pay close attention to the amount of caffeine and the use of over-the-counter vitamins. It is not unusual for patients to erroneously believe they can protect their liver with use of over-the-counter vitamins and herbal supplements. It is also not unusual for them to be taking amounts that are in themselves toxic to the liver. If they take more than one supplement containing quantities of oil soluble vitamins, levels of these vitamins can quickly build up far past RDA recommendations. It takes careful consideration of the answers to these questions during the history taking to determine these risk factors. Dehydration, unfortunately, increases the effects of such hypervitaminosis.

Excessive caffeine adds to the diuretic effects of alcohol, promoting further washout of medications and electrolytes, and contributes to blood pressure problems both in elevation and orthostatic situations caused by dehydration. Caffeine can also cause increased anxiety when taken, but will also cause a significant headache on withdrawal if the quantity the patient normally consumes is high.

Be aware that patients who have been drinking significant amounts for significant periods of time may not show symptoms of withdrawal for several days from the point where they stop drinking. This is due to several factors, but essentially due to the fact that the damaged GABA-A system may take time to recover enough that it can respond to not being sedated with a depressant. Thus patients may not go into withdrawal for three to seven days after stopping drinking, even though their blood alcohol levels are zero the entire period of time. Now this is unusual, but definitely not unheard of, and the patient's history is the key to this danger as patients will tell you this fact, IF you ask.

Also note the word 'significant' in the above paragraph. There is no specific figure I can substitute for this word to make the decisions absolute. The fact is that 'significant' varies for every patient.

Finally, patients who have a past history of a significant head injury may also have a delayed withdrawal response as above, PLUS they are at a higher risk of withdrawal seizures, even if they have not had a seizure before. Therefore extra care, and time, needs to be taken when evaluating and detoxing these patients.

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Chapter 4

ACUTE intoxication

While I have defined that detox in itself is not primarily a problem of intoxication but rather of the withdrawal, every detox deals with patients who present in an intoxicated state.

Getting a patient safely detoxed is both easier and harder than I can describe on paper. It is harder because sometime it can get very complicated and the complications can sometime compound each other. It can also be easier than I describe, because if you aggressively seek out the problems and treat the problems before the patient gets into trouble, it is relatively easy. I like to think of it much like landing a plane. If the weather is fine and the runway clear, then things should go smoothly; but it is when all the factors are against you that training and experience will determine if you walk or are carried away.

Detox from alcohol is much the same. There are rules and parameters to follow and, in most cases, these work just fine to get even complicated detox patients with scary alcohol levels and histories safely down. Other times, multiple complications arise and you will need every tool you have ever developed to get a good outcome.

Not surprisingly, the levels of intoxication vary greatly and the effects the patient shows also vary greatly even for patients with similar blood alcohol levels. For a patient with little tolerance, blood alcohols of 0.15 can cause significant disturbances in gait, speech, emotional lability and coordination. Other patients with a blood alcohol over 0.45 mg/dl can appear to be affected in only a minor way and have no perceptible changes in coordination or orientation. Thus one canNOT predict a blood alcohol level based on the outward clinical appearance of the patient.

Additionally, the levels gotten on a breathalyzer may have little correlation with the blood alcohol, not because of any inherent problems with the breathalyzer machine, but rather with the fact that the veteran may have consumed a large quantity just prior to being escorted to the detox center. Thus his blood alcohol will still be rising as they are being processed. Because it usually takes the laboratory service some time to collect the blood sample, compared to the quick collection of the breathalyzer, the alcohol tends to be absorbed and thus the readings of actual alcohol levels are more correct.

Alcohol Poisoning

Alcohol poisoning is defined as a condition in which a toxic amount of alcohol has been consumed. In reality it is an overdose of an alcohol. The body is overwhelmed by the amount of alcohol in the system and cannot metabolize it quickly enough.

Symptoms of alcohol poisoning include:

1. Confusion
2. Vomiting
3. Seizures
4. Slow or irregular breathing
5. Blue-tinged skin or pale skin
6. Unconsciousness ("passing out")

In reality, the condition is, having more alcohol in your system than your system can handle. However, the real danger in the level of blood alcohol is related directly to the patient's tolerance. When patients consume quantities that they are totally unable to process, they develop the situation of alcohol poisoning. When this happens, the patient can suffer from system depression and especially respiratory depression that, if not treated quickly, will lead to total system collapse.

Patients with alcohol poisoning will develop lethargy to the point where they are not arousable even with deep stimulation. Such patients will show decreased Babinski reflexes, followed by decreasing respirations and oxygenation levels. The cascade of such progression is obvious, leading to death if not treated quickly.

Experience has taught me that despite levels found in the books, patients can suffer from alcohol poisoning with a wide range of levels. Some patients can handle amounts (blood alcohol levels well over 0.4 mg/dl) that are considered toxic in most books with little outward effects and definitely no lethargy. Other patients will get in trouble with blood alcohol levels less than 0.3mg/dl. The difference results from the patient's personal tolerance and the present state of their liver's ability to break down alcohol.

Therefore it is ONLY by a careful examination of the patient's level of consciousness that one can determine if they are in danger from this condition. Patients who are questionable need to be followed closely and serially. This ensures that they do not get into trouble and that if symptoms of alcohol poisoning occur that they get treated for this immediately. Patients who do develop symptoms of alcohol poisoning need to be supported with oxygen and transferred immediately (by ACLS ambulance) to an intensive care setting that has the ability to support respiration and dialyze the patient if needed.

Chapter 5

Common Deficiencies Found in Detox Patients

THIAMINE

Another situation that will be covered again in much greater depth in later chapters is the neurological condition of patients entering detox. Because the effects of alcohol can make neurological assessment difficult due to the confusion that the intoxicated patient displays, all patients should be given thiamine on admission, especially patients who display nystagmus.

This is because alcohol actively washes circulating thiamine out of the blood stream and creates a deficiency that becomes acute once the patient begins to sober up.

Unfortunately, most patients will not accept an IM injection of thiamine due to the fact that it does produce a burning symptom. This will be so in spite of repeated attempts to explain the seriousness of the situation. However, attempts should be made to try and convince them of such and if they will not agree, they should be started on 100mg of oral thiamine per day with first dose being as soon after admission as reasonably possible.

NOTE: Patients who need to be given boluses of Glucose (for example diabetics with low blood sugars who are detoxing) need to be given thiamine at the same time because the administration of glucose can cause the sudden onset of Wernicke's encephalopathy in a patient who is critically deficient of thiamine.

(Wernicke's encephalopathy is a syndrome of mental disturbance, ataxia, nystagmus and lateral rectus palsy, which will be covered in more details in a later chapter.)

Use of Benzodiazepams

I wish it could be as easy as it is to say that any patient who is still intoxicated cannot go into DTs. However, if you look back on the last chapter, you can see that if the over stimulation of the RAS is great enough (due to high levels of prolonged drinking or other depressants), in fact, the patient can go into full blown delirium tremens even while they have what the average person would consider to be relatively high blood alcohol levels.

The problem with this situation is that the use of benzodiazepams can cause an erratic response due both to tolerance and to the ability of the liver to detoxify the benzodiazepams. Therefore, the use of these compounds is risky when the patient still has alcohol in their system. If at all

possible, it is better to use adjunct medications to control the withdrawal symptoms in this situation.

Personally, I find the clinically appropriate medications are atenolol and also gabapentin. Atenolol should be titrated based on the patients pulse and blood pressure. Gabapentin should be administered at a dosage range of 1800 to 3600 mg per day in divided doses. However, if there is legitimate evidence of hallucinosis, then the patient absolutely needs to be treated with something that will suppress the RAS to prevent further progressions of symptoms.

While it is common for many facilities to gravitate toward the short acting benzodiazepams, my personal experience is that this is a mistake. Because of the fast drop of short acting benzodiazepams, cells of the inhibitory neurotransmitter γ -aminobutyrate A (GABA-A) system become sensitized. Thus it takes considerably longer and more medications to stabilize and safely detox patients than if you aggressively prevent them from experiencing hallucinosis in the first place.

Electrolyte Imbalances

One of the (many) significant problem with chronic alcoholism is the tendency for patients to wash out significant amounts of electrolytes. Especially in diets that are less than adequate, the patient will be come depleted of electrolytes. Therefore laboratory analysis is crucial to the evaluation of the detoxing patients.

Unfortunately, there are some significant complications from depleted electrolytes, like possible seizures and cardiac rhythm problems, but there can also be problems from too rapidly replacement them, especially with sodium.

SODIUM

Hyponatremia can be caused by a collection of syndromes, which include (but are not limited to) chronic alcoholism, psychogenic polydipsia, postoperative hyponatremia, renal failure, liver failure, heart failure, nephrotic syndrome and the syndrome of inappropriate secretion of vasopressin (SIADH). So one part of the underlying questions to be answered is to determine the cause of the hyponatremia.

If the cause is correctable, then sodium must be replaced slowly or a syndrome called “central pontine myelinolysis” or “osmotic demyelination syndrome” may occur. The syndrome of central pontine myelinolysis is characterized by flaccid quadriplegia, dysphagia and dysarthria. The mechanisms predisposing this neurologic complication are not completely understood. Some theories suggest that the rate of correction of hyponatremia is implicated in the development of such syndrome, while others consider the cause as the magnitude of correction (the absolute change in sodium concentration over a given period) as the main predisposing factor. Therefore, attention to both the rate and the magnitude of correction are warranted.

Please note, however, that despite the name the lesions found in patients who received too rapid of corrections for hyponatremia are not confined to the pons. Also know that any drug that has a diuretic action, including caffeine, can cause hyponatremia. So therefore histories need to pay attention to and include caffeine and other diuretic usage histories.

Therefore any patient with sodium of less than 130mmol/L who is NOT symptomatic should be allowed to correct their own sodium via natural (their own) renal methods and not given IVs to correct this situation. If the patient is symptomatic, then the use of hypertonic saline aiming to increase the serum sodium concentration by 0.5 to 1mmol/L/h with the upper limit being an increase of no greater than 20 mEq in 24 hours (or preferentially, over 48 hours) may be warranted. The use of a loop diuretic should be considered if the possibility of excessive fluid load exists (cardiac failure or renal failure).

POTASSIUM

Potassium is one of the body's major ions. Nearly 98% of the body's potassium is intracellular. The normal potassium level is 3.5-5.0 mEq/L, and total body potassium stores are approximately 50 mEq/kg (3500 mEq in a 70-kg person).

Hypokalemia may result from many different conditions including, but not limited to, renal or GI losses, inadequate diet, cellular shift (movement of potassium from serum into cells), medications and diuretic effects particularly of alcohol. Cases of hypokalemia due to excessive and usually prolonged alcohol consumption are well documented.

Hypokalemia is defined as a potassium level less than 3.5 mEq/L.

Moderate hypokalemia is a serum level of 2.5-3 mEq/L.

Severe hypokalemia is defined as a level less than 2.5 mEq/L.

Up to 14% of outpatients are mildly hypokalemic, while approximately 80% of patients who are receiving diuretics become hypokalemic, especially when using alcohol.

