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A test about the knowledge of some concepts of Evolutionary Medicine in the medical field

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Abstract
The correct knowledge in the medical field of some basic concepts of Evolutionary Medicine is tested with the answers of physicians of various professional qualifications to a group of 14 questions. The answers obtained show not only that there is an almost complete ignorance of some basic concepts of Evolutionary Medicine, but that current opposite ideas are prevalent. The consequence is that diseases are prevented and cured assuming an erroneous framework in a health maintenance system organized on unscientific assumptions with disastrous consequences for the rates of morbidity and mortality.

Keywords: evolutionary medicine, hygiene hypothesis, antibiotics, vaccines.

Introduction

Evolutionary Medicine is not an alternative medicine, but a Medicine that wants to be thoroughly and consistently based on sound scientific ideas and therefore duly integrated with concepts derived by Evolutionism. In fact, as Medicine is an applicative branch of Biology and Evolutionism is the backbone of Biology, it is not conceivable that Medicine may be organized without taking into due account the results and the logic of Evolutionism.
According to the current view and teaching of Medicine, Evolutionism is of little or no practical importance to this discipline: it is useful to understand the anatomy of certain organs, to explain better the physiology of some functions. Yet, considering the nature of the disease, which is something that does not evolve and hits as an anomaly the living being, Evolutionism is irrelevant for the understanding and the treatment of diseases.
On the contrary, the thesis of Evolutionary Medicine is that only taking into account that the living being is the result of evolution it is possible to understand the primary causes of the diseases and their real essence and from this to derive the most effective preventive and curative measures.
Those unfamiliar with the Evolutionary Medicine could argue that diseases are currently understood in their primary causes, preventive measures are mostly well-known, and treatments are certainly improvable, but that a good knowledge of Evolutionism in the medical field could be of little use for this purpose. Yet, this opinion is heavily wrong, as the careful Reader will observe in the next pages.
This paper wants to pinpoint on some biological-medical problems for which the discrepancy between the traditional medical view and that of Evolutionary Medicine is strong, with serious consequences for the prevention and the treatment of many diseases.

Method

A series of 14 questions with multiple answers (all in Italian language) was submitted by e-mail to over 200 Italian physicians of various professional qualifications (general practitioners, specialists of various type, hospital workers, researchers and scholars,

etc.). The choice of the person addressed was random and no information was given about the aims of the test before the answers. Only 48 doctors replied to the questions, expressing as requested one answer for each question. The goal was to detect if there was convergence or divergence between the traditional medical view and that of Evolutionary Medicine. Each question had four possible answers of which one was correct and the others wrong. In one case (question 11) two answers were correct, and in another case (question 3) three answers were correct. In these last cases, the fact that two or more answers were correct was not communicated.

Results for each question

For each question, it is now presented the formulation of the question and of the possible answers (all in the English translation) for which it was asked to make a single choice for the one deemed most appropriate. Immediately after, I report the responses obtained and then synthetic considerations that expose why the proposed answers are correct or not.

In each of the tables of the answers, it is also shown the expected correctness of random answers ("ECRA"), given by the number of correct answers divided by four.

The overall results are shown in the next section.

Question 1) Vaccines stimulate organism defences against bacteria, viruses and other pathogens and constitute the more effective medical means of defence against the diseases caused by them. Disregarding the cases when vaccines are ineffective (e.g., when they do not activate defences against appropriate antigens) or harmful (e.g., when they provoke allergic reactions or because sometimes the pathogen survives and rouses a noxious infection), in the other cases vaccines ...:

Answers:

A) as they cause undue risks for vaccinated subjects, should be used in restricted ways, should never be compulsory and their use should be subordinated to the consent of the subjects or of their tutors;

B) are always advantageous, and pathogen germs cannot develop more or less virulent mutants because totally blocked in their reproduction;

C) in addition to an immediate advantage, cause the selection of less virulent mutants and, therefore, in prospect may eliminate even the future danger of severe infections;

D) are advantageous against infections, but are potentially harmful if not well designed as they may provoke the selection of more virulent pathogens;

[For all the questions only one answer was required: A / B / C / D]

Table 1

Answers obtained:

A = 11 (22,91%);

B = 6 (12,5%);

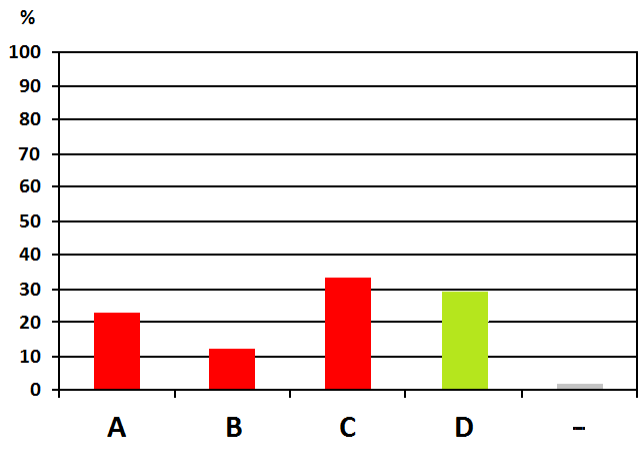
C = 16 (33,33%);

D = 14 (29,16%);

No answer = 1 (2,08%);

