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Review

Mediterranean diet and the French paradox: Two distinct biogeographic concepts for one consolidated scientific theory on the role of nutrition in coronary heart disease

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1. Introduction

Scientists and physicians have long been debating the Mediterranean-style diet and the French paradox for coronary heart disease (CHD). However, folksy they sound, these two biogeographic concepts can still be very useful to explain unexpected or controversial medical and scientific data, such as the low mortality rate from CHD in Mediterranean Southern Europe and in France as compared with other European countries. Understanding these concepts may help improve our ability to treat and prevent CHD. Most of the present confusion probably comes from the consistent underestimation by physicians and scientists of the role of nutrition in CHD. This article is not aimed at giving a comprehensive review of these two complex notions, which have to be analyzed in a broad geographic, climatic, agricultural, historical and socioeconomic context. We will only provide a superficial overview, in relation to the epidemiology of CHD. Finally, we will try to introduce the two concepts as a fundamental premise of a new scientific theory on the role of nutrition in CHD, a theory that remains to be fully formulated.

2. The Mediterranean-style diet

2.1. Definition

The definition of the Mediterranean-style diet varies according to the particular Mediterranean area that is considered. For instance, the Greek version of the Mediterranean diet is dominated by the consumption of olive oil and by a high consumption of vegetables and fruits [1]. Since antioxidants are common in these foods, an antioxidant action may provide a plausible explanation for the apparent benefits of that diet [1]. According to another version, however, the Mediterranean diet is a non-strict vegetarian diet rich in oleic acid, omega-3 fatty acids, fiber, vitamins of the B group and various antioxidants, but low in saturated and polyunsaturated fat [2]. With that wider definition, the expected benefits for the prevention of CHD go far beyond an antioxidant effect and include lipid and blood pressure lowering effects, anti-inflammatory effects, the prevention of arterial plaque rupture and thrombosis, as well as protection against malignant ventricular arrhythmia and heart failure.

2.2. Historical overview

Interest in the concept arose from the finding that CHD

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mortality in southern Europe was considerably lower than that in northern Europe [3,4]. In 1987, the age-adjusted CHD mortality rate in Finland or the UK was still about three times as high as in Spain or Portugal (Table 1). Historically, the Seven Countries Study, with its cross-cultural investigation comparing middle-aged men from northern and southern Europe, has played a major role in the recognition of the evidence [4]. This unique study dealt not only with the interaction of classic CHD risk factors with the dietary habits of the studied populations, but also with their combined effects on the occurrence of CHD complications and death. The relative protection noted in southern Europe was initially thought to be largely due to the relatively safe and even protective dietary traditions of Mediterranean populations, although interpretation of the data essentially focused on the role of cholesterol in CHD [4,5]. Major emphasis was placed on the low animal fat content of the Mediterranean diet, on the high consumption of vegetable food (including whole cereals, pulses and vegetables), and on the regular use of olive oil. All of these do help in lowering serum cholesterol levels [5]. Later on, it appeared that the classic risk factors of CHD such as blood lipids [5], blood pressure [6] and smoking were not very different in the populations of southern Europe and in other Western countries. This suggested that those factors could not fully explain the difference between CHD mortality rates in the north and south of Europe. The conclusion was that unexplored factors and pathological mechanism(s) other than the accumulation of cholesterol within the arterial wall are favorably affected by this diet [2,5–7].

Since epidemiological studies provide only associations between risk factors and diseases, and not causal relationships, there has long been doubts as to the true effect of the Mediterranean diet itself on CHD. Other characteristics of the Mediterranean lifestyle were assumed to be protective as well. The economic situation and the presence of extensive welfare and health systems, for instance, were put forward as possible explanations for the low prevalence of CHD in certain Mediterranean countries. Although an effect of these factors cannot be totally excluded, recent data from Albania, where a low CHD rate is associated with economic misery and modest health services, disagree with this assumption [8,9]. Nevertheless, as for any therapeutic strategy, randomized trials are the only way to make sure that a given dietary pattern results in a significant protective effect. The Lyon Diet Heart Study is a randomized single-blinded secondary prevention trial aimed at testing whether a Mediterranean-style diet may reduce the risk of recurrence after a first myocardial infarction. A surprising 50 to 70% reduction in the risk of cardiovascular complications was reported [10–12], while no major bias was detected in the trial [12]. This strong protective effect was confirmed in the GISSI trial, where the risk of death was three times as low among CHD patients on a traditional Mediterranean diet as among patients following a Western diet [13]. The major impact of that diet on survival was also confirmed in various aging populations [1]. Finally, the Lyon trial suggested that patients following the Mediterranean-style diet might also be protected from cancer [14]. Although further trials are warranted to confirm the cancer data, those of the Lyon trial are in line with epidemiological studies emphasizing the role of nutrition in the prevalence (and prevention) of many cancers [15,16].

Table 1
Age-adjusted mortality rates from ischemic heart disease (per 100 000 males or females) in 1987 in countries of northern and southern Europe. From the Eurostat database [3]

Country	Ischemic heart disease	
	Males	Females
Finland	386	169
Norway	307	123
Ireland	372	169
UK	340	157
Italy	144	65
Spain	109	48
Portugal	108	52
Greece	132	58

2.3. A consensus about the concept of the cardioprotective Mediterranean diet

Following the publication of the final report of the Lyon trial [14], the American Heart Association Science Advisory and Coordinating Committee stated that ''*it would be short-sighted not to recognize the enormous public health benefit that the Mediterranean-style diet could confer*'' and that ''*there is a pressing need to identify unknown risk factors and effective intervention strategies*'' [17]. Thus, the experts of the American Heart Association and of the European Society of Cardiology are now on the same line in recommending the adoption of a Mediterranean-style diet for the prevention of CHD.

