

Abstracts

Papers and Posters Presented at the International Congress on Health and Wine. Wine as Part of a Healthy Diet and Lifestyle, 13 - 16 September 2005, Spier, Stellenbosch, South Africa

PAPER PRESENTATIONS

THEME: Social Responsibility / Wine Biochemistry

SESSION I: Wine Derived Phenolic Compounds

The Chemistry of Wine

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Wine is a very complex fluid, often described as the second most complex in nature. It contains quite a large number of polyphenolic substances—most of these are derived from the grape, but if oak is used, this contributes hydrolyzable tannins as well. The complexity increases with fermentation and aging as the grape derived phenolics react with the acid and oxygen in wine to produce many new substances as well, and many of these substances are poorly characterized at best. The grape derived polyphenolics are categorized into several groups, and a major distinction are the flavonoids and non-flavonoids. Among the non-flavonoids, the hydroxycinnamates constitute the largest group. These are the major phenolic substances present in the juice of the grape and this means these are also the principal phenolics in white wine. These occur as phenolic acids conjugated with tartaric acid, and during fermentation and aging these conjugates hydrolyze and partially esterify with the alcohol present in wine. The hydroxycinnamates are also key substrates for polyphenol oxidase, and are rapidly oxidized if oxygen is present during the crushing operation. Other non-flavonoids include the benzoic acids, a relatively minor constituent. Gallic acid is the principal component. In grapes it occurs as an ester conjugate of epicatechin in seed condensed tannin, but in the aqueous acidic environment of wine, is released as the free acid. The stilbenes are also relatively minor in quantity, but its principal component, resveratrol, appears to have many important effects on cancer mechanisms, although it is unclear if the amount in wine could impart any protection against the disease. The stilbenes occur in the grape mostly as glucosides, and these conjugates also undergo hydrolysis once wine is made. The human absorption of resveratrol has been measured. The absorption and mammalian metabolism of phenolic

substances can be generalized to include the methylation of the phenolic hydroxyl groups, as well as their glucuronidation and sulfation. The latter two conversions make polar products likely to be eliminated, and conversions rates are generally very high (>90%) except with high doses. In general, absorption rates as determined by total derived products in the urine is generally 1-5% of the consumed material. In terms of mass, the flavonoids far outweigh the non-flavonoids in the grape berry, and these skin and seed constituents are extracted by the maceration process in red wine production where these tissues are left in contact with the fermenting must, and in some cases, the wine after fermentation, in order to transfer these substances into the wine. The flavonoids include the flavonols, and of those, quercetin and its glucosides is the most abundant. As with the other conjugates mentioned above, these also hydrolyze once wine is made so that while the grape contains only the glycosides, wine contains these and the aglycones. These are produced in the grape skin in response to sunlight, and considering the necessity of sunlight for high quality fruit, can be used as a marker for red wine quality. Quercetin is particularly reactive to oxidation, and can be depleted by oxidative wine treatment. The absorption of quercetin is enhanced by the presence of glucose as a conjugate, but other sugars are absorbed like the aglycone. The forms present in plasma and urine are universally converted to the methylated or the polar conjugates mentioned above. The anthocyanins are the red-colored pigments in grapes, and they form the basis of red wine color, reacting with other phenolics in wine to form the poorly characterized wine pigments. Recent work has begun to reveal the identity of these substances, and there are many different forms present in wine. Malvidin-3-glucoside is the major anthocyanin in grapes, with 3 other anthocyanin forms and multiple glycoside forms. These substances are absorbed and surprisingly, the natural forms are the most abundant observed, although some of the common conjugates are also detected. The flavanols form the largest group of polyphenolic in grapes and wine. These include the monomeric catechins, but the majority exist as the oligomer-

The abstracts are published as received. The names of presenting authors are in **bold**. Full-length papers of the presentations will be published in a special edition of the South African Journal of Enology and Viticulture

ic and polymeric forms, variously called the proanthocyanidins and condensed tannins. These abundant polyphenolics contribute to the astringent and bitter taste of red wine. They also react with the anthocyanins over time to produce wine pigments. These occur mostly in the berry non-conjugated forms, although a small proportion are esterified to gallic acid. These compounds are absorbed as the monomers and dimers, but higher oligomers are not observed intact in the blood or urine. The usual conjugates are observed and the free flavanols are scarcely measurable. In addition, the flavonoid structure appears to be extensively degraded by gut microflora to simple phenolics that are absorbed. It also appears that the oligomeric and polymeric forms are de-polymerized in the gut by microbial action. Most characterization and absorption studies have addressed the substances native to the fresh fruit. The products of processing, both fermentation and aging, have only been directly investigated in a few cases, such as wine pigments. From these few lines of study the complexity of the products is daunting, much as it is with tea and cocoa. However, to properly understand the physiological effects of wine polyphenols, these derived substances must not be ignored.

Antioxidants – What They Do and What They Don't

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Antioxidant products abound, and are purveyed to the public-at-large as providing near-miraculous benefits for the treatment of almost every ill, as also for the prevention of ill health and for the maintenance of optimal health. In fact very few clinical studies have shown anything like significant benefits, and some have shown that adverse effects can certainly accrue. That these clinical studies have put various antioxidants to the test as though they are regular allopathic pharmacotherapeutic agents, lies at the heart of the disappointing and disadvantageous outcomes. We humans have evolved over the millennia requiring a vast array of macro- and micro-nutrients along with antioxidant-laden foodstuffs. Ingesting single isolated antioxidants in large amounts creates imbalances among these agents within our bodies, which may well be expected to be un-physiological – we might say unnatural, and not surprisingly, even deleterious. Only an intake of a good diet rich in fruits and vegetables and herbs and spices, along with a better content of omega-3 fatty acids, and avoiding excess saturated fats and especially trans-fatty acids, seems capable of providing all essentials for health. It behoves all responsible healthcare practitioners to counter the 'hype' that surrounds the marketing and use of isolated antioxidants, and to actively prescribe good diets and wholesome lifestyles. The benefits of such a lifestyle cannot be mimicked by any 'pill or potion'.

Red Grape Varieties Differ Both in the Amount and in the Structure of their Skin and Seed Tannins Extractable from the Wine

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Red wine is a very rich source of flavanols, consisting of catechins, oligomeric and polymeric proanthocyanidins (PAs). The

aim of this study was to investigate the composition of the fraction of flavanols which is extractable from the grape into the wine. By HPLC-DAD-MS analysis, carried out before and after thioacidolysis, it was confirmed that grape extracts of the varieties Cabernet Sauvignon, Carmenere, Marzemino, Merlot, Pinot Noir, Syrah and Teroldego are mainly rich in monomers and small oligomers (mDP < 7). Grape seeds extracts contain three monomers (catechin, epicatechin and epicatechin gallate) and procyanidin oligomers. Grape skins extracts contain four monomers (catechin, epicatechin, gallo catechin and epigallocatechin), procyanidins and prodelphinidins oligomers. Upper and extension units of PAs are constituted mainly or only of epicatechin units, in the seeds and skins respectively. The terminal units of the grape PAs are a mixture of five compounds, the same found also as monomers. Catechin gallate, gallo catechin gallate and epigallocatechin gallate, which are found in other flavanol-rich, plant-derived foods and beverages, are not present in grape extracts. The grape variety determines both the amount and the structure of wine flavanols, leading to differences in the composition which are likely to play an important role in the nutritional and sensorial properties of the wines.

Le vin rouge est un produit très riche en flavanols comprenant les catéchines et les proanthocyanidines oligomériques et polymériques (PA). L'objectif de cette étude consistait à examiner la composition de la fraction de flavanol que l'on peut extraire du raisin dans le vin. Par le biais d'une analyse HPLC-DAD-MS, menée à bien avant et après thioacidolyse, il a été confirmé que les extraits de raisin prélevés sur les cépages Cabernet Sauvignon, Carmenere, Marzemino, Merlot, Pinot Noir, Syrah et Teroldego sont essentiellement riches en monomères et en oligomères de petite taille (mDP < 7). Les extraits de pépin de raisin contiennent trois monomères (catéchine, épicatechine et épicatechine gallate) et des oligomères procyanidines. Les extraits de peau de raisin contiennent quatre monomères (catéchine, épicatechine, gallo catechine et épigallocatechine) et des oligomères procyanidines et prodelphinidines. Les unités supérieures et d'extension des PA sont principalement ou uniquement constituées d'unités épicatechines, pour ce qui est des pépins et de la peau respectivement. Les unités terminales des PA de raisin sont un mélange de cinq composants, les résultats sont les mêmes pour les monomères. Les catéchine gallate, gallo catechine gallate et épigallocatechine gallate, que l'on trouve dans d'autres aliments et boissons dérivés des plantes et riches en flavanols, ne sont pas présentes dans les extraits de raisin. Le cépage détermine à la fois la quantité et la structure des flavanols, entraînant des différences dans la composition susceptibles de jouer un rôle important dans les propriétés nutritionnelles et sensorielles des vins.

Influence of Technology on Estrogenic Activity of Red Wines

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The activation of the estrogen receptor by different isoflavones and stilbenes is well documented. Estrogenic activity of this com-

pounds is effected through activation of estrogen receptor a and estrogen receptor b. Mainly *trans*-resveratrol has been made responsible for the estrogenicity of red wines. Using a screening system mimicking the transactivation of estrogen receptor a the estrogenic potency of a selection of red wines was tested. The aim of the study was to find out if there is a difference between red barrique wines and red wines made without oak barrels. The polyphenols of the wine samples were enriched by solid phase extraction on C 18 columns. These extracts were then tested for their estrogenic activity with a yeast transactivation assay. The extremely permeably *Saccharomyces cerevisiae* strain 188 R1 transformed with an estrogen receptor a expression plasmid and the corresponding reporter plasmid was used. Incubation of yeast with an estrogenically active substance leads to binding of the estrogen receptor a dimer to the estrogen response element and thus to expression of b-galactosidase. The specific enzyme activity is equivalent to the amount of estrogenic activity. Both red wines with and without barrique contact were able to transactivate human estrogen receptor a and the arylhydrocarbon receptor in yeast. We hypothesised that other estrogenic compounds than resveratrol are present in this wines. A negative or positive health impact must be discussed with care. These compounds are present in low concentrations compared to plant extracts used as herbal remedies.

