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EDITORIAL

# Alcohol: social lubricant and pharmacological blind spot

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## Introduction

Alcohol, born from the fermentation of sugars in grains, fruits or vegetables, is one of the world's most widely used and socially accepted psychoactive substances, found in beverages such as beer, wine and spirits. Across many cultures, it has a long history of use for leisure, ritualistic and therapeutic reasons. Ethanol, the active ingredient in alcoholic drinks, acts swiftly on the central nervous system, triggering noticeable shifts in mood, behaviour and cognitive function.

Although moderate drinking may hold social and cultural value, heavy or prolonged consumption carries serious health consequences such as alcohol use disorder, liver cirrhosis, pancreatitis, cardiomyopathy, neurological damage (Wernicke-Korsakoff syndrome), Foetal Alcohol Syndrome and increased risks of death and certain cancers.[1,2] Alcohol is estimated to be responsible for approximately 4% of cancers worldwide, with notable links to cancers of the pharynx, larynx, oesophagus, liver, colorectum and breast. Its carcinogenic potential stems from multiple biological pathways, most prominently the DNA-damaging effects of its metabolite acetaldehyde, along with ethanol's ability to disrupt DNA methylation, trigger oxidative stress and inflammation and impair one-carbon metabolism and folate-dependent processes.[3]

As general practitioners, we do not have the luxury of viewing alcohol as a distant social concern or an occasional emergency room nuisance. Alcohol is ubiquitous, in our communities, our hospitals, our consultations and our patients' lives. In South Africa, we face a particularly high burden of alcohol-related harm from trauma, injuries and accidents, interpersonal violence, cardiovascular events, liver disease, mental health issues (depression, anxiety) and premature death.[4,5] Despite this, alcohol remains a legal and socially accepted substance, deeply entrenched in our culture and commerce.

The pharmacology of alcohol, how it is absorbed, distributed, metabolised and exerts its effects on the brain, is often poorly understood or overlooked in everyday practice. This article places that science front and centre, offering a clear, practical account of alcohol's journey through the body and its relevance to the cases we encounter daily. But beyond the pharmacology lies an uncomfortable truth: we are probably not treating alcohol seriously enough in our clinical practice.[5] Understanding its effects is only the first step; recognising its footprint in every area of healthcare and acting decisively, is the challenge we must meet.

## Pharmacokinetics: what the body does to alcohol

When ethanol is consumed, whether in a glass of wine or a binge-drinking session, its path through the body is deceptively simple. It is absorbed rapidly, influenced by stomach contents, beverage concentration and the pace of consumption. Most of it enters through the small intestine, finds its way into the bloodstream with a maximum concentration reached between 10 and 90 minutes, and then rapidly bathes every organ, especially those that are highly vascularised, including the brain where it exerts its intoxicating effects.[6]

The body processes drugs mainly to clear them and reduce their harmful effects. In the case of ethanol, this clearance rate, though it varies between individuals, is roughly equivalent to one standard drink per hour, corresponding to a blood alcohol concentration (BAC) of about 0.01 g/dL- 0.03 g/dL (average 0.02 g/dL or 20 mg/100 mL).

However, contrary to popular belief, there is no universal definition of a standard drink or alcohol unit. While a standard drink contains roughly the same amount of ethanol as found in a 330 ml beer, a 90 ml glass of 12 % white wine, a 75 ml glass of 14 % red wine or a 25 ml measure of spirits, definitions vary internationally: in the EU an alcohol unit is set at 10–12 g of ethanol, in the UK at 8 g, in Australia at 10 g, and in the USA at 14 g per drink. In South Africa, a unit is 12 g. In many restaurants, a single glass of red wine is often served in a 250 ml pour, equivalent to more than three units (0.06 g/dL) of alcohol. At this volume and typical strength (14% ABV), most individuals would exceed the legal driving limit of 0.05 g/dL BAC after just one glass.

Binge drinking refers to a drinking pattern that results in BAC reaching or exceeding 0.08 g/dL.[7] This typically corresponds to the consumption of about four or more standard drinks for women, and five or more for men, within roughly two hours.[8,9] (As an aside, many patients and even clinicians remain unaware that the recommended weekly intake is no more than 14 units, preferably spread over three or more days, limits frequently exceeded with little recognition of their cumulative harm.)

Although some ethanol is excreted unchanged in urine, sweat and the breath (hence the rationale for a breathalyser test), the liver takes on the brunt of ethanol metabolism. It begins with alcohol dehydrogenase (ADH) converting ethanol into the toxic intermediate acetaldehyde, followed by aldehyde dehydrogenase (ALDH) turning that into acetate, which is a less harmful by-product, carbon dioxide and water. But this system has its limits. While under usual conditions, ethanol is mainly broken down by ADH, with heavy or long-term alcohol use, additional pathways such as the cytochrome P450 isoenzyme CYP2E1 and catalase become increasingly involved in its metabolism.[10] Once the enzymes are saturated, metabolism proceeds at a fixed rate of roughly one unit per hour. Anything beyond that overwhelms the system.[8]

Acetaldehyde accumulation, due to either rapid consumption or genetic variations in metabolism, is not just unpleasant, it is toxic. Flushing, nausea, vomiting and tachycardia are common signs, but chronic exposure escalates to organ damage, particularly in the liver and heart. Some patients, especially those on medications like disulfiram or metronidazole which inhibit ALDH, or those with impaired liver function, are at heightened risk.

