prolune
PROTEINES À LA >UNE<

Issue 15, October 2005

In vino veritas

"Wine rejoiceth the heart of man", so sang the psalmist. And still today, wine lovers happily raise their glasses. The psalmist however had no car to drive home after some joyful gathering. What is more, in those days, life expectancy was far shorter than now so there was no need to worry about the long term effects of alcohol. In 2004, about one third of the road accidents in Switzerland were due to drinking and driving. Alcohol affects the functions of vital organs, either globally or more specifically by attacking particular proteins. A number of target proteins have been identified and this has opened up a new field of investigation : genetic predisposition to the ill-effects caused by alcohol. Already 2'500 years ago, Hippocrates recommended wine to his patients, "wondrously appropriate to man", on the condition though that it was taken "within reason and with due moderation each according to his own constitution". That advice still stands.

7'000 years of history

The first known traces of wine were found in North-East Iran, in the bottom of jars which date back 7'000 years… Wine certainly has accompanied the history of humanity! It has inspired many a poet and thinker. It has been associated for as long as we can remember with religious rites and, in the Christian Church, wine ranks with bread, as food for both body and soul. A gift of the gods in Ancient times for man's well-being, it was used as a remedy for numerous aches and pains.

For a long time, fermented beverages were the only kind fit for drinking ; beer was for the people and wine was reserved for the élite. As a consequence, alcohol was consumed without any qualms right up to the 19th century. Even Louis Pasteur is known to have stated that "wine is the healthiest and the most hygienic drink of all".

It was only with the onset of the industrial revolution that people became aware of alcoholism as such. There is a thin line between drinking for pleasure and drinking out of need. Some drink wine because it tastes good, while others indulge in it to relax and forget their worries. The mood, however, is short-lived, and more and more drink is needed to sustain it. Which is where the problem lies…. Alcohol is toxic. It has both direct and side effects, which are many and complex. It causes vital organs to dysfunction and even its elimination produces molecules that can be harmful.

Sloane 2435 f.44v. By permission of the British Library

Fig.1 *"Better to drink a little wine out of necessity than a lot of water out of greed." St. Benoît (5th century)*

"Whatever the flask…

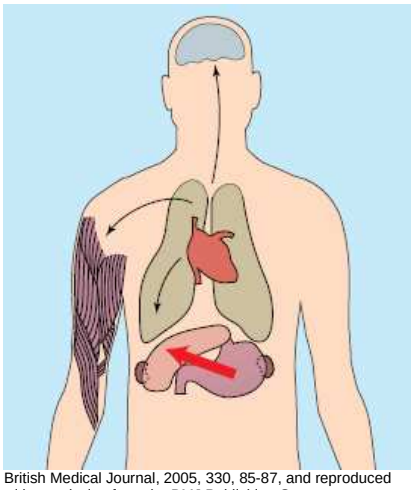
The scientific name of the alcohol we drink is ethanol. It is a small molecule, soluble in water but not in fats and absorbed by the stomach and the intestines. The rate at which it is absorbed depends on several factors, one being the contents of the stomach and its concentration in alcohol. It is most quickly absorbed both on an empty stomach and with a beverage which contains 20% to 30% alcohol[1]. This is why a glass of beer which contains 3% to 8% alcohol is absorbed more slowly than sherry, for instance, which harbors about 20%.

Champagne does go to your head quickly. It is not just an impression. Fizzy alcoholic drinks – like champagne, or a whisky and soda – are absorbed faster. Food, in particular various sugars, slows down the process. Consequently, alcohol is best taken with a meal if you wish to enjoy it and not suffer too much from its negative side effects.

…so long as we get merry"

On an empty stomach, the highest concentration of alcohol in the blood is observed one hour after it has been ingested. Then, it decreases progressively. An individual's rate of elimination is not only personal but also depends on the amount of alcohol that has been taken. However, on an average, the elimination rate is 0.15‰[2] per hour, meaning that an evening's excessive intake of alcohol can still have an effect on our physiological functions the next day..

Once the alcohol has crossed the gastric and intestinal barriers, it is distributed wherever possible. Most of our tissues – such as the heart, the brain and our muscles – are exposed to the same concentration as is the blood. The liver is an exception since the alcohol absorbed is conveyed to it by the hepatic portal vein. As a result, it is far more exposed. Alcohol diffuses relatively slowly in the organs except in those that are well irrigated by blood such as the brain and lungs.