*L'activation des récepteurs aux oestrogènes par différents isoflavones et stilbenes sont bien documentés. L'activité oestrogène de ces composés s'effectue au travers de l'activation des récepteurs aux oestrogène a et b. C'est principalement le trans-resveratrol qui est tenu pour responsable de l'activité oestrogène du vin rouge. En utilisant un système de criblage imitant la transactivation des récepteurs aux oestrogènes a, le potentiel d'activité oestrogène d'une sélection de vins rouges a été testé. L'objectif de ce travail était de déterminer s'il existe une différence entre les vins rouges affinés en barrique et les vins ne subissant pas ce traitement. Les polyphénols des extraits de vins furent enrichi par extraction en phase solide sur colonne C18. Ces extraits furent ensuite testés pour leur activité oestrogène en utilisant un système de transactivation chez la levure. La souche extrêmement poreuse 188 R1 de *Saccharomyces cerevisiae* transformée avec un plasmide d'expression du récepteur a à l'oestrogène et avec le plasmide rapporteur correspondant a été utilisée. L'incubation des levures avec une substance à activité oestrogène conduit à la fixation du dimère de récepteur a à l'oestrogène à l'élément de réponse à l'oestrogène et de ce fait à l'expression de b-galactosidase. L'activité spécifique de l'enzyme est proportionnelle à l'activité oestrogène de la substance testée. Les vins des deux origines, affinés ou non en barriques se révélèrent capables de transactiver le récepteur a humain à l'oestrogène et le récepteur à l'arylhydrocarbone chez la levure. Nous émettons l'hypothèse que d'autres substances oestrogènes que le resveratrol sont présentes dans ces vin. Un impact négative ou positif sur la santé humaine doit donner lieu à une discussion attentive. Ces substances sont présentes à de faibles concentrations en comparaison des extraits de plantes à usage.*

Unravelling the Total Antioxidant Capacity of Pinotage Wines – the Contribution of Phenolic Compounds

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Pinotage is a South African red wine cultivar with a unique phenolic profile. An understanding of the contribution of individual phenolic compounds on the total antioxidant capacity of Pinotage wines, is important for determining guidelines for the production of Pinotage wines with optimal total antioxidant capacity. These aspects were the main focus of the study. The Trolox equivalent antioxidant capacity (TEAC) of individual phenolic compounds, namely gallic acid, caffeic acid, caftaric acid, *p*-coumaric acid, (+)-catechin, (-)-epicatechin, procyanidin B1, delphinidin-3-glc, petunidin-3-glc, cyanidin-3-glc, peonidin-3-glc, malvidin-3-glc, quercetin-3-glc, myricetin-3-glc, quercetin-3-gal, quercetin-3-rham, myricetin, quercetin, kaempferol and isorhamnetin, were determined using the ABTS^{•+} scavenging assay. The individual phenolic content and total antioxidant capacity (TAC) of 139 Pinotage wines were determined using HPLC and the ABTS^{•+} scavenging assay, respectively. The contributions of the quantified compounds were calculated from their concentrations in the wine and TEAC values. The contribution of polymeric compounds was determined by separating the monomeric and phenolic compounds in three wines using ultrafiltration. Possible synergistic interactions were tested by combining individual phenolic compounds to mimic the phenolic profile of three wines and measuring the TAC of the mixture. The TEAC values of quercetin-3-gal, isorhamnetin and peonidin-3-glc are reported here for the first time to the best of the authors' knowledge. Esterification of caffeic acid with tartaric acid, i.e. caftaric acid caused a decrease in TEAC value. Quercetin-3-rham and quercetin-3-gal also had much lower TEAC values than quercetin as is the case for quercetin-3-glc. Peonidin-3-glc has a TEAC value higher than malvidin-3-glc due to one less electron-withdrawing methoxy group, but a TEAC value lower than delphinidin-3-glc and petunidin-3-glc due to less hydroxyl groups. Of the compounds found in Pinotage wines, *p*-coumaric acid and procyanidin B1 had the lowest and highest TEAC values, respectively. The highest contributions to the TAC of Pinotage wines were either compounds present in large concentrations such as caftaric acid and malvidin-3-glc, or compounds with high TEAC values such as gallic acid and procyanidin B1. The total calculated TAC was, however, only between 11 and 24% of the measured TAC. The contribution of polymeric phenolic compounds and other unknown large compounds isolated from three wines using ultrafiltration were 54% indicating that unknown small compounds also contribute to the TAC of Pinotage wines. Some synergism was detected in mixtures mimicking the concentrations of 12 phenolic compounds in three wines. The total antioxidant capacity of Pinotage wines is influenced by several factors, namely individual phenolic compounds, polymeric compounds, unknown compounds and possible synergistic interactions between compounds.

SESSION II: Social Responsibility of Wine Consumption

Our Operating Environment: Snapshot of Countries' Public Health Policies and Guidelines on Alcohol and Hence Wine Consumption

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Worldwide, approximately 2 billion people consume alcoholic beverages such as wine, beer and spirits. The mean adult global per capita consumption of 'pure' alcohol is 5.1 L, which is divided approximately equally between beer, spirits and wine. The pharmacological textbooks list alcohol as a drug that has dose-dependent effects. When the dose is low to moderate, the effect can be considered as a benefit to health but when the dose is high or abusive, the effect is considered as a harm to health. Of those 2 billion people that consume alcoholic beverages worldwide, approximately 76.3 million or 3.8% have alcohol-related problems due to alcohol abuse, and 1.8 million or 0.09% will die from alcohol-related harms. Clearly public health policies on alcohol consumption are necessary to address the economic, health and social impacts of alcohol-related harms. Coronary heart disease, however, is the leading cause of death in developed countries and its incidence is increasing in developing countries. While high alcohol consumption increases the incidence of hypertension, cardiac arrhythmias, congestive heart failure and haemorrhagic stroke, low to moderate alcohol consumption actually decreases the risk of coronary heart disease. Moderation is consistently defined as 20–40g ethanol per day. The beneficial health effects of alcohol consumption thus provide significant challenges for alcohol policy but these data are gradually being accepted and considered when countries are developing and subsequently reviewing their public health policies on alcohol consumption. This paper focuses on the evolution of public health policy and associated guidelines in those countries which have based them on recent review of the medical and scientific literature. It is suggested that a legitimate role for researchers in policy development is to understand and provide detailed knowledge of the biological mechanisms of alcohol consumption in order to provide a context for the policies, and to aid in educating the consumer.

Alcohol and Emotions: Friend or Foe?

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The first draught serveth for health, the second for pleasure, the third for shame, the fourth for madness" Sir Walter Raleigh 1552-1618. Man has known for many years that alcohol has a stabilizing effect on the mood. It is also true that moderate drinkers tend to have better health and live longer than those who are either abstainers or heavy drinkers. The positive effects of alcohol on the mood of some people, re-inforces the regular use of the substance in many. In most people this would lead to a life-long happy relationship. During the presentation the mood stabilizing effects of alcohol will be highlighted. Healthy drinking patterns and the causal factors for the development of alcohol dependency will be explored. "Wine makes daily living easier, less hurried with fewer tensions and more tolerable" Benjamin Franklin.

Industry Action through the ARA in Addressing Alcohol Abuse

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A social aspects organisation (SAO) like the ARA inevitably faces the challenge in having to decide where to direct its efforts in addressing the consequences of alcohol abuse. Areas of prevention, treatment and rehabilitation make demands on its resources. The ARA is an example of an SAO which has made a conscious decision to focus on prevention. This paper explains why this area was chosen for its strategic focus and how it has succeeded in doing so in partnership with other stakeholders. A brief outline of programmes in the areas of education, industry self-regulation, research and alcohol abuse prevention is presented.

Self Reported Surveys of Alcohol Consumption – Methodologies to Improve Reliability of the Data from Surveys of the General Population of Alcohol Consumers

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It is a general opinion that survey data on alcohol consumption is generally an underestimate of actual alcohol consumption behaviour. The reasons usually relate to a consumer reticence to admit real consumption levels due to forgetfulness, or that they are threatened by a perceived societal prejudice towards alcohol consumption generally. In order to overcome this expected consumer propensity to underestimation, there is a growing literature suggesting that utilising specific methodologies of questionnaire design, sample design, timing of the research contact and the method of questionnaire administration, when combined in a study of the general population, can elicit quantity - frequency consumption data that more closely relate to actual consumption behaviours. This paper will first outline a review of the literature where differing methodologies of quantity - frequency measurements are tested and validated. The paper will then demonstrate how these various methodologies can be effectively combined in a national study of Australian alcohol consumption behaviours (n = 1005). The objectives of the Australian study were first to develop and test a set of measurement scales to elicit consumer attitudes towards alcohol and social-based control measures, and at the same time to measure quantity - frequency consumption behaviours. The overall aim was to compare these consumption levels with consumers' attitudes to alcohol and social control measures in order to understand the relationship between the two. The outcomes of the research are designed to provide policy makers with more effective guidelines when encouraging a culture of moderate consumption of alcohol generally. The methodology techniques to be discussed will be the use of focus groups to understand the scope of the elements of alcohol consumption behaviour and how they were understood by the consumer. Each question in the final

measuring instrument (questionnaire) was tested during the period and before the major field work commenced. The survey method used was a telephone interview (25 minutes duration) with specially trained interviewers used to conduct the study. The times when telephone contacts were made were carefully selected to best reflect the expected behaviours of the randomly targeted respondents and their expected propensity to be interviewed. The conclusions drawn will provide guidance to future researchers in the development of the measuring instrument (questionnaire) by discussing the structure and composition of the focus groups, the

analysis of the focus group outcomes as a mechanism to develop the individual questions to be included in the final questionnaire. The questionnaire was constructed in such a way that consumption ranges were able to capture heavy, light and occasional users in the same survey. Similarly the attitudinal questions were structured to measure the level of attitudes (1 – 7 Likert Scales) so that direct relationships between consumption and attitude could be made. The results of the study show that demographic factors have more influence on attitudes than the norms of consumption (heavy, medium, light) on moderate behaviours.