Tot. = 48 (100%);

ECRA = 25%



Correct answer: D

Vaccines are generally advantageous against infections, but it is a serious error to overlook that they act on entities that evolve and not on inanimate objects [Read and Mackinnon, 2008]. It is not true that pathogens against which vaccines are aimed are always totally blocked in their reproduction and, therefore, cannot develop mutations making them more or less virulent: e.g., in the case of hepatitis B virus, mutants not blocked by vaccine-induced immunologic defences are spreading [Francois et al., 2001; Hsu et al., 2004; FitzSimons et al., 2005] (Answer B is false). Moreover, it is not true that vaccines always favour the prevalence of less virulent mutants and so make less and less dangerous the pathogen opposed: e.g., in a well-documented case, Marek's disease virus, a disease caused by a herpes virus that provokes a form of poultry cancer, two generations of vaccines, after an initial phase of seeming success, have provoked the onset of more virulent and harmful stocks [Witter, 2001; Davison and Nair, 2004, 2005] (Answer C is false).

In shorts: "Rightly, vaccination is viewed as a medical triumph. Yet it is argued that the long-term control of acute childhood diseases like smallpox, polio, and measles does not mean vaccines are evolution-proof. The pathogens now being targeted are quite different from the organisms responsible for those diseases, and some of the vast evolutionary experiments currently being conducted with vaccines are generating pathogen evolution. As shall be seen, a variety of evolutionary responses to vaccination are possible, including the evolution of more virulent pathogens." [Read and Mackinnon, 2008]

In spite of these limits and reservations, which impose a careful evaluation of the consequences on the evolution of pathogens opposed by vaccines, advantages deriving from their use are generally much greater than risks caused by them. For certain types of diseases, in particular, we should not make exceptions to vaccine compulsoriness or trust in the free will of people that have no qualification to evaluate correctly about the best decision and that could decide from a personal point of view even in contrast with the public good (Answer A is false).

This question requires a critical evaluation of vaccine action in an evolutionary scenery, avoiding the serious error to consider pathogen germs as simple inanimate targets that cannot evolve. Carelessness of this concept can induce to serious errors of evaluation, which can jeopardise vaccine effectiveness or even cause harsh consequences (Answer D is correct).

Question 2) In subjects that are not elderly or suffering for a disease, refraction defects that reduce the eyesight (myopia, astigmatism, hypermetropia) are very frequent. Such defects ...:

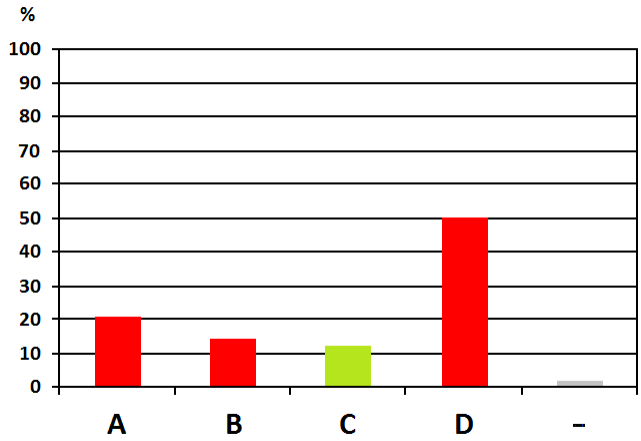
Answers:

A) are caused by the interaction of pathological genes predisposing to myopia / astigmatism / hypermetropia and environmental factors (weariness of the eyesight, unfit lighting, etc.);

B) are caused by pathological genes while environmental and nutritional factors are rarely the cause;

C) are caused by environmental factors while pathological genes and nutritional factors are rarely the cause;

D) are caused by the interaction of pathological genes predisposing to myopia / astigmatism / hypermetropia, environmental (weariness of the eyesight, unfit lighting, etc.) and nutritional (scarcity of particular vitamins and micronutrient) factors;

Table 2 Answers obtained: A = 10 (20,83%); B = 7 (14,58%); C = 6 (12,5%); D = 24 (50%); No answer = 1 (2,08%); Tot. = 48 (100%); ECRA = 25%	

Correct answer: C

“Animal models in multiple species show that early visual experience affects growth of the eye and eventual refraction. ... It has been hypothesised that prolonged reading or the retinal blur of prolonged near work leads to the development of myopia. This is supported by evidence showing an increase in the prevalence of myopia from near 0% to rates found in the Western population in aboriginal peoples exposed to a Western curriculum of education. ... Whether using primates (monkeys, marmosets, or tree shrews) or chickens, investigators have shown that when a clear, formed image is not allowed to be focused on the retina (by suturing up eyelids or placement of translucent goggles) high myopia will develop in the eyes of young animals.” [Fredrick, 2002]

In chickens forced from 5 to 12 days of age to use spherical lenses with –10 to + 10 of dioptric value, this visual manipulation caused astigmatism, myopia or hyperopia in 66-100% of the animals [Kee and Deng, 2008].

Myopia frequency varies by country and by ethnic group, from near 0% in Eskimo populations living in ancestral conditions [Young et al., 1969] and 0.8% in some Solomon Islands in 1966 [Verlee, 1968] up to 70-90% in some Asian populations [Chow et al., 1990; Wong et al., 2000].