British Medical Journal, 2005, 330, 85-87, and reproduced with permission from the BMJ Publishing Group.

Fig.2 *Most tissues, such as the heart, brain and muscles, are exposed to the same concentration of alcohol as the blood.*

[1] Since one cubic centimeter of alcohol weighs approximately one gram, the 'percentage' or 'degree' of alcohol may be stated as the number of grams of ethanol per deciliter (dl) that is 100 milliliters. For example, wine has a strength of about 12%, so that a 1dl glass of wine contains about 12g of pure alcohol. Spirits, which have much higher degrees of alcohol, are served traditionally in correspondingly smaller glasses, so that the amount of alcohol per glass is similar. In general, when we speak of a "standard glass", we imply a quantity of alcohol of 10g to 12g.

[2] The measure "per thousand" (o/oo) is used to determine the amount of alcohol circulating in the body. It is expressed in grams of alcohol per liter of "water" (blood and other physiological fluids). In fact, to estimate the quantity of alcohol circulating in the body, one must take into account the total volume in which the alcohol can diffuse; that is to say, the total volume of water of the organism. This corresponds to about 70% of body weight for a man and 60% for a woman. For example, a man of 70kg contains 49 l of water (70kg x 0.7), of which some 5 is blood. If the man drinks 2 glasses of wine, that is about 24g of alcohol, his alcohol level will be bout 48g per liter, i.e. 0.48 o/oo. These values are only an estimate which takes no account of efficiency of absorption, age of the subject, state of health and so on.

"A drink…

The brain is alchohol's first target, starting with the peripheral areas. In small quantities, alcohol is a stimulant. It acts upon the reward centers and frees molecules such as dopamine and serotonin, conferring a sense of well-being and relaxation, thereby lessening inhibitions and increasing self-assurance. Jean Clavel, a contemporary wine grower and historian, qualifies wine as a "social lubricant". In a "social" context, changes in behavior due to drunkenness are familiar to us. It is nevertheless surprising to note that these changes can occur – as in Pavlov's conditioned reflex – as soon as we start drinking, well before even a single molecule has reached the brain!

Our reward centers are not the only ones to be affected in the peripheral zones; alcohol also influences our sensory perceptions and good judgment.

…or two?"

When the intake of alcohol increases, the deeper regions of the brain are affected, and in particular the limbic system which controls our emotions and memory. Anger, sadness and aggressiveness become almost unmanageable. Progressively, the alcohol reaches the cerebellum which controls muscular coordination and the sense of balance; our movements become jerky and our walking unsteady. If alcohol intake continues, a fourth region begins to dysfunction – the hypothalamus – and with it a well-known phenomenon: diminished libido.

MacDuff: What three things does drink especially provoke?
Porter: Marry, sir, nose-painting, sleep, and urine. Lechery, sir, it provokes and unprovokes: it provokes the desire but it takes away the performance. […]
Shakespeare, in Macbeth (Act II, Sc.3)

And what about urine? Its volume does indeed increase a good deal after drinking alcohol because the brain produces less antidiuretic hormones. Under normal circumstances, as the kidneys produce urine, they start by filtering the blood. They also absorb a large amount of water which contains not only waste that the body must eliminate but also a number of other substances, such as sugars and mineral salts, that could still be of use. The process continues; everything that can be "recycled" is reabsorbed while only waste matter is evacuated. The brain informs the kidneys to reabsorb water, by way of an antidiuretic hormone – a very small protein – called vasopressin. Without vasopressin, the kidneys do not reabsorb as much water as they should and as a result produce much more urine. Ultimately, the drinker is dehydrated.

From an alcohol level of 4 o/oo upwards, the medulla oblongata, which forms the lower part of the brain stem, is affected. This particular part of the brain controls vital functions such as breathing, cardiac frequency, blood pressure, body temperature and consciousness. Disorders in the medulla can lead to alcoholic coma, and even death.

A long list of ill effects indeed for only one drug… However, the brain alone is not the only organ to be affected. Irritation of the stomach and the intestines cause vomiting; concomitantly, an influx of blood to the said organs stimulates their secretions, in particular acid gastric secretions. Blood also rushes to the skin, giving rise to hot flushes, unsightly red blotches and perspiration although – paradoxically – the body temperature is lowered. On the other hand, the muscles are less well irrigated, which can bring on muscular pains.