Symptoms of hypokalemia include:

1. Palpitations
2. Skeletal muscle weakness or cramping
3. Paralysis, paresthesias
4. Constipation
5. Nausea or vomiting
6. Abdominal cramping

7. Polyuria, nocturia, or polydipsia
8. Psychosis, delirium, or hallucinations
9. Depression
10. Electrocardiogram changes -
 - T- wave flattening or inverted T waves
 - Prominent U wave that appears as QT prolongation
 - ST segment depression
 - Ventricular arrhythmias (eg, premature ventricular contractions [PVCs], torsades de pointes, ventricular fibrillation)
 - Atrial arrhythmias (eg, premature atrial contractions [PACs], atrial fibrillation)

There has also been shown to be a correlation of potassium levels as a predictor of pending DTs.

It has also been shown that low potassium levels can lead to seizure activity.

Hyperkalemia is not as common in the alcoholic, but can frequently be seen in patient's taking supplements or eating foods high in potassium.

Hyperkalemia results from increased consumption or decreased or impaired potassium excretion. It is a potentially life-threatening illness that can be difficult to diagnose because of a paucity of distinctive signs and symptoms.

Hyperkalemia is defined as a potassium level greater than 5.5 mEq/L.

Mild Hyperkalemia is 5.5 - 6.0 mEq/L

Moderate Hyperkalemia is 6.1 - 7.0 mEq/L

Severe Hyperkalemia is 7.0 mEq/L and greater

In determining the cause of hyperkalemia, you must be suspicious of renal failure, possibly due to acute dehydration (from alcohol consumption) and dialysis.

It is also important to rule out pseudo-hyperkalemia caused by hemolysis (in the lab tube), thrombocytosis, leukocytosis and venipuncture technique (i.e., ischemic blood draw from prolonged tourniquet application).

An abnormal EKG may be the first of an abnormal potassium level.

EKG Changes (dependent on the severity of the Hyperkalemia):

Peaked T waves, shortened QT interval, and ST segment depression

Bundle branch blocks causing a widening of the QRS complex, increases in the PR interval, and decreased amplitude of the P wave

EKG changes reverse with appropriate treatment. Without treatment, the P wave eventually disappears and the QRS morphology widens to resemble a sine wave. Ventricular fibrillation

or asystole follows. EKG findings generally correlate with the potassium level, but potentially life-threatening arrhythmias can occur without warning at almost any level of hyperkalemia.

The primary cause of morbidity and death is potassium's effect on cardiac function. The mortality rate can be as high as 67% if severe hyperkalemia is not treated rapidly.

CONCLUSION

Be aware that the relationship between serum potassium and symptoms is not consistent. For example, patients with chronically elevated potassium levels may be asymptomatic at much higher levels than other patients. The same is true with chronic hypokalemic conditions. Therefore it is essential that laboratory analysis of electrolytes including potassium levels be obtained as soon as practically possible on detoxing patients. Also supplementation should be started for patients with hypokalemia.

MAGNESIUM

It is common for patients showing up to acute detox frequently have total body (versus only serum) deficits of magnesium. Evidence shows the incidence of hypomagnesemia among people with alcohol dependence is approximately 25% and mainly is due to magnesium diuresis caused by alcohol.

NOTE: Since less than two percent is present in the extracellular fluid, serum levels do not necessarily reflect the status of total body stores.

Magnesium is absorbed in the small bowel by both active and passive transport mechanisms. Absorption of dietary magnesium takes place mainly in the ileum. Normal serum concentration typically ranges from 1.8-2.5 mEq/L. It is excreted in stool and urine (predominantly urine) and regulation of serum magnesium is by renal control. However, the kidney has a strong capacity to reabsorb magnesium, under normal circumstances. Alcohol directly impairs the ability to re-absorb magnesium.

However, other factors that may also impair renal re-absorption of magnesium are volume expansion, hypercalcemia, and diuretic administration and must be ruled out as causes for hypomagnesemia.

At serum magnesium levels less than 1.0 mEq/L, patients may have tremor, hyperactive deep-tendon reflexes, CNS hyper-excitability, muscular fibrillations, positive Chvostek sign progressing to tetany, cardiac arrhythmias, psychosis, ataxia, vertigo, nystagmus, and seizures. Hypomagnesaemia has also been implicated in insulin resistance making such situation even harder to control.

NOTE: Chvostek's sign is a sign of a latent tetany shown by contraction of the muscles of the eye, mouth or nose, elicited by tapping along the course of the facial nerve. The examiner taps gently over the facial nerve in front of the ear.

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Chapter 6

NEUROLOGICAL COMPLICATIONS of Alcoholism

Two of the more well known major complications of alcohol withdrawal are Wernicke's encephalopathy and Korsakoff's syndrome. Luckily, both of these syndromes are rare today due to vitamins being present in many food substances, but one must be aware of the passivity of them.

Although Wernicke's and Korsakoff's may appear to be two different disorders, they are generally considered to be different stages of the same disorder, which is called Wernicke-Korsakoff syndrome. Wernicke's encephalopathy represents the "acute" phase of the disorder, and Korsakoff's amnesic syndrome represents the "chronic" phase.

Wernicke's encephalopathy

Wernicke encephalopathy is the "acute" phase of the acute degenerative neurologic disorder resulting from a deficiency in vitamin B-1 (i.e., thiamine), an essential coenzyme in intermediate carbohydrate metabolism. Alcohol interferes with active GI transport of thiamine. Untreated Wernicke's encephalopathy can be fatal.

A common misconception of Wernicke's encephalopathy is that it is only seen in alcoholics. Anything that causes prolonged loss of thiamine can cause the syndrome, especially in an already deficient patient. Common causes include prolonged vomiting and inanition associated with chemotherapy, eating disorders, and elderly patients living alone who do not maintain their nutritional status.

It should be noted that Wernicke's encephalopathy can be precipitated by administration of glucose to a patient who is significantly thiamine deficient. The condition has also been described in patients receiving dialysis, on hyperalimentation, with AIDS, and with malnutrition. It also can occur in chronic alcoholic patients who present to the ER who are treated with IV fluids.

Wernicke's encephalopathy can also occur secondary to a genetic abnormality resulting in a defective form of transketolase that diminishes binding of the coenzyme thiamine pyrophosphate.

SYMPTOMS

1. **Ocular abnormalities** are the hallmarks of Wernicke encephalopathy. Horizontal nystagmus and paralysis of lateral rectus muscles are common. Less frequently noted are sluggishly reactive pupils, ptosis, and anisocoria.
2. **Global confusional state :**
 - a. Apathy
 - b. Impaired awareness of the immediate situation
 - c. Inability to concentrate
 - d. Retrograde amnesia (inability to recall information)
 - e. Antero-grade amnesia (inability to assimilate new information)
 - f. Confabulation
 - g. Spatial disorientation
3. **Ataxia**, (loss of equilibrium) seen in the **early** stages of the disease, results from vestibular paresis, which is uniformly found. The wide-based ataxic gait seen in the subacute and chronic phases of the illness results from cerebellar dysfunction, either and/or combined with vestibular dysfunction. The Romberg sign is quite positive, again implicating more than just the cerebellum as the cause of the ataxia.
4. **Hypothermia**, from involvement of the temperature-regulating center, is characteristic.
5. **Hypotension**, caused by a defect in efferent sympathetic outflow and decreased peripheral resistance, may be present.
6. **Coma** may be the sole manifestation of Wernicke encephalopathy. Of patients surviving Wernicke encephalopathy, 80% have Korsakoff psychosis.
7. Other manifestations of thiamine deficiency involve the cardiovascular system and peripheral nervous system (nutritional polyneuropathy).

CLASSIC TRIAD

Patients with Wernicke's encephalopathy **may** exhibit the classical characteristic clinical triad of ophthalmoplegia, ataxia, and global confusion. However, in reality, only one third of patients with acute Wernicke's encephalopathy present with the classic clinical triad.

1. Involuntary, jerky eye movements or paralysis of muscles moving the eyes
2. Poor balance, staggering gait or inability to walk
3. Drowsiness and confusion.

The mental changes, initially and commonly found, are a quiet apathy, which may convert to confabulation similar to that seen in patients have with Korsakoff's psychosis.

The major cognitive deficit is one of memory. The predominant problem is with incorporating new memories.

However it is very important to note that patients may have a change in mental function as their only sign of Wernicke's disease.

The differential diagnosis includes:

1. Various brain stem and cerebellar syndromes, due to vascular disease, including both hemorrhages and infarction and drug intoxications (especially anticonvulsants).
2. Basilar meningeal bacterial infections
3. Viral encephalitis, acute hydrocephalus
4. Paraneoplastic syndromes
5. Rarely a peripheral vestibular disturbance.

Other less common etiologies.

6. Forced or self-imposed starvation
7. Protein-energy malnutrition resulting from inadequate diet or malabsorption
8. Conditions associated with protracted vomiting
9. Chronic renal failure
10. Carbohydrate loading in the presence of marginal thiamine stores (feeding after starvation)
11. Transketolase function abnormalities

Imaging Studies:

A head CT scan is the definitive test for emergency diagnosis of focal neurologic disease. In patients who are comatose, a CT scan can detect not only intracranial lesions, but also fractures of the skull and minute amounts of blood.

Other Tests:

- Always do an EKG as a baseline
- Consider EEGs for some patients to exclude status epilepticus and nonconvulsive status epilepticus as causes of coma and altered mental status.

TREATMENT

The treatment of Wernicke's disease is immediate large doses of intramuscular thiamine. However, it should be noted that if magnesium is deficient, thiamine alone will not be adequate to control the syndrome.

Wernicke encephalopathy must be viewed as a medical emergency, even if other competing diagnoses of CNS processes are being considered. Because the condition is potentially reversible, start immediate treatment in patients exhibiting any combination of the above-mentioned symptoms and signs, particularly if the patient is in a high-risk population.

As little as 2 mg of thiamine may be enough to reverse the ocular symptoms (which generally begin to improve in 1-6 h), but initially administer doses of at least 100 mg Thiamine solution. Ataxia and acute confusional state may resolve dramatically, although improvement may not be noted for days or months.

NOTE: IM Thiamine produces a burning or stinging sensation that causes many patients to refuse to take it. In serious cases of need, you **MUST** exercise your persuasive powers and get patients to agree to IM thiamine as it takes up to 3 days (or more in pancreatic problems) for patients to get adequate absorption from oral dosage even if you give higher doses.

Start thiamine prior to treatment with IV glucose solutions, and continue until the patient resumes a normal diet. Glucose solutions may precipitate Wernicke disease in a previously unaffected patient. For this reason, administer thiamine to all patients with alcoholism who require parenteral glucose.

- The final step in treating Wernicke's encephalopathy is attending to and correcting magnesium deficiency.
- For safety carefully monitor the cardiovascular status of each patient.

Complications:

- Korsakoff psychosis

Prognosis:

- Patients with Wernicke encephalopathy have a 10-20% mortality rate.
- Of patients surviving Wernicke encephalopathy, 80% have Korsakoff psychosis.