“The marvellous vision of these primitive people [Australian Aborigines] is illustrated by the fact that they can see many stars that our race cannot see. In this connection it is authoritatively recorded regarding the Maori of New Zealand that they can see the satellites of Jupiter which are only visible to the white man's eye with the aid of telescopes. These people prove that they can see the satellites by telling the man at the telescope when the eclipse of one of the stars occurs. It is said of these primitive Aborigines of Australia that they can see animals moving at a distance of a mile which ordinary white people can not see at all.” [Price, 1939]

“Epidemiological surveys have shown that myopia is more prevalent in individuals who spend more time reading or performing close work than those who spend more time not using their eyes at near. Myopia has been correlated with the amount of school work and level of educational attainment. The process continues into the third decade of life with graduate students, microscopists, and military conscripts becoming more myopic with more near work. Studies of Aboriginal peoples and Inuits have shown increasing incidence of myopia correlating to the increased near work demands.” [Fredrick, 2001]

In shorts, evidence indicates that with the prolonged and frequent use of the eyes to see too much near objects in the childhood and in the juvenile age (reading of books, use of monitors, etc.), physiologic genes that have the beneficial function of regulating precisely eyeball growth to optimise the eyesight, cause an abnormal eyeball growth

determining refraction defects. Such refraction defects increase their frequencies insofar as the eye is used for too much near objects or, however, forced in ways for which the eye is not adapted.
But, studying two groups of 6- and 7-year-old school children of Chinese ethnicity, the first living in Singapore and the other in Sydney, with only two significant differences (Sydney children made more near-work activity and spent more time in outdoor activities), it was observed that the prevalence of myopia was only 3.3% in Sydney children and 29.1% in Singapore children [Rose et al., 2008b].
The idea that the direct exposition to natural light was the key factor has been confirmed by other studies [Rose et al., 2008a; Dirani et al. 2009].
In the absence of conditions of vision to which our species is not adapted, refraction defects are not developed, as shown by the case of Inuit populations living in ancestral conditions with near 0% myopia frequency [Young et al., 1969] and its increased frequency in correlation with near work demands [Fredrick, 2001]. “The increase in myopia prevalence observed in Hong Kong, Taiwan, Japan, and Singapore over the past few decades suggests an environmental risk factor, since the gene pool has not changed.” [Saw et al., 1996]
Consequently, except rare particular cases, the so-called “pathological” genes predisposing to myopia or to other refraction defects are indeed physiologic beneficial genes, favoured by natural selection, which on the contrary determine refraction defects in non-physiologic conditions to which the organism is not adapted.
Nutritional lacks (e.g., vitamin A deficiency) are important only in rare and particular cases.
The above-said considerations indicate that answers A-B-D are wrong and mirror well-established opinions according to which a great part of the human population would be unlikely afflicted by “pathological” genes causing refraction defects, whereas human populations living in non-modern conditions would be oddly exempt from such “pathological” genes. Moreover, these well-established opinions do not explain the extraordinary increase of refraction defects frequency observed in many populations in few decades and therefore without an impossible genetic general degeneration.
Negative definitions as (pathological) gene “predisposing to the defect of refraction X” should be substituted by positive definitions as (physiologic) gene “regulating ocular development”.
Evolutionary Medicine discriminates between “evolutionary” or “primary” causes (e.g., in the case of refraction defects: prolonged and frequent use of the eyes to see too much near objects in childhood and in juvenile age, and other conditions to which our eyes are not adapted) and “proximate” or “near” causes (in our case, physiologic genes that regulate precisely eyeball growth to optimise the eyesight and that in altered conditions determine refraction defects).
The meaning of genes as causes of refractive defects should be clearly specified. Except particular cases, physiologic and not pathological genes are essential in the pathogenesis, in combination with altered conditions that are the “primary” causes. Therefore, to document and maintain that those genes (without other specifications) are essential in refraction defects pathogenesis is misleading: this creates the wrong idea that there are largely diffuse pathological genes needing medical treatment while, on the contrary, pathological alterations of our ecological niche are the “primary” cause of refraction defects and preventive measures should be studied and applied. For evolutionary medicine: 1) refraction defects are the consequence of the inexistence or of the bad application of preventive measures; 2) medical treatment of refraction defects is the second-rate treatment of a medical failure.
In shorts, the present extraordinary epidemic of refraction defects is not a consequence of insufficient medical treatment, but an outcome of the absence of preventive

measures, which would be an application of an essential statement of evolutionary medicine: it is absolutely necessary to identify and to modify alterations of ecological niche for which our genes are mismatched and that therefore cause diseases!

Question 3) Decays, crowded teeth and related complications are common diseases. Which of the following statements is true?