While it strongly supports the validity of the epidemiological data cited above [1–7], the Lyon trial again illustrated the importance of a dietary pattern giving preference to fresh fruit and vegetables, bread and cereals, as well as to fish and plants rich in alpha-linolenic acid [18]. The authors of the AHA Advisory also stated that the experimental diet used in the Lyon trial was comparable to food patterns that were typical of many regions in Greece and Southern Italy in the early 1960s, but uniquely different in that is was high in alpha-linolenic acid. The point is important when assessing the potential protective effect of specific nutrients, in particular n-3 fatty acids, against CHD. In fact, in 1993, Sandker et al. reported that the serum cholesteryl ester levels of the Greek cohort in the Seven Countries Study included an amount of alpha-linolenic acid (the main plant n-3 fatty acid) three times as high as that of the Dutch cohort [19]. Simopoulos showed

that, at that time, the Greeks obtained alpha-linolenic acid from wild leafy greens gathered in the field in any season of the year, from the eggs of range-fed chickens that also obtained alpha-linolenic acid from wild plants and grains, and also from walnuts [20]. We know that populations of Southern Italy and Spain did the same. Thus, the traditional Greek and Mediterranean diets are richer in alpha-linolenic acid than the Western diet, and the experimental diet tested in the Lyon trial was not different from the traditional Mediterranean diets as regards the intake of alpha-linolenic acid, though the sources of alpha-linolenic acid were not the same in the Lyon trial experimental diet (essentially canola oil and canola oil-based margarine) and in the traditional Mediterranean diet.

2.4. Geographic variations

The Mediterranean area, with its hot climate and fertile soil, supports exceptionally diverse food crops. Seafood are also popular in the Mediterranean food culture, although not in the same way everywhere. Thus the agricultural and fishing characteristics of the regions were basically (but not exclusively) the origin of what we now call the Mediterranean-style diet. Also, the conditions for food production, transport and trade have varied considerably (and still vary) around the Mediterranean shores. While there is no room here to fully discuss each of these points, it is obvious that, at present, Mediterranean countries (including Portugal for the purpose of our study) still vary not only with respect to geography, culture, religion, agriculture and economy, but also in their health and welfare systems. Five of these countries belong to North Africa and another three to the Middle East. These non-European countries are not directly comparable with most European Mediterranean countries (at least in terms of health indicators) because of many differences in their present social, agricultural and economical situations. Among European countries, France spans a large area, stretching from what would otherwise be called northwestern Europe to its southern Mediterranean shores. In fact, when carefully looking at the French territory in terms of geography (Fig. 1), climate (Fig. 2), agriculture and food habits, it is obvious that more than 80% of France is practically outside of any important Mediterranean influence [21]. Furthermore, olive cultivation, a symbolic feature of the traditional Mediterranean agriculture and food culture, has not been important in France since most of the trees were destroyed by frost circa 1950.

Countries such as Egypt (essentially African) or Turkey (essentially Asian) are also not typical Mediterranean countries. Several other particularities and inconsistencies further complicate the overall picture, but some of them may still provide useful information. For instance, the CHD mortality rate in the Mediterranean island of Malta differs from typical rates in other Mediterranean countries and is rather similar to those of northern Europe (Tables 2 and 3). Malta does not, however, have a typical Mediterranean food pattern because the island is not self-sufficient and depends on food imports. Historically, Malta was successively conquered by several different nations, the last being England, and each conqueror brought along their own food preferences. The result is a unique, mixed dietary pattern, and also a mortality pattern that differs from typical figures in the region [22]. The example of Malta illustrates the predominant role of the dietary pattern of a population in the prevalence of CHD, whatever the geographic situation or the climate. The same applies to Israel, home to large numbers of people who grew up in other countries and in foreign food cultures. For instance, the consumption of polyunsaturated vegetable oils (rather than olive oil) in Israel is one of the highest among industrialized countries, whereas the consumption of animal fat is low. While the CHD mortality rate in Israel is not as high as in Malta, it is consistently high as compared with Spain, Portugal and France (Tables 2 and 3). This ''Israeli paradox'' makes it difficult to draw conclusions about diet-related disease patterns in that specific country [23].

The CHD mortality rate in Greece and Macedonia is relatively high at present as compared with other European countries (Tables 2 and 3), which is rather surprising. This is probably the result of recent changes in the lifestyle of the adult population in these countries, including their dietary habits [24]. This is clearly documented by the DAFNE database for Greece [25]. In contrast, Portugal is a country open to the Atlantic Ocean (and with no Mediterranean coasts), where traditional food habits (in particular the high consumption of olive oil, wine, bread and fish) are similar to the typical Mediterranean model and where the CHD mortality rate is low (Tables 2 and 3). Thus, in order to understand the relations between CHD and geography, the main question is not whether a population lives in the south or the north of Europe but whether this population is following the essential rules of the Mediterranean dietary pattern. In other words, a Mediterranean population that gives up the Mediterranean diet (as is the case in Greece) is no longer protected, while a non-Mediterranean population living in the south of Europe can be either protected (in Portugal) or not (for instance, in Malta, Bulgaria or Romania), depending mainly on their dietary habits. Thus, contrary to common belief, the climate or geographic situation is not a direct major risk (or protective) factor of CHD. Living in a sunny country is not a safeguard against CHD, whereas living in ''glacial polar conditions'' does not automatically result in a high risk of CHD, as illustrated by the heart disease history among the Eskimos (Inuits). A striking variation in CHD mortality rates by geographic region has also been reported in the United States. A west-to-east gradient is observed, with high CHD rates markedly clustered in the Appalachia and Ohio, but also in the Mississippi delta, in Georgia and in the Carolinas [26]. Thus, in America as well as in Europe,