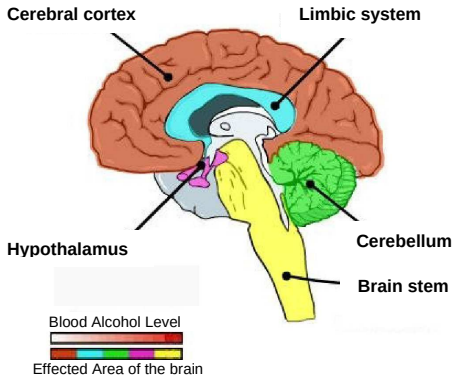


Fig.3 *The effects of alcohol on the brain*

Feeling dizzy…

Certain symptoms of drunkenness simply arise from a change in the properties of the liquids in which the alcohol is dissolved. The loss of balance is one. Balance is orchestrated by our inner ear in which there resides a specific structure called the cupula. The cupula looks like a small jellylike balloon on a fixed base, which is immersed in a viscous liquid called the endolymph. Every movement of our head moves the endolymph and, as a result, the cupula bends. Thanks to such coordinated movements our body perceives its own movement and can readjust its balance. The diffusion of alcohol in the middle ear modifies the comparative density of the cupula with respect to the endolymph – thus causing loss of balance with every movement of the head.

Chemical relays work as electric signals

Many of the effects of alcohol are the result of it attacking certain proteins found on the surface of specific cells and within a well-defined biological context. Although the molecular processes of the neurological effects of alcohol on the nervous system are far from being solved, it is clear that alcohol does affect the transmission of the nervous influx at several levels, with the sole aim of slowing it down.

A nervous signal has two components: one electric, the other chemical. The nervous influx that runs through a nerve cell, or neuron, does so by electric impulse. Once the impulse has reached the other end of the neuron, the nature of the signal changes. Small molecules, known as neurotransmitters, are freed and take over. The freed neurotransmitters bind to proteins called receptors, which are found on the surface of the neighboring neuron. If the signal is a stimulant, the binding of the neurotransmitter to its receptor will produce a further electric signal. If, on the other hand, the signal is an inhibitor, neurotransmitter binding will check the nerve influx. Hence, the nature of the neurotransmitter determines whether the signal is a stimulant or, on the contrary, an inhibitor. Not all neurons make use of the same chemical relays. Consequently, they can be divided into groups according to which neurotransmitter they use.

Regarding the neurological effects of alcohol, two groups in particular have been investigated into: the glutamate neurotransmitters and the GABA neurotransmitters.

A signal sent by a glutamate neurotransmitter to its receptor stimulates a neuron; the nerve impulse is therefore transmitted further. However, in the presence of alcohol, the glutamate receptors are strongly inhibited and the nerve influx is blocked!

Contrary to the glutamate signal, the GABA neurotransmitter is an inhibitor. When alcohol interacts with the GABA receptor, the negative signal transmitted by GABA is intensified so the nerve influx is interrupted. Alcohol is not the only drug to interact with this receptor; barbiturates and certain local anaesthetics do also and always with the same sedative effect. In this light, it is not difficult to understand why doctors always recommend not mixing sedatives with alcohol: the effects are doubled!

In short, the information given to us by our brain is the result of the maintenance of a delicate balance between stimulating and inhibiting signals. To put it simply, the effect of alcohol tends to block stimulating signals and increase inhibiting ones, the result of which is a slowing down of the brain's functions.

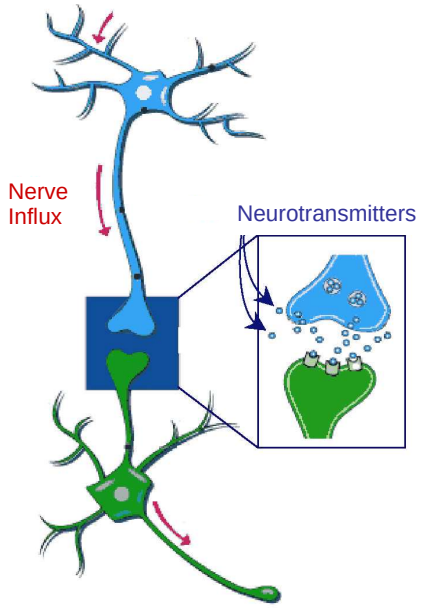


Fig.4 *Transmission of the nerve influx. The blue neuron propagates the influx as an electric impulse. At the end of the neuron, the neurotransmitters (blue circles) are released, and bind to their receptors on the surface of the green neuron. In this way, a nerve impulse is propagated.*