Korsakoff's Syndrome

Korsakoff's syndrome is the "chronic phase" of the degenerative neurological memory disorder, which is caused by a deficiency of vitamin B1, also called thiamine. Another term for Korsakoff's is 'alcohol amnestic syndrome.'

In the United States, the most common cause of thiamine deficiency is alcoholism. Other conditions that cause thiamine deficiency may occur quite rarely, and most commonly can be seen in patients undergoing dialysis. Korsakoff's syndrome may also occur in other conditions where there is severe malnutrition, but this is extremely rare.

- Korsakoff's syndrome is caused by lack of thiamine (vitamin B1). Excessive use of alcohol is most commonly the cause of the thiamine deficiency. Alcohol can inflame the stomach lining and impede the body's ability to absorb the key vitamins it receives.

Although Korsakoff's syndrome is not strictly speaking a dementia, people with this condition experience short-term memory loss.

As noted above, Korsakoff's is part of the Wernicke-Korsakoff syndrome, which consists of two separate but related stages: Wernicke's encephalopathy is the first part and Korsakoff's psychosis is the follow-on condition. However, not all cases of Korsakoff's are preceded by an episode of Wernicke's.

What is Korsakoff's psychosis?

Korsakoff's differs from most dementias, in which there is often damage to a large area of the cortex. Thus this dementia affects a much wider range of abilities. The main symptom is memory loss, particularly of events arising after the onset of the condition. Sometimes, memories of the more distant past can also be affected.

Korsakoff's psychosis may follow if Wernicke's encephalopathy is untreated or is not treated soon enough. It may also develop gradually. Brain damage occurs in important small areas in the mid-part of the brain, resulting in severe short-term memory loss. Many other abilities may remain intact

Other symptoms may include:

1. Difficulty in acquiring new information or learning new skills.
2. Lack of insight into the condition. Even a person with great gaps in their memory may believe their memory is functioning normally.
3. Inventing events to fill the gaps in memory. This is more common in the early stages of the illness and is known as 'confabulation'.
4. Apathy, in some cases, or talkative and repetitive behavior in others.
5. People usually retain skills that they acquired before developing the disorder, so they are often able to manage with appropriate support.
6. Of patients with Korsakoff psychosis, 25% do not recover and require long-term institutionalization.

Only about 20% eventually recover completely during long-term follow-up care.

How is Korsakoff's diagnosed?

1. **Korsakoff's syndrome cannot be diagnosed until the person has abstained from alcohol for at least four to five weeks** to enable the acute symptoms of alcohol withdrawal to subside.
2. Psychological tests of the person's memory and other abilities will then be carried out to see whether they may have Korsakoff's or some other condition.

ONSET

It has been suggested that whereas it may take around 20 years for a man to develop Korsakoff's syndrome, it may take about half that time for a woman.

It is not yet clear why some heavy drinkers develop Korsakoff's syndrome and others do not, although this may relate to diet.

Treatment

While it remains unclear whether additional thiamine helps people improve once the brain damage has already occurred, it may help prevent further damage occurring.

Prognosis

Improvement usually occurs within a period of up to two years.

It has been estimated that about a quarter of those affected with Korsakoff's make a very good recovery.

About half make a partial recovery and need support to manage their lives.

Another quarter make no recovery and may need long term care.

Korsakoff's will continue to progress if the person continues to drink heavily and has poor nutrition.

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CHAPTER 7

MEDICINES in the TREATMENT of the WITHDRAWAL SYNDROME

The goal of treatment of withdrawal is to prevent the patient from developing DTs or other neurological conditions. In short, I have personally found that appropriately aggressive treatment will prevent patients from having these complications and while that will not prevent every complication, this will dramatically decrease the morbidity and mortality rates and also the length of patient stays.

Also, aggressive treatment allows such patients to be treated on less intensive wards. Meaning, that unless a patient has other serious medical conditions, they should not need to have IV's placed or be on telemetry or ICU units.

While every detox specialist will develop their own protocols, here are some of the medications I have found helpful.

Suggestion of medications to use includes but is not limited to;

1. **Benzodiazepines: Valium, or Librium** – dosage – use whatever dose required.

Do not expect to control all symptoms with benzodiazepams. That is what the other medications are for. Expect that you will need to add other medications. Not using a combination of medications and only using more benzodiazepines is a classic mistake of the non-detox specialist.

Unfortunately, this medication is usually under-dosed due to concerns of it building up. If the patient has even a moderately intact liver function (monitor the patient's GGT) there is small concern. However, the real concern should be the patient's level of consciousness, which should be monitored by nursing staff. If the patient appears over-sedated or intoxicated, the medication should be lowered dramatically or stopped. Because of the long half-life of this medication, there is very small risk of withdrawal complications even with sudden stopping of Valium.

Many people like the drug Librium because of a shortened half-life and therefore they feel there is less chance of build up in a patient with questionable liver status. Because of the moderately long half life of this medication there is very small risk of withdrawal complication from sudden stopping of Librium.

Short acting Benzodiazepines (like Ativan) should be reserved for patients with a KNOWN problem of breaking down benzodiazepines as otherwise the short half-life will make this drug unable to protect the GABA-A system from rebound over-activation as they wear off (quickly).

2. **Gabapentin** ... starting dosage of 600mg TID to a maximum of 3600 mg per 24 hours – used to treat withdrawal anxiety, protect from seizures and also treat pain. Gabapentin is a superior and unique drug because it helps control the GABA-A system without the side effect of irritating the pancreas like divalproex does or the complications of other anti-seizure drugs.
3. **Beta-blockers:** Beta-blockers are the first line antihypertensive medication to be used, not only because they are centrally active, but also because they decrease portal hypertension, thus decreasing the incidence of bleeding from esophageal varices.

Atenolol produces a long, even curve for control of blood pressure, pulse control, anxiety and prevents many arrhythmias that such patients are prone to, by decreasing work load of the heart. Atenolol is preferred due to its longer half-life compared to shorter acting beta-blockers. Care has to be taken to ensure that use of a beta-blocker is not counter-indicated in patients, especially diabetics and severe COPD patients who are on bronchodilators.

Additional blood pressure control can be accomplished **once these above medications are in effect** with the full range of other blood pressure medications. However, the use of diuretics is hazardous unless the patient's present electrolytes and kidney function are known first.

Pancrealipase should be used in patients who have pancreatic dysfunction without evidence of gastric or duodenal ulcers. See the chapter on Alcoholic Pancreatitis for more details.

Obtain blood levels of all anti-seizure medications as soon as possible, but unless you can determine clinically that they should not be given, it is best to continue these medications. Restart them if the patient has not been taking them unless there is clinical evidence against this.

Even though you are going to give gabapentin, you should also use the anti-seizure medication they are supposed to be on. However, special attention needs to be placed on medications that may have serious liver or bone marrow dyscrasias like carbamepazine.

Psychotropic medications should be stopped as they decrease seizure thresholds.

Obviously, there are other medications that will be used to treat the myriad of medical problems that develop or are already apparent in the detox patient. However, it is best to pay particular attention to those that can cause irritation of either the liver and/or the pancreas because use of such medications can further complicate the issue. For example, divalproex can irritate the pancreas, statins, which may be very safe in most cases, can cause increased problems and even myositis during the detox period. In fact, many drugs may obtain higher than normal levels (and thus have complications one would not expect in therapeutic levels) due to delayed breakdown during detox periods.

The patient's liver may have had problems breaking down medications for a significant period of time while they were drinking, but the diuretic actions of alcohol may have been washing the excessive medications out. However, once they stop drinking, they are no longer protected by this diuretic action.

Once patients are in active DTs then it is best to seek advice from an Addictive Psychiatrist due to the complications involved. Additional consults to internal medicine are indicated as appropriate.

Haloperidol, a dopamine blocker, should be considered in patients in DTs who do not respond to a combination of benzodiazepines, gabapentin and beta-blocker therapy. Of the major psychotropic available, haloperidol has lower anticholinergic side effects, less effect on myocardial function, respiratory drive and less propensity to lower seizure thresholds.

Chapter 8

Alcoholic Pancreatitis

One of the problems that you will definitely encounter when working with the chronic drinking patient is that of alcoholic pancreatitis, both chronic and acute. In fact, heavy alcohol consumption seems to account for 55 % to 80% of chronic pancreatitis. The two most common major causes of pancreatitis are long-standing alcohol consumption and biliary stones.

Unfortunately, management of chronic pancreatitis is an evolving and frequently confusing issue because of the varied opinions and sometimes conflicting research that is available. Thus, recommended treatments will vary and I can only give you the best advice based on today's knowledge.

NOTE: We are not going to deal with non-alcoholic pancreatitis in this book, as that condition seems to be a generalized attack (probably autoimmune) against the entire pancreas. However, an autoimmune form of chronic pancreatitis referred to as lymphoplasmacytic pancreatitis has been increasingly recognized in many middle-aged patients with no apparent risks factors for pancreatitis.

Alcohol increases both the protein content of the pancreatic digestive enzymes excreted and concomitantly decreases bicarbonate levels and trypsin inhibitor concentrations. This leads to the formation of protein plugs which obstruct pancreatic enzyme outflow. On the cellular level, alcohol leads to an increase of intracellular pancreatic enzymes and their premature activation and release. On the ductal level, alcohol increases the permeability of ductules, which allow enzymes to reach the parenchyma of the pancreas, resulting in pancreatic tissue damage.

Biliary stone disease is the other major cause of acute pancreatitis is (eg, cholelithiasis, choledocholithiasis). A biliary stone may lodge in the pancreatic duct or Ampulla of Vater and obstruct the pancreatic duct, leading to a build up of pancreatic enzymes, increased ductal pressures and an extravasation of enzymes into the parenchyma. Reports show that the incidence of fluid collections and pseudocysts were both less frequent after biliary pancreatitis than with an alcohol cause.

Some of the reasons why pancreatitis is so concerning is that:

- 1) The pancreas is located in the retroperitoneal space and has no capsule; therefore inflammation can spread easily to the surrounding peritoneum and organs.

- a. In acute pancreatitis an edematous pancreatitis can cause parenchymal edema and peripancreatic fat necrosis.
 - b. When necrosis involves the parenchyma, it can cause hemorrhage and dysfunction of the gland,
 - i. This can result in hemorrhagic or necrotizing pancreatitis.
- 2) Necrotizing pancreatitis can cause pseudocysts and pancreatic abscesses because of damaged tissue being walled off by granulation.
- a. Pancreatic abscesses can also result because of bacterial seeding of pancreatic or peripancreatic tissue (i.e., pancreatic abscess formation).
 - b. An ultrasound or, preferably, a CT scan can be used detect both.
- 3) The inflammatory process can cause systemic effects because of the presence of cytokines, such as bradykinins and phospholipase A.
- a. These cytokines may cause vasodilation, increase in vascular permeability, pain, and leukocyte accumulation in the vessel walls.
 - b. Fat necrosis may cause hypocalcemia.
 - c. Pancreatic B cell injury may lead to hyperglycemia.
 - d. Acute respiratory distress syndrome (ARDS), acute renal failure, cardiac depression, hemorrhage, and hypotensive shock all may be systemic manifestations of acute pancreatitis in its most severe form.
- 4) Chronic pancreatitis is characterized by progressive and irreversible loss of pancreatic exocrine and endocrine function.