SESSION III: Epidemiological Studies of Wine and Health

Amount and Type of Alcohol and Morbidity and Mortality – Results from Epidemiological Studies

M. Grønbæk (Keynote Speaker)

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The association between alcohol intake and cardiovascular disease has received quite some attention the last decade. Far most of the studies conclude that moderate drinkers of alcohol have a decreased risk of developing cardiovascular disease compared to those who do not drink alcohol. While there is an increasing body of evidence that alcohol (ethanol) itself has cardioprotective properties, the question whether there are different risks and benefits associated with the different types of alcoholic beverages; beer, wine and spirits, is still unresolved. However, during the last years both epidemiological and experimental studies have brought support to the hypothesis that substances in wine have cardio- as well as cancer-protective effects. Both case-control and cohort studies have consistently shown that light to moderate drinkers are at lower risk of cardiovascular disease and death than non-drinkers. Most agree that this declining risk curve can be interpreted as a causal relation, although the strength of the apparently protective effect is still disputed. However, many studies report a decline in risk of cardiovascular disease in the range of twenty five to thirty percent. Several plausible mechanisms for the apparently cardio-protective effect of a light to moderate intake of alcohol have been suggested. Subjects who drink alcohol have higher serum-levels of high density lipoprotein and lower of low density lipoprotein than abstainers. Thus, high density lipoprotein has been suggested to be a mediator of 40-60% of the effect of alcohol on ischemic heart disease. Also, alcohol has a beneficial effect on platelet aggregation, and thrombin level in blood is higher among drinkers than among non-drinkers. Recently, the largest of the prospective studies have shown that the effect of alcohol and cardiovascular disease may be modified by age and gender. Hence, two large American studies have shown that the apparent cardioprotective effect seems stronger among the elderly. Therefore, while the cardioprotective effect of a light to moderate alcohol intake is quite evident based on a large number of epidemiological studies, there are several factors which may influence the strength of the effect. A number of recent cohort studies have addressed the question whether there are differences in the effect of drinking wine, beer and spirits. Most of those having been able to address the question

in populations with a variation in intake of all three types of beverages have found wine drinkers to be at lower risk of all cause mortality and in some instances also of mortality from cardiovascular disease. A larger number of studies of the effect of alcohol on incidence of cardiovascular disease have superficially addressed the question of different effects of the different types of beverages. Substances in wine have been shown to have the platelet aggregation inhibiting effect also found to pertain to ethanol. Further, an inhibiting effect on low density lipoprotein oxidation of unknown factors in wine was shown. Also other mechanisms related to not specified factors in wine, have been suggested to play a role in the prevention of cardiovascular disease. Apart from the effect on platelet and low density lipoprotein oxidation, a vasodilating effect has been proposed, perhaps due to an effect of wine on the endothelium. The suggestions from the experimental studies have only been sparsely reproduced in population studies. Thus, one of the first studies on flavonoid intake in humans, found a lower risk of coronary heart disease among subjects who had a high dietary intake of flavonoids, while data from the Nurses Health Study did not support the findings. Further, several other antioxidant effects which may inhibit carcinogenesis but also may have an effect on cardiovascular disease have been proposed. Several of these antioxidants are present in both fruits and vegetables, as well as in wine. When reviewing the different epidemiological papers on type of beverage and cardiovascular disease, the question still remains whether it is the drink or the drinker? As mentioned above, several biological mechanisms from substances present in wine but in beer and spirits may explain the epidemiological findings. However, recently a few studies have shown that other factors, differently distributed among wine drinkers and non-wine drinkers may confound the above mentioned relations. A high intake of fruits, vegetables and fish and a low intake of saturated fat has been suggested to reduce the risk of cardiovascular disease. The so-called Mediterranean diet which includes fruits and vegetables has in six out of ten cohort studies been found to have a weak protective effect on cardiovascular disease. In studies from US and Denmark preference of wine was associated with a high intake of fruit, vegetable, fish, salad and a high frequent use of olive oil for cooking compared with preference of beer and spirits in both men and women. However, the confounding effect of dietary factors should be very strong to explain the above mentioned findings. Further, recent studies from Italy and France suggest that diet is not a strong confounder in

these countries, where wine has also been found to have additional effect compared to beer and spirits. Self-reported subjective health has in several studies shown to be a strong predictor of cardiovascular disease and all-cause mortality. In studies from both Helsinki and Copenhagen it was shown that beer drinkers were more likely to have suboptimal health than those who preferred wine. Another factor which may be of importance drinking pattern. A recent very large Danish study have shown that binge drinkers have a higher mortality from all causes than steady drinkers. With regard to coronary heart disease, a study from Harvard University shows that those who were steady drinkers had an apparently beneficial effect of drinking light to moderate-

ly. Hence, if wine drinkers were steady drinkers and beer drinkers more likely binge drinkers, this may itself explain the above mentioned differences. However, a recent study from Denmark showed that this does not seem to, since wine drinkers were more likely to binge than beer drinkers.

In conclusion most epidemiological studies support the clinical and the experimental suggestions of an effect of wine in addition to a light to moderate alcohol intake on cardiovascular disease, and some newer studies show that carcinogenesis may be impaired by wine intake, although the differences between the effects of the different types of alcohol to a large extent may be due to confounding.

THEME: Cardiology / Endocrinology

SESSION IV: Cardiovascular Implications of Alcohol / Wine Consumption

Alcohol and Cardiovascular Diseases: A Historical Review and 2005 Update

L. Klatsky (Keynote Speaker)

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Study of the history of a subject seldom fails to provide insights about current knowledge. One important result is recognition of past mistakes, creating the potential for avoiding their repetition. Attempts to generalize and simplify about alcohol and cardiovascular (CV) diseases have slowed progress. Disparities in relations of alcohol drinking to various CV conditions are now clear. A basic disparity between the effects of lighter and heavier drinking always cuts through alcohol-health relations. In this brief overview, the following will be considered: cardiomyopathy, arsenic and cobalt beer drinkers' disease, cardiovascular beri-beri, systemic hypertension (HTN), cardiac arrhythmias, cerebrovascular disease, atherosclerotic coronary heart disease (CHD), and heart failure.

Monocyte Function in Hypercholesterolemic Patients – Influence of GM-CSF

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Monocytes are known to play an essential role in atherosclerosis but also to orchestrate collateral artery growth (arteriogenesis). In both settings, monocyte adhesion to the vascular endothelium, their transmigration into perivascular tissue and secretion of growth factors and cytokines has been shown. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is known to strongly stimulate arteriogenesis, modifying monocyte function and prolonging their life span. While effects of circulating cholesterol on atherosclerosis are well known, the effects on arteriogenesis are yet unresolved. In this study we analyzed the effects of GM-CSF on monocyte surface marker expression and gene

programming. Monocytes were isolated using magnetic beads from peripheral blood mononuclear cells of patients with familial hypercholesterolemia and of age, gender and race matched controls. Surface marker expression was analyzed by flow cytometry after staining with fluorescent monoclonal antibodies for CD11b, CD14 and CD44. Also mRNA was isolated from these cells and gene expression was investigated using real-time PCR. Surface protein expression of the adhesion molecule CD11b was significantly higher in patients with hypercholesterolemia at baseline. 48h of culture resulted in equal cell surface expression of this marker in controls as well as patients. GM-CSF stimulation caused a marked increase in monocytes from controls, compared to monocytes from patients. Gene analysis of the surface markers supported the protein data, presenting a significantly lessened decrease of CD11b gene expression after culture with GM-CSF in both patients and controls. The expression of genes known to play an important role in arteriogenesis (MMP-12, CISH, MCP-1) in response to GM-CSF was increased in controls compared to hypercholesterolemic patients. Monocytes from hypercholesterolemic patients respond less vigorously to the arteriogenic stimulus GM-CSF with regard to the expression of the cell-adhesion molecule CD11b, as well as activation of genes associated with arteriogenesis. This may indicate that cholesterol suppresses the ability of monocytes to activate arteriogenesis.

Red Wine and Heart: A Journey from Grape to Resveratrol

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The consumption of wine, particularly red wine, imparts beneficial effects in the prevention of coronary heart disease. Our study determined that mild to moderate wine consumption (equivalent to one to two glasses of wine/day) rendered the heart resistant to ischemia and heart failure. This gave rise to what is now popularly termed as the *French Paradox*. A recent study determined that regular consumption of grapes also render the myocardium resistant to ischemic heart disease. In this study, the rats were given

(orally) Standardized Grape Extract (SGE) (obtained from California Table grape Commission) for a period of one month. After 30 days, the rats were sacrificed, hearts excised and made ischemic for 30 min followed by 2 hrs of reperfusion. At 100 mg/kg and at 200 mg/kg, grapes provided significant cardioprotection as evidenced by improved post-ischemic ventricular recovery and reduced amount of myocardial infarction. SGE reduced the malonaldehyde content of the heart indicating reduction of oxidative stress during ischemia and reperfusion. The cardioprotective effects of red wine have been attributed to several polyphenolic antioxidants including resveratrol and proanthocyanidins that are present in the wine and the grapes. Our study determined that these polyphenolic antioxidants provide cardioprotection by their ability to function as *in vivo* antioxidants. These phenols as well as red wine triggered a signal transduction cascade initiated by the activation of adenosine A1 and A3 receptors thereby activating MAP kinase signaling leading to a reduction of proapoptotic transcription factors and genes such as JNK-1 and c-Jun and inducing redox-sensitive transcription factor NFkB thereby potentiating ischemia-mediated anti-death signal. This results in the reduction of cardiomyocyte apoptosis. Resveratrol mediated anti-apoptotic signal appears to be potentiated by an upregulation of nitric oxide leading to the initiation of an angiogenic signal triggered by an induction of vascular endothelial growth factor. The results, thus, indicate that not only do the red wine and grapes provide cardioprotection through their antioxidative properties, but also they have ability to trigger a survival signal through the polyphenolic antioxidants, especially resveratrol.