It is not so simple

Certain neurons that make use of the GABA neurotransmitters are highly sensitive to alcohol, whereas others located only a few microns away (one thousandth of a millimeter) are totally insensitive to them. So the phenomenon seems to be very specific. One hypothesis is that the effects of alcohol depend on the composition of the GABA receptor. Indeed, GABA receptors are an assembly of five different proteins – or subunits – selected from 19 possible subunits. The choice of the subunits may determine a receptor's sensitivity to alcohol. Experiments to this effect carried out on rats show surprising results that suggest individual genetic predispositions regarding neurological responses to alcohol. Such predispositions appear to be connected with the presence of polymorphisms in the GABA receptor.

Similar yet unique

What is a polymorphism? Proteins, such as the GABA receptor subunits or indeed any other protein, are made up of a chain of molecules – or amino acids – selected from a choice of 20 amino

acids. A protein's sequence determines the structure and function of the protein, in the same way as a sequence of notes in a music score determines a tune.

However, even though we all sport the same kind of proteins, which ensure the same kind of functions, there are details which vary from one person to another. For instance, a protein can have the same function though it may differ by one amino acid in two different people. Much in the way that a varying note in a symphony is not a false note but just the composer's fantasy. Such a note is called a polymorphism in biology. Polymorphisms are often without consequence. However, they can convey a particular resistance to stress and illness or, on the contrary, make a person more susceptible to them.

Genetically programmed?

There is a species of rat known for its intolerance to alcohol. Indeed, when ingested, they have an acute problem of motor coordination. Researchers have observed that the rodents have a polymorphism in one of the subunits of the GABA receptor, GABRA6, which could be at the root of their hypersensitivity to alcohol. The GABRA6 subunit is located on the surface of neurons situated in the cerebellum, precisely the part of the brain which is involved in the coordination of movement.

This finding confirms the importance of GABA receptors in mediating certain effects of alcohol. The action of alcohol on GABA receptors is always the same. It increases inhibiting signals, which will either result in sleepiness or uncoordinated movements according to which neuron it affects.

This kind of polymorphism has not been identified in humans. However, rats are known to be a very good model and it should not be ruled out that the same thing may well apply to humans. Everyone has difficulty in coordinating their movements after drinking too much alcohol but the presence of genetic predispositions in some may considerably worsen the effects.

Overcoming the handicap

Our organism can put up with an occasional slowing down of our brain's activity, but following the repeated abuse of alcohol it has to adapt in order to allow the nerve impulse to propagate nevertheless. To do this, the number of specific proteins located on the surface of the neurons is modified. As a result, those that are stimulated by alcohol – the 'blocking' receptors – decrease in number, while those that are inhibited - the stimulating receptors – will increase. In this way, the "protein make-up" of an alcoholic is progressively altered as opposed to the occasional drinker's. With time, an alcoholic shows little of the neurological effects of alcohol observed in an occasional drinker, and even acquires a certain tolerance to it.

Once accustomed to alcohol, our organism finds it difficult to do without. Indeed, an alcoholic is faced with a substantial increase in nerve stimulation and he must drink for his nervous system to re-establish a normal rate of stimulation. It's a vicious circle: the more an alcoholic drinks, the more his or her organism adapts to the amount of alcohol that has been drunk…and the more he or she needs to drink.

Moreover, a sudden absence of alcohol leads to the hyperstimulation of the nervous system. Withdrawal brings about a state of anguish, insomnia, epileptic fits and hallucinations and the well-known delirium tremens. Untreated, a number of these symptoms can be fatal.

Is alcoholism hereditary?

The children of alcoholic parents seem four times more likely to become alcoholics themselves, whether or not they grow up in their biological family. Researchers have found an association between a predisposition to alcoholism and the GABRA3 protein, another GABA receptor. The idea behind this research is that some people's nervous system could be hyperstimulated by nature. Such hyperstimulation could be genetic, and hence hereditary. Since alcohol has a stabilising effect on excitability, these people drink to moderate their brain signals. This is the beginning of the end: from small tots to fits of drunkenness, they risk becoming dependent to alchohol. And yet there seems to be no genetic curse that condemns to alcoholism. A person can very well be predisposed without ever becoming an alcoholic.

And what about pink elephants?