In addition, numerous experimental studies have shown that even moderate alcohol abuse stimulates diffuse pancreatic fibrosis which is intralobular without other important lesions; this fibrosis is different from that seen in alcoholic chronic pancreatitis in which fibrosis is mainly perilobular initially and only intralobular in more advanced stages.

TREATMENT

Evidence does not support the use of nasal gastric suction for treatment of pancreatitis. Studies showed no statistically significant differences between the groups that received nasogastric suction and the groups that did not, in duration of abdominal pain, anorexia, abdominal tenderness, ileus, presence of abdominal masses, or elevated serum amylase and lipase. However, there was a significant increase in subjective complaints and duration of nausea and vomiting in patients with nasal gastric suction in place.

Instead, treatment of alcoholic pancreatitis seems to be best accomplished with enzyme supplementation with pancrealipase. (Versus treatment of non-alcoholic pancreatitis, which seems to be absolute abstinence of food.) In addition, use of enzyme supplementation allows for faster restoration of electrolyte balance in the detoxing alcoholic patient simply due to restoration in dietary intake.

Dosage of pancrealipase should be titrated to the point to control clinical symptoms and laboratory studies should be followed to ensure that lipase levels are decreasing and clinical symptoms are under good control. Please note that lipase levels do not correlate very well with pain symptoms, especially in chronic pancreatic patients. Patients who are having significant pain that does not correlate with lipase levels should have a CT or MRI to rule out significant pathology.

NOTE: If amylase levels are used to monitor the pancreas, they should be fractionated to ensure that pancreatic components are being observed.

Usually three to six capsules of pancrealipase with every meal should be prescribed. In most situations, if the patient is clinically symptom free on a dose of less than three capsules they can be taken off the Pancrealipase supplementation all together.

Significant symptoms or significantly elevation of (fractionated) amylase or lipase levels should be assessed with an abdominal x-rays, especially if the levels are increasing. Evidence of possible cysts should be further evaluated with ultrasound and/or CT. If symptoms persist or suspicious findings are noted on ultrasound or CT, the patient should be referred to the gastroenterologist.

RESEARCH

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Chapter 9

Alcoholic Hepatitis

Alcoholic hepatitis is a syndrome of progressive inflammatory liver injury caused by alcohol consumption. It is characterized by necrotizing inflammatory hepatic lesions and acute hepatic decompensation. Alcoholic hepatitis usually occurs with long-term heavy drinking, but in susceptible individuals, may occur rapidly with only moderate intake of alcohol. In severe cases, alcoholic hepatitis is associated with a high mortality in hospitalized patients.

It well known is that steatosis, or fatty liver, and cirrhosis frequently accompany alcoholic hepatitis. Steatosis invariably appears if consumption of alcohol exceeds 80 g per day. It is estimated that 90-100% of heavy drinkers will show some evidence of fatty liver. However, only 10-35% of heavy drinkers develop alcoholic hepatitis and only 8-20% will develop cirrhosis.

Alcoholic hepatitis usually persists longer than the period of time of actual drinking and progresses to cirrhosis if heavy alcohol use continues. However, if the use of alcohol stops, alcoholic hepatitis tends to resolve over weeks to months, sometimes without permanent damage to the liver. The reason for this is not completely understood.

MECHANISM OF ACTION

Alcohol is readily absorbed from the GI tract, and greater than 90% is metabolized by the liver through oxidative mechanisms. Alcohol and its main metabolite acetaldehyde cause damage to liver cell membranes. In fact, acetaldehyde may be the principal causative agent of alcoholic liver injury. Alcohol can alter the activity of membrane-bound enzymes and cell membrane transport proteins and affect the ability of cell membranes to function properly.

Acetaldehyde-modified proteins and lipids on the cell surface may also behave as antigens and trigger immunologic injury. This typical histologic picture includes hepatocellular necrosis and ballooning degeneration, Mallory's hyaline bodies (abnormal aggregations of cellular intermediate filament proteins) and an inflammatory reaction with many polymorphonuclear leukocytes.

Most patients with alcoholic hepatitis show signs of malnutrition. In the past, nutritional deficiencies were thought to play a major role in the development of liver injury. This assumption was supported by several animal model studies where susceptibility to alcohol-induced cirrhosis could be produced by diets deficient in choline and methionine. This view changed in the early 1970s after key studies by Lieber and DiCarlo performed in baboons showed that alcohol ingestion could lead to steatohepatitis and cirrhosis in the presence of a nutritionally complete diet.

Active alcoholic hepatitis often persists for months after the patient stops drinking. In fact, its severity may worsen during the first few weeks of abstinence. This observation suggests that an immunologic mechanism may be responsible for the injury. Levels of serum immunoglobulins, especially the immunoglobulin A class, are increased in persons with alcoholic hepatitis.

SYMPTOMS

Mild forms of alcoholic hepatitis frequently do not show any symptoms and the determination will be made based on laboratory studies alone. Severe cases present with subacute onset of fever, hepatomegaly, leukocytosis, jaundice, coagulopathy, ascites, hepatic encephalopathy, and esophageal varices, possibly with hemorrhage.

Labs

Because of the frequent lack of other clinical symptoms, diagnosis is frequently made on the basis of laboratory studies. Aspartate aminotransferase (AST, formerly SGOT) will be increased - typically in the 100 IU/mL to 200 IU/mL range, even in severe disease. The AST level is higher than the ALT (or SGPT) level but rarely exceeds 400 IU/mL. The ALT level may even be normal, even in severe cases.

One useful ratio in determining if a patient has alcoholic hepatitis is that if the AST to ALT ratio is 2:1 the diagnosis can be made. However, an important corollary of this observation is that significant AST or ALT elevations, for example, 1000 IU/mL are not likely to be explained by acute alcoholic hepatitis, even in an alcoholic. When this is the case, other causes must be determined.

Other signs of alcoholic hepatitis are:

1. Elevated alkaline phosphatase
2. Gamma glutamyl transferase (GGT) is markedly elevated
3. Hypo-albuminemia
4. Mean Corpuscular Volume (MCV) is elevated

The level of bilirubin elevation and prolonged prothrombin are better indicators of severity of disease than the level of enzyme elevation.

Treatment

The treatment of alcoholic hepatitis is largely symptomatic, with emphasis on improving nutrition and stopping all alcoholic intake. There is clear research showing that poor nutrition

dramatically worsens the prognosis. Therefore, during the recover period, meticulous attention needs to be paid to ensure that the patient has an appropriate nutritional status.

Corticosteroids have been the most controversial therapy in alcoholic hepatitis. Recent studies seem to (slightly) favor use of corticosteroid therapy for patients with severe disease and spontaneous hepatic encephalopathy. Steroids may work by decreasing the inflammatory reaction and immunologic injury. However, while steroids seem to have a beneficial effect on short-term survival, some studies have indicated that they do not seem to improve long-term survival rates. Other studies suggest that enteral or parenteral nutritional supplementation was associated with a better long-term survival compared with corticosteroids in patients with alcoholic hepatitis

Emerging research shows that Tumor Necrosis Factor Alpha, or TNF-a, is also a factor in liver damage. In fact, increasing TNF vales are associated with a high mortality in hospitalized patients. TNF-a can induce programmed cellular death (apoptosis) in liver cells. Several studies have shown extremely high levels of TNF and several TNF-inducible cytokines in the sera of patients with alcoholic hepatitis. TNF and other inflammatory cytokines and hepatic acute-phase cytokines have been thought to play a significant role in modulating certain metabolic complications in alcoholic hepatitis. They are felt to be instrumental in the liver injury of alcoholic hepatitis and cirrhosis.

Therefore, TNF inhibitor medications, such as pentoxifylline or cilostazol can potentially improve short-term survival in patients with severe alcoholic hepatitis. The benefit appears to be related to a significant decrease in the risk of developing hepatorenal syndrome and doses of these medications should be considered. However, it is NOT appropriate to consider stronger TNF inhibitors that are known to compromise the immune systems. Neither should TNF inhibitors be considered in patients with hepatitis C, as so far, there is no research to show that this is a safe practice.

Therefore, it is recommended that for patients with ascites and with a total bilirubin level greater than 8-gm/dL, prompt consideration should be given to the use of corticosteroids or a TNF inhibitor (like pentoxifylline) to reduce mortality. Recommended dosage of pentoxifylline to be used is 400 mg orally 3 times daily, or an equivalent dose of cilostazol. No single therapy has had a universally miraculous success.

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Chapter 10

Cirrhosis

There is no way that you are **not** going to have to deal with the patient with cirrhosis, so the subject has to be addressed in this manual. However, cirrhosis is a subject that can and has covered entire medical manuals, so there is no way I am going to be able to do justice to the subject in the short space I have here. Therefore, I plan to cover the highlights and refer you to both complete medical texts on the subject and also recommend that you consult with a gastroenterologist, or preferably a hepatologist, for patients who have severe complications of their cirrhosis.

Cirrhosis (from all causes) is the twelfth leading cause of death by disease. In the USA it kills about 26,000 people each year. However, in the USA the leading cause of cirrhosis is alcoholism. While there are many causes of cirrhosis (see a partial list below) we are going to limit the discussion to those caused by alcohol.

Alcoholic cirrhosis usually develops after more than a decade of heavy drinking. The amount of alcohol required to damage the liver varies greatly from person to person. In women, as few as two to three drinks per day have been linked with cirrhosis and in men, as few as three to four drinks per day.

Causes of Cirrhosis

Although most often associated with alcohol abuse (as I stated above, it is most common cause in the U. S.), cirrhosis of the liver can result from many causes. Almost any chronic liver disease can lead to cirrhosis. Some of the more common causes are:

- Alcoholic liver disease
- Chronic viral hepatitis B, C and D or autoimmune hepatitis
- Inherited metabolic diseases (example, hemochromatosis)
- Chronic bile duct diseases
- Chronic congestive heart failure
- Non-alcoholic steatohepatitis
- Long term exposure to toxins or toxic drugs
- Parasitic infections (example, schistosomiasis)
- Metastatic cancer with liver involvement
- Hepatic or portal vein thrombosis

Suspicious (but not diagnostic) symptoms of cirrhosis include:

- Telangiectasias. However, spider telangiectasias are not diagnostic and can be seen in individuals without liver disease.
- Jaundice
- Ascites
- Esophageal varices are strongly suggesting cirrhosis
- An enlarged liver, or abnormally nodular livers
- An enlarged spleen
- Reduced level of albumin (usually levels below 3.2 are very suspicious)
- Evidence of reduced blood clotting (based on INR and platelet levels)
- Abnormal elevation of liver enzymes in the blood (such as ALT and AST)
- Elevated levels of iron in the blood (the patient may have hemochromatosis)
- Auto-antibodies (antinuclear antibody, anti-smooth muscle antibody and anti-mitochondrial antibody) may be a clue to the presence of autoimmune hepatitis or primary biliary cirrhosis.
- Liver cancer (hepatocellular carcinoma)
- Wilson's disease (a genetic disease in which there is abnormal handling and accumulation of copper throughout the body, including the liver)

Unfortunately making the diagnosis of cirrhosis is not clear-cut and only presumption of the diagnosis can be made from symptoms. The single best test for actual diagnosing cirrhosis is a biopsy of the liver, which should be performed by the gastroenterologist. Liver biopsies, however, do carry a small risk for serious complications (primarily bleeding), and therefore, biopsy often is reserved for those patients in whom the diagnosis of the type of liver disease or the presence of cirrhosis is not clear.