The Relation of Alcohol Consumption to Calcified Atherosclerotic Plaque in the Coronary Arteries and Aorta

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There have been conflicting results on the relation of alcohol consumption to the presence of calcified atherosclerotic plaque in the coronary arteries (CAC), which is increasingly being used as a non-invasive index of atherosclerosis. Previous studies have suggested that wine and/or alcohol reduce, increase, or have no effect on CAC. We evaluated the relation of alcohol intake to the presence of CAC and calcified plaque in the aorta among 3,166 white and African-American subjects from the National Heart, Lung, and Blood Institute Family Heart Study who underwent cardiac CT scans. With adjustments for age, race, study center, BMI, hyperglycemia/diabetes, hypertension, and smoking, odds ratios

(and 95% CI) for CAC scores > 100 for non-drinkers and consumers of 1-3, 4-7, 8-14, and > 14 drinks per week were 1.0, 0.8 (0.4, 1.3), 1.1 (0.6, 1.9), 0.9 (0.5, 1.5), and 1.5 (0.9, 2.5) for men and 1.0, 0.9 (0.5, 1.6), 1.3 (0.8, 2.3), 1.3 (0.7, 2.2), and 2.1 (0.8, 5.9) for women. Sensitivity analyses with other cut-points for calcified plaque gave similar results. Analyses of alcohol and aortic calcification showed similar, non-significant associations. We conclude that despite its beneficial effects on coronary artery disease risk, moderate alcohol consumption does not relate significantly to calcified atherosclerotic plaque in the coronary arteries or in the aorta. These findings suggest that the protective effects of moderate alcohol consumption against cardiovascular events may occur through different mechanisms than those associated with the development of calcified atherosclerotic plaque.

Moderate Wine Drinkers Have Lower Hypertension Related Mortality: A Prospective Cohort Study in 36 000 French Men

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For a given blood pressure, risk of death from coronary heart disease in Northern Europe and USA is much higher than in Mediterranean Countries. In this prospective cohort study, we tested the hypothesis that regular wine drinking might reduce hypertension-related risk of death. We used data on 36, 583 consecutive healthy middle-aged men with a normal electrocardiogram, not taking drugs for cardiovascular risk factors. These subjects underwent comprehensive health appraisal in a Center for Preventive Medicine between January 1st, 1978 and December 31st, 1985. Mortality from all-causes and specific causes during a 13 to 21 years follow-up was recorded. In a Cox model adjusted for six confounding variables, moderate wine drinkers (<60 g alcohol/day and no beer), compared with abstainers, have a lower risk of death from all-causes by 23% with SBP of 158 mmHg [RR 0.77 (CI 0.62-0.96, p<0.02)], 27% with SBP of 139 mmHg [RR 0.73 (CI 0.58-0.91, p<0.01)] and 37% with a SBP of 116 mmHg [RR 0.63 (CI 0.51-0.78, p<0.001)]. Even for the highest quartile of blood pressure, moderate wine drinkers and only them, are protected from all causes mortality. No significant reduction in all causes mortality in relation to SBP was observed in other drinkers (≥60g alcohol/day or consuming beer and wine), particularly in the highest quartile of blood pressure, where the non moderate drinkers (≥60g alcohol/day) have a higher risk [RR 1.26 (CI 1.01-1.57, p<0.04)] for the wine and no beer drinkers and [RR 1.34 (CI 1.07-1.67, p<0.01)] for the beer drinkers. A moderate intake of wine is associated with a lower risk of hypertension related mortality from all-causes.

SESSION V: Haemostasis, Endothelial Function

Endothelial Activation, Vascular Inflammation and Coronary Artery Disease

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Current evidence suggests that most significant risk factors for heart disease have been identified. Indeed, the majority of new cases of acute myocardial infarctions can today be predicted by the presence and the level of nine risk (or cardioprotective) factors that can easily be assessed and, most importantly, modified. These risk factors are the same in almost every geographic region and in every racial/ethnic group worldwide, and are consistent in men and women. Eight out of these nine risk factors are influenced by diet, and most act promoting atherogenesis, which is the most important background condition for cardiovascular disease. Dietary interventions mostly impact on atherogenesis by modulating pro-inflammatory processes at the cellular level that initiate and perpetuate endothelial dysfunction, plaque formation and, eventually, plaque rupture. As an example, there is now enough evidence, both epidemiological and clinical, for the beneficial effects of omega-3 fatty acids, monounsaturated fatty acids or Mediterranean diet antioxidant polyphenols.

The Influence of a Mediterranean Diet With and Without Red Wine on the Haemostatic and Inflammatory Parameters of Subjects With the Metabolic Syndrome

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Some antithrombotic effects of the Mediterranean diet complemented by red wine could be proved on normal subjects. In a later study, addition of red wine did not add to the benefits of the Mediterranean diet except for prolongation of the bleeding times. Platelets play an important role in thrombosis and in myocardial infarction and the effect of wine consumption on platelet activity has been reviewed by previous researchers. Procoagulants and anticoagulants also participate in thrombogenesis: FVII (affected by dietary triglycerides), FVIII and fibrinogen (both affected by inflammatory responses) and von Willebrand's factor (vWF) that is also used as a marker of endothelial function. CRP and fibrinogen are markers of vascular inflammation in atherogenesis and in the metabolic syndrome. Finally the fibrinolytic pathway's efficiency to resolve a formed thrombus, plays an important role via tPA and PAI-1 activities. Variable results in these fibrinolytic markers in relation to wine and/or alcohol consumption were described before. This study examined whether a Mediterranean-like diet supplemented with red wine, complemented with mild exercise had an acute impact on patients diagnosed with the metabolic syndrome. In this study, 12 non-smoking patients between the ages 32 to 60 years with diagnostic criteria of the metabolic syndrome on minimal medication, consumed a Mediterranean-like diet for 4 weeks respective-

ly without and with red wine. During the experimental periods the subjects increased their intake of vegetables, cereals, fruit, mono-unsaturated fatty acids and fish at the expense of red meats and dairy products. Patients were motivated to include 20 – 30 minutes of mild exercise (walking) into their daily routine. Dietary control was through 4 times 3-day dietary record during the study period. The amount of red wine added to the diet was 250 ml (26 grams of alcohol) per day for male and 180 ml (19 grams) per day for female participants. A genetic profile for cardiovascular risk factors was performed on all the subjects to identify specific familial disorders and as selection criteria to confirm the clinical diagnosis. Risk reduction assessment linked to nutrition and lifestyle that target the interaction between genes and the environment was done for each participant. Biochemical and haemostatic assessments were determined on all participants to compare the effect of their habitual and newly acquired lifestyles and diet with and without wine. Fasting blood samples were taken at base line, after 4 weeks of diet and after another 4 weeks of diet plus moderate red wine consumption. Weight, abdominal circumference and blood pressure were measured at each visit. Contrary to the literature findings, wine demonstrated no additional anti-atherogenic or antihaemostatic effects in our subjects in this study. Our study aimed at the longterm beneficial effects of moderate wine consumption on biological parameters. It could be that the effect of diet and wine is not clearly demonstrable in such a short term intervention period. It is also probable that the diet showed more favourable effects on health parameters as the anti-oxidant capacity of the plasma because the diet was continued for double the period of time for that of wine intake. However, wine was added last in the intervention and the beneficial anti-oxidant effect of the diet alone was probably partially reversed by the addition of alcohol. This would be further resolved when the genotypes like ApoE4 of our study subjects become known.

Alcohol, Wine, Platelet Function and Haemostasis

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Red wine is rich in the complex polyphenols and these compounds have attracted attention as potential cardiac-protective compounds. The present review summarizes the literature on wine polyphenols and the evidence for a protective effect on blood platelets. In fact, while the mechanisms underlying the effects of alcohol on cardiovascular disease have been limited to lipid metabolism and the haemostatic system, those related to wine consumption have also been extended to specific anti-inflammatory, antioxidant and nitric oxide related vaso-relaxant properties of its. In addition, it has become evident that blood platelets contribute to the rate of development of atherosclerosis and CHD through several mechanisms. Several studies carried out on humans and animals have shown that wine phenolics could exert their effects by reducing prostanoid synthesis from arachidonate. In addition, it has been suggested that wine phenolics could reduce platelet activity mediated by nitric oxide. Moreover, wine phenolics increase vitamin E levels while decreasing the

oxidation of platelets submitted to oxidative stress. However, a rebound phenomenon of hyperaggregability is observed after an acute alcohol consumption which is not observed with wine consumption. We shall summarize here the experimental studies with wine or wine-derived products aimed at finding biological explanations for the supposed effects on blood platelets of wine consumption.