Besides its neurological and psychotropic effects, alcohol also has an effect on sugar metabolism in the brain. Some areas of the brain are particularly affected, amongst them the occipital lobe. In the presence of alcohol, this part of the brain uses about 30% less sugar than it should. And this is the center of the faculty of vision… Undernourished nerve cells do not function well so they are unable to interpret images appropriately…which entails vision disorders, i.e. hallucinations.

Alcohol, hypoglycaemia and diabetes

The effects of alcohol on sugar consumption and its concentration in the blood are not confined to the brain. Excessive intake of alcohol can lead to hypoglycaemia.

Our organism has set up a complex system for controlling the amount of sugar in the blood (glycaemia). When we eat sugar, the pancreas frees a hormone: a protein called insulin. Insulin signals to various organs that sugar must be stored so as to ensure that its concentration in the blood is maintained at an acceptable level. When there is insufficient sugar in the blood, another hormone sets the stocks free. Too much sugar in the blood causes diabetes with all its long term disastrous consequences; too little sugar causes hypoglycaemia which can be fatal.

Both the liver and the pancreas play a role in maintaining the level of sugar in blood. On an empty stomach, the liver produces sugar in order to diffuse it in the blood stream. In the presence of alcohol though, all the liver's resources are summoned for detoxication so it is in no position to synthesize the amount of sugar needed. As a consequence, the level of sugar in the blood falls. Fasting and drinking are the ideal combination to bring on hypoglycaemia… This is a particularly high risk with alcoholics. They can replace 60% of their daily quota of calories thanks to alcohol. So, not only is their liver detoxicating full time but their sugar reserves are practically non existent.

Needless to say, a diet based on alcohol creates numerous other problems such as serious deficiencies in vitamins and mineral salts, which are directly responsible for the destruction of nerve cells, for instance, or bad blood coagulation. It also seems that alcohol affects the hormonal control of glycaemia. A number of studies seem to point to the fact that alcohol could indeed diminish insulin secretion and our sensitivity to it. But the results of these investigations are sometimes contradictory, and the consequences difficult to assess. What is certain though is that diabetics must take every precaution with alcohol.

Cleaning out the system

As seen above, alcohol is a real threat to the normal function of many organs, which is why it is vital to get rid of it. There is nowhere in our organism where alcohol can be stocked while awaiting treatment. So action must be taken immediately. The liver is the principal alcohol purification plant, and it destroys 90% of the alcohol absorbed. 2% to 5% of the remainder is eliminated in the urine, perspiration and in our breath – where it can be measured by means of a breathalyser.

The liver has two ways of detoxicating alcohol: by way of alcohol dehydrogenases or the Microsomal Ethanol Oxidising System (MEOS). Each pathway uses different proteins.

The alcohol dehydrogenase pathway consists of two consecutive chemical reactions. The first turns alcohol into acetaldehyde. Acetaldehyde is toxic and is what is at the heart of the disagreeable symptoms which accompany a hangover. In normal conditions, acetaldehyde is rapidly converted into acetate, which is quite harmless. It is then used by our metabolism and transformed into CO_2 and water. As is the case with several other chemical reactions in our body, these reactions are not spontaneous. They are triggered off by specific proteins – called enzymes – which act as catalysts. Slight variations in these enzymes determine a person's sensitivity to alcohol.

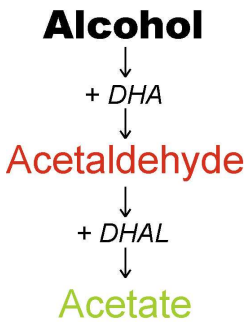


Fig.5 *The detoxication of alcohol by DHA (alcohol dehydrogenase) and DHAL (aldehyde dehydrogenase)*

Alcohol dehydrogenases

The enzymes that convert alcohol into acetaldehyde are alcohol dehydrogenases, or ADHs. There are many forms which are found mainly in the liver but also in the stomach, the intestines and the skin. The quantity of ADH varies with a person's drinking habits – it is greater in regular drinkers than occasional drinkers. It can also depend on a person's origin. Indeed, ADH is generally less abundant in Asians and South Americans than it is in Caucasians.

'Chi va piano va sano'

Some ADHs, and in particular ADH1B, bear polymorphisms that either heighten or lower the enzyme's activity, thus influencing the effectiveness of alcohol detoxication. One would have thought that people who have a high rate of converting alcohol into acetaldehyde, and who carry this type of polymorphism, stand up well to an evening's drinking. But it is not so! In such a

case, the quantity of acetaldehyde increases so much that the protein which converts it into acetate cannot keep up. This leads to intoxication whose symptoms include sudden hot flushes, headaches, vertigo, vomiting and a rapid heartbeat. Although the link between forming a habit of drinking and these polymorphisms is still not clearly defined, they do seem to play a preventive role: intoxication due to acetaldehyde is so disagreeable that it is a powerful deterrent in itself!