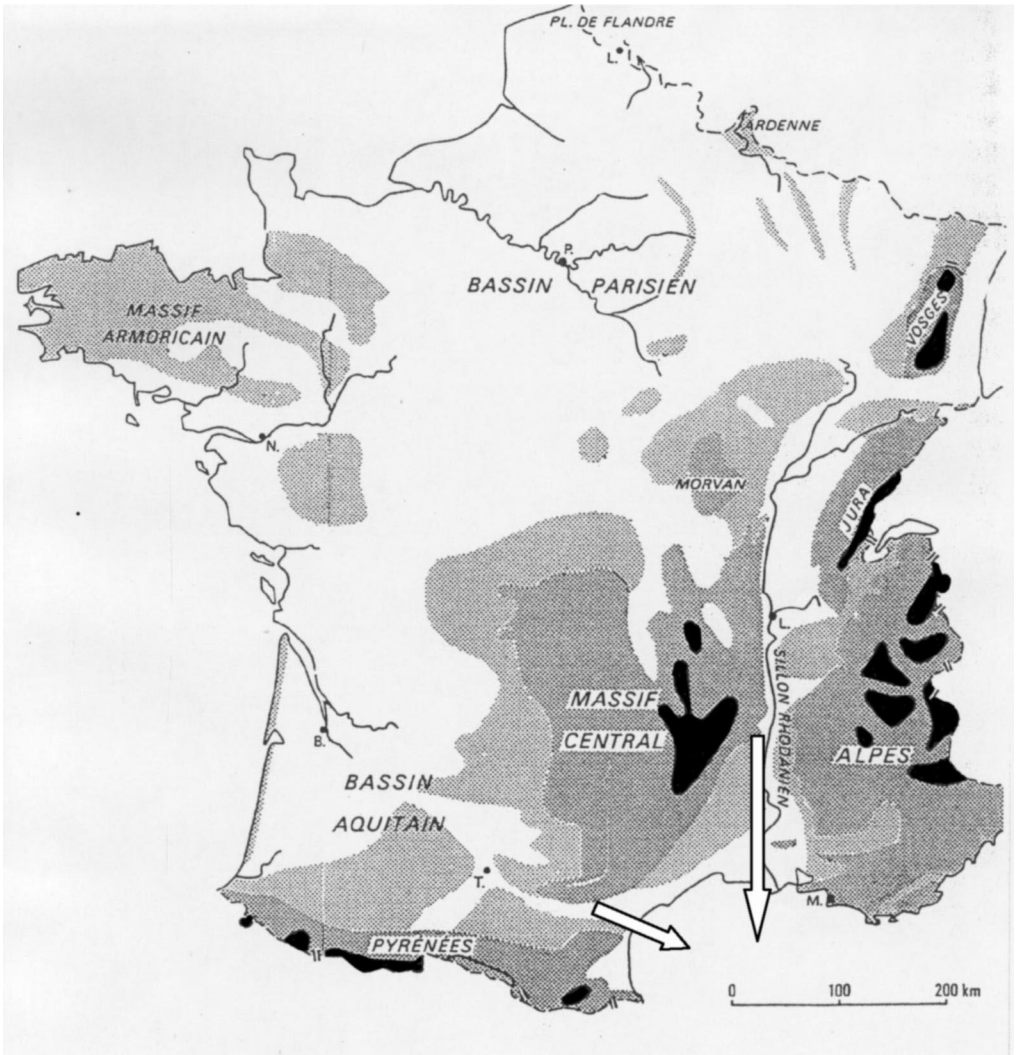

Fig. 1. Main physical characteristics of France. Gray areas represent zones of moderate or high relief resulting in difficulties for transport and agriculture. Arrows indicate major geographic passages or shelves (''seuil'' in French), e.g. the Seuil du Lauragais between the Pyrenees and the Massif Central. Another important passage is the ''Sillon Rhodanien'', another name for the Rhône Valley. As shown on the map, the French Mediterranean area is small and separated from the rest of the territory by high mountain ranges close to the sea. Cold winter winds passing between the mountains through the Seuil du Lauragais and the Sillon Rhodanien (Tramontane and Mistral winds, respectively), and steep altitude increases in the mountains prevent northward extension of the Mediterranean-type agriculture and food crops from the Mediterranean shores. See text for comments.

living in the south is obviously not a protective factor against CHD.

2.5. Variations in time

The lifestyle of most Europeans, particularly in northern Europe, has changed a great deal during the last decades. Over the same period, there have been major trends in the incidence and severity of CHD. Is there a causal relationship? According to the recent report of the WHO MONICA Project, the estimated contribution of changes in conventional CHD risk factors (smoking, hypertension, cholesterol) seems to only partly explain the variation in population trends for CHD [27]. It can be assumed that risk factors other than the conventional ones have played an important role in these trends. For instance, significant changes in the dietary habits of certain populations have indeed been documented from various sources and may have played an important role [25,28,29]. As a probable (but not exclusive) result of these major dietary changes, the mortality rates from CHD actually decreased in most North European countries but tended to increase in some countries of southern Europe. For instance, mortality rates from cardiovascular diseases for men in 1992 were surprisingly similar in Greece (531 per 100 000), Iceland (511) and Belgium (542), as they were for women in Greece (279), Denmark (275) and Finland (297) [30]. In addition to the confirmation of a well-identified east-to-west gradient (data not shown), the striking point of these data is that the apparent north-to-south gradient for CHD in Europe (Table 1) had already ceased to exist in 1992 [30]. On the other hand, there are South European countries