Wine Dilates the Brachial Artery but Does Not Increase Flow Mediated Dilatation Over Two Hours

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There is epidemiological evidence for possible cardiovascular benefits from consumption of alcoholic beverages, but corroboration by functional and outcome studies is still outstanding. We performed non-invasive functional tests on the brachial arteries of healthy volunteers before and for two hours after consuming red wine, calculated to deliver 0.35g alcohol/kg body mass. An Acuson 128 ultrasound machine (7.5MHz transducer) generated images of the brachial artery. Brachial artery dimensions were taken at baseline, 30, 60 and 120 min. Similarly, FMD was assessed after 5 min of

forearm occlusion by a sphygmomanometer cuff inflated to 50mm Hg above systolic blood pressure. Putative minimum and maximum lumen diameters were determined after ice immersion and sublingual trinitroglycerine (TNG) at baseline and 60 min after wine consumption. 16 subjects had a mean \pm SD resting brachial artery diameter of 3.84 ± 0.61 mm that significantly increased on wine to 4.44 ± 0.58 at 30min, 4.39 ± 0.62 at 60 min and 4.49 ± 0.62 at 120 min ($P < 0.0001$). The calculated blood flow rates during the study did not differ significantly over the measured intervals. The baseline mean diameter with TNG was not significantly different from the dilation with wine. The vasoconstrictor response varied widely, with a $-2.6 \pm 2.9\%$ change from baseline diameter. There was appreciable variation of the diameter relative to the range found with the individual ice and TNG. The calculated FMD (% changes) for the study were 10.8 ± 4.6 , 6.1 ± 2.9 , 5.6 ± 4.2 and 7.5 ± 2.7 indicating statistically significant effects of wine ($P < 0.0001$). We conclude that red wine consumption leads to arterial dilation even under vasoconstrictory conditions. FMD is significantly reduced within 30 min of consumption and is significantly depressed for at least 2 hours. Since red wine is a complex beverage, further studies need to be done to discriminate the effects of alcohol and phenolic compounds on vascular function. The potential beneficial effects of wine may relate to different doses or other mechanisms than FMD.

SESSION VI: Wine and Lipid Metabolism

From the Ancient Wisdom of Greek and Roman Civilization the Recommendations for a Healthy Diet, Where Post-prandial Oxidative Stress and Cellular Stress Response is Prevented

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The "modern" notion of Mediterranean diet has been introduced by Ancel Keys as a nutritional approach to prevent chronic degenerative diseases, mainly atherosclerosis. The major features of Mediterranean diet are a high intake of vegetables, legumes, fruits, cereals, the use of olive oil, a low intake of meat and finally a regular intake of wine at meals. The antithetic counterpart is the typical diet of Northern Europe and Northern America, where meat consumption is higher, the fats are either animal or hydrogenated, the intake of fruit and vegetables is low and spirits and beer substitute for wine. Remarkably, the same antinomy among nutritional habits is observed when eating pattern of ancient Greeks and Romans is compared with that of emerging Northern barbarian populations. The notion of producing foods by cultivating fields had to compete with the notion of catching what is available in the forest. Hunting and eating large amounts of meat was the pattern of warriors that eventually conquered the Roman Empire. Thus, we have now to "rediscover", as the legacy of an ancient wisdom, the Mediterranean diet. Searching for the molecular mechanisms of health benefits of this diet, already unquestionably identified in epidemiological studies, it could be convenient introducing the recent concept of "post-prandial oxidative stress". Several foods containing partially oxidized fat and cata-

lysts of lipid peroxidation (i.e. meat, mainly bovine) increase the oxidation and oxidability of lipids in plasma lipoproteins, eventually leading to a misfolding of apo B. An altered oxidative balance in plasma leads to endothelial dysfunction (an early hallmark of atherogenesis) and, in general, to a cellular response to stress. This stress response is nowadays seen as the biological mechanism of an alteration of homeostasis, eventually leading to chronic diseases. Fruit, vegetables, olive oil and wine taken with foods bring all the elements to counteract such a response. The post-prandial increase of lipid hydroperoxides is minimized and the cellular stress response is turned down. Such a view of a healthy effect of a diet as a whole could also eventually explain why nutritional supplements, usually taken while fasting, are only minimally active in disease prevention.

Dyslipoproteinaemia in South Africa

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The link between lifestyle and plasma cholesterol and atherosclerotic vascular disease is clearly demonstrated by studies within and between populations. Dyslipoproteinaemias impart much higher risk of cardiovascular disease. Genetic dyslipidaemias have been well-characterised over the past 25 years. Having initially been described from the clinical evaluation, plasma lipoprotein patterns allowed insight into dyslipidaemias according to defects in proteins functioning as receptors or enzymes and ultimately have been clarified at the genetic level. Genetic dyslipidaemias are enriched in the South African population as a result of founder effects in several of its ethnic groups. Familial hypercholesterolaemia (FH) is the best studied of these disorders. It is recognised by premature heart dis-

ease, tendon xanthomata and low density (LDL) cholesterol hypercholesterolaemia (>5mmol/L). Mutations in the LDL receptor have been identified in the Afrikaner, Jewish, Indian, Black and mixed ancestry population. Cardiovascular disease in these subjects is influenced by lifestyle as well as many other risk factors. Although statins have made a dramatic impact on the control of dyslipidaemia in FH, adopting a healthy lifestyle remains important.

Nutritional Genetics: Development and Application of an Individualised Approach for Cardiovascular Disease Risk Reduction

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A rapid DNA test has been developed which screens for familial hypercholesterolaemia (FH) and other genetic risk factors that can be triggered into cardiovascular disease (CVD) by lifestyle risk factors, if left untreated. This multi-gene CVD test consists of four components – dyslipidaemia, folate metabolism, coagulation and iron overload – that are evaluated in the context of family and medical history (e.g. hypertension, obesity, diabetes), biochemical parameters and relevant environmental risk factors. Testing for specific genetic alterations involved in lipoprotein and lipid metabolism are particularly useful to identify individuals who may not benefit from certain dietary measures to lower CVD risk, such as moderate alcohol drinking. Convincing evidence has been provided that the common E4 allele of the apolipoprotein E gene, which occurs in approximately 30% of the general South African population, modulates the effect of alcohol intake on plasma lipids and consequently CVD risk. Apart from alcohol, a diet high in saturated fat and cholesterol as well as smoking should be avoided because the risk imposed by these factors is significantly increased in the presence of the Apo E4 allele. By combining genetic testing for both monogenic and multifactorial conditions, it has become possible to distinguish between patients with FH requiring life-long drug treatment and those at increased CVD risk as a consequence of other factors that can be treated effectively by dietary and lifestyle intervention.

Modification of Cardiac and Stroke Risk Factors through the Implementation of a Lifestyle Intervention Programme: A Gene Based Phased Approach

H. Avenant

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Current medical infrastructure has been inaccessible to cater for preventative care. This caused individuals to look for advice elsewhere. This situation left the medical fraternity on the sideline in terms of creating and using opportunities to contribute to a healthier population in general. The morbidity of cardiovascular disease and strokes was recently reiterated by data provide by the World Health Organization, when they were respectively listed first and forth on the list of the 10 most prevalent diseases causing disability. The occurrence of these diseases depends largely on interaction between the environment and the genetic predisposition of an individual. By modifying the environment, it is possible to modify or minimise the expression of many deleterious gene mutations. Knowledge of our genetic heritage now provides a sound basis for proactive long term planning to invest in one's health, the most

valuable asset of any person. Healthcare practitioners will have to emphasize the fact that preventive care pays, both in terms of cost and quality of life. Consequently, serious consideration is called for to pursue avenues by which some advances can be made in bettering the cardiovascular health of individuals. An integrated lifestyle intervention programme was developed to provide practical strategies to support the numerous studies that document cost effective, improved outcomes of lifestyle intervention over secondary intervention techniques. An important aspect of this program is to foster the realization that this health principle should be applied in families across the board. Expanding awareness to the community at large as to what a healthy lifestyle should consist of is not only a philanthropic act, but also an economic one.

Effects of a Polyphenols-Enriched Chardonnay French White Wine and a Sparkling Pinot Noir Brazilian Red Wine on Early Atherosclerosis in Hamsters

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The aim of this work was to assess the protective effect on early atherosclerosis in hamsters of 2 different specific wines : a polyphenols enriched chardonnay french white wine (PCWW) produced by Virginie-Castel and a sparkling pinot noir brazilian red wine (SPRW) produced by Chandon do Brazil in comparison with a solution of ethanol 12% vol. (A), or only water (W). These 2 wines contains total phenols (expressed in gallic acid equivalent) : 1425 mg/L for PCWW and 570 mg/L for SPRW. Levels of Tanins (catechin, epicatechin and procyanidins dimers : B1,B2,B3,B4) were 371.9 mg/L for PCWW. Contents of Catechins and anthocyanines monomers was 217.4 mg/L and 272.1 mg/l for red polymers in SPRW. Hamsters fed an atherogenic diet for 12 weeks. Four groups of 8 hamsters fed such a diet received by force-feeding PCWW, SPRW or A mimicking a moderate consumption of wine (500mL/Day/70kg Adult Body weight). Controls (W) received water. After 12 weeks of feeding and 18 h of food deprivation, the hamsters were anesthetized. Plasma apolipoprotein A-1 (Apo A-1) and apolipoprotein B (Apo-B) concentrations were determined using Sigma turbidimetric immunoassay kits. The plasma antioxidant capacity (PAC) in hamsters fed the atherogenic diet was measured using a kit from Randox Laboratories. The aortic arches were carefully dissected and lipids stained with Oil red O. Each aortic arch was then directly displayed on a glass slide, endothelium side up and observed *en face* by light microscopy. All segments were photographed using a video digitizer. The area covered by foam cells (aortic fatty streak lesion) was analyzed quantitatively using a computer-assisted morphometry system and expressed as a percentage of the total area surveyed. Cholesterol levels were reduced significantly for PCWW and SPWR groups. The ratio Apo-A1/Apo-B increased in

the group receiving Alcohol A (significantly) and with both wines SPWR and PCWW indicating a potential beneficial effect. Plasma antioxidant capacity was increased significantly in the groups A and SRPW compared with controls. Aortic fatty streak area was significantly reduced in the groups receiving SPRW (-85%), PCWW (-85%) and A (-58%) in comparison with controls. Our

findings demonstrate that chronic ingestion (nutritional moderate consumption) of a polyphenol enriched white wine (rich in catechins) prevent the development of atherosclerosis in hamsters the same way that a red wine (containing anthocyanines and catechins). The phenolic compounds family involved in such a beneficial effect can be attributed to the catechins – tanins family.

