



MINI-REVIEW ARTICLE

The Roseto effect: An Italian-American version of the French paradox?

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ABSTRACT

Clinicians worldwide continually have to respond to questions about the potential benefits on health from the moderate consumption of alcohol, and the “French paradox” has often been cited as supporting this premise. We wish to briefly comment on findings from the last several decades that provide evidence that moderate drinking may have some beneficial health effects, starting with a new analysis of the observation of “Unusually Low Incidence of Death From Myocardial Infarction” – a study of an Italian American community in Pennsylvania published in the Journal of the American Medical Association in 1964.

KEYWORDS: Wine, moderate drinking, French Paradox, coronary heart disease



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INTRODUCTION

Located on one of the foothills of the Appalachian Mountains in the United States, Roseto, Pennsylvania, was settled in 1882 by immigrants from an Italian hilltop town, Roseto Val Fortore, and surrounding villages in the southern Italian province of Foggia. Dr Benjamin Falcone, a local physician who had been practising for 17 years in the Roseto area, had observed that coronary artery disease was uncommon among Rosetans compared to the inhabitants of the adjacent town of Bangor. His observation aroused the interest of Stewart Wolf and his colleagues from the University of Oklahoma. Their survey of Roseto and the surrounding communities covering a seven-year period from 1955 to 1961 found a remarkably low death rate from myocardial infarction in the Italian-American community of Roseto – less than half that of four surrounding villages (Stout *et al.*, 1964).

1. Unusually low death rates from myocardial infarction in Roseto

The early comparative studies of diet and heart disease indicated that a high-fat diet was key in the genesis of atherosclerosis and myocardial infarction (Keys *et al.*, 1954). In Roseto in the United States, where 95 % of the inhabitants were Italian, the fat percentage of total calories was 38 % in men and 43 % in females, which was similar to the average fat percentage of calories in Minnesota (42 %) and the United States (40 %). Cooking was done in most families with lard rather than olive oil as the principal shortening and fatty meats were common. The mean values of serum cholesterol by age and sex corresponded closely to those reported in the Framingham study, and Rosetan men and women over age 21 were found to be overweight (Stout *et al.*, 1964).

Even so, when the number of deaths from myocardial infarction (proven anatomically, established clinically, and presumed) were compared by town for the seven-year period, the values for Roseto were found to be significantly lower than the values for the other four towns in the area ($p < 0.001$), especially for men. From 1955 to 1961 the age-adjusted mortality due to myocardial infarction in Roseto was 1 per 1000 men and 0.6 per 1000 women as compared to the average in the United States of 3.5 per 1000 for men and 2.09 per 1000 for women (Bruhn, 1965).

2. A low-fat diet or “a sensible way of life”?

Stout *et al.* (1964) stated: “The reason for the relatively salubrious condition of the Rosetans is not clear at the present moment;” however, the authors suggested a possible explanation: “Their sensible way of life, with social support and close family ties reflecting Old World values, might act as a buffer against the deleterious effects of stress and life change”. Ancel Keys, the Minnesota physiologist who put saturated fat on the map as a major cause of heart disease, was not pleased: “Those of us who emphasise the importance of diet have not claimed that dietary fat is the only etiological factor and, conceivably, the influence of the diet could be overcome by other influences, including the suggested favourable effect of a happy psychosocial situation such as

is purported to prevail in Roseto. But before concluding that dietary fats and calories have no effect, it is necessary to examine more critically the data published by the team from the University of Oklahoma Medical Center” (Keys, 1966). Keys criticised the lack of data on saturated fatty acids, however, in a rebuttal, Wolf (1966) stated that “No claim was made that diet is unimportant in the pathogenesis of coronary atherosclerosis. There was the implication that factors other than diet, including social factors, might be significant, but no unsupported inferences were drawn”.

Other contemporary studies have confirmed the importance of diet. For example, during the Second World War (when Norway was occupied by German troops) there was a considerable decline in the consumption of meat and meat products, whole milk, cream, margarine and other fats, cheese and eggs resulting in a reduction in the fat component of the average diet from 159 to 71 g per day; this was accompanied by a sharp fall in mortality from circulatory diseases from 1941 onwards to a nadir in 1943-45 (Strøm & Jensen, 1951).

When the war ended, mortality rose sharply and there was a close correlation between the curve for consumption of fat contained in these foods and the curve for mortality from circulatory diseases. This occurred despite, during the harsh German occupation of Norway, “there was increased nervous strain which has been held to provoke circulatory diseases” according to Strøm and Jensen (1951).

