Chapter 1 : Learning Theory of Addiction and Recovery Implications:

Theoretical and Generic Considerations for Hospital Life- Sustaining Treatment Policies ï»¿ Silfen, Eric () Hospital Policies on Life-Sustaining Treatments and Advance Directives in Canada ï»¿.

This article has been cited by other articles in PMC. Abstract The ECG is a rapidly available clinical tool that can help clinicians manage poisoned patients. Specific myocardial effects of cardiotoxic drugs have well-described electrocardiographic manifestations. In the practice of clinical toxicology, classic ECG changes may hint at blockade of ion channels, alterations of adrenergic tone, or dysfunctional metabolic activity of the myocardium. This review will offer a structured approach to ECG interpretation in poisoned patients with a focus on clinical implications and ECG-based management recommendations in the initial evaluation of patients with acute cardiotoxicity. Poisoning, defined as exposure to any drug, chemical, or toxin that results in injury, is the second leading cause of injury-related fatality in the United States of America USA behind only motor-vehicle collisions [1]. Cardiotoxicity from poisoning is one of the leading causes of death among these patients [2 , 3]. It is thus crucial for clinicians to rapidly recognize cardiotoxicity and be prepared to face management decisions that require prompt action despite access to limited clinical data. Although poisoning is an infrequent cause of cardiac arrest in elderly patients, it is the leading cause of cardiac arrest in patients under 40 years of age [1 - 4]. Many recommendations for the emergency cardiovascular care of poisoned patients are based on expert consensus, not scientific evidence [4] though some toxin-specific recommendations for life support measures based on limited scientific evidence have been made [5]. Additionally, because standard guidelines for emergency cardiovascular care may not be optimal for the management of acute poisoning and overdose, urgent consultation with a medical toxicologist or regional Poison Control Center is recommended for patients with cardiovascular toxicity by the American Heart Association, the American Academy of Clinical Toxicologists, and the American College of Emergency Physicians [4 , 6 , 7]. According to recently published guidelines from the American Heart Association, the emergency cardiovascular care of myocardial injury should change in both diagnostic evaluation and therapeutic management if the patient has a history of drug or toxin exposure [8]. The initial evaluation of the poisoned patient is based on the constellation of vital signs, symptoms and signs on physical examination, which may be a daunting task especially without formal training in toxicology or when faced with a rare exposure. Care of the patient takes on another element of complexity when one considers that toxicity may change during the course of evaluation depending on the particular exposure. For example, a patient with tricyclic antidepressant toxicity may undergo several phases of multi-organ toxicity prior to ultimate cardiovascular collapse. Toxidrome identification, rather than focusing on toxins or suspected toxins, allows for a more rational approach to the poisoned patient. Including ECG interpretation in the initial approach can provide key information to guide management. This review describes the role of ECG in poisoning, summarizes specific toxic effects on the myocardium and provides a systematic interpretation of the ECG and the identification of ECG toxidromes. Management issues in those patients identified to suffer from cardiotoxic effects are also addressed. One of its most attractive characteristics for emergency medicine and critical care is that electrocardiogram ECG results are rapidly available in a matter of minutes. The waveforms and intervals produced by the electrical forces of depolarization and repolarization and their behavior over time enable physicians to identity normal and abnormal patterns that may represent cardiac or extracardiac disturbances. In medical toxicology, the ECG plays an important role in the evaluation of poisoning to identify or exclude cardiotoxicity, as well as to take fundamental steps in initial management. A sound understanding of ECG interpretation and the characteristics of cardiotoxicity is necessary to establish a basis for the utility of the ECG in drug overdose. A recent study found that the initial interpretation of ECGs reported to a poison center was frequently inaccurate and suggests that correct interpretation would imply changes in management recommendations [9]. Therefore, treatment implications including consultation with medical toxicologists or Poison Control Centers should be based on correct interpretation in order to lay a sound foundation for management. ECG interpretation is well established in patients with chief complaints of chest pain and