In cirrhosis of the liver, damaged and dead liver cells are replaced by fibrous tissue, which leads to fibrosis or scarring. Liver cells regenerate in an abnormal pattern forming nodules that are surrounded by fibrous tissue. This distortion of the normal liver architecture interferes with normal blood flow through the liver and thus prevents it from working as it should.

Decreased blood flow to the liver can cause increased portal pressures and cause blood to back up in the portal vein and portal circulation. This is purely a hydraulic pressure effect. This, in turn, leads to some of the more serious complications of cirrhosis. Blood can also back up in the spleen causing it to enlarge and sequester blood cells. Most often, the platelet count falls because of splenic sequestration; however direct poisoning of bone marrow by alcohol plays a significant factor in platelet decreases. Patients with platelet levels lower than 20 should be considered for a transfusion of platelets.

If the pressure in the portal circulation increases enough, blood can flow backwards from the portal circulation to the systemic circulation. This can cause varicose veins in the stomach (gastric varices), esophagus (esophageal varices) and the rectum (hemorrhoids). Gastric and esophageal varices can rupture, bleed massively and even cause cardiovascular events or death.

Hypertension in the portal circulation, along with other hormonal, metabolic, and kidney abnormalities in cirrhosis, can also lead to fluid accumulation the abdomen (ascites) and, if severe enough, also in the peripheral tissue (peripheral edema). Additionally, ascites fluid in

the abdomen often becomes infected with bacteria normally present in the gut (spontaneous bacterial peritonitis).

The reason why beta-blockers are recommended for all patients with cirrhosis is because they decrease portal hypertension and thereby decrease some of these complications. Dosage should be titrated based on the patient's pulse and other clinical conditions.

Decreased bilirubin secretion from hepatocytes in cirrhosis leads to the back up of bilirubin in the blood. This leads to jaundice, the yellow discoloration of the skin and eyes. As the water-soluble form of bilirubin also backs up in the blood, bilirubin can also spill into the urine giving it a bright yellow to dark brown color.

Abnormal biochemical function of the liver in cirrhosis can lead to several complications. The serum albumin concentration falls, which can lead to aggravation of ascites and edema. The metabolism of drugs can change, requiring dose adjustments. In men, breast enlargement (gynecomastia) sometimes occurs because metabolism of estrogen in the liver is decreased. Decreased production of blood clotting factors can lead to bleeding complications. Derangements in the metabolism of triglycerides, cholesterol and sugar can occur. In earlier stages, cirrhosis frequently can cause insulin resistance and diabetes mellitus. In later stages, or in severe liver failure, blood glucose may be low because it cannot be synthesized from fats or proteins. Incidentally, as a compounding problem, cirrhosis causes increased resistance to insulin

Cirrhosis can also lead to kidney dysfunction and failure. In end-stage cirrhosis, a type of kidney dysfunction called hepatorenal syndrome can occur. Hepatorenal syndrome is almost always fatal unless liver transplantation is performed.

Cirrhosis, especially in advanced cases, can cause profound abnormalities in the brain. In cirrhosis, some blood leaving the gut bypasses the liver as blood flow through the liver is decreased. Metabolism of components absorbed in the gut can also be decreased as liver cell function deteriorates. Both of these derangements can lead to hepatic encephalopathy as toxic metabolites, normally removed from the blood by the liver, can reach the brain. In its early stages, subtle mental changes such as poor concentration or the inability to construct simple objects occurs. In severe cases, hepatic encephalopathy can lead to stupor, coma, brain swelling and death.

Treatment of cirrhosis must be directed at the complications. The incidence of bleeding esophageal varices can be decreased with the use of beta-blockers and those who do bleed can be treated with endoscopic sclerotherapy or rubber band ligation. Ascites and edema are often responsive to a low sodium diet. More advanced ascites and edema should be treated with diuretic therapy, but particular attention must be paid to electrolyte imbalances that can occur. Further treatment including the possibility of transplant should be referred to the gastroenterologist.

A low protein (40 to 60 gram) diet and use of agents such as lactulose may keep ammonia levels in the normal range and thus help hepatic encephalopathy. All such patients should also

be on a low salt (3-4 gram) diet. Infections, such as spontaneous bacterial peritonitis, must be rapidly treated with appropriate antibiotics. Coagulation disorders will sometimes respond to vitamin K.

Please be aware, though, that all drugs metabolized in the liver must be given with caution because of the dramatic changes in metabolic half-life which can occur

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Chapter 11

Hepatic encephalopathy

The question of the best treatment modalities for the patient with hepatic encephalopathy is one that still remains unanswered. Unfortunately, while some significant progress has been made in regards to this, studies have seemed to raise as many questions as they have answered. So while much is known, much still remains to be known.

However, despite not knowing the exact cause of hepatic encephalopathy, we know that hepatic encephalopathy can occur as an acute, potentially reversible disorder or as a chronic, progressive disorder usually associated with chronic liver disease. Hepatic encephalopathy is characterized by various neurologic symptoms that range from tremor and asterixis to hyperreflexia and decerebrate posture, changes in consciousness, and behavior changes that can range from mild to severe. Neuromuscular hepatic encephalopathy can rapidly progress to become an emergency condition!

In people with otherwise stable liver disorders, hepatic encephalopathy may be triggered by anything that increases protein intake, including episodes of gastrointestinal bleeding, and excessive intake of dietary protein. Hepatic encephalopathy can also be triggered by electrolyte abnormalities (especially a decrease in potassium, which may result from vomiting or treatments such as diuretics or paracentesis), infections, renal disease, and surgical procedures that shunt or bypass blood past the liver.

However hepatic encephalopathy may also be triggered by any condition that results in alkalosis, low oxygen levels in the body, use of medications that suppress the central nervous system (such as barbiturates or benzodiazepine tranquilizers), surgery, and sometimes by co-occurring illness.

CAUTION/Making the Diagnosis

Hepatic encephalopathy must be differentiated from disorders that mimic or mask symptoms of hepatic encephalopathy. These include (but are not limited to) alcohol intoxication, sedative overdose, complicated alcohol withdrawal, Wernicke-Korsakoff syndrome, subdural hematoma, meningitis, and metabolic abnormalities such as low blood glucose. An electroencephalogram (EEG) may help in diagnosing early encephalopathy. Even in mild cases, an EEG shows abnormal brain waves. Blood tests also usually show abnormally high levels of ammonia, but this is not always the case and the diagnosis is made on the combination of findings and symptoms, not ammonia levels or absence of elevated ammonia alone.

Typical (Possible) Symptoms of Hepatic Encephalopathy:

Changes in mental state, consciousness, behavior, personality
Forgetfulness
Confusion, disorientation
Delirium
Dementia
Changes in mood
Decreased alertness, daytime sleepiness
Decreased responsiveness, progressive stupor
Coma (May be life-threatening)
Decreased self-care ability
Deterioration of handwriting or loss of other small hand movements
Coarse muscle tremors
Muscle stiffness or rigidity
Seizures (rare)
Speech impairment
Movement, uncontrollable
Movement, dysfunctional
Agitation
Jaundice and ascites may be noted
Signs of cerebral edema may be noted (cerebral edema may be present even if papilledema is absent)

Occasionally, there is a characteristic musty odor to the breath and the urine.

Neurologic symptoms may fluctuate. A coarse, "flapping" muscle tremor may be observed during voluntary movement, such as when the person attempts to hold the arms out in front of the body (also exhibited as a positive Babinski's reflex).

Mental status examination will be abnormal, particularly cognitive tasks such as connecting numbers with lines.

Blood tests may be nonspecific, or may show liver failure. Frequently, blood chemistries may show low albumin, high bilirubin, and other abnormalities (including AST and ALT and GGT) are possible but are variable. Serum ammonia levels are usually high. Prothrombin time may be prolonged, but is not correctable with Vitamin K.

CT scan of the head may be normal, or may show general atrophy (loss of tissue).

Forms of Hepatic Encephalopathy

Acute hepatic encephalopathy may be reversible, while chronic forms of the disorder are often slowly progressive. Both forms MAY result in irreversible coma and death. There is approximately an 80% chance of fatality if coma develops. Recovery and recurrence are variable. Acute hepatic encephalopathy is associated with fulminant liver failure and is characterized by quick progression to profound coma, seizures, and decerebrate rigidity.

In acute liver failure, hepatic encephalopathy is strongly associated with development of cerebral edema. Unfortunately papilledema is often absent even cerebral edema is severe. Acute hepatic encephalopathy, which is accompanied by cerebral edema in the late stages, has a high mortality rate. Deaths of patients with fulminant liver disease are due to cerebral herniation and hypoxia, both of which are caused by increased intracranial pressure and reduced cerebral perfusion pressure.

Acute hepatic encephalopathy presents as overt clinical changes in mental status but progresses at a variable rate. Correction of the causative factors (if possible) usually allows return to the sub clinical state. Chronic hepatic encephalopathy presents as a mild alteration of mental status that may only be discovered on psychomotor testing. The chronic form is characterized by persistence of neuropsychiatric symptoms despite adequate medical therapy.

Understanding the Mechanisms of Hepatic Encephalopathy

What is known is that hepatic encephalopathy is a condition of brain and nervous system damage that occurs as a result of abnormal levels of metabolic toxins and naturally occurring substances crossing the Blood Brain Barrier (BBB). Some of these compounds are toxins; nitrogenous substances, like ammonia other compounds are naturally occurring compounds like gamma-aminobutyric acid (GABA). Other compounds that have been found to cross the BBB are benzodiazepams and methyl-benzodiazepam.

It is known that the main requirement for most hepatic encephalopathy conditions is significant liver disorders (the most common being cirrhosis or hepatitis), which reduce liver function. However, conditions that cause blood circulation to bypasses the liver can be equally responsible. At one time it was felt that ammonia, produced by the body when proteins are digested, was responsible for all the toxic effects to the central nervous system. Thus treatment with a low protein diet would be corrective. Unfortunately, this was not found to be the case. Further research reveals that as much as 40 percent of the body's ammonia comes from gut flora, so even with low protein diets, increased levels of circulating ammonia can be present.

Ammonia is not the only factor in the development hepatic encephalopathy even though ammonia does 1) inhibit excitatory postsynaptic potentials, thereby depressing overall central nervous system function and 2) cause cerebral energy failure due to inhibition of key rate-limiting tricarboxylic-acid-cycle enzymes. At the same time, ammonia does not fit the profile for the cause of hepatic encephalopathy because 1) There is poor correlation of ammonia levels with severity of hepatic encephalopathy, 2) hepatic encephalopathy can exist in the absence of elevated ammonia levels and finally 3) low ammonia levels actually produce neuro-excitatory effects rather than the neuro-depressant effects seen in hepatic encephalopathy.