3. The devotees of Bacchus

In the early editions of his “Practice of Medicine” Osler stated that arteriosclerosis appears among the devotees of Venus (syphilis), Bacchus (alcohol), Mars (the military life) and Vulcan (the strenuous life). However, there was early evidence from Cabot (1904) of a protective effect of alcohol on atherosclerosis. In his autopsy study of 283 cases of chronic alcoholism (excluding those over 50 years of age) only 18 cases (6 %) showed evidence of arteriosclerosis. Out of the several hundred cases of arteriosclerosis examined by Cabot at Massachusetts General Hospital, 45 were under 50 years of age and only 6 of these (13 %) had any history of alcoholism. During the discussion after Cabot’s lecture at the 55th Annual Session of the American Medical Association, Dr. Meltzer from New York City expressed fear “...that Dr. Cabot’s assertion, that arteriosclerosis may be less among alcohol consumers, is a myth that will be misinterpreted and has made him a persona non grata in Massachusetts and elsewhere with men and women averse to the use of alcohol in health and disease” (Cabot, 1904).

In retrospect, the data from the Roseto cohort were similar to the results from the Paris Prospective Study (1967–77). The observation from that study that the high consumption of saturated fatty acids did not lead to a high risk of myocardial infarction among police officers from Paris was named “Le paradoxe français” by investigator Jacques L. Richard (1987), and it is the central question behind the French paradox concept. For a similar level of risk factors – age, blood pressure, cholesterol, cigarette smoking and diabetes – the incidence of hard CHD events in the Parisian prospective

study was 36 % lower than in U.S. railroad workers and 55 % lower than in the Pooling Project (Ducimetière *et al.*, 1980).

The same paradox was observed in Roseto: while conventional risk factors – consumption of animal fat, lack of exercise, obesity and cigarette smoking – were no less in Roseto than in nearby communities, the Rosetans experienced a significantly lower death rate from myocardial infarction than that of their neighbours. The meals in Roseto were family meals where the pasta and meatballs were washed down with wine and conversation. In 1963, nearly half of the households in Roseto made their own wine; the average daily intake of alcohol for Rosetan men was 34 g (approximately 3 glasses of wine) and for women 7 g, equal to a small glass of wine (Wolf & Bruhn, 1993).

4. Wine and the French Paradox

In 1979, St. Leger *et al.* (1979) surprised the world with the results of a study of risk factors for cardiac mortality in 18 developed countries: the principal finding was a strong and specific negative association between ischaemic heart-disease deaths and alcohol consumption, which was shown to be wholly attributable to wine consumption. The clue might be the effects of wine on the components of the haemostatic system: the coagulation system, endothelium and regulatory proteins, platelets and fibrinolysis. In pilot studies, Renaud *et al.* (1986) compared farmers from Var, southern France (low in CHD mortality), with farmers from south-west Scotland (high in CHD mortality) for platelet reactivity. The clotting activity of platelets was closely related to the intake of saturated fat while the intake of alcohol was inversely related to epinephrine and collagen-induced aggregation. Consumption of alcohol was 45 g per day in Var (mostly in the form of wine) vs. 20 g per day in Scotland, and platelet aggregation (secondary aggregation to ADP) was 55 % lower in Var than in Scotland.

It was already known that a meal with fatty foods (bacon & eggs and buttered toast) inhibited fibrinolysis conspicuously (Greig, 1956). Meade *et al.* (1979) reported favourable associations between habitual consumption of moderate amounts of alcohol and the haemostatic system with lower plasma fibrinogen concentrations and increased fibrinolytic activity. Such findings have been replicated in hundreds of experimental studies since.

5. 60 Minutes and “Le Paradoxe Français”

In November 1991, Professor Serge Renaud, director of the INSERM Research Unit 63 in Bron (Lyon), France, who was by then recognised as the international leader in research on alcohol, wine, and health, was asked on US television (the CBS Newsweekly program, 60 Minutes) about his explanation of the “French paradox”. “I think it is the alcohol”, he replied. “It’s well documented that, really, an intake, a moderate intake of alcohol, prevents coronary disease by as much as 50 percent.” The CBS report had followed the publication of an article, “Le Paradoxe Français”, in which Dolnick (1990) spelt out essentially the same conclusions as 60 Minutes based on interviews with Renaud and other experts, including an extended dinner conversation with Jacques L. Richard, an

authority on heart disease rates in France and father of the “French paradox” phrase. On the 60 Minutes broadcast about the French Paradox hypotheses, which was discussed by both Professor Renaud and Professor R. Curtis Ellison of Boston University School of Medicine, the concept achieved instant national fame followed by broad international recognition.