dyspnea and in those with metabolic disturbances. In the poisoned patient, the same systematic approach to the ECG can also be useful. Poisoned patients can present ECG changes common in coronary artery disease, electrolyte abnormalities or causes of dyspnea. This can be illustrated by the example of a cocaine user presenting with chest pain and dyspnea, since consequences of cocaine use may include myocardial infarction, pulmonary embolism or pneumothorax [10]. Some caveats should be taken into account when analyzing the role of the ECG in poisoned patients. Factors besides direct cardiotoxicity may influence ECG changes. Severely poisoned patients with substances that do not have specific cardiac effects can present with cardiotoxicity in the context of multiorgan failure. Sympathomimetic and anticholinergic effects are commonly seen in drug overdose as well as hypovolemia and hyperthermia, all of which can cause tachycardia. Anxiety and pain may also be exacerbating factors. Repeated ECG evaluation should be performed in patients with suspected cardiotoxicity or in those with ECG changes suggestive of toxicity. Patients that have ingested sustained release preparations of suspected cardiotoxic drugs or those who have ingested drugs with known delayed toxicity should also undergo serial ECGs. All such patients should be continuously monitored in an appropriate setting until toxicity resolves. Cardiotoxic agents have effects on specific ion-channels particularly sodium, calcium, and potassium that produce important changes in the action potential as well as resting potential. What follows will be a brief review of the primary mechanisms of toxins on the myocardial ion channels and the subsequent consequences that lay the basis for ECG interpretation in poisoned patients. Sodium Channel Blockade The upward stroke of the myocardial action potential is a result of the conformational change and opening of voltage dependent sodium channels in response to an electrical stimulus from adjacent cells, thus causing depolarization. This phase 0 of the action potential is delayed, demonstrating a less steep slope of depolarization Fig. There are several ECG changes suggestive of delayed ventricular depolarization. QRS morphology, duration and axis changes due to sodium channel blockade will be described in the interpretation of the ECG in poisoning.

Chapter 2 : Phase 0 clinical trials: theoretical and practical implications in onc | OAJCT

Drug-drug interactions (DDIs) related to altered drug absorption and plasma protein binding have received much less attention from regulatory agencies relative to DDIs mediated via drug metabolizing enzymes and transporters.

According to learning theory, addiction is simply a learned behavior. In other words, people learn to engage in addictive behavior according to well-established learning principles. There are two fundamental types of learning that apply to humans and animals alike: A third type of learning is called social learning. Social learning occurs when we learn something by observing others. Unlike classical conditioning and operant conditioning, only humans and certain animals e. People may learn addictive behavior through classical conditioning by pairing the pleasure of addictive substances or activities, with environmental cues. For example, suppose someone always smokes marijuana in the car after work. The enjoyment of smoking marijuana forms a paired association with riding in the car. The timeframe "after work" also forms a paired association. By repeatedly pairing marijuana-with-car, and marijuana-after-work, both the car and after-work will become cues to smoke marijuana. Then these cues getting into the car, getting off work may create powerful cravings for marijuana. Fortunately, what we learn can also be unlearned. For instance, if after-work has become a "cue" to smoke pot, then doing a different activity repeatedly after-work will form a new association. Someone could practice riding in the car without smoking. The power of a cue is diminished through a process called cue exposure. Cue exposure repeatedly presents a person with the cue, without pairing. Therefore, riding in the car and not smoking pot will reduce powerful cravings over time. Counter-conditioning is a special type of classical conditioning. An addictions recovery application of counter-conditioning is called taste aversion a strong dislike of a specific taste. Toxic foods make us sick. They lead to the development of an aversion to the taste of that food. Taste aversion is somewhat more complex than classical conditioning. Classical conditioning pairs the stimuli together within seconds of each other. The association between a toxic food and subsequent nausea will indeed develop. However, these two events may occur several hours apart. Schick Shadel Hospital has developed and advanced this approach. Patients taste and smell alcohol or other addictive substances. This is followed by induced nausea. Patients receive medication to bring about the nausea. Operant conditioning is a second type of learning. A system of rewards and punishments forms the basis for this learning. If the first use of a substance is a rewarding experience, we are more likely to return to it. Likewise, without unpleasant consequences to addiction, there is little reason to stop. We know that people can enhance recovery efforts by allowing natural consequences to occur. For instance, loved ones can stop shielding someone from the negative consequences of their addiction; i. Similarly, we can reward healthy choices so they become more appealing than addictive behavior. For example, a person may be permitted to return to their family and comfortable home; but only if they have demonstrated a period of sustained abstinence. Questions for personal reflection from learning theory: Since I may have learned addictive behaviors, how can I unlearn them? How can I replace them with healthier, life-affirming activities? Maybe I should get some professional help with these cues and cravings. What will happen if important people in my life learned to reinforce my positive behaviors? What will happen if they stop enabling me? Maybe I could find a professional who could help them.