The pharmacology provides valuable insight, but just as important is how often we apply this knowledge in clinical practice. How frequently do we take the time to explore alcohol use in meaningful detail when faced with a patient presenting with unexplained fatigue or liver dysfunction?

## Pharmacodynamics: what alcohol does to the brain

Ethanol exerts broad and complex effects on the central nervous system by altering intracellular signalling pathways, which in turn influence gene expression, chromatin structure and protein synthesis. These molecular changes disrupt neuronal circuit function and contribute to lasting cellular adaptations within the brain.[11] At its core, though, ethanol is a nervous system depressant. It mimics the effects of sedatives and anti-epileptics by inhibiting neuroexcitatory NMDA receptors and voltage gated calcium channels while enhancing GABAergic inhibition. The result is slowed neuronal firing, reduced alertness, impaired coordination and depending on the dose, anything from disinhibition to respiratory arrest and death.[12,13]

Ethanol can begin to affect receptor and ion channel activity at concentrations as low as 1 mM/L, equivalent to approximately 4.61 mg/dL (0.00461 g/dL).[12] As BAC rises, so does the severity of central nervous system depression. When blood alcohol levels are below 50 mg/dL (a BAC of 0.05 g/dL), the effects can feel deceptively pleasant including enhanced sociability, a sense of euphoria and increased talkativeness. This early stage of intoxication, known as disinhibition, can also tip into risky territory, sometimes fuelling impulsivity, aggression or even violence.

At levels between 50–100 mg/dL (0.05–0.10 g/dL), individuals may show impaired coordination, slowed reaction time and reduced concentration. This range approaches or exceeds the legal driving limit in many regions (typically 50–100 mg/dL).[10] Between 100–150 mg/dL (0.10–0.15 g/dL), more marked effects occur, including ataxia, slurred speech and impaired memory and motor function. Above 150 mg/dL, sensory responsiveness may diminish, and the risk of unconsciousness, respiratory depression and death increases due to ethanol's direct effects on the brainstem respiratory centres.[10,14]

Severe intoxication typically occurs at BAC levels exceeding 200 mg/dL (0.20 g/dL), with symptoms such as amnesia, diplopia, vomiting, hypotension and hypothermia. At 300–400 mg/dL (0.30–0.40 g/dL), the risk of life-threatening complications such as coma, respiratory failure, arrhythmias (notably atrial fibrillation[15]) and sudden cardiac death, significantly increases.[16] Fatalities are most common when BAC exceeds 500 mg/dL, although individual tolerance varies widely. In those with low tolerance, death may occur at levels around 300 mg/dL, while chronic users may survive levels exceeding 1200 mg/dL. The presence of other CNS depressants such as opioids and benzodiazepines significantly lowers the threshold for fatal outcomes.

We must understand these dose-dependent effects not just to assess severity but to interpret behaviour. A patient who seems just sleepy may actually be slipping into respiratory failure. A teenager who presents with just alcohol in their system could very well be teetering on the edge of asphyxia.

### *Tolerance*

Perhaps the most insidious aspect of chronic alcohol use is tolerance. Those who drink chronically may seem fine at BACs that would render others unconscious, but their respiratory centres remain vulnerable. Patients who drink daily may no longer feel intoxicated, but they remain at high risk. Their motor coordination may improve with experience, but their respiratory centres do not adapt the same way. Tolerance to the euphoric effects of alcohol does not protect against death. As clinicians, we must be vigilant. A patient who insists they are fine at 300 mg/dL may be one drink away from collapse. Let us not be lulled into complacency by confident self-reporting or apparent sobriety. Objective assessment and caution must guide our approach.

## Intoxication

Alcohol intoxication is a daily reality in many South African emergency units. Presentations range from disorientation and slurred speech to violence, unconsciousness and respiratory failure.[17] Alcohol toxicity accounts for a significant share of alcohol-related deaths. Although the exact fatal threshold varies, a BAC of ≥ 0.300 g/100 mL can cause profound respiratory depression. In addition to respiratory failure, high BACs increase the risk of aspiration, positional asphyxia and hypothermia. Underlying medical conditions such as cardiac arrhythmias or impaired alcohol metabolism may further heighten the risk of death.[18]

Too often, patients are stigmatised, minimised or simply parked until they sober up. But intoxication is a clinical emergency. Assessing mental status, vital signs including oxygen saturation, and ruling out trauma or concurrent pathology is essential.[19]

Ethanol levels alone may not tell the full story. In practice, elderly patients may present with profound symptoms at low concentrations, while young adults may appear deceptively stable at levels that would floor others.