Answers:

A) In 1932, in St. Moritz valley, girls were advised to extract all the teeth and to use a beautiful denture because with the marriage they would have lost all their teeth;

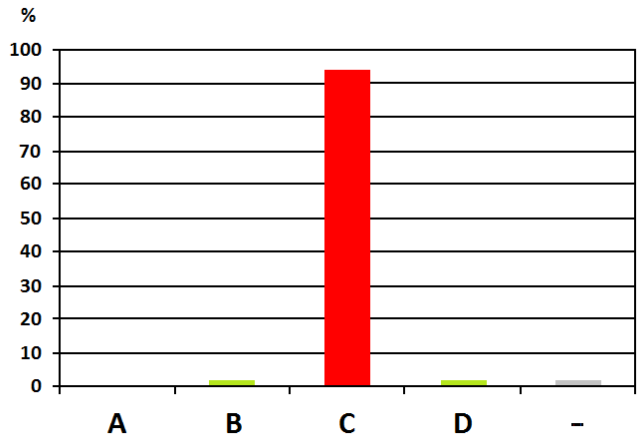
B) In 1935, in Fiji islands, because the lack of dentists, the only cause of suicide was toothache;

C) Modern dentistry and common rules of oral hygiene have greatly improved teeth conditions in comparison with preceding centuries and prehistoric age;

D) It is possible to have healthy teeth practically for a whole population without dental treatments and without the use of toothpaste, toothbrush and any form of oral hygiene, in particular, not removing the tartar and the remainders of food between the teeth;

Table 3
Answers obtained:
A = 0 (0%);
B = 1 (2,08%);
C = 45 (93,75%);
D = 1 (2,08%);
No answer = 1 (2,08%);
Tot. = 48 (100%);

ECRA = 75%



Correct answers: A, B and D

The correct answers are given with exceptional evidence by the extraordinary book of Dr. Price [Price, 1939] that, although published in 1939, is of real weight and relevance to the present and should be read with great care by all. It is documented that in prehistoric populations the teeth were practically exempt from caries, while in Neolithic populations, with the introduction of agriculture and the consequent modifications of diet, the teeth conditions worsened [Richards, 2002]. In modern populations, with the wide use of sugary drinks, foods with high sugar contents and poor in fibres, etc., the mean condition of teeth has further worsened in a catastrophic way. In the last decades, with the diffusion of modern dental treatment, the mean state of the teeth is in part improved without reaching the optimal condition of the Paleolith neither that partially deteriorated of the Neolithic.

Some quotations from Price's book (see also fig. 1):

(Chapter 2 – The progressive decline of modern civilization):

<In South Africa> "In not one of a very large collection of teeth from skulls obtained in the Matjes River Shelter (Holocene) was there the slightest sign of dental caries. The indication from this area, therefore, bears out the experience of European anthropologists that caries is a comparatively modern disease and that no skull showing

this condition can be regarded as ancient. [DRYER, T. F. Dental caries in prehistoric South Africans. Nature, 136:302, 1935.]”
(Chapter 5 – Isolated and modernized Eskimos):
“The excellence of dentitions among the Eskimos has been a characteristic also of the skulls that have been excavated in various parts of Alaska.
It might be expected that such wonderfully formed teeth would maintain so high an immunity to dental caries that their proud possessors would never be troubled with tooth decay. This, unfortunately, is not the case, a fact of great significance in evaluating our modern theories of the causes of dental caries. When these adult Eskimos exchange their foods for our modern foods, which we will discuss in Chapter 15, they often have very extensive tooth decay and suffer severely. This is clearly illustrated in Fig. 11, for these Eskimos' teeth had been seriously wrecked by tooth decay. They had been living on modern foods and were typical of a large number who are in contact with the Bering Sea ports. Their plight often becomes tragic since there are no dentists in these districts.
...
It is a matter of great significance that the Eskimos who are living in isolated districts and on native foods have produced uniformly broad dental arches and typical Eskimo facial patterns. Even the first generation forsaking that diet and using the modern diet, presents large numbers of individuals with marked changes in facial and dental arch form. In Fig. 12 will be seen four Eskimo girls who are of the first generation following the adoption of modernized foods by their parents. All have deformed dental arches. It is important to note the pattern of the settling inward of the lateral incisors and the crowding outward of the cuspids. This facial design is currently assigned to a mixing of racial bloods. These girls are pure-blooded Eskimos whose parents have normally formed dental arches.”
(Chapter 6 – Primitive and modernized North American Indians):
“This collection contains also skulls from several places and from prehistoric periods. The teeth are all splendidly formed and free from dental caries. The arches are very symmetrical and the teeth in normal and regular position.
It was important to study the conditions of their successors living in the same general community. Accordingly, we examined the teeth and general physical condition of the Indians in a reservation in North Vancouver, so situated that they have the modern conveniences and modern foods. In this group of children between eight and fifteen years of age, 36.9 per cent of all the teeth examined had already been attacked by dental caries. No people were found in this group who were living largely on native foods.”
(Chapter 10 – Isolated and modernized Australian aborigines):
“Another important source of information regarding the Aborigines of Australia was provided by a study of the skeletal material and skulls in the museums at Sydney and Canberra, particularly the former. I do not know the number of skulls that are available there for study, but it is very large. I examined many and found them remarkably uniform in design and quality. The dental arches were splendidly formed. The teeth were in excellent condition with exceedingly little dental caries.”
For modern Australian aborigines: “Those individuals, however, who had adopted the foods of the white man suffered extremely from tooth decay as did the whites.”
(Chapter 12 – Isolated and modernized New Zealand Maori):
“Since over 95 per cent of the New Zealanders are to be found in the North Island, our investigations were limited to this island. Our itinerary started at Wellington at the south end of the North Island and progressed northward in such a way as to reach both the principal centers of native population who were modernized and those who were more isolated. This latter group, however, was a small part of the total native population. Detailed examinations including measurements and photographic records were made in twenty-two groups consisting chiefly of the older children in public schools. In the

examination of 535 individuals in these twenty-two school districts their 15,332 teeth revealed that 3,420 had been attacked by dental caries or 22.3 per cent. In the most modernized groups 31 to 50 per cent had dental caries. In the most isolated group only 2 per cent of the teeth had been attacked by dental caries. The incidence of deformity of dental arches in the modernized groups ranged from 40 to 100 per cent. In many districts members of the older generations revealed 100 per cent normally formed dental arches. The children of these individuals, however, showed a much higher percentage of deformed dental arches.