These reasons all cast doubt on ammonia as the complete cause of hepatic encephalopathy. In fact, no single toxin or compound seems to fulfill all criteria for the cause of hepatic encephalopathy; therefore the pathogenesis is believed to be multifactorial.

Interestingly enough, it is found that normal gut flora produces GABA and also low levels of benzodiazepams and methyl-benzodiazepams. Normally these compounds are detoxified in the intact liver and naturally remaining circulating levels do not pass the blood brain barrier. However, in hepatic encephalopathy, the integrity of the BBB may be poor, so that even though circulating plasma levels of GABA, benzodiazepams and methyl-benzodiazepams may be normal, the substances may accumulate in the brain and be involved in the pathogenesis of hepatic encephalopathy.

This may explain why sometimes treatment with flumazenil (a benzodiazepine antagonist) may reverse hepatic encephalopathy. It can also help explain why patients who had not been treated with benzodiazepams have been found to have levels of benzodiazepams and methyl-benzodiazepams in their cerebrospinal fluid.

While the role of ammonia in changing the BBB is not clear, early studies in Rhesus monkeys studies have suggested that NH_4^+ is responsible for 20% or even more of the transport of ammonia from plasma to brain.

These claims were based on finding that transport protein mediated translocation of NH_4^+ is predominant in locations, such as in the thick ascending limb of Henle's loop and in isolated astrocytes. Many of the ion-transporters involved in renal NH_4^+ reabsorption are also present in brain capillary membranes and could mediate uptake of NH_4^+ .

Astrocytic uptake of NH_4^+ is associated with increased extracellular K^+ , which is a potent cerebral vasodilator. Such interference between transport of NH_4^+ and other cations could be clinically important because increased cerebral blood flow often precedes cerebral herniation in acute liver failure.

The results obtained indicate that hyperammonemia may disrupt BBB integrity not only to AIB and EB but also enhance the transport of other solutes

This last paragraph is extremely important for it show the danger for increased medication potency effects in patients with disruptions in the BBB integrity.

However, ammonia may not be the only answer because some (rat) studies have also shown a link between portal hypertension and BBB permeability, which seems to exist regardless of ammonia levels.

So the question of why the changes in permeability of the BBB remains. While it is noted that ammonia, particularly in conjunction with elevated potassium levels, cause changes in BBB permeability, this subject is definitely not yet fully answered. It is best to be clinically suspicious if the patient exhibits unexplained confusion or lethargy.

Treatment

The obvious goals of hepatic encephalopathy treatment include life support, elimination or treatment of precipitating factors, and removal or neutralization of ammonia and other toxins or compounds causing the problem. Life support may be required for severe cases, including support of breathing or circulation, particularly if coma develops. Cerebral edema may develop, which can be life-threatening.

Precipitating factors must be identified and treated as quickly as possible. Gastrointestinal bleeding must be stopped. The intestines must be emptied of blood because blood breaks down into protein components that are converted to ammonia. Treatment of infections, renal failure, and electrolyte abnormalities (especially hyper-potassium states) is critical. However, attention to magnesium levels must not be over-looked.

In patients with severe or repeated cases of encephalopathy, the patient may be advised to reduce protein in the diet (usually to a 40 to 60 gram protein diet) in order to reduce ammonia production. However, dietary counseling is important, as too little protein in the diet can contribute to malnutrition. Specially formulated intravenous or tube feedings may be necessary for critically ill patients.

The role of antibiotics to control gut flora remains controversial but neomycin has been used to reduce ammonia production by reduction of intestinal bacteria. Lactulose may be given to prevent intestinal bacteria from creating ammonia, and as a laxative to evacuate blood from the intestines.

Treatment with flumazenil (a benzodiazepam receptor agonist) should be considered. While studies show that flumazenil had a significant beneficial effect on short-term improvement of hepatic encephalopathy in patients with cirrhosis, it had no significant effect on long-term recovery or survival.

Sedatives, tranquilizers, and any other medications that are metabolized or excreted by the liver should be avoided if possible. Medications containing ammonium (including certain antacids) should also be avoided. Other medications and treatments may be recommended, with variable results.

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Chapter 12

ANEMIA

A major problem that you definitely will encounter is anemia. The short answer is that patients who have ischemic cardiac or other ischemic conditions should be considered for transfusion when they reach levels of 10 grams of hemoglobin per cu/mm or less. Other patients should be considered at the level of 8 grams of hemoglobin per cu/mm or less.

Patients who present with overt anemia are relatively simple to sort out and treat. However, the major problem is those patients who have slow progressive decreases in their hemoglobin over time, but who do not have the trigger values that clearly indicate what to do.

In determining the cause of the decreased hemoglobin, one must remember that there almost always WILL be a drop in hemoglobin values reported by the laboratory during the first day or two of admission. This drop is due to re-hydration. No diuretic effect of alcohol and water intake will cause re-hydration, especially if caffeine is limited.

However, if the hemoglobin continues to fall, then the obvious issue to determine is if the patient is having a bleed, or if the problem is with their bone marrow. Unfortunately, this is not always easy to tell. While a fecal occult blood test can pick up the presence of blood, this test is not always specific, nor is a single test always accurate. An additional issue is whether the decreasing hemoglobin is being caused simply by metabolic damage to the bone marrow and the liver with the resultant decrease in erythropoietin.

In most cases, determining whether the cause of the decreasing hemoglobin is caused by a bleed or by metabolic reason can be answered through use of the serial FOBT testing and reticulocyte counts. Serial FOBT should detect any significant blood loss. So any time the patient is having persistently decreasing hemoglobin, either the bleed is significant and will be detected on the FOBT, or the problem is the bone marrow. A negative FOBT should mean that the patient is not having a significant bleed. Note I did not say any bleeding and a single FOBT is not adequate. Therefore a series of at least 3 days testing should be done.

An intact bone marrow and adequate supplies of erythropoietin should cause the release of increased reticulocytes and platelets. The problem is with a very small but persistent bleed in a patient who does not have enough bone marrow production capabilities to produce reticulocytes. This is a mixed-cause anemia and needs to be watched serially as, hopefully, time will reverse the course. However, it is best to ensure the patient is not getting any NSAIDS at all (including acetaminophen) and place the patient on both a H2 blocker and a PPI to protect the gastric mucosa.

An additional concern is the iron supplies and an iron panel should be run on all patients with an anemia. Unfortunately, due to other vitamin deficiencies, the lack of microcytic cell size does not rule out the possibility of low iron values. Patients who show iron deficiencies should be treated with such, but patients with known cirrhosis should not be placed on high level of iron prophylactically because they will develop hemociderosis, a condition of iron deposits in the liver compounding the cirrhosis. Therefore, iron panel findings should be monitored (in the long term care setting).

Iron overload is very common in many types of non-biliary cirrhosis but rare in biliary cirrhosis. The hemociderosis of affected livers seems to be acquired and to occur rapidly once cirrhosis has developed; cirrhosis alone may cause iron accumulation.

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Chapter 13

Cardiac Consideration in Detox patients

Evidence began to emerge in the 1950s that supported the idea of a direct toxic myocardial effect of alcohol. Research during the last 25 years has been particularly productive in characterizing the disease entity of alcoholic cardiomyopathy (AC).

Alcohol use has also been shown to have numerous effects on the cardiovascular system other than heart failure. It has been associated with arrhythmia (such as atrial fibrillation, atrial flutter, other supraventricular arrhythmia, premature ventricular contractions), sudden death, hypertension, and stroke.

On the other hand, there are also numerous studies that have demonstrated that light-to-moderate alcohol consumption (i.e., 1-2 drinks per day or 3-9 drinks per week) decreases the risk of cardiac events such as myocardial infarction.

One significant problem with long-term use of alcohol is the development of alcoholic cardiomyopathy. This is a long-term problem, and it will present a significant increased risk of cardiac complications during detox periods, especially in patients with angina and cardiac events. Patients who present with symptoms of this or other cardiac conditions need to have at least the minimum work up to ensure that they are not in crisis, regardless of patient reports of negative symptoms.

Special care needs to be taken in the more common situation of a patient with long standing cardiac problems presenting for detox. This is especially true with patients who have congestive heart failure. The reason is that laboratory studies are not able to adequately show the entire picture of the fluid and electrolyte depletion in the patient who has been chronically drinking. Thus, when the patient acutely stops drinking, fluids that are normally lost from the use of alcohol will now be retained. This will significantly decrease the concentration of cations in their body, making a bad situation worse and effectively increasing congestive heart failure and stress on the heart. Add the loss of dilation effect of alcohol, which actually had a temporarily protective effect on the blood flow to the heart, and the patient is suddenly at a sudden increased risk for a cardiac event.

Nitrates (and calcium channel blockers) run the risk of increasing edema and peripheral pooling, thus worsening congestive heart failure. Thus nitrates should be used when clinically warranted but with care. Patients who are suspected to be in significant congestive heart failure, especially low volume failure, should be referred to a cardiologist or internal medicine specialist on an immediate basis. The use of the BNP test is advantageous, but should not be relied upon to give the complete answer to determine if the patient is in congestive failure.

Chapter 14

Psychiatric Problems

This book would not at all be complete if it did not address the issue of mental illness that is so very common in the inpatient detox setting. The link between mental illness and drug and alcohol use has been well established and thus a significant portion of patients you will deal with will have significant mental illness as a co-morbid condition that will definitely impact both their presentation and their risk of detox.

One of the most pressing issues that must be dealt with is the use of psychotropic medications in the detox setting. Because of the high percentage of patients who present with a psychiatric illness, many of them will present requesting to start back on their medications if for no other reason than to help them sleep. I will say that in my opinion it is initially best not to use any psychotropic medication that you can avoid.

Please note that this comment is meant for the short-term and not the long-term situation. The patient's mental illness condition must be addressed or their probability of abstaining from drug and alcohol abuse is extremely low. However, since most psychotropic medications lower seizure thresholds, the initial use of these drugs will complicate the detox process. The actual treatment of the psychiatric illness needs to be under the care of a psychiatrist who is not going to be able to assess the patient adequately during the acute detox phase.

That being said, there are, of course, those patients who present with an acute threat of violence to staff and other patients. In these patients you, of course, must control the situation and the use of these medications is not only justified but also necessary.

Be aware that you MUST weigh the usage of these medications carefully; you do not know what other drugs the patient has taken and in some cases the medications needed to control the situation carry their own inherent risk. For example, droperidol, which is seemingly safe, does carry a black box warning due to its potential to cause torsades des pointes in patients with low potassium levels, the risk of tardive dyskinesia, and the potential for respiratory depression. If droperidol is used, then it is imperative to have immediate determination of the serum potassium. Do NOT use droperidol if you do not have immediate lab capabilities to determine potassium levels.

The risk for the patient, other patients, and staff must be considered for a patient who is out of control and thus there will be times when such chemical restraints must be used in the best interest of the patient. In these times I prefer the use of a cocktail as I have found that the combination allows me to use less medication than if I had used a single medication and thus incurs less risk.