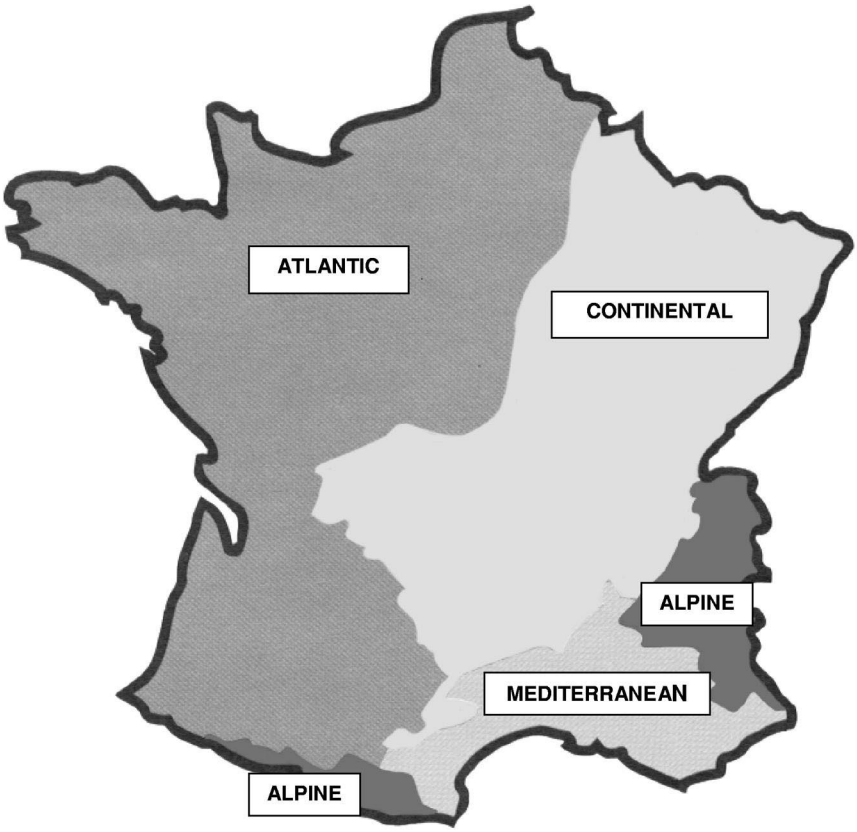

Fig. 2. Simplified presentation of the main climatic and biogeographic areas in France. The area of Mediterranean climate is small. See text for comments.

(Spain, Portugal, Italy) where there has been resistance to the westernization process and the lifestyle of the adult population has remained basically unchanged as compared with Greece. In these countries, CHD rates have remained stable and low until recently [30]. These recent and rapid changes in both the dietary habits and the CHD rates in European populations should be born in mind when trying to interpret and theorize the effect of nutrition on CHD. Over a short period of time, CHD mortality rates have changed rapidly in many European countries, which suggests that the classic theory of the effects of risk factors taking a long time before being apparent is wrong. Furthermore, these rapid changes in the CHD rates were reproduced experimentally in several trials where the diet

Table 2
Chances (per 1000 males) of eventually dying of heart diseases, cerebrovascular diseases and diseases of the circulatory system at age 0, in 1996 or 1997. From the WHOSIS database [48]

	Heart diseases	Cerebrovascular diseases	Diseases of the circulatory system
Finland	325	87	442
Norway	311	93	443
Ireland	335	75	444
United Kingdom	304	87	430
Italy	251	110	415
Spain	210	100	348
Portugal	159	193	379
Israel	261	107	389
Malta	342	94	461
Greece	309	153	488
Macedonia	328	190	558
France	197	71	308

Table 3
Chances (per 1000 females) of eventually dying of heart diseases, cerebrovascular diseases and diseases of the circulatory system at age 0, in 1996 or 1997. From the WHOSIS database [48]

	Heart diseases	Cerebrovascular diseases	Diseases of the circulatory system
Finland	309	137	483
Norway	284	134	451
Ireland	303	116	459
United Kingdom	264	132	430
Italy	279	159	515
Spain	261	153	472
Portugal	178	273	492
Israel	247	130	412
Malta	359	124	504
Greece	327	232	584
Macedonia	350	225	640
France	228	102	377

of randomized patients was changed and where the biological consequences of these dietary changes were evident within a few weeks after starting the trial [11,31–33]. While further studies are warranted to document these points, we can assume that the inhibition of lipid oxidation and of arterial plaque inflammation, the prevention of plaque rupture, arterial thrombosis, myocardial ischemia and ventricular arrhythmia, as well as the retardation of heart failure could be achieved very rapidly provided that adequate dietary changes are actually implemented [21,34–37].

2.6. Comments

Despite regional variability and disparities, it is now well accepted that the food culture is one of the few common denominators in the Mediterranean region. Although the concept may seem artificial, both local residents and foreign scientists have described a Mediterranean ''food culture'' and have stressed its benefits for health [22,38]. A Mediterranean diet pyramid (a graphic representation similar to that used by the US Department of Agriculture) was modeled by an international group of experts, on the basis of the diet of the early 1960s in Greece and southern Italy [7]. Fundamentally, the traditional Mediterranean diet pattern has been, and still is, closely tied to traditional areas of olive cultivation and there is no doubt that its benefits are closely related to the extensive use of the monounsaturated fatty acid-rich olive oil. Actually, monounsaturated fatty acids favorably affect a number of CHD risk factors [39]. Also, vegetable foods (including bread) make up most of the daily intake. Finally, minimum processing, seasonal use and the freshness of foods are expected to maximize their contents in dietary fiber, antioxidants and other micronutrients.