These data are in striking contrast with the condition of the teeth and dental arches of the skulls of the Maori before contact with the white man and the reports of examinations by early scientists who made contact with the primitive Maori before he was modernized. These reports revealed only one tooth in 2000 teeth attacked by dental caries with practically 100 per cent normally formed dental arches."

(Chapter 13 – Ancient civilizations of Peru):

"When we have in mind that from 25 to 75 per cent of individuals in various communities in the United States have a distinct irregularity in the development of the dental arches and facial form, the cause and significance of which constitutes one of the important problems of this study, the striking contrast found in these Peruvian skulls will be seen to constitute a challenge for our modern civilizations. In a study of 1,276 skulls of these ancient Peruvians, I did not find a single skull with significant deformity of the dental arches."

(Chapter 3 – Isolated and modernized Swiss):

"When parents were asked to permit their children to have one meal a day reinforced, according to a program that has proved adequate with my clinical groups in Cleveland, the objection was made that there was no use trying to save the teeth of the girls. The girls should have all their teeth extracted and artificial teeth provided before they were married, because if they did not they would lose them then." (Answer A is correct!)

(Chapter 7 – Isolated and modernized Melanesians):

<in the years 1934-1936, in Fiji islands> "Abscessed teeth often cause suicide." "No dentists or physicians are available on most of these islands. Toothache is the only cause of suicide." (legend of fig. 32). (Answer B is correct!).

Modern dentistry has improved the teeth conditions in comparison with the dreadful state of the previous centuries, but certainly has not led back to prehistoric condition (Answer C is false). Lastly, it is true that Paleolithic populations, and those modern populations that live in conditions Paleolithic-like, have had, and have, healthy teeth without using any specific oral hygiene or dental treatment (Answer D is correct).

It is well documented that dental caries is caused by acid-producing bacteria (e.g., *Lactobacillus species*, *Streptococcus mutans*, etc.) acting in the presence of fermentable carbohydrates such as glucose, sucrose, and fructose [Rogers, 2008]. Evolutionary Medicine discriminates between "primary" causes (diet alterations) and "proximate" causes (acid-producing bacteria, which are physiologic commensal microbes and which without diet alterations do not cause dental caries): oral hygiene contrasts partially "proximate" causes and not "primary" causes and therefore its effectiveness is limited.

This question is peculiar because only one of the possible answers is wrong while the other three are correct. Therefore, a random reply had a 75% probability to be correct. In spite of this, the rate of wrong answers was 93,75%!

Figure 1 – A collage of photos from Price's book. In the upper side, living natives and skulls of individuals from people observing ancestral dietary habits (without any form of oral hygiene), while in the lower side natives following modern diets.

Question 4) There are various pathological genes (and some malformations determined by genes) predisposing to atherosclerotic diseases in non-old subjects and to arterial hypertension.

Answers:

A) This is true and the known number of such genes increases from year to year;

B) Except for sporadic cases, the above-said diseases are not caused by pathological genes;

C) The above-said diseases are caused by the interactions between pathological predisposing genes and excesses in alimentary habits;

D) A mild hypertension and small atherosclerotic lesions are common and practically normal even in young subjects. Unfit drinks and foods in subjects with pathological genes predisposing to the above-said diseases increase this basic vulnerability up to pathological conditions;

Table 4

Answers obtained:

A = 8 (16,66%);

B = 1 (2,08%);

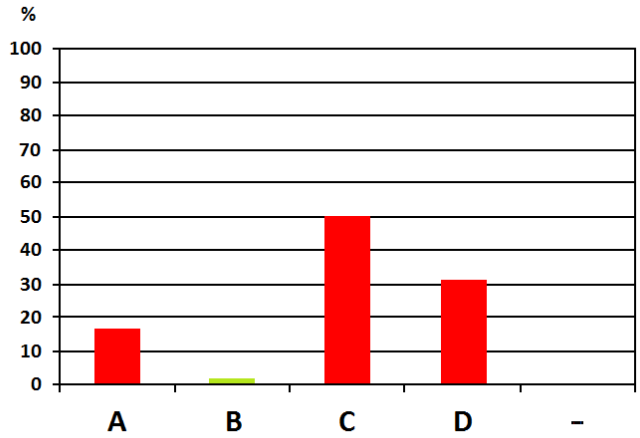
C = 24 (50%);

D = 15 (31,25%);

No answer = 0 (0%);

Tot. = 48 (100%);

ECRA = 25%



Correct answer: B

In modern populations living in Paleolithic-like conditions, that is hunting and gathering peoples (e.g., some Australian aborigine populations, Hadza in Tanzania, !Kung of Kalahari desert in Botswana, Ache of Paraguay, Efé of the Democratic Republic of Congo, Agta of the Philippines), atherosclerotic diseases in non-old subjects and arterial hypertension are practically unknown [Trevathan et al.,. 2008]. This is not a consequence of short life spans as in these peoples more than 8% of the population exceeds 60 years of age [Blurton Jones et al., 2002]. Systolic arterial blood pressure found in !Kung populations is practically always about 120 mmHg at all ages [Truswell et al., 1972] [see fig. 2].