I tend to use a combination of a short-acting benzodiazepam and a typical antipsychotic (such as haloperidol) to control such violent patients. A combined dose of 1-2mg of lorazepam and 5-10 mg of haloperidol seem to work the best. The dosages should be altered, of course, based on the patient and the clinical situation. The reason why this combination works well is that psychiatric patients who are used to doses of psychotropic medications are susceptible to the calming action of the benzodiazepam where as the non-psychotic patient who has a long history of alcohol abuse may very well be resistant to the actions of the benzodiazepam but is still is susceptible to the haloperidol effects.

Of course, it may be necessary to restrain the patient while the medication you are giving them take effect or even so that you can actually give the patients these medications. In such cases I recommend that you leave the physical control of these patients to those who are specifically trained in controlling them without causing harm to themselves, the patient, or associated staff. The old practice of having numerous staff members jump on the patient should be avoided because of increased risks of injury to the patient and staff members.

Along with violent situation there are also other considerable dangers to the detoxing psychiatric patient in terms of the risk of suicide. It is well established that chronic alcoholism, in itself, causes depression. Further, it is easy to understand the worsening of a previously existing depression by chronic alcohol consumption both directly, as above, and also from the washing out any medications that are used to treat the depression.

Like any significant depressive syndrome, there is some (questionable) increased risk of suicide once the patient begins to feel better. This is due to the fact that while the full depression has not abated, the patient may have the energy to impulsively do an act they think will cure their situation.

NOTE: while there are studies and findings that actually dispute this conclusion, many antidepressants do list this possibility in their PDR warnings. Thus, it is good medicine to pay attention to this possibility.

It is my personal opinion that any psychotropic medication that can be delayed until after the patient is out of the acute detox phase should be. Little is to be gained by starting most of these medications immediately and much risk can to be avoided by waiting the few days needed to bring the risk down. The psychiatrist should be consulted if there is a question of what medications to use or what can be delayed.

Another issue that must be addressed in the detox patient is the issue of competency. While this is not meant to imply that you should be doing competency exams on all detoxing patients, it is noted that chronic alcohol usage, in itself, can cause significant brain damage and deterioration, which is visible on CT. Add to this the considerably increased risk for falls and fights, and the detoxing patient may be at serious risk for making decisions that are not rational. Care must be taken to allow the patients who do not have the capability to make sound decisions to have as much of their legal rights as possible, without allowing patients to have their way, (like leaving or refusing medical care). It is suggested that you work closely with a psychiatrist to determine the competency status of all patients in question.

Research

- 1) OMH Letter to Parents Concerning the FDA Warning About Using Antidepressants in Children and Adolescents
- 2) Cocaine-Related Psychiatric Disorders : Christopher P Holstege, MD -[eMedicine](#)
- 3) BIPOLAR AFFECTIVE DISORDER: Stephen Soreff, MD,; Lynne Alison McInnes, MD - [eMedicine](#)

CHAPTER 15

AMPHETAMINES

Another one of the chemicals of abuse you will run into in a detox program, whether inpatient or outpatient, will be amphetamines. Use of amphetamines seems to wax and wane in a popularity that seems to change over decades (rather than in months or years) and we presently are in the upswing of such a popularity increase. This is probably due to the ease of making such and also the relatively ease of creating a powerful euphoric.

In short, amphetamines are D1 and D2 sympathomimetic amines receptor stimulants with a simple structure that have multiple biological effects, including hyperthermic, anorectic, cardiovascular and central nervous system stimulant actions. The mechanism of action is to cause the release of dopamine from presynaptic axon terminals, block dopamine reuptake, inhibit the storage of dopamine in presynaptic vesicles, and inhibit the destruction of dopamine by enzymes. Because of massive D2 receptor stimulation amphetamine users can exhibit all positive symptoms of schizophrenia.

Additionally, amphetamines have a false transmitter effect where they are re-absorbed into the presynaptic nerve terminal membranes. The problem with this is that, while the chemicals are close enough to be reabsorbed, they are not effective as neurotransmitters when they are released from the vesicles. Thus, the amphetamine user gets a prolonged depressive effect after the usage.

Other drugs which fall into the same classification as amphetamines are: MDMA, Ecstasy, or Adam. However, MDMA differs from the other amphetamines in that it interferes with the reuptake of serotonin in the brain.

Historically: The ma huang plant (*Ephedra vulgaris*) had been used in China for centuries to treat people with asthma. The ma huang plant contains ephedrine. In 1920 "ephedrine" was released as a drug used to treat asthma.

In 1932, synthetic ephedrine was sold "over-the-counter" and was available without a prescription until 1954.

Amphetamines were initially used in 1935 to treat narcolepsy, and later Parkinsonism, obesity, and fatigue. With the advent of more therapeutic drugs, its use in Parkinsonism and narcolepsy was discontinued. Unfortunately, by that time a large market had already developed for the use of amphetamines in treatment of obesity, hence the nickname still present on the street is "diet pill". Adding to the usage, amphetamines were given to soldiers and pilots during World War II to keep them alert and to fight off fatigue.

Actions: A major action of amphetamines is to inhibit sleep and fatigue. Thus, amphetamines have been used as self-medication by truck drivers, students and businessmen, to stave off normal fatigue and enable them to work for days with little sleep or food.

Street amphetamines (for illicit usage) come in several different types. The form found on the street varies with the latest popularity. However, SOME of the names of oral forms are benzedrine or "bennies" and dextroamphetamines or "white cross". The latest upswing in amphetamine usage has been in the form of methamphetamines, which are known as "crystal" or "meth" or "ice". Meth has become the most widely used form of illicitly produced amphetamines.

All forms of amphetamines are stimulants. Methamphetamine, which is the latest upsurge in usage, is only produced in illegal drug laboratories. There is no known medical advantage to methamphetamines and they are not used by medical personnel for treatment of any medical condition. Methylphenidate (note 1) which is a similar compound to amphetamines is sometime abused on the street but definitely not preferred by illicit drug users as it does not produce the profoundly euphoric effect than amphetamines do.

Benzedrine or dextroamphetamines are usually taken orally or they may be snorted. Methamphetamines are usually injected or smoked.

The initial oral dosage of amphetamines is usually 20 - 40mg. However, as usage or abuse continues, an increase in dosage is required as rapid tolerance occurs.

Immediate effects at low doses

- Sensations of euphoria
- Enhanced self awareness and self confidence
- Increased visual awareness
- Heightened alertness
- Increased capacity for concentration
- Greater energy
- Users become hyperactive, talkative, excited, irritable and restless
- Reduction of appetite
- Increased breathing and heart rate
- Raised blood pressure
- Dilation of the pupils.

Effects at high doses

The reason for the symptoms that occur with a high dose, or possible overdose, of amphetamines is the massive stimulation of the nervous system. The massive release of

chemicals from the nerves not only stimulates the nerves they are supposed to, but also increases stimulation of other nerves throughout the body.

- Dry mouth
- Fever
- Stereotyped movements
- Sweating
- Headache
- Blurred vision
- Dizziness
- Flushing
- Pallor
- Tachycardia
- Tremor
- Loss of coordination
- Jaw clenching/tension
- Nausea/vomiting
- Gastrointestinal disturbances
- Insomnia
- Rapid or slurred speech
- Seizures
- Hyperthermia

Cerebrovascular accidents can result from hemorrhagic stroke or ischemic events secondary to vascular occlusion due to excessively high blood pressure during episodes of usage. At high doses, amphetamine abusers may experience distortions and gross alterations in body image, which are often extremely frightening.

Additionally amphetamines can produce a paranoid psychosis with disorientation that resembles schizophrenia. Symptoms include delusions of persecution, ideas of reference, and often bizarre visual and auditory hallucinations. Amphetamine psychosis can often only be distinguished from paranoid schizophrenia by the fact that the symptoms do disappear, usually a few days or weeks after drug use is stopped.

Long-term effects

Malnutrition – since amphetamines suppress appetite, illnesses related to nutrition and vitamin deficiencies occur and there is increased susceptibility to disease. Anemias should be investigated as well.

Violence – intense and sudden acts of aggression can occur. Aggressive acts are often related to paranoia, feelings of persecution, and distortion of perception.

Blockage of blood vessels – impure amphetamines may contain foreign particles, which can block small blood vessels and lead to kidney damage, lung emboli or stroke.

Depression – often a vicious cycle exists. A patient suffering from chronic depression takes amphetamine for relief, becomes dependent, tries to discontinue its use, suffers depression as a withdrawal symptom, and renews amphetamine use.

The possibility of Subacute Bacterial Endocarditis: a bacterial infection from IV usage, is a real risk, although, luckily, not common. However, patients with cardiac murmurs or symptoms of failure must have workups. Subacute bacterial endocarditis is usually (but not always) caused by a viridians streptococci. If untreated, it can become fatal within six weeks to a year.

FALSE TRANSMITTER EFFECT

Another proven effect of amphetamines is the depression and damage that remains after the user recovers from the acute effects of amphetamines. This effect happens because when chemicals are normally released from the presynaptic ends of nerves, they stimulate the post synaptic receptors and then are either destroyed (by enzymes) or are reabsorbed back into the presynaptic nerve terminals to be incorporated into (presynaptic) vesicles and used for future release. However, when amphetamines are used, not only do amphetamines cause an increase in the breakage of vesicles and an initial release of the normal chemicals released, but the amphetamine is also re-absorbed into the (presynaptic) vesicles nerve ends along with a decreased amount of normal chemicals as part of the normal process.

When this happens and the next normal stimulus causes a release of chemicals out of the nerve end, the amphetamine particles are also released. The stored amphetamine particles not only won't stimulate the next nerve in sequence, like normal neurotransmitters, but also they interfere with the function of the other normal chemicals released. This causes an overall decrease in ability to function that persists for weeks, or even months, after heavy amphetamine usage has stopped. There is some evidence to support the hypothesis that some of the damage done to the nerve terminals is never fully recovered from. The percent of damage done seems to be directly related to the dosage of amphetamine used and the accumulative effect.

EFFECTS OF WITHDRAWAL FROM AMPHETAMINE USE

Psycho-stimulant withdrawal is generally described in three phases – crash, burn and recovery. The characteristics of these phases are as follows:

Crash– the initial period which classically follows a period of use. The most common effects experienced include fatigue and exhaustion. Effects may last several hours to several days. This is a period when the body does not have enough catecholamines in the pre-synaptic nerve terminals to maintain normal function. Therefore the body will become sedated and attempt to rebuild supplies by sleep.

These symptoms are compounded by the "speed freaks" sleep deprivation (caused by inability to sleep while using amphetamines), and the feeling of paranoia, which becomes more evident with every day the subject abuses amphetamines. Other positive symptoms are also possible but not as common.