Chapter 3 : "Theoretical Considerations in Qualitative Interviewing" by Robin Cooper

Theoretical Considerations and Practical Approaches to Address the Effect of Anti-drug Antibody (ADA) on Quantification of Biotherapeutics in Circulation Marian Kelley, Ago B. Ahene, Boris Gorovits, John Kamerud, Lindsay E. King, Thomas McIntosh, and Jihong Yang.

General systems theory stresses the importance of groups and their influences over individual people. We all exist within a set of nested social systems. These nested social systems can include families, organizations, neighborhoods, societies, cultures, etc. According to this theory, we can only understand individual behavior by considering these group influences. According to general systems theory, addiction is caused by larger social systems that surround an individual. To illustrate this somewhat confusing concept, consider a single cell within an organism. In order to understand the behavior of a single cell, we need to understand the tissue, the organ, the organ system, and the body, in which the cell is functioning. Systems theory proposes that all systems like the maintain balance and harmony. Therefore, every individual within any given system participates in the maintenance of that balance. However, if the natural balance status quo of a system is dysfunctional, then the system serves to maintain that dysfunction. In other words, it would "rock the boat" if we tried to improve the systems functioning. This is how some dysfunctional systems can promote and foster addictive behavior for some individuals in that system. With respect to addiction, the principal system of interest is the family system. Like all systems, families operate to maintain a balance. Usually this entails activities and pressures to avoid conflict, hostility, aggression, or other things that leads to disharmony. The cost of maintaining this balance can be quite high. When someone in a family attempts to discontinue their addiction, it affects all the family members. In other words, recovery "rocks the boat. This evaluation serves to uncover hidden forces that serve to continue dysfunction. These forces have allowed addiction to flourish. Once these forces are identified, family members work together to foster a more functional family system that does not promote addiction. For instance, mom may drink in the evening because she is lonely. This is how she copes with raising three children by herself. Meanwhile, her husband spends most of his time watching TV. Whenever her husband complains about her drinking a conflict erupts. In response to this unbalancing conflict, mom drinks more, and so the cycle continues. A systems approach would suggest the husband delay watching TV until all the children have finished their homework and are in bed. The therapist may ask husband and wife may to spend time together in the evening sharing an activity they both enjoy. These activities help the family system maintain a more functional balance. Questions for personal reflection from general systems theory: Everyone says they want me to get better. Yet, the moment I try to recover, she has a mile-long list of things she wants me to do. Every time I start to get better, I swear they do things that push me back in. Maybe a good family therapist can help us.

Chapter 4 : General Systems Theory of Addiction and Recovery Implications

Psychopharmacologia (Berl.) 46, () - 9 by Springer-Verlag Theoretical and Methodological Considerations on Drug Discrimination Learning.

Chapter 5 : Theoretical and Generic Considerations for Hospital Life- Sustaining Treatment Policies

Theoretical Considerations and Practical Approaches to Address the Effect of Anti-drug Antibody (ADA) on Quantification of Biotherapeutics in Circulation.