Excessive salt intake, hypercaloric and hyperlipidic diet, stress (in shorts, the so-called risk factors for hypertension and atherosclerosis) are all conditions to which our species is not adapted. Genes that are physiologic and favoured by selection in natural condition (otherwise their existence would not be justifiable) in such anomalous conditions provoke the above-said diseases [Eaton, Konner et al., 1988; William and Nesse, 1991; Nesse and Williams, 1994; Trevathan et al., 1999, 2008]. The use of negative terms as (pathological) genes “predisposing to atherosclerotic diseases / hypertension” is misleading and should be substituted with terms that describe positively their functions in the ecological conditions to which our species is adapted. Disease origin is in the alterations of the ecological niche and not in genes that are not pathological but physiologic and advantageous in natural conditions.

For these considerations, with certain exceptions, the attribution of the above-said diseases to the action of “pathological” genes or to the interaction between

"pathological" genes and risk factors is misleading. In the pathogenetic mechanisms underlying atherosclerotic diseases and hypertension, physiologic genes are certainly involved, but they are "proximate" and not "primary" causes and, however, they are physiologic and not "pathological" in the natural conditions to which our species is adapted (Answers A, C and D are wrong). Except for sporadic cases, the above-said diseases are always caused by alterations of the ecological niche to which our species is adapted (Answer B is correct).

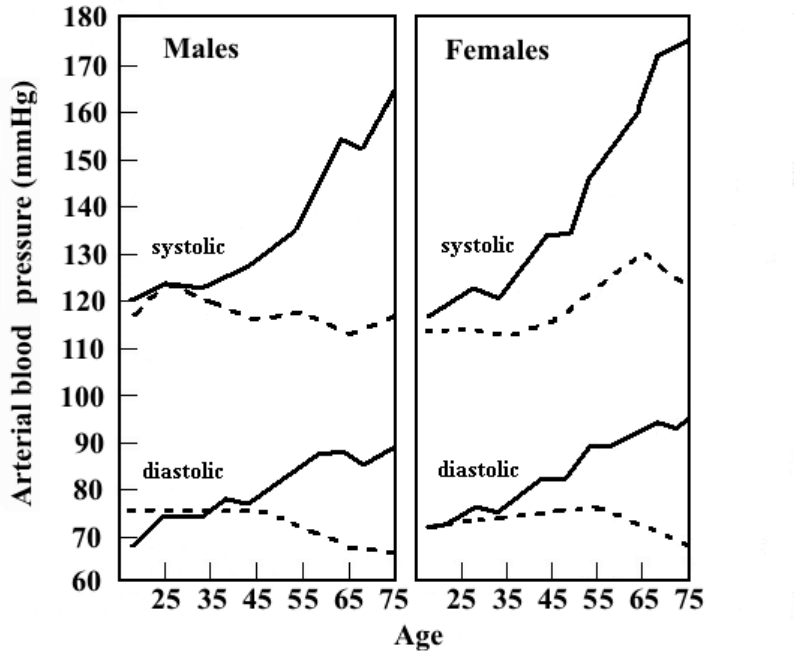
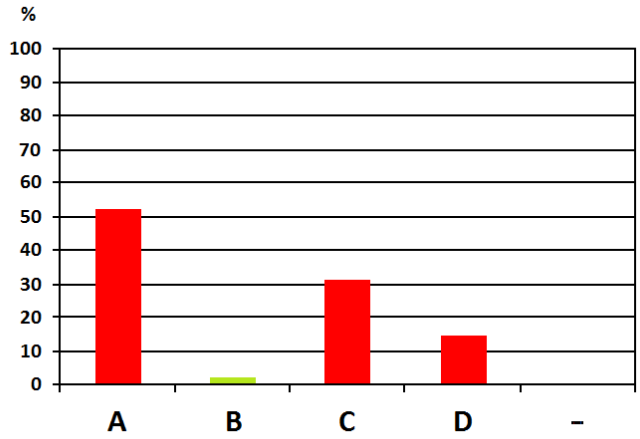


Figure 2 - Arterial blood pressures in !Kung individuals (dashed lines) and in London citizens (continuous lines) [Truswell et al., 1972] (partially redrawn).