3. The French paradox for coronary heart disease

3.1. Definition

The French paradox is usually defined as the lower-than-expected CHD mortality rate in a country where classic CHD risk factors are not less prevalent than in other industrialized countries and where, in addition, the diet has historically always been rich in saturated animal fat [40].

The concept of the French paradox conflicts with the conventional theory on the role of classic risk factors in CHD. Thus, questioning the concept of the French paradox is not just a rhetorical exercise, and understanding it may help clarify some of the mechanisms underlying the development of CHD. In the absence of interventional studies, only hypothetic and indirect arguments can be put forward. However, cross-cultural and geographic comparisons, comparisons of men and women in France and the close examination of local and regional variability and disparities in France may help to explain, at least partly, the French paradox.

Another important clinical aspect of the French paradox that is emerging is the observation that French patients suffering from acute coronary syndromes may have a better outcome (death, heart failure, recurrent infarction) than patients from other countries [41,42]. No difference in the use of modern therapeutic procedures during the acute phase of the disease has been evidenced so far to explain this discrepancy [42]. Again, some unidentified factors may contribute to the different outcome in France.

3.2. Historical overview

The possibility that the French may be protected in some way against CHD was suggested by British authors more than 40 years ago and was initially based on crude comparisons of national official statistics [43]. More recently, other investigators have provided cross-cultural population data by studying the incidence of CHD among middle-aged French men in comparison with men included in the US Pooling Project and the international Seven Countries Study [44]. These cohort data confirmed the national statistics, and thereby the existence of a French paradox. However, the question is still the subject of an ongoing debate among epidemiologists, who regularly propose new—and sometimes fancy—theories to explain it. There is no room here to summarize the different stages of this long controversy. Among the serious explanations that were proposed over time, two were based on methodological concerns and should be briefly commented. The first one was that not all deaths caused by CHD in France were classified as such. It was argued that French physicians, in the absence of autopsy data, tended to certify some deaths that may have been attributable to CHD as death from unspecified or unknown causes [45]. Whether that undercertification bias may, at least partly, account for the low prevalence of CHD in France (as seen through the national statistics) as compared with Britain has been further investigated in a recent British study [46]. The authors eventually concluded that the excess proportion of all deaths attributed to unspecified causes in France was equivalent to 19% of the difference in mortality from CHD between France and Britain (Table 4). After correcting for that bias, mortality from CHD in France was about one-third of that in Britain in 1992, while the major classic risk factors of CHD were similar [46]. Thus undercertification definitely cannot explain the French paradox.

The second methodological concern was about the cross-cultural comparisons of cohorts from different countries [44]. It may be argued that small regional cohorts were not representative of the whole countries, even if post-hoc adjustments were performed. For instance, the middle-age men recruited in the Paris Prospective Study, who were active policemen, were not representative of the French male population at risk of CHD [44]. The same

Table 4
Mortality (number of deaths/100 000) from ischemic heart disease and ill-specified causes among people aged 55–64 in France and Britain in 1992. French data were obtained from the French National Institute for Health and Medical Research (INSERM). Modified from Ref. [46]

Certified causes of death (ICD-9 code)	Men			Women		
	France	Britain	Ratio	France	Britain	Ratio
Ischemic heart disease	128	487	1:4	27	153	1:6
All poorly specified or unspecified causes	71	3	24:1	25	2	12:1
Ischemic heart disease plus all poorly specified or unspecified causes	199	490	1:2.5	52	155	1:3

could be said about the comparison of regional data in the MONICA Project, in which, for example, the French centers, whether taken separately or pooled together, are obviously not representative of France as a whole [47]. Thus, to discuss the concept of the French paradox, it is certainly better to only use the official data provided by the World Health Organization (WHO).

Tables 2, 3 and 5, where the mortality data are expressed in accordance with the new methods adopted by the WHO (WHOSIS database), provide a fresh (in 1997) quantitative picture of what the French paradox means for men and women. Interestingly, the chance of eventually dying of CHD at age 0 (Tables 2 and 3) is not very different from the chance of eventually dying of CHD at age 65 (Table 5) in most European countries [48]. This suggests that the age factor is not, at present, a fine discriminating factor between countries with different CHD mortality rates. From these data, it is possible to conclude that the French paradox definitely does not result from spurious statistics or from a dilution bias.

3.3. What is the role of the diet in the French paradox?

Many authors have proposed various hypotheses to explain the French paradox [40,46,49–51]. Briefly, the main assumptions that have been explored relate to the lifestyle of the French, in particular their drinking and dietary habits. Curiously, for many authors, discussing the French paradox only means discussing the beneficial versus deleterious effects of ethanol in general and of wine in particular. The French are indeed known to drink more than other Europeans (Table 6). However, other dietary aspects are probably important in the French paradox and the next sections will only briefly discuss the alcohol–heart disease issue which has otherwise been the subject of recent reviews [52,53].

A recent assumption was that the French may be protected simply by their dietary habits, in the same way as the other South European populations [47]. Although respectable, that explanation raises many questions. First, among the South European populations, only those with a consistent Mediterranean-type diet still have a low CHD mortality rate. As discussed above, living in a sunny country is not a safeguard against CHD. Second, the diet of the French is not Mediterranean at all. This is hardly surprising, since France is not a Mediterranean country either geographically or in terms of climate. In fact, contrary to common belief, the greatest part of the French territory is not influenced by the Mediterranean Sea. High mountains, separated by narrow passages, prevent the Mediterranean influence reaching the northern and central parts of France (Fig. 1). It has been said that ''*the Mediterranean influence ends where olive trees can no longer grow*'' (Georges Duhamel). Because of the cold winters and chilly north winds, olive cultivation has never been well developed in France except in a narrow strip