Managing patients presenting with substance intoxication poses several challenges including obtaining a reliable history which is often limited or inaccurate, especially when the patient is confused, uncooperative or unable to communicate. Other concerns include suicidal intent, uncertainty about diagnostic thresholds and questions of decision-making capacity, specifically, the patient's ability to understand, evaluate and convey informed choices. Co-ingestion of multiple substances, limited access to appropriate support services and legal implications associated with certain drugs further complicate management.

We need to be more nuanced about managing these cases. Intravenous fluids, glucose supplementation (oral glucose or intravenous dextrose), temperature control and oxygen support are simple measures, but often inconsistently applied.[19] Arrhythmias like holiday heart syndrome may be missed. And agitation, when it occurs, can quickly escalate to dangerous levels for both staff and patient.

Alcohol-related aggression is often linked to disinhibition and impaired judgment or coexisting psychiatric or medical disorders. Yet too often, our response is reactive - restraints, security or inappropriate sedation. Verbal de-escalation should be our first approach, using a calm, non-confrontational style in a safe and quiet space.[19] When medication is needed for agitation or violence, antipsychotics like haloperidol (5 mg) combined with promethazine (50 mg) should be considered.[17] Benzodiazepines, while effective, should preferably be avoided or must be used cautiously and orally. The synergistic respiratory depressant effect of combining ethanol and sedatives is not just theoretical – it kills. Intravenous diazepam, though occasionally required, carries additional serious risks and should therefore be administered slowly, not exceeding 5 mg per minute, or actually preferably not at all. Just as important is vigilant monitoring after sedation; (very) frequent assessment of respiratory rate, oxygen saturation and level of consciousness is essential to ensure patient safety.[20]

Restraints, when unavoidable, must remain a last resort, used ethically, documented meticulously and never mistaken for clinical care. As clinicians, we must commit to retraining ourselves and our teams in safer, more compassionate approaches to managing alcohol-related behavioural crises.[19]

## Withdrawal

Alcohol withdrawal syndrome is one of the most under-recognised yet dangerous syndromes in medicine. It does not affect every chronic drinker, but in those who are dependent, abrupt cessation can precipitate a cascade of symptoms that may begin as early as 6 to 12 hours after the last drink. Initial signs include tremor, anxiety, irritability, sweating, palpitations and insomnia, often dismissed or misattributed. By 12 to 24 hours, more severe manifestations may appear, including visual, auditory or tactile hallucinations without disorientation (alcoholic hallucinosis).

Within 24 to 48 hours, some patients develop withdrawal seizures, typically generalised tonic-clonic in nature. The most severe form, delirium tremens (DTs), marked by confusion, agitation, fever, tachycardia, hypertension and hallucinations, usually peaks between 48 and 72 hours and constitutes a medical emergency with a high mortality risk if untreated.

High-risk patients (those with past withdrawal seizures, concurrent illness or long-standing dependence) should be considered for prophylactic benzodiazepines.[21] But we must resist the urge to prescribe sedatives indiscriminately. For low-risk patients, unnecessary benzodiazepine use carries its own set of dangers: prolonged sedation, respiratory suppression and extended hospital stays.

As always, clinical monitoring is paramount, not only for emerging signs of withdrawal but also for the risks of over-sedation. Respiratory status, hepatic function and the concurrent use of opioids or other sedative-hypnotics must all be considered. And we must not forget the pharmacological fundamentals: thiamine should be administered pre-emptively to prevent Wernicke's encephalopathy, a condition that remains tragically overlooked in patients with chronic alcohol use.[19,21]

## Concluding remarks

In a country where alcohol is both a social lubricant and a public health crisis, general practitioners are uniquely placed. We see patients before, during and after the consequences of excessive drinking. We hold the keys to early screening, brief interventions, referral to treatment and long-term support.

We must routinely ask about alcohol use, not just quantity, but pattern and impact; use brief interventions to reduce risky drinking in motivated patients; identify those at risk of withdrawal, liver disease or dependency; advocate for harm reduction, from safe drinking messages to community interventions; and challenge stigma in ourselves, our teams and our systems. Yes, we need more policy, more resources and better addiction services. But that does not absolve us from doing what we can in our rooms, wards and waiting areas.

Alcohol is not just a beverage. It is a neurotoxin, a metabolic disruptor, a social driver of disease and death. It is both legally consumed and tragically misunderstood. We owe it to our patients and to our communities to understand it fully and to treat it seriously. Let us not wait for the unconscious, the agitated or the hypoxic to appear in our casualty departments. Let us act earlier, speak frankly and intervene wisely. In doing so, we can turn clinical knowledge into compassionate care, and reactive treatment into proactive prevention. Because in the fight against alcohol harm, general practitioners are not just the first line, they are the only line many people will ever cross.

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