Question 5) Type 2 diabetes or mature diabetes is determined by the interaction of pathological genes predisposing to diabetes and bad alimentary and lifestyle habits (excess of calories and fats in the food, sedentary lifestyle, etc.). Type 1A diabetes or immune mediated juvenile diabetes (the most common form of type 1 diabetes) is exclusively caused by predisposing pathological genetic factors. This is ...:
Answers:
A) completely true;
B) completely false. Except for sporadic cases due to genetic defects, both types of diabetes are caused by changes of life conditions to which man is adapted;
C) true only for statements about type 1A diabetes. For type 2 diabetes, except for sporadic cases due to genetic defects, it is caused by changes of life conditions to which man is adapted;
D) true only for statements about type 2 diabetes. For type 1A diabetes, except for sporadic cases due to genetic defects, it is caused by changes of life conditions to which man is adapted;

Table 5 Answers obtained: A = 25 (52,08%); B = 1 (2,08%); C = 15 (31,25%); D = 7 (14,58%); No answer = 0 (0%); Tot. = 48 (100%); ECRA = 25%	

Correct answer: B

Worldwide diabetes frequency is high and rapidly increasing. It has been estimated to be 2,8% in 2000 (171 million cases) and 4,4% in 2030 (366 million cases) [Wild et al., 2004]. On the contrary, in populations living in Paleolithic-like conditions (e.g., "Broaya pastoralists who maintain a traditional nomadic life in the Sahara") diabetes is practically unknown [Eaton, Shostak and Konner, 1988].

The rapid increase in diabetes frequency cannot be justified by a rapid increase in a single generation of the frequency of pathological genes. Likewise, the extreme difference in diabetes frequencies between populations living in ancestral-like conditions and those living in modern conditions cannot be caused by hypothetical pathological genes absent in some populations and largely present in others.

Hypercaloric and hyperlipidic diets, the use of food with high glycemic index (namely nourishment that provokes a rapid absorption of sugar), the scarcity of physical activity are all modern conditions to which our species is not adapted. Genes that are physiologic, advantageous and favored by selection in natural conditions (otherwise their existence would not be justifiable) cause in such anomalous conditions type 2 or mature diabetes [Eaton, Shostak and Konner, 1988].

The assertion that some genes (not defined as pathological) are involved in type 2 diabetes pathogenesis is correct but misleading as these physiologic genes are "proximate" and not "primary" cause of the disease.

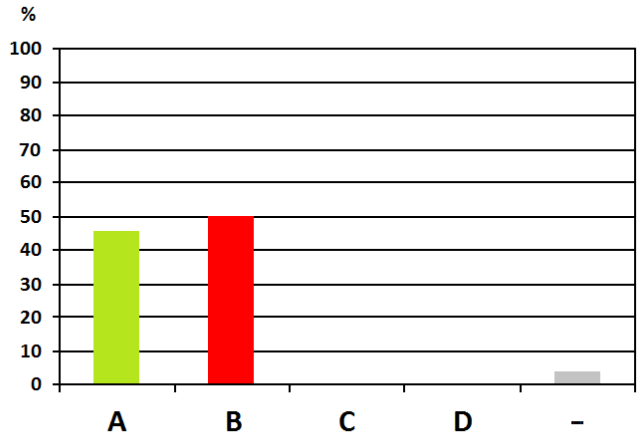
Less known alterations of the ecological niche cause autoimmune diseases that provoke the destruction of beta cells of Langerhans and so type 1A or immune mediate juvenile diabetes.

"A wide (over 400-fold) variation exists in worldwide incidence rates of type 1 diabetes, with the highest occurring in Finland (over 45 per 100,000 under the age of 15 years) and the lowest in parts of China. In many countries (e.g. in Europe, the Middle East, Australia) the incidence of autoimmune-mediated type 1 diabetes in children <15 years of age has risen by 2-5% per annum." [Silink, 2002]

"Type 1 diabetes is associated with other autoimmune conditions; the most common association is with thyroid disease. The Belgian Diabetes Registry indicated that the prevalence of thyroid peroxidase autoantibodies is 22% in patients with type 1 diabetes. Approximately 1 in 10 patients with type 1 diabetes express transglutaminase IgA autoantibodies, and more than half of these patients have coeliac disease on intestinal biopsy. Approximately 1 in 50 people with type 1 diabetes have 21-hydroxylase autoantibodies, and approximately 25% of these patients progress to Addison's disease." [Devendra et al., 2004]

“The steady rise in the incidence of T1D [Type 1 Diabetes] in developed countries over the last three decades is a matter of major public health concern (Gale, 2002). Taken together with a very uneven distribution of the disease worldwide, with a North–South gradient, this increase in incidence prompted epidemiologists to determine the factors that could possibly explain this unfortunate trend. The fact that similar epidemiological features have been observed for other autoimmune diseases, notably multiple sclerosis, and for allergic diseases (Bach, 2002), suggests that the explanation is probably not essentially specific to T1D. There is epidemiological evidence for the causal role of the decrease of infections in the increase of incidence of T1D.” [Feillet and Bach, 2004]
According to “hygiene hypothesis”, helminth eradication and a too clean environment for young infants lead to an abnormal immunoregulation that causes autoimmune diseases as type 1A diabetes and allergy [Gale, 2002; Bach, 2002].
The weight of certain genes in type 1A diabetes pathogenesis is well known [Dejkhamron et al., 2007] but these genes are “proximate” and not “primary” causes of the disease. They cannot be defined “pathological” genes, as in the ancestral conditions to which our species is adapted both type 1A and type 2 diabetes are practically unknown [Eaton, Shostak and Konner, 1988].
The use of negative concepts as “genetic predisposition” to type 1A diabetes [Dejkhamron et al., 2007] and “genes responsible for type 2 diabetes” [Virally et al., 2007] is misleading and they should be substituted with terms that describe in a neutral or positive way their function in the ecological conditions to which our species is adapted. Type 1A diabetes origin, or “primary” cause, is in alterations of the ecological niche and not in genes that are not pathological in natural conditions.
For these considerations, to attribute, with certain exceptions, the two types of diabetes to the action of “pathological” genes or to the interactions between “pathological” genes and risk factors is misleading (Answers A, C and D are wrong). Except for sporadic cases, the two types of diabetes are always caused by severe alterations of the ecological niche to which our species is adapted (Answer B is correct).