“The French pattern of life seems to encapsulate wine, food and lifestyle,” Dr Ellison said on the 60 Minutes segment. “While the full picture is yet clear, we know that the French are regular consumers of moderate amounts of alcohol, especially red wine, primarily with meals; eat more fresh fruit and vegetables and use less sugar; eat more cheese and drink less whole milk; and they spend more time with their meals and snack less. Of all of these factors, the link with moderate and regular consumption of wine with meals is the strongest and most scientifically proven.” When the 60 Minutes host Morley Safer closed the segment holding a glass of red wine and saying, “The protection of the French from heart disease may lie in this inviting glass!”, the response in the US was remarkable. For the following month, red wine sales were up 44 per cent over the same month of the previous year (Kolpan, 2016).

Professor Renaud was well aware of the dangers of higher levels of alcohol consumption. In the 60-minute segments, he pointed out that, “At the present time, a considerable number of men in France consume more than a bottle of wine per day putting them at risk of, for example, certain cancers and liver disease”. According to WHO’s World Health Statistics Annual 1989, the death rate from cirrhosis of the liver in the United States was 17 per 100,000 while the French cirrhosis rate was 31 per 100,000. In comparison, cardiovascular disease killed 464 per 100,000 in the U.S. and 310 per 100,000 in France. The WHO statistics actually hide a striking pattern in the French cirrhosis rates. Dr. Renaud said that INSERM studied the rates on a regional basis and found the highest cirrhosis rates (50 – 100 per 100,000) were in the northern regions of Alsace and Lorraine which have the highest consumption of beer and spirits. However, the regions with the highest wine consumption, such as Provence, Haut-Garonne and other wine-producing regions, had the lowest cirrhosis rates in France: 7 – 14 per 100,000.

6. Building the evidence base

Less than one year later Renaud published a review of the French paradox in the *Lancet* (Renaud & De Lorgeril, 1992). The paper defined the French Paradox: for a level of risk factors higher than or similar to those of the United Kingdom and the United States (cholesterol, saturated fat consumption, blood pressure, smoking), France had a lower coronary heart disease mortality rate. With the low risk of CHD in Toulouse (78/100,000), verified in the MONICA project, in comparison with Stanford, USA (182/100,000) as an example, the authors focused on the role of wine. The average consumption of alcohol in Toulouse was about 38 g per day, 34 g in the form of wine, and Renaud proposed a haemostatic mechanism rather than an interaction with the atherosclerotic process: “An alternative explanation is that because wine is mostly

consumed during meals it is absorbed slowly, and thus has a prolonged protective effect on, for example, blood platelets at a time when they are under the influence of alimentary lipids that are known to increase their reactivity. It has been shown in prospective and case-control studies that moderate intake of alcohol can prevent myocardial infarction, and by inference coronary thrombosis, but not stable angina pectoris, which is primarily the result of atherosclerotic lesions.”

Investigating the rebound phenomenon of increased platelet response to aggregation after alcohol withdrawal, Ruf *et al.* (1995) compared the effects of red and white wine to that of alcohol in studies in rats. Platelet aggregation was inhibited to the same extent in three groups of rats receiving the same amount of alcohol in the form of 6 % ethanol, white wine or red wine. However, when the rats were fasted and deprived of alcohol for 18 hours, the rebound effect on platelet function was not observed in animals given red wine and only partly observed with white wine. In a prospective, randomised cross-over study, a daily glass of red wine for 3 weeks significantly reduced plasma viscosity and fibrinogen concentrations. The decreased viscosity levels were maintained after 3 weeks of abstinence, suggesting a sustained viscosity-lowering effect of red wine (Jensen *et al.*, 2006). Recently Xanthopoulou *et al.* (2017) in a cross-over study with 10 healthy men found that wine consumption reduced postprandial platelet sensitivity against platelet activating factor independently of alcohol.

7. A randomised controlled trial of the preventive effects of wine?

Interpreting study results is difficult and it is particularly difficult to advise the general public when the advice must be based on ecologic surveys and observational evidence from population studies. Thus, whether or not a moderate regular intake of wine with a meal is associated with healthier outcomes by cause or consequence is still debated. The “Roseto effect” has been cited as evidence for the positive effects of social cohesion and social support on coronary artery disease, and a review found some support for the influence of social support on coronary heart disease mortality (Greenwood *et al.*, 1996). However, in a study of psychosocial risk factors for heart disease in France and Northern Ireland, a multivariate analysis indicated that, contrary to prediction, France had a substantially more negative psychosocial risk profile than Northern Ireland. The psychosocial risk factors were not successful at predicting (at a 5-year follow-up) the hard clinical endpoint of definite fatal/non-fatal myocardial infarction (Sykes *et al.*, 2002).