Table 5
Chances (per 1000) of eventually dying of heart diseases, at age 65, in 1996 or 1997. From the WHOSIS database [48]

	Men	Women
Finland	344	328
Norway	323	302
Ireland	345	324
United Kingdom	311	279
Italy	269	296
Spain	224	276
Portugal	174	189
Israel	273	263
Malta	351	379
Greece	325	347
Macedonia	357	377
France	220	245

Table 6
Consumption of alcohol (as liters per person and per year) and wine (as grams per day per person) in 1988 in South and North European countries. Adapted from the OECD database [28] and the Eurostat Directory [3]

Country	Alcohol	Wine
France	15.7	195
United Kingdom	9.4	33
Spain	14.1	129
Italy	11.4	144
The Netherlands	10.2	38
Greece	10.3	84
Sweden	6.7	33

along the Mediterranean coast. In fact, more than 80% of France has none of the characteristics of the Mediterranean climate (Fig. 2) and agriculture and, as a result, the diet of most of the French is not a Mediterranean diet. Table 7 shows the mean consumption of some food groups typical of either the Mediterranean or the Western diet in some South and North European countries. As expected, Mediterranean countries were clearly different from other countries, with a high consumption of olive oil and a low consumption of butter and dairy products on average. They also had a higher consumption of cereals, pulses, nuts, legumes and vegetables but a lower consumption of meat (particularly beef) than northern countries. At that time, there was no clear difference between the two groups of countries as regards the consumption of fruit, fish, rice and potatoes (and also of pork, not shown in the table). France was obviously not a Mediterranean country when looking at the consumption of olive oil (so low that it is not reported), butter and beef (higher than in any northern country). In addition, the French were not as high consumers of pulses and nuts as the Mediterranean populations. Finally, the French were among the lowest consumers of cereals, rice and fruit among Europeans (Table 7).

Caveats about the use of national food balance data to compare the true consumption of foods between populations (or countries) are well known. Cohort and cross-sectional surveys in specific regions should therefore help to confirm the data. For instance, in EURALIM, a collaborative European survey, the dietary habits of the French are similar to those of the Belfast cohort and very different from the Italian and Spanish ones [54]. In particular, the consumption of fruit and the intake of fiber by the French appear to be very low, whereas the intake of saturated fatty acids is very high (16% of energy). These data are in accordance with the first French national dietary survey, called ASPCC [55]. In this survey, the mean fat intake of adults made up about 39% of the total energy intake, while saturated fats represented 16% of intakes, mainly because of a high consumption of butter (30% of saturated fat intakes), confirming the food balance data (Table 7). Finally, Gerber developed a ''diet quality index'' and studied the diet of a population sample from southern France (Languedoc area). Only 10 out of the 146 subjects had a wholesome diet, which indicates that even in the south of France, the dietary habits of the population are not in line with the main characteristics of the traditional Mediterranean diet [56]. Interestingly, the age-standardized mortality rate from CHD for men and women in the Languedoc region in 1990 (Table 8) was similar to that of the Paris area and higher than that of Poitou-Charentes—both are situated north of Languedoc [57]. Questioning why the CHD mortality rate is the same in Paris (north of France) and Montpellier (south) is another way of seeing the French paradox.

Table 8
Age-standardized mortality rate from CHD in professionally homogeneous populations in different French regions in 1990. Adapted from Ref. [57]

Region	Men	Women
Poitou-Charentes	101	59
Midi-Pyrenees	104	50
Provence-Côtes d'azur	105	50
Aquitaine	114	56
Rhônes-Alps	118	55
Paris area	119	54
Languedoc	119	59
Limousin	122	63
Auvergne	129	59
Brittany	137	73
North	154	78
Alsace	155	81

Table 7
Food consumption (1988) in South and North European countries expressed as calories per day per person. Food balance data describe the amounts of foodstuffs produced in the country, less the amounts exported and stored, plus the amounts imported. Thus these data provide direct information about the availability of foods, but only indirect information about the true dietary intake by the population. They should therefore be considered as approximations. In addition, to simplify the picture for non-specialist readers, we use OECD data [28] which are already a summary of FAO data [29]. For instance, olive oil consumption in France is not indicated in the OECD data, not because nobody uses olive oil in France but because consumption is much lower than in typical Mediterranean countries

Country	Total cereals	Rice	Potatoes	Pulses and nuts	Legumes and vegetables	Total fruit	Total meat	Beef	Fish	Butter	Olive oil
Finland	653	40	143	18	36	56	536	124	62	167	–
Norway	710	28	181	25	37	78	400	111	43	75	–
Denmark	626	26	131	26	48	62	896	100	120	156	–
Germany	720	26	144	32	53	130	880	136	24	154	–
UK	795	39	209	70	39	85	528	128	32	93	–
Italy	1104	54	77	67	101	108	583	151	28	49	271
Spain	700	71	185	78	87	89	700	67	81	8	264
Portugal	958	180	180	72	40	65	449	72	120	12	73
Greece	995	48	166	108	136	143	513	96	14	39	472
France	766	40	182	29	74	73	740	169	43	174	–

Thus, the current data do not support the view that the French are protected against CHD because their diet is of the Mediterranean type.