SESSION VII: Wine, the Metabolic Syndrome and Degenerative Diseases

Wine and the Mediterranean Diet's Protection Against the Metabolic Syndrome is Mediated by Endothelial Nitric Oxide Synthase

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The positive health effects derived from moderate wine consumption are pleiotropic. They appear as improvements in cardiovascular risk factors such as plasma lipids, haemostatic mechanisms, endothelial function, and antioxidant defences. The active principles would be ethanol and mainly polyphenols. Results from our and other laboratories, support the unifying hypothesis that the improvements in risk factors after red wine consumption are mediated by endothelial nitric oxide synthase (eNOS). Many genes are involved, but the participation of eNOS would be a constant feature. In cells in culture, red wine enhances both, function and expression of eNOS in a process dependent on phenolic antioxidants and largely regulated at the transcriptional level. In vivo, both mediterranean diets and red wine enhance endothelial function in human volunteers. It has also been shown that eNOS mediates the antithrombotic effect of red wine. The metabolic syndrome is a cluster of metabolic risk factors associated to high risk of cardiovascular disease (CVD). The National Cholesterol Education Program's Adult Treatment Panel III (NCEPATP III) clinical definition of the metabolic syndrome requires the presence of at least three risk factors, from among abdominal obesity, high plasma triacylglycerols, low plasma HDL, high blood pressure, and high fasting plasma glucose. The molecular mechanisms responsible for the metabolic syndrome are not known. Much emphasis has been given to insulin resistance. Also oxidative stress does play a role, and oxidative damage in metabolic syndrome has been described and was also found in our observations. Since metabolic syndrome apparently affects 10 to 30% of the population in the world, research on its pathogenesis, molecular mechanisms and possible therapeutic and preventive measures, is needed. The recent finding that eNOS knockout mice present a cluster of cardiovascular risk factors comparable to those of the metabolic syndrome, suggests that defects in eNOS function may cause human metabolic syndrome. These mice are hypertensive, insulin resistant and dyslipidemic. Further support for a pathogenic role of eNOS comes from the finding in humans that eNOS polymorphisms associate with insulin resistance and diabetes, with hypertension, with inflammatory and oxidative stress markers, and with albuminuria. Epidemiological studies as well as recent intervention studies, provide evidences that mediterranean diets and wine consumption are associated with reductions in metabolic syndrome car-

diovascular risks. Moreover, it has been observed that light to moderate alcohol consumers show a favourable insulin profile, when compared with non-drinkers and heavy drinkers. From recent studies addressing directly the relationship among alcohol consumption and the prevalence of metabolic syndrome, in Sweden and USA, it can be concluded that moderate alcohol consumption is significantly and inversely associated with metabolic syndrome, as shown for several of its components: low serum HDL cholesterol, elevated serum TAGs, high waist circumference, hyperinsulinemia, and hypertension. It has also been shown in recent trials of mediterranean diet, in patients with the metabolic syndrome, a decrease in vascular inflammation markers and an improvement in endothelial function. So, the overall data sustain the hypothesis that eNOS enhancement should reduce metabolic syndrome incidence and its consequences. Therefore red wine and mediterranean diets, since they improve endothelial function in volunteers, and enhance eNOS function in vitro, presumably a consequence of their high content of phenolic antioxidants, should be considered as potential tools for the control of metabolic syndrome. Initial results from other groups, support our proposal.

Alcohol, Wine and the Skeleton

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Osteoporosis is a common, costly and serious disorder characterised by a low bone mineral density (BMD), increased bone fragility and susceptibility to fracture, which typically involves the wrist, spine or hip. Osteoporosis involves one in four postmenopausal women and one in six men. Up to 20% of hip fracture patients die within one year of the event. Even more disconcerting is the fact that less than 50% of patients are capable of leading an independent life following a hip fracture. The direct medical costs of acute fracture care in the USA exceeds \$15 billion per year. A decrease in bone mass (BMD) and strength is generally the result of either genetic, environmental and/or ageing factors. Up to 70% of the variation in peak bone mass is genetically determined. Genetic factors are also involved in the age-related decrease in bone mass and in BMD-independent factors which predispose to fracture. Age-related factors largely involve the acute decrease in serum oestradiol levels following the menopause (↑bone resorption), and osteoblast incompetence with ageing (↓bone formation). Environmental factors include diseases/drugs and life-style changes (diet, physical inactivity, smoking, alcohol) known to adversely influence bone.

The Acute Influence of a Mediterranean-like Diet With and Without Red Wine on Patients With the Metabolic Syndrome

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This study examined whether a Mediterranean-like diet complemented with red wine and mild exercise had an acute impact on patients diagnosed with the metabolic syndrome. In this study, 12 patients between the ages 32 to 60 years with the metabolic syndrome, consumed a Mediterranean-like diet for 4 weeks respectively with and without red wine. During the experimental periods the subjects increased their intake of vegetables, cereals, fruit, mono-unsaturated fatty acids and fish at the expense of red meat and dairy products. Patients were motivated to include 20 – 30 minutes of mild exercise (walking) into their daily routine. Dietary control was through 4 times 3-day dietary record during the study period. A genetic screen was done on all participants for genetic markers of cardiovascular disease (CVD). Weight, BMI, abdominal circumference and blood pressure were measured at each visit. Fasting blood samples were taken at base line, after the diet and after the diet plus wine periods. The following biochem-

ical parameters were determined at baseline, after 4 weeks of diet and after another 4 weeks of diet plus moderate red wine consumption: total cholesterol(TC), triglycerides(TG), HDLC, LDLC, TC/HDL ratio, uric acid, fasting blood glucose, insulin, and the glucose/ insulin ratio. Hypersensitive C-reactive protein (HS-CRP), FVIII, fibrinogen and von Willebrand's factor (vWF) were measured as inflammatory markers. The haematological parameters measured were: platelet count, platelet coagulation, platelet membrane fluidity, plasma TxB2, tPA, PAI-1, FVII, FVIII, fibrinogen, and vWF. The oxygen radical absorbent capacity (ORAC) was determined to measure the antioxidant effect of the diet and wine intervention. There was a statistical significant ($p=0.044$) increase in the ORAC after the experimental period. Body weight decreased significantly ($p=0.0403$), and a trend in decrease in the abdominal circumference ($p=0.059$) was observed. A statistically significant decrease in systolic blood pressure ($p=0.0446$) was observed. This study indicates that diet can reduce weight and blood pressure, but do not influence the atherogenic lipoprotein and pro-coagulant haematological profile in patients with the metabolic syndrome on the short term. Red wine had no additional benefits during this short intervention period. It appears that wine consumption is rather a biological marker of a healthier lifestyle pursued by its devotees than an actual cause of superior health *per se*.

THEME: Nutrition, Lifestyle, Wine and Health Relationships

SESSION VIII: Mediterranean Diet and Wine

Mediterranean Diet, Wine in Moderation, and Health

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In my presentation, I will consider first what is the Mediterranean diet and what is the role of the Mediterranean wine drinking pattern. Next, I will present evidence indicating how Mediterranean diet, that integrates moderate alcohol consumption, affects longevity in a clearly Mediterranean country, Greece. Subsequently, I will provide data that a Mediterranean- inspired diet can be beneficial even for people living outside the Mediterranean region. I will present data supporting Mediterranean diet, including moderate wine consumption, as an appropriate diet for those who have already suffered a coronary attack. I will conclude with examination of the role of moderate wine drinking in the Mediterranean diet and the associated longer survival.

Alpha-Linolenic Acid in the Prevention of Coronary Artery Disease and Arrhythmia: What's New from the Lyon Study?

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The low mortality rate in the Cretan cohort of the 7 country study was in relation with a high plasma level of the precursor of the

omega 3 fatty acid (FA) family : alpha-linolenic acid (ALA) coming from an ALA rich food chain. In the duplication of the Cretan diet on 600 coronary patients, we replaced butter and oils by rapeseed oil and rapeseed margarine, rich in ALA. We did not observe any sudden death as compared to 10 in the control group with the prudent diet. Singh confirmed recently this results, with mustard seed oil. He observed 6 sudden cardiac death, versus 16 in the control, and 8 versus 30 other non-fatal ventricular arrhythmia (ventricular ectopics 8/min). Comparing the intervention trial with fish or fish oil omega 3, and plant omega 3 : RR of cardiac death = 0.7 (DART), 0.8 (GISSI), 0.24 (Renaud) and 0.33 (Singh). RR = 1.26 in the last study of Michael Burr with fish or fish oil, unexplained results, RR of sudden death being 1.54, significant. Animal studies have confirmed that ALA supplied under the form of rapeseed oil, was the most efficient FA to reduce vulnerability to cardiac arrhythmia in rats. The mechanism of the antiarrhythmic effects of omega 3 FA, in normal and Ca²⁺ overloaded cells, appears to be primarily by reducing the Ca²⁺ entry. A daily consumption of 2 grams of ALA is central in a healthy diet (2 spoons of rapeseed oil or mustard oil a day).

Oil and Olive Health

Nola Dippenaar

Fat is an important component of the daily diet of humans, and recent research has clearly illustrated that it is not the quantity of fat taken in daily, but the type of fat consumed that is vital for

health. Over the past decades, due to the high incidence of cardiovascular disease, the general recommendation was to limit the intake of fat, in particular the intake of saturated fat, and to replace this with carbohydrate. This inevitably led to a greater intake of refined carbohydrates, which wrecks havoc with glucose and insulin levels in the human body. More recently the Mediterranean Diet and lifestyle of the people of Crete became the recommended lifestyle to follow, with the food pyramid symbolizing the best and worst choices in daily nutrition. From the ongoing research in this area, it once again became apparent that the recommended 30% of daily energy intake in the form of fat should not be reduced, but rather better balanced, with saturated fat supplying no more than 10%; the bulk in the form of mono-unsaturated fat (10-15%) and the remainder as polyunsaturated fat (omega 3 and omega 6). This would also ensure that the daily intake of cholesterol was below the recommended level of 300 mg/day.