In the discussion of their observation of a strong and specific negative association between ischaemic heart disease deaths and wine consumption, St. Leger *et al.* (1979) suggested an experimental approach: “If wine has a protective effect against I.H.D. [ischemic heart disease] death then this is, in view of our results, more likely to be due to constituents other than alcohol in alcoholic beverages. Wines are rich in aromatic compounds and other trace components which give them their distinct character and it may be to these that we should look for the protective effect. All this is, of course,

speculation and wine drinking is said to be related to a relaxed way of living but we firmly believe that our evidence, and that from other studies, justifies an experimental approach to this question.”

Erik Damberg, a young Danish doctor, spent some years with the Medical Research Council Epidemiology Unit in Cardiff, Wales, in the late 1970s as part of his education for a career in public health. He shared an office with Selwyn St. Leger and had frequent meetings with Archie Cochrane to discuss future research projects. To this day, Damberg has a clear memory of the discussions about a potential randomised controlled trial of the preventive effects of moderate wine consumption on myocardial infarction (personal communication). The number of participants required was estimated to be about 16,000 middle-aged persons, and the French “De Luze company” had shown an interest in being a sponsor of the trial. However, due to problems with gaining ethical clearance in the UK, the matter disappointingly was taken no further. Similarly, a recent attempt by Kenneth Mukamal at Harvard and a group of international co-investigators to carry out a large clinical trial of alcohol and cardiovascular disease was terminated by NIH (Oppenheimer & Bayer, 2020; Miller *et al.*, 2021).

8. Proof by example: Roseto

In his book “Le Regime Santé” Serge Renaud (1995) gave a vivid description of the catastrophic change of lifestyle in Roseto. The text below has been translated from French by his co-worker Dominique Lanzmann. “It was well noted that Roseto differed in diet from other Pennsylvania cities. These dietary habits were those of Italy in the XIX century. They ate mainly cereals, vegetables and fruits. More than half of the families used olive oil (57 %). All drank wine. At that time, in the early sixties, 50 % of the Rosetans still made their own wine; they gave half of it to their relatives and friends. The grapes used came in part from private gardens where a wide variety of vegetables and fruits were also grown: lettuces, cabbages, peppers, onions, peas, beans, endives, radishes, zucchini, tomatoes, corn, beets, cucumbers, parsley, figs, peaches, pears, apples, cherries, plums and much more. The two bakers in Roseto also made bread, pizza, fish pies, pasta and pretzels every day.

Suddenly, between 1965 and 1974, coronary mortality in Roseto increased dramatically. When a new survey on eating habits was carried out in 1985, it was discovered that the consumption of olive oil had decreased by 50 %, as well as that of lard, butter and eggs. Informed, like the rest of the American population, of the harmful role of fats and cholesterol in coronary heart disease, Rosetans had changed their diet to what the American Heart Association calls the “prudent diet. The number of smokers had also decreased as did wine consumption. In 1961 – 1963, 32 % of Roseto men and 12 % of women smoked; by 1985, only 22 % and 9 % did so. The number of Rosetans who produce wine had also dropped from 50 % to 10 %, and consumption had fallen proportionately. In a few years, Roseto’s eating habits had shifted from the Mediterranean type to the cautious type,

the number of smokers had decreased, wine consumption had decreased, blood cholesterol had increased and coronary mortality had risen by more than 100 %. This is the sad experience offered by Roseto, a city blessed by heaven and which has remained so as long as it has remained faithful to its ancestral customs!”

Even without a clinical trial, besides the Roseto proof by example, there has been an amazing degree of replication of results from a multitude of cohort studies for many decades, and an increasing number of randomised clinical trials, as well as the verification of proposed mechanisms from experimental studies. All of these support the premise that the moderate intake of alcohol, especially regular wine consumption with meals, is a safe and potentially important lifestyle factor for the reduction of the risk of cardiovascular diseases. We contend that, while not specifically prescribing alcohol, physicians should not withhold from their middle-aged and elderly patients who are at risk of such diseases scientifically sound information on the relation of light-to-moderate drinking to cardiovascular health.

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