Combined with the other problems of the amphetamines is the fact that the user of amphetamines has no appetite, making food - both liquid and solid - extremely difficult, if not impossible to eat. The lack of sleep plus the lack of nourishment to maintain the body causes a severe strain on the heart and other organs of the body. This strain keeps increasing as long as the user keeps maintaining themselves on amphetamines until the body can no longer sustain the load. When this happens, if the user is lucky, he will merely collapse into a state of exhaustion and sleep until the body has rejuvenated enough to at least function properly. However, there is also the definite possibility that one organ system of the body will fail under the strain. If one of the body's organs does fail, the results are fatal. Hence, the slogan on the street is "speed kills!" Even the average heroin addict has a longer life span than the devout speed freak.

Burn – This phase may last for a number of weeks or even months and is typically characterized by:

- lethargy/fatigue
- Long but disturbed sleep
- Irritability
- Strong hunger
- Deep depression that may lead to attempted suicide
- Fits of violent action
- Anxiety attacks
- Headaches
- Sweating
- Muscle cramps
- Gastrointestinal cramps

Recovery - normal mood and behavior is interrupted by episodic craving often in response to conditioned cues. These cravings may last minutes or hours and may continue to occur months or years after cessation of amphetamine use. The most florid symptoms usually dissipate within a few days or weeks of cessation of use of amphetamines. Often, a significant improvement in mood, energy, and paranoid thinking occurs within days.

Other symptoms such as normal sleep patterns, memory loss, confusion and paranoid thinking and perceptual abnormalities may persist for perhaps six to twelve months. After that time, residual symptoms, if present, are generally slight and not disabling, and are noticed primarily by the user.

TREATMENT (acute)

Treatment from the acute standpoint is definitely different than treatment to prevent further usage. In the acute setting, the idea is to prevent complications from the over stimulation of the body (for example: hypertension, tachycardia and agitation). Beta blockers are the drug of choice in this regard, if there are no contradictions to such. Additionally, it is important that all patients have an immediate EKG to assess for any ischemia. Physically such patients are at small but obviously higher risk for development of aneurisms and varices simply due to the episodes of induced significant hypertension. Therefore a good neurologic and abdominal exam needs to be done on every admission.

Positive psychiatric symptoms can be treated with the same protocols for schizophrenia (D2 receptors blockers like haloperidol).

Psychiatrically, the question of psychosis as a baseline versus drug-induced psychosis and treatment of such is best handled by a psychiatrist. Evaluations must include a determination of depression and suicide risk for all patients withdrawing from amphetamines. This is especially true for patients with an underlying bipolar disorder- especially the rapid cycling type and those patients with a previous suicide attempt history, because these patients are at a much higher risk for suicide due to the induced depression. Laboratory studies should also include a CPK to assess such.

Note 1: Methylphenidate is a central nervous system (CNS) stimulant. It has effects similar to, but more potent than, caffeine and less potent than amphetamines. It is used because of proven calming and “focusing” effect on those with ADHD, particularly children.

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CHAPTER 16

COCAINE

Another frequent drug of abuse that you must have some familiarity with is cocaine. Cocaine is a purified extract from the erythroxyloncoca tree. The natives of Peru and Bolivia have used the leaves of this tree for centuries, chewing them for their stimulant effects.

ACTIONS: Cocaine is a strong central nervous system stimulant that interferes with the re-absorption process of dopamine. The buildup of dopamine causes continuous stimulation of receiving neurons, which is associated with the euphoria commonly reported by cocaine abusers. Cocaine binds to sites in areas of the brain that are rich in dopamine synapses such as the ventral tegmental area (VTA) and the nucleus accumbens.

While it is not completely known why, cocaine differs from amphetamine in the important fact of its D1 and D2 receptor nerve receptor stimulation. Because of this, except in very high doses of cocaine, where stimulation of D2 receptors occurs after total saturation of D1 receptors, there is very little risk of the positive schizophrenic symptoms (like hallucinations and delusions) found with amphetamine usage. However, repeated cocaine administration reduces levels of postsynaptic D2 receptors.

Cocaine has two main effects on the nerve junctions. The first action is on the presynaptic nerve junction blocking of the nerve's ability to reabsorb the chemicals that it releases whenever it is stimulated. The second effect is to block the post-synaptic nerve junction, thereby finally blocking all nerve impulses in the nerve. This causes a state of anesthesia (loss of feeling) in all areas where cocaine is applied. This has significant implication in terms of cardiac risk! It is also why many cocaine addicts are unaware of the holes in their nasal septum (due to necrosis from vasoconstriction). This also has long-term implications in that nerve receptors are changed and can set off muscle chest wall spasms, which may mimic the chest pain of an MI.

Cocaine is most commonly snorted; however, it can be smoked, injected or eaten. It is absorbed in all surfaces to which it is applied. However, the greatest absorption rate occurs when it is applied to mucosa. The duration of cocaine's immediate euphoric effects depend on the route of administration. The faster the absorption, the more intense the high. However, the faster the absorption, the shorter the duration of action. The high from snorting may last 15 to 30 minutes, while that from smoking may last 5 to 10 minutes. Increased use can reduce the period of time a user feels high and increases the risk of addiction.

Physical symptoms: Cocaine causes a mydriasis (dilation of the eye), decrease in fatigue, increase in mental alertness, increase in heart rate, and also a numbness at the site where the cocaine was applied. Cocaine also causes a vasoconstriction of all blood vessels in the site to which it is applied. What this means is that all blood vessels in the area where cocaine touches become constricted and thereby decrease the amount of blood flowing through them.

This vaso-constrictive effect has been used for years by doctors to help control nose bleeds or in dental operations to help control the bleeding of the gums. However, when the person on the street uses cocaine, he is not using it in the concentration that is normally used in a medicinal setting, but in a much higher concentration. Therefore, the blood vessels to which the cocaine is applied are constricted to a much greater degree. As the person who abuses cocaine frequently snorts the drug through the nose, this causes a constriction of the blood vessels in the mucosa of the nose. Unfortunately for the user, this constriction of blood vessels can cause a death of the skin lining the nose, because that skin (or mucosa) is totally dependent upon those blood vessels for its nourishment. When this necrosis happens, the user sets himself up for a chronic sinus condition with the strong possibility of recurrent and severe infections; as the nasal mucosa which normally protects the user from such infections has been destroyed.

The above symptoms noted are only for those users who use a small to moderate amount of cocaine and do not have the misfortune to overdose on it. Since cocaine is a very expensive drug and is usually “cut” numerous times before reaching the user on the street, the true concentration of cocaine in the powder, which the user buys is unknown. Therefore, the possibility of overdose exists. The listed fatal dose of cocaine is approximately 1.2 gm (or 1200 mg), but toxic symptoms have been reported with as little as 20 mg. Since street concentration usually varies from 5- 35%, it becomes fairly easy for the heavy user to approach the levels of possible overdosing.

The signs and symptoms of an overdose are: excitation, restlessness, anxiety, fever, irregular respiration, nausea, vomiting, rapid heart rate, possible paranoid psychosis (identical to that of amphetamine psychosis), possible convulsions, and possible death.

ADDICTION: In the past, it was widely believed that cocaine was not physically addicting because of the lack of physical effects on abstinence, but it was believed that a person could get psychologically addicted to the high cocaine produced. Unfortunately, it was also erroneously believed that such symptoms could be relatively easy to overcome. With the advent of devices like the P.E.T. scanner, it has been proven that cocaine is not the relatively innocuous drug it was once believed and that cocaine directly stimulates and damages the neuro-pathways of the pleasure and related emotional centers of the brain. Actual physical changes of post synaptic nerve end plates occur with the use of cocaine and those changes are accumulative with every usage. While initial changes may occur with only 1-2 usages of cocaine (depending on personal and genetic susceptibility), the changes may last for decades or more. In some cases anadonia may result from the accumulated damage. Although it has been proven that prolonged treatment for cocaine dependency has better statistics than short term

treatment, at present there is NO cure for cocaine dependency, even with prolonged treatment. The addict remains addicted for life.

What is particularly important from the detox point of view is that unless the user presents with evidence of overdose, or cardiac involvement, withdrawal from cocaine causes few, if any, life threatening symptoms and does not in itself warrant admission to the detox ward. Like amphetamines, however, the rapid cycling bipolar patient and those patients with a history of impulsive suicide attempts need to be evaluated carefully for possible admission due to psychiatric reasons.

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CHAPTER 17

Marijuana

Depending on the reports you read, up to 40% of Americans have used marijuana at some point in time and approximately 10% of the population uses it on a regular basis. Marijuana is (in many areas of the country) the third most popular substance chosen by young people for regular use, superseded only by alcohol and tobacco. Therefore, there is no way you are going to be able to avoid dealing with the effects of marijuana in the patients admitted to the detox center.

The source of marijuana is the hemp plant (*cannabis sativa*). The active ingredient is THC (delta-9-tetrahydrocannabinol), which is found in the leaves and flowering shoots of the plant. However, other cannabinoids are also found. Hashish, another common form of THC, is the resinous substance taken from the tops of female plants. It contains the highest concentration of THC.

When used, the concentration of THC taken varies greatly and, in fact, may vary as much as a hundred-fold, depending on the route used (smoked versus ingested) and the concentration found in the material that is used and also any contaminating materials.

The drug is used primarily because of induced effects of euphoria and relaxation. However, increased visual, auditory, and taste perceptions may also occur with low-to-moderate doses. THC also frequently stimulates the appetite.

Because marijuana does not cause hallucinations or direct anger-center stimulation, patients who exhibit delirium, hallucinations, or violence should be questioned for the suspicion that the marijuana had been laced with another agent, usually as PCP.

However, unpleasant effects may also occur, including changed body image, disorientation, acute panic reactions and paranoia (rarely severe). Visual tracking is impaired and sense of time is typically prolonged.

Marijuana effects may also include:

- Increased heart rate and blood pressure
- Bronchodilatation (widening of the airways)
- In some users, bronchial (airway) irritation leading to bronchoconstriction (narrowing of the airways) or bronchospasm (airway spasms, leading to narrowing of the airways)
- Pharyngitis, sinusitis, bronchitis, and asthma in heavy users (due to bronchial and upper airway irritation)
- Possible depressive effects on the immune system (particularly the WBC's).

The metabolite of THC/marijuana is stored in the body's fat tissue, and evidence of marijuana may be found in users through urine testing up to 1 month after the last use of the drug.

One study has indicated that an abuser's risk of heart attack more than quadruples in the first hour after smoking marijuana. The study suggest that the effect might occur from marijuana's effects on increased blood pressure and heart rate and reduced oxygen-carrying capacity of blood. However, this effect is short-lived and quickly returns to baseline.

While initial use of marijuana causes a calming effect, the feelings are replaced by withdrawal effects, which include agitation, insomnia, irritability, and anxiety. This is because of rebound irritation of the limbic system. Withdrawal symptoms in chronic THC use leads to an increase in the activation of the stress-response system and changes in the activity of nerve cells containing dopamine.

Other marijuana effects on the detox ward are minimal and easily overcome with the use of Gabapentin due to the anti-anxiety effects of this medication. Respiratory effects need to be considered, but effects are other wise negligible. Reversal effects on the actions of psychotropic medications are significant but are not relevant or treatable on the detox ward. In fact, this situation is best left to the psychiatrist to deal with, as it relates to the patients appropriate use of his medications more than his detox issues.

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