Small is beautiful

To perform well, ADH needs a small auxiliary molecule: a cofactor. It so happens that this cofactor is also necessary for many other chemical reactions in the body – such as the metabolism of fats for instance – and it is to be found in limited quantity. Consequently, when the auxiliary cofactor is mobilized for alcohol detoxication there are not many available for other reactions which, as a result, are slowed down. This is why heavy drinkers put on weight very early on. In the long run, the liver is clogged up with fatty deposits (steatosis) as do the blood vessels, paving the way to cardiovascular disorders.

Janus-faced enzyme

Before we proceed further on our molecular tour in the liver, let us pause and take a look at the amazing complexity of the ADHs. These enzymes belong to a large family of proteins found not only in humans and potatoes, but also in yeast and bacteria. In humans as in other animals, ADH converts ethanol into acetaldehyde. However, ADH can do exactly the reverse in other organisms… This last property is at the heart of one of the most ancient biotechnologies: alcoholic fermentation. When grape juice is given to yeast as a source of energy, the yeast breaks down the sugars to produce acetaldehyde and CO2. ADH converts the yeast acetaldehyde to alcohol, and the result is wine. So, this two-faced enzyme either produces or breaks down alcohol, depending on the biological context!

Acetaldehyde dehydrogenase

Acetaldehyde is neutralized in the liver by yet another family of enzymes – the acetaldehyde dehydrogenases (ALDH) – to produce acetate. As with ADH, there are many types of ALDH which could be expected to be interchangeable. However, as an example, ADHL2 is not found in many Asians, which would explain their intolerance to alcohol. Indeed, acetaldehyde is converted inadequately into acetate, so it accumulates and causes intoxication. It is a drawback but it does have the advantage of dissuading people to drink. If, on the other hand, they persist in drinking, the damage incurred on the liver, in particular, is far greater than in people who are "fitted" with ADHL.

The toxic effects of acetaldehyde are put to use in alcohol withdrawal. There are molecules, such as disulfirame (Antabuse) which inhibit the action of ADHL thus causing an accumulation of acetaldehyde. Vomiting is guaranteed after the first drop of alcohol!

Best is the enemy of good

The ADH pathway prevails up to 0.3o/oo of alcohol in the blood. Beyond this level, the liver triggers off an alternative mechanism of detoxication: the MEOS or cytochrome P450 system. This particular system involves a protein called CYP2E1. The MEOS system detoxicates other substances, especially drugs such as paracetamol, for instance. It is therefore strongly advised not to associate drugs with alcohol in order to avoid saturation. In occasional drinkers, the ADH and MEOS pathways are very similar. But for alcoholics, the MEOS pathway is prevalent.

Paradoxically, although the finality is to neutralize alchohol, detoxification via CYP2E1 produces even more toxic substances – a fact which most probably contributes to liver damage in the event of chronic alchohol abuse.

A saturated sewage plant

Our organism can cope with environmental agressions but only up to a point. A reasonable consumption of alcohol can be dealt with by both the ADH and MEOS pathways discussed above. However, an excessive and chronic intake of alcohol will progressively saturate our ingenious "sewage plant": our liver.

After summoning all its resources to detoxicate alcohol, lesions appear in the liver due to the accumulation of acetyldehyde. As time passes, the liver cannot fulfill its basic functions, i.e. processing food into energetic reserves, producing coagulation factors as well as other proteins, breaking down toxins and other waste matter resulting from our metabolism, etc. In other words, subjects suffer from hepatic deficiency.

The liver's cells begin to suffer, causing the overproduction of a protein called collagen, which settles in a fibrous mass between cells. In a limited amount, the existence of such fibres is normal and even necessary. Indeed, they give structural support to our cells and organs while

preserving a certain flexibility. However, an overproduction of collagen stifles cells and hardens the liver making it rigid and impermeable to the circulation of blood, and causing cirrhosis. What is more, the blood vessels in the liver are flattened, which causes hypertension and the blood is forced to go through other inappropriate channels. The ensuing complications are varied: varicous veins, oedema…

Are women more vulnerable to alcohol than men?