3.4. May alcohol and wine drinking have a role in the French paradox?

An inverse association between light to moderate alcohol consumption and CHD risk has been consistently demonstrated in many epidemiological studies, independently of age, gender and smoking habits [52,53,58]. Since the consumption of alcohol, in particular wine, is high in France compared with most Western countries (Table 6), it has been proposed that their drinking habits may protect the French against CHD [40,45]. In addition, it is noteworthy that adult French women drink less than men, with more than 60% of them drinking only one glass or less per day on average in one study [57]. Rigaud reported that the mean consumption of alcoholic beverages in France was about 30 g of pure ethanol per day for men and only 10 g per day for women [59]. In ASPCC, alcohol made up 8% of the energy intake for men and 3.5% for women [55]. Therefore, because they drink more moderately, French women do not suffer from the same alcohol-related diseases as men and their life expectancy is one of the best in the world. In contrast, the life expectancy of French men is not better than that of other Europeans (Table 9). Thus, in relation to alcohol, we have to consider two distinct French paradoxes, depending on the gender and, if we accept the idea that the difference between French men and women in their way of drinking partly explains the difference between the male and female French paradox, we can also say that wine drinking may be a factor to explain the French paradox in general.

3.5. Dietary diversity and attitudes to food and drink

Human eating and drinking behaviors are a complex and multidimensional matter. If the French paradox does have a dietary explanation, the answer may lie in the overall quality of the diet (a combination of factors that can vary throughout time and from one region to another) rather than in a single food or beverage.

In recent studies, low dietary diversity scores, characterized by the omission of several food groups, were shown to be associated with increased CHD mortality [60]. It was reported that the percentage of the French adult population with a high dietary diversity score is remarkably high as compared with a similar US population (90% against 33%). French women had the highest dietary diversity score [61]. The way by which dietary diversity may influence CHD likely involves some of the particularities described for the Mediterranean diet, such as the freshness of the foods, seasonal use and minimum processing of food. These factors are not taken into account when analyzing the food consumption (Table 7) and nutrient intakes by the classical methods, although they may be crucial in terms of the bioavailability of certain nutrients. Also not taken into account are the local sources of fresh and natural foods such as those produced in the kitchen garden of many French families. Gardening is actually very popular in France and about 30% of French adults are claimed to regularly garden [62]. In contrast to most Western populations, for which gardening means beautiful flowers and lawns, the primary motivation of the French gardeners is to grow fruits and vegetables for familial consumption. In addition to the resulting light or moderate physical activity, shown to be associated with a lower risk of all-cause mortality in men with established CHD [63], kitchen gardening provides a number of fresh non-processed foods rich in micronutrients that are partly lost during storage and transportation to the supermarket.

Another aspect of the French paradox relates to the cultural importance of food in the daily life of most people. Food is actually a critical contributor to physical well-being and a major source of pleasure, concern and stress. Eating and drinking take up much of people's waking time around the world. In an international study, populations were surveyed with questions dealing with beliefs about the diet–health link, their concerns about food, and many other items [64]. The group associating food most with health and least with pleasure was the Americans, and the group most pleasure-oriented and least health-oriented was the French. Ironically, the Americans, who make the greatest efforts to alter their diet for the sake of health, are the least likely to classify themselves as healthy eaters [64]. Actually, the way the French drink (essentially wine, every day, during meals and rarely alone) is very different from the way that is prevalent in many Western countries (binge drinking on Saturday nights, to make a caricature). As often cited, binge drinking is a way of trying to forget a difficult life, whereas wine drinking is often associated with pleasure and conviviality, two aspects of a happy lifestyle. Whether a happy life may protect against CHD is an open question that warrants further investigation.

3.6. Comments

In summary, the low rate of CHD mortality in France is not explained by technical or methodological difficulties in

Table 9
Life expectancy (years) for men and women in 1996 in some European countries. Adapted from Ref. [3]

Country	Male	Female
France	74.1	82.1
United Kingdom	74.3	79.3
Spain	74.4	81.6
Italy	74.9	81.3
The Netherlands	74.7	80.3
Greece	75.1	81.4
Sweden	76.5	81.5

the assessment of CHD. Indirect (but convergent) data suggest that the dietary habits (taken as a general behavior rather than as an enumeration of nutrients) of the French are involved in that relative protection.

4. Conclusion and prospects

The Mediterranean diet and the French paradox are two biogeographic and nutritional concepts that conflict with the conventional theories about CHD. They are, however, the basis of a consolidated scientific theory that includes both the classic risk factors of CHD and the nutritional and biogeographic (ethnic) aspects of CHD. Among them are not only the Mediterranean diet and the French paradox, but also other ethnic or regional characteristics discussed (or not) in the present article, such as the Albanian, Maltese, Israeli, Macedonian, Greek, Eskimos, Asian and Japanese, and many other exceptions.

Briefly, the conventional theories assume that, on the basis of assessments of the classic major CHD risk factors, a precise and quantitative relationship between these risk factors and CHD has been elucidated [65]. Accordingly, a preventive strategy targeted at these risk factors can then be designed and adapted for each individual [65,66]. Curiously, in most scientific statements approved by national and institutional Scientific Committees, the lists of modifiable risk factors do not include any dietary factors, and the question of the dietary prevention of CHD is either discussed rather naively or totally ignored [65–68]. Also ignored is the major issue of the interactions between dietary (and other lifestyle) factors and the genetic predisposition to develop CHD [69,70]. Genetic (non-modifiable) factors should indeed be considered even when designing a preventive strategy aimed at correcting modifiable risk factors because the effects of these factors are very dependent on the genetic background of each individual. For instance, a recent study has shown that a polymorphism in the gene for alcohol dehydrogenase type 3 partly explains the protective effect of moderate ethanol consumption [70]. Polymorphisms in the genes of apolipoproteins B and E also seem important in the deleterious effect of dietary factors on the risk factors of CHD [69]. These genetic and nutritional aspects should obviously be incorporated in a modern theory of heart disease, since their interactions might be the key factors responsible for the development of CHD in many patients.