Omega-6 vs Omega-3 Fatty Acids: The Margarine Debacle

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Margarine is a major human innovation whereby plant oils and fats are converted to a semi-solid spread which has been consumed on a large scale at the expense of unhealthy animal fats in butter and lard that were clearly shown to enhance the risk of

heart disease. Unfortunately margarine has two main intrinsic lipid flaws, i.e. the presence of trans-fats formed during the hydrogenation process and the relative absence of omega-3 fatty acids due to inappropriate choice of plant oils. Evidence exists that systemic inflammation is involved in the etiology of diseases such as atherosclerosis and cancer. Much of this inflammation is programmed by the activation of the NF-kappaB transcription factor, which in turn activates a host of pro-inflammatory genes. PPARgamma is another transcription factor, which when activated can inhibit NF-kappaB. In normal cells PPARgamma should be active and NF-kappaB inactive. Trans-fats inhibit PPARgamma; omega-6 fatty acids activate NF-kappaB, omega-3 fatty acids stimulate PPARgamma and saturated fats activate NF-kappaB. Resveratrol from red wine inhibits NF-kappaB. It follows that too much trans-fats and omega-6 fatty acids can undermine health by inducing systemic inflammation, whereas an absence of trans-fats and a close to parity ratio of omega-6 to omega-3 fatty acids could enhance health by keeping NF-kappaB dormant. This lipid imbalance is referred to as the "margarine debacle" in this document. Fortunately more modern margarines have been manufactured which are trans-fat free and have ratios of omega-6 to omega-3 less than 10:1. Legislation is needed to set the norms for healthy margarine. It is predicted that future margarines will act as vehicles not only for beneficial lipids but also for many different natural products, over and above vitamins, such as resveratrol and curcumin – both of which are potent inhibitors of NF-kappaB.

SESSION IX: Alcohol and Health: Is Wine really Good for You?

From French Paradox to Cretan Miracle

S. Renaud (Keynote Speaker)

When I first arrived in Canada in 1951 to continue my college education, I was struck by the high proportion of heart attacks suffered by young hockey players and the population at large. The origin could not be genetic since the inhabitants of Quebec share the same genetic characteristics as the French. Therefore, an environmental factor had to be responsible. I observed the huge difference in eating habits, especially the large consumption of saturated fats, the very small consumption of fruit and the absence of wine compared to the Bordeaux region I was from where one gladly brought a good bottle of wine to a hospitalized relative. In those years, the only way to study nutrition was to embark on veterinary studies since nutrition was not taught to future doctors. After finishing first in my class at the Veterinary College, I chose to devote myself entirely to research. I started my career with Hans Selyé, the inventor of "stress," who wanted me to become his main assistant, but I preferred to study the relationship between nutrition and coronary heart disease. Indeed, the war years had shown the astonishing reduction in thrombosis in periods when food is scarce and less rich in saturated fat. I was convinced that the quality of fats was a major factor determining health. I was quickly promoted to a post-graduate teaching position and became Professor of pathological anatomy and Professor of nutrition at the Medical School of Montreal. My experience in

pathological anatomy at the Cardiology Institute of Montreal and experimental studies in rat confirmed to me the major role played by thrombosis in myocardial infarction, independent of cholesterol, thirty years before it became fashionable. After years of laboratory research on the nutritional factors responsible for thrombosis, I developed a method of research on platelet activity in humans: reaching rural populations thanks to a laboratory on wheels. The study of the behaviour of blood platelets requires delicate and immediate analyses and it would have been vain to imagine rural populations travelling to research laboratories. In this way I was able to compare different regions of Western Europe (Moselle, Var, Belgium, Wales, Scotland) and put these populations on diets based on rapeseed oil. I thus proved that platelet aggregation was the factor most closely linked to coronary disease and demonstrated the effects of alpha-linolenic acid (omega 3) on the lowering of platelet aggregation. Everything was ready to organize the Lyon diet heart study on the Cretan diet, which was confirmed in 2002 by an Indo-Israeli study. In this study, I demonstrated that the Cretan secret was not in their siestas, nor in their genes, but in their diet. Olive oil is not the key. Their eating habits, dating back at least thirty-five centuries, are responsible for their low level of cardio-vascular disease, a twentieth of that experienced elsewhere. Wild greens on the island are the starting point of a traditional food chain. They naturally enrich animal products and by-products with essential fatty acids. The inhabitants' plasma is three times richer in alpha-linolenic

acid, the precursor of the family of omega 3, than in other European countries. It is said to be essential because it cannot be synthesized. The Lyon diet heart study showed that in adding this fatty acid to the diet of heart patients (1.3 grams a day more than in the control group), 75% of coronary recurrences and 100% of sudden deaths were prevented. Yet, after a six-month follow up period, the cardiologist in charge of monitoring the patients wanted to change their diet, unconvinced of its usefulness because their cholesterol level did not get down! I refused to modify the programme, which represented the culmination of thirty years of deductions, and I was vindicated by the unprecedented results. It is easy to have a diet rich in alpha-linolenic acid. One need only use rapeseed oil in cooking and seasoning. Two soup spoons of rapeseed oil contain 1.8 grams of alpha-linolenic acid, or 100% of the recommended daily intake. While I was visiting professor at Boston University, I learned of the results of the Framingham study in which alcohol, supposedly a harmful factor in coronary heart disease, seemed, on the contrary, to protect from it, this to the huge astonishment of the epidemiologists at the N.I.H. (National Institute of Health). The information was wilfully kept secret for several years but I considered it extremely important as it could partially explain the cardio-vascular protection of the French. I then launched studies of alcohol and wine in animals in the framework of my research on thrombosis before embarking on research on humans in Wales. In 1991 while I was working on several studies, journalists from 60 Minutes, the CBS television programme, came to my laboratory, Unit 63, in Lyon, to ask me my opinion on the cardio-vascular protection of the French. I suggested, taking great precautions, that alcohol could be one of the protective factors. The expression, the French Paradox, was heard on the air for the first time in the U.S. during this interview on the famous 60 Minutes programme. At the request of thousands of Americans, it was re-broadcast several times and watched by more than fifty million Americans. A direct consequence of this highly successful programme was that the U.S. government (Federal Bureau of Alcohol, Tobacco and Firearms) asked me to justify my words in a request made through the French Ministry of Finance. It was then that I published an article in the *Lancet* in which I explained my reasons. Following the appearance of this article, I never received any other requests from the American government. However, two years later, the U.S. Surgeon General suggested that a moderate intake of alcohol could be beneficial to health. In the 1992 *Lancet* article, I thus defined the French Paradox : for a level of risk factors similar to that of countries such as England and the U.S. (cholesterol, high blood pressure, smoking, saturated fat consumption), France has a lower coronary heart disease mortality rate than in the majority of the rest of the industrialized world. I then developed my hypothesis that the habit of drinking moderate amounts of wine with meals could be beneficial to health, an hypothesis backed up by numerous observation studies. I continued to study this concept both in animals, in particular on the positive role of alcohol on blood platelets and especially wine, in the prevention of the platelet rebound effect and in humans. Over ten ago, I launched a vast epidemiological population follow-up study with the Center of Preventive Medicine in Nancy. Thanks to this institution and to the head of statistical programmes, René Guéguen, we have been able to gather data on 100,000 subjects over a 20 – 25 year period. This study consists in monitoring the causes of death since 1978 of a

group of 45,000 men and 55,000 women aged now between sixty and ninety and whose drinking habits and main biometric and biological health parameters are known from the beginning. It was the first study in France to have demonstrated that a moderate consumption of alcohol, particularly wine, was associated with a 40% reduction in cardio-vascular mortality in middle-aged men. The analysis of this group showed, for the first time, that a daily intake of between 1 and 3 glasses of wine, and only wine among alcoholic beverages, was linked to a 20% reduction in death from cancer. These surprising results were confirmed in Denmark. The conclusions of Gronbaeck are similar to ours : only wine in moderate amounts is associated with a reduction in deaths from all causes including cancer. Beer does not have the same effects, especially concerning deaths from cancer. This regional French group is one of the few in the world (2 or 3) comprising enough subjects to be broken down into sub groups composed of only moderate wine drinkers and thus able to differentiate the consequences of moderate wine drinking from other alcoholic beverages on mortality. The Eastern region of France presents the particularity of having both an important group of wine drinkers and also beer drinkers. Until now only the results of studies on humans have been able to be published on deaths from all causes and from cancer as well as on deaths related to high blood pressure. Today, my work is now continued by Dr Dominique Lanzmann-Petithory, who takes over all the programme of the Nancy study. We are looking for funding in order to continue this study. Recently, in March 2005, American friend cardiologists under the guidance of Dr Tedd Goldfinger made me the honour to create the Renaud Society <http://www.renaudsociety.com>, an association of physician passionate about wine and research on wine. The association was launched at the Culinary Institute of California on Saturday, 5 March 2005, in the presence of my friends Morten Gronbaeck, Curtis Ellison, François de Booyse and Arthur Klatsky (from right to left on the photograph).

Deleterious Influence of Wine on the Human Dentition

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The purpose of the study was to investigate the erosion effect of wine on human teeth using multidimensional research approaches involving epidemiological tools, Microhardness tests, Scanning Electron Microscopy (SEM) and Confocal Laser Scanning Electron Microscopy (CLSM). Differences in erosion between teeth of wine-makers and those who are not wine-makers, was clearly demonstrated. The continuous, frequent exposure of wine-makers' teeth to wine is the major factor in the differences obtained. Microhardness tests and microscopic investigations conducted confirmed the deleterious influence of enamel exposed to wine. A clear 'dose-response' relationship was demonstrated by means of the Microhardness tests. Differences were also demonstrated in the surface morphology of enamel with respect to the exposure to the wines investigated in the SEM and CLSM studies. Differences with respect to severity were shown with the SEM investigations. Subsurface lesions were observed with the aid of CLSM on the enamel exposed to the wines.