Women have always been scorned for "not holding their liquor" as well as men. But is there a biological truth behind this? Well, yes. Women absorb and metabolize alcohol differently.

In men and women of the same build and weight, the volume of blood is less in women. Also, women have more subcutaneous fat. No point in going on a diet. These reserves are physiological and nothing can be done about it! As a consequence, the volume in which alcohol can diffuse is smaller in women. Hence, despite the fact that a woman has ingurgitated no more alcohol than her fellow man, there will be more circulating in her blood than in his.

ADH is found in the stomach where it breaks down ethanol before it is absorbed. Gastric ADH in women is less active than in men, so the quantity of alcohol neutralized before absorption is in fact lower. In other words, women absorb more alcohol than men do, though they may drink the same amount... As a result, following two glasses of wine, a man of 60kg will have about 0.5o/oo of alcohol in his blood while a woman of the same size and weight would have about 0.6o/oo.

Lastly, the hormonal variations which take place during the menstrual cycle also affect the speed at which alcohol is metabolized. Indeed the level of alcohol circulating in the blood differs at different stages of the cycle, the climax being at the time of ovulation and just before menstruation.

1 standard glass = 3 dl of beer / 1 dl of wine / 2 dl of spirits

Women (in per thousand)

Glass	40 kg	45 kg	50 kg	60 kg	70 kg	80 kg
1	0,45	0,40	0,35	0,30	0,25	0,25
2	0,90	0,80	0,75	0,60	0,50	0,45
3	1,40	1,25	1,10	0,95	0,75	0,65
4	1,85	1,65	1,50	1,25	1,00	0,90

Men (in per thousand)

Glass	50 kg	60 kg	70 kg	80 kg	90 kg	100 kg
1	0,30	0,25	0,25	0,20	0,15	0,15
2	0,60	0,50	0,45	0,40	0,30	0,25
3	0,95	0,75	0,65	0,55	0,50	0,45
4	1,25	1,00	0,90	0,75	0,65	0,60

Fig.6 *Table of o/oo published by the Federal Office of Public Health*

Together, we drink…

There are great names that are the stuff of dreams: Château Margaux, Château Petrus, Romanée Conti… and others that we discover on holiday from the local wine-grower … A good wine is bottled sunshine to share with friends and family. It is a delight for all our senses, a conversation piece and an excuse for reminiscences! But, alas, friend and foe are close companions and the misfortunes of alcohol lurk in the wake of its joys. *"Wine is akin to man. Is it to be commended or despised? Loved or hated? There is no knowing nor will it ever be told how many sublime feats or dreadful deeds it has inspired…"* (Charles Baudelaire).

To which we raise our glasses. With moderation…

Anne Estreicher*

*Translation: Geneviève Baillie

For further information:

On the Internet:

- Effects of alcohol on the brain (McGill University in Montréal): http://www.lecerveau.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_par/i_03_m_par_alcool.html#drogues
- INSERM: http://www.futura-sciences.com/comprendre/d/dossier147-6.php

A little more advanced:

- Alex Paton and Robin Touquet, "ABC of Alcohol", februar 2005, Blackwell publishing, ISBN: 0727918141

Illustrations:

- Heading illustration (Bacchus by Michelangelo Merisi, "Le Caravage"), Source: http://www.ibiblio.org/wm/paint/auth/caravaggio/bacchus.jpg
- Fig.3, Source: http://science.howstuffworks.com/alcohol6.htm
- Fig.4, Adaptation: http://www.drogues.gouv.fr/fr/savoir_plus/livrets/action_drogues/action_page2.html
- Fig.5, Source: http://www.suchtundaids.bag.admin.ch/imperia/md/content/kampagnen/allesimgriff/04/3.pdf?PHPSESSID=100b9caeb1dc9b88742c5fd845523aba

At UniProtKB/Swiss-Prot:

- Vasopressin-neurophysin 2-copeptin, Homo sapiens (human) : P01185
- Alcohol dehydrogenase class II pi chain, Homo sapiens (human) : P08319
- Alcohol dehydrogenase beta chain (ADH1B), Homo sapiens (human) : P00325
- Aldehyde dehydrogenase, mitochondrial (ALDH2), Homo sapiens (human): P05091
- Cytochrome P450 2E1, Homo sapiens (human): P05181
- Gamma-aminobutyric-acid receptor gamma-3 subunit, Homo sapiens (human) : Q99928

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