According to the conventional theories [65–67], it is possible to estimate an ''absolute risk'' of CHD and a ''relative risk'' of having CHD which is the ratio of the absolute risk in a group to that of a ''low-risk group''. The Framingham definition of a ''low risk state'' is claimed to provide a useful denominator to determine the effect of risk factors on an overall patient's risk [66]. From these simple calculations, it would be very easy to determine the intensity of the preventive intervention for a given individual. The main caveat is that the Framingham scores are derived from measurements made several years ago in a very specific population, namely middle-aged white Americans living in the New England area, and that the absolute risk for any other population may not be the same. Figs. 3 and 4 illustrate the point by showing the relationships between CHD mortality and either blood cholesterol or blood pressure in different populations. Obviously, the absolute risk of CHD was very different in the different populations at each level of the risk factors. At any level of blood pressure or blood cholesterol, the risk of death caused by CHD was considerably lower in the Mediterranean (or Japanese) populations than among North Europeans or Americans [71]. We can conclude that the predictive equations developed from the Framingham data are not very useful for any population living anywhere else than in the USA, at any other time than the period when the Framingham data were collected. These equations should not be extrapolated to other populations and the same applies to other regional prediction algorithms such as, for instance, PROCAM in Münster [67]. Finally, this

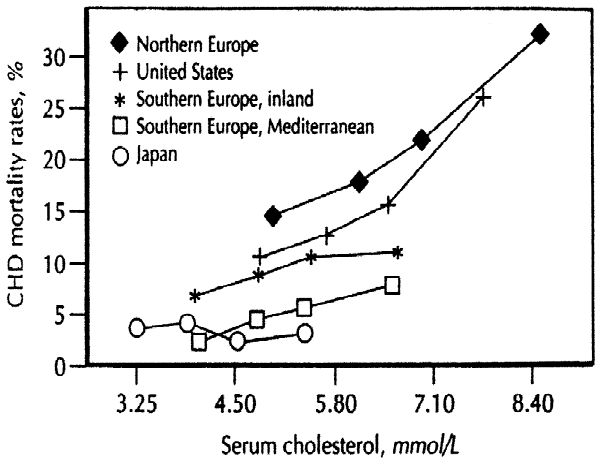

Fig. 3. Rate of 25-year mortality due to CHD (adjusted for age, smoking and blood pressure) per quartile of serum cholesterol in pooled cohorts of the Seven Countries Study. Adapted from Ref. [5] (with permission).

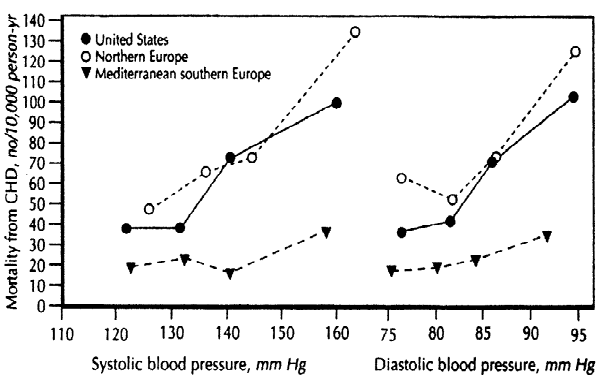

Fig. 4. Mortality due to CHD per quartile of systolic blood pressure in three populations of the Seven Countries Study. Adapted from Ref. [6] (with permission).

also indicates that the scientific theories about CHD derived from observations made in the USA and Northern Europe do not provide a universal view of the disease. A valid scientific theory should provide a universal explanation of CHD and should therefore include the biogeographic and nutritional concepts developed (among many others) about the Mediterranean-style diet and the French paradox.

There is no room here (and we do not wish) to extensively formulate a new diet–heart theory based on biogeographic and genetic variation concepts. In a few words, that theory states that CHD results from a tragic interaction between genetic (endogenous) and environmental (exogenous) factors. Among the environmental factors, we believe that the dietary factors are preponderant. Further research programs are obviously warranted to delineate, from a theoretical and clinical point of view, the main ''lines of force'' of the theory. New studies should be designed using clinically meaningful endpoints instead of surrogate endpoints such as blood pressure and serum cholesterol. Actually, the risk factors do not have the same impact on different cardiac complications [71]. Also, the main determinants of the risk factors should be used instead of these risk factors for the evaluation (calculation) of the risk when designing preventive strategies. For instance, to treat hypertension, it would be more logical (in terms of physiology), less toxic (side effects) and more effective (to reduce CHD mortality) to educate patients to drastically reduce sodium intake, to increase magnesium, potassium and calcium intakes and to adopt a dietary pattern similar to the DASH diet [72], rather than using blood pressure lowering drugs, the simplest but not the less toxic means. The sodium intake issue is particularly relevant as it acts independently [73] on blood pressure and left ventricular hypertrophy, two independent predictors of CHD death. We can therefore speculate that such a non-drug approach might reduce the CHD risk associated with high blood pressure and left ventricular hypertrophy without side effect and at a very low financial cost. Trials specifically designed to test this kind of hypothesis are urgently warranted.

Finally, the discrepancy between the current practice of certain physicians and dieticians and the ''official'' scientific statements discussed above is puzzling. In fact, many observational and interventional studies have evidenced the importance of nutrition in the prevention of CHD, not only in the management of the classic risk factors (e.g. lipid-lowering diets) but also beyond these factors [71]. The problem is probably that traditionalist scientists (and physicians) consistently underestimate the role of nutrition in CHD, and that the potential of dietary counseling in the prevention of CHD is hardly recognized. Confusion and misunderstanding also arise from the exaggerated emphasis laid on classic (and drug-modifiable) risk factors, such as hypertension and elevated blood lipids. That exaggeration partly results from the pressure exerted by the pharmaceutical industry and the agrofood business on physicians and scientists and also from their insufficient knowledge of nutrition [74].

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