Alcohol, Wine, Hypertension (HTN) & Coronary Heart Disease. (CHD)

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Since wine is an alcoholic beverage, the theme of this session and of this presentation needs to focus on the relative role of beverage choice (wine, liquor, or beer) in the relations to health measures or outcomes. Thus, "good for you" translates into "better for you" where alcohol drinking (usually light-moderate) is beneficial or "less bad for you" when alcohol drinking (usually heavy) is

harmful. This dichotomy is illustrated well by relations to HTN and to CHD. Ecological studies provide strong evidence that wine drinkers fare better than beer or liquor drinkers with respect to CHD risk and some cohort studies contribute to this hypothesis. All available outcome data are from observational studies. Possible residual confounding by drinking pattern, diet, physical activity, behavioral traits, or psychosocial factors cannot yet be completely ruled out. Issues include: 1) How appropriate is inferential assumption of confounding? 2) How appropriate is inference of benefit via non-alcoholic wine ingredients? 3) How might a satisfactory randomized prospective controlled clinical trial be designed and executed?

SESSION X: Healthy Wine Production

The Importance of Food Allergens in the Liquor Industry

H. Steinman (Keynote Speaker)

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Early recorded history documents the addition of various substances to food for a variety of technical reasons. These include salt, sugar and vinegar for food preservation, and sulphur dioxide, which was used during the Roman era for sterilisation of wine vats. Today there are more than 20,000 additives available that can be utilised in food for a variety of technical grounds. Usually the intake of these is small. A number of additives are utilised in the manufacture of various types of liquor. Many of these are sourced from foods that have well-documented allergenic potential, for example, egg when used as a clarifying agent. The resulting additive may retain the allergenic potential of the original substrate and consequently the manufactured food may contain a 'hidden' allergen. Furthermore, a number of substances are formed or altered during the manufacturing process, e.g., histamine. These may result in non-allergenic intolerance effects in individuals. Some substances, such as alcohol, even when not abused, may result in a variety of adverse effects depending on the pathophysiological mechanism. For example, approximately 45% of oriental individuals have a partial to complete absence of a vital enzyme required for the metabolism of alcohol. Examples of allergens and additives that may be found in the liquor industry of which a number may result in adverse effects in individuals are: Alcohol, Barley, Egg, Grape, Histamine, Hops, Isinglass, Nitrates, Sulphur dioxide, Tyramine, Wheat and Yeast. Further, a number of allergens, such as mites and moulds, may affect workers in occupational settings. Adverse effects may be confined to oral and gastrointestinal effects, but in occupational settings, 'inhalant' allergens may result in respiratory symptoms and may be vitally important for the well-being of workers. Understanding the importance of additives or natural ingredients that have been implicated in adverse reactions, whether exerting their adverse effects due to an allergic or intolerance mechanism, will result in a deeper understanding problems experienced by consumers and workers in the industry.

What about Biogenic Amines, Ochratoxin A etc.

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It is generally accepted that moderate wine drinking can be beneficial to human health. However, some unwanted compounds, including potential carcinogens, such as ethyl carbamate, mycotoxins such as ochratoxin A, neurotoxins, such as biogenic amines, and asthmatic chemical preservatives, such as sulphites, can sometimes also be found in wine. Biogenic amines are basic nitrogenous low molecular weight compounds with biological activity that may be formed or catabolised during the normal metabolism of animals, plants and micro-organisms. Biogenic amines are derived mainly from amino acids through substrate-specific decarboxylase enzymes. Amines may be formed by yeasts during the alcoholic fermentation (mostly putrescine); by lactic acid bacteria (LAB) during malolactic fermentation (MLF) and during maturation of wines. Biogenic amines can also be present in the must, such as putrescine in grapes is associated with potassium deficiencies in the soil. The main biogenic amines in wine are histamine, tyramine, putrescine, cadaverine and phenylethylamine. In view of this certain countries/supermarkets are imposing upper legal levels of histamine in wines. To elucidate the current situation in South African wines a twofold strategy was followed. Firstly, the biogenic amine-producing ability of 400 lactic acid bacteria (LAB) isolated from South African wine was determined, using a decarboxylase screening plate method. Tyramine was the main amine formed by the LAB strains investigated. Putrescine was also produced. *Lactobacillus hilgardii* strains were shown to be mainly responsible for biogenic amine formation. Two *Lactobacillus brevis* strains also produced biogenic amines. None of the LAB produced histamine or cadaverine. The effect of temperature and pH on the formation of biogenic amines were also tested. Secondly, 300 commercial South African wines were tested for the presence of histamine, tyramine, putrescine and cadaverine. A low percentage of wines contained concentrations higher than the suggested levels. Fungi can produce mycotoxins, which are regarded as

carcinogens, and thus a matter of great concern with consumers. Therefore discussions are ongoing in the European Union to establish maximum limits for the presence of Ochratoxin A in wine. The two genera of fungi associated with infected grapes that can produce these mycotoxins (such as aflatoxins, patulin and ochratoxin A) are *Aspergillus* and *Penicillium*. It is therefore important to evaluate the levels of ochratoxin A in wine to establish a base line level. Ethyl carbamate received much attention in 1970's when high levels was detected in fruit distillates and brandies destined for Canada. Ethyl carbamate levels can be influenced by physical parameters during ageing and storage of wine or by the yeast and bacteria. These two wine microorganisms have different mechanisms to produce this compound. The amount of ethyl carbamate produced by yeast is mostly negligible, but a study conducted by Uthurry et al. in 2005 showed the levels increased significantly after MLF, irrespective of the starter culture used. Today there are also legal limits for the level of ethyl carbamate for different wine styles.

Organic Viticulture and Winemaking in South Africa

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This paper deals with all aspects of Organic wine from definitions, methods of organic viticulture, production in the cellar to the marketing and sale of organic wine. There are as many definitions as certifying bodies but they all have at their core the production of a crop without the use of synthetic chemicals. The organic wine definition is not as clear cut, as a distinction can be made between 100% organic and "Wine made from organically produced grapes". Production of organic grapes is really about controlling fungal diseases so it makes sense that most of the larger organic farms are in the warmer drier areas. This presents problems with an activity common to most organic farms: compost making. Strategies in the vineyards have been developed to make compost making unnecessary. Organic substitutes have been developed for most chemicals used conventionally. The problem is that does one want a total destruction of pests and diseases or does one want to develop a natural balance that obviate the need for a spray, organic or not. Organic vineyards are often more expensive to establish, but once a balance has been achieved, the production costs fall below conventional production. In the cellar there are not as many enforced rules as might be imagined. The most obvious and the easiest to test is the Sulphur dioxide level. Strategies must be developed to bottle the wine with the correct amount of SO₂ to ensure a normal shelf life whilst still coming below the 80-100ppm total limit. This invariably means not using much SO₂ early in the process. This can have an impact on wine style and the production of biogenic amines. Self enforced restrictions include the avoidance of fining agents from eggs, gelatine, fish etc. This is to cater for the significant numbers of vegetarian customers who are attracted to organic wines assuming they will not have these in them in the first place. There are no restrictions on the packaging for organic wines. The certifier is interested in the product and not the packaging. Most producers are mindful of the connection in people's minds between organic products and traditional production. Plastic closures, allowed for organic wines, are generally avoided as their image does not sit well with traditionalists or environmentalists. Organic wines producers should take care not to create too separate an image from conventional

wines. It is possible to saturate the dedicated organic consumer. Real growth will come from normal wine drinkers who choose organic because the price, quality, image combination is right. It is difficult to justify that drinking organic wine is healthier than conventional or that organic wines will always taste better. They should also be realistically priced as consumers automatically expect organic produce to be more expensive. Organic wine production is undoubtedly more environmentally friendly and with more and more people trying to live healthier lives, the presence of organic wines on shelves or on wine lists helps them to fulfil their chosen lifestyle.

Scheme for the Integrated Production of Wine as a Consumer Guarantee of Sustainability and Food Safety

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The Scheme for Integrated Production of Wine was introduced in South Africa in 1998. Fifteen guidelines for production of grapes and 13 for production of wine form the technical base of IPW. Compliance with guidelines is evaluated by producers and wine-makers themselves, and audited by ARC Infruitec-Nietvoorbij and Enviroscientific Auditing Services on a spot check basis. Evaluation of the agrochemical spray records is based on IP coding of registered agrochemicals, which assesses the environmental impact of each product. This system enables producers to minimize the environmental impact of agrochemical applications by selecting the products and application methods that are least detrimental to the environment.

Wine, Lifestyle, and Health

R.C. Ellison (Keynote Speaker)

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Epidemiologists have known for several decades that the moderate consumption of alcohol is associated with less coronary heart disease (CHD). In 1974, after the Framingham Heart Study had been in operation for more than 25 years, a report on the factors related to deaths from coronary heart disease (CHD) was prepared. It contained strong evidence that individuals who smoked cigarettes, had high levels of blood cholesterol, and/or had high blood pressure were much more likely to die from CHD. These became known as major "risk factors" for heart disease. In the same paper prepared by the Framingham Study investigators, there were also data showing a marked reduction in the risk of CHD mortality for consumers of alcohol. Because officials at the National Institutes of Health feared that releasing the latter information would lead to increased alcohol abuse in the US, they required that the alcohol-CHD data be removed, and the fourth major risk factor, "abstinence from alcohol," was omitted from the paper. Many other scientists, however,

began to publish information showing an inverse association between alcohol intake and CHD, with reports coming from studies by Arthur Klatsky in California and from around the world. The number of publications on moderate drinking increased markedly after the *60 Minutes* program on the “French Paradox” in 1991, when the American public first became aware of potential beneficial aspects of alcohol. At the same time, many scientists apparently felt

that it was now “politically correct” to report data demonstrating beneficial health effects of alcohol. Of hundreds of studies published in the scientific literature over the past decade, the results have been amazingly similar: almost uniformly, they have demonstrated that moderate drinkers have much less CHD. And new data show that, for people who already have CHD, moderate alcohol intake reduces the chances of repeat angioplasty and death.