Question 6) The theory of evolution, or evolutionism, has a huge weight to understand biological phenomena. Moreover, it has real importance for the comprehension of the origin of various genetic diseases (e.g., thalassemia). However, beyond its great weight for the scientific knowledge in general, and excluding some particular case as the explanation of the origin of some genetic diseases, which is the effective importance for everyday life and for ordinary medical practice?
Answers:
A) It is indispensable for medical daily practice and for any branch of medicine. A profound knowledge of evolutionary mechanisms is essential for health safeguard;
B) It has no direct importance for the ordinary medical practice and for health safeguard. However, the knowledge of evolutionary mechanisms is fundamental to the biological essential bases of medical knowledge.
C) It is important only in the case of antibiotic therapy strategies and in the treatment of infections and of worm parasitosis;
D) It is important only in the treatment of allergies and of autoimmune diseases;

Table 6 Answers obtained: A = 22 (45,83%); B = 24 (50%); C = 0 (0%); D = 0 (0%); No answer = 2 (4,16%); Tot. = 48 (100%); ECRA = 25%	

Correct answer: A

"*Evolution in Health and Disease* describes how evolutionary thinking gives valuable insights and fresh perspectives into human health and disease, establishing evolutionary biology as an essential complementary science for medicine. Integrating evolutionary thought into medical research and practice helps to explain the origin of many medical conditions, including diabetes, obesity, cardiovascular disease, asthma, allergies, other autoimmune diseases, and aging. It also provides life-saving insights into the evolutionary responses of pathogens to antibiotics, vaccinations, and other human interventions." (from the back cover of the book of Stearns and Koella [Stearns and Koella, 2008]).

Evolutionary or Darwinian Medicine [Williams and Nesse, 1991; Nesse and Williams, 1994], a modern development of the work of Charles Darwin (1809-1882), is the practical application of evolutionary concepts to medicine.

With a shrewd reference to a famous statement of Dobzhansky [Dobzhansky, 1973], Nesse and Williams concluded their book saying "... nothing in medicine makes sense except in the light of evolution." [Nesse and Williams, 1994]

Other clever statements from the same source are:

(Medical Education) "When evolution is included, it will give students not only a new perspective on disease but also an integrating framework on which to hang a million otherwise arbitrary facts. Darwinian medicine could bring intellectual coherence to the chaotic enterprise of medical education."

(Clinical Implications) "An evolutionary approach does, however, suggest that many such treatments are unnecessary and that we should do the research to see if the benefits are worth the costs."

(Public Policy Implications) "New ways of organizing medical care may finally provide incentives for dedicating substantial clinical resources to preserving health based on principles of Darwinian medicine."

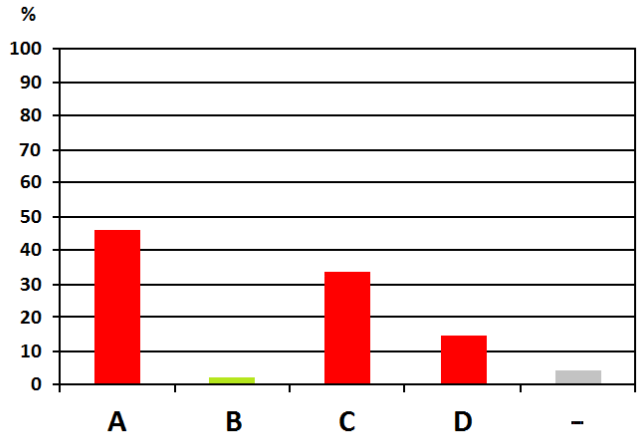
In 1983, it was written [Libertini, 1983]:

"... any biological phenomenon that is not strictly contingent, is after all an aspect, a side of the evolutionary process. With such assumption, the question about the possible definition of pathology in evolutionary terms comes out spontaneously. In other terms, the question is if disease phenomenon is an anomaly, an exception or, on the contrary, a phenomenon that is integral part of the evolutionary process. ...

From an evolutionary point of view, diseases are not something outside the norms, but, on the contrary, a set of various categories of phenomena, each evolutionarily "predictable" in its general essence. ...

Evolutionary approach to the concept of disease is the most rational and general possible. Any other more limited approach, even if more useful as regards a specific pathological problem, just because more limited and specifically oriented, must not be conceived in terms in contrast with evolution theory. ...
Evolutionary approach to the concept of disease originates spontaneously suggestions and basic interrogatives about prevention and treatment of the various categories of diseases." (Ch. V — Evolution and pathology; translated from Italian; original text available at Library of Congress; digital copy at: http://www.r-site.org/ageing/index_e.htm.)
Many arguments about the practical utility of Evolutionary Medicine are expounded in the books of: a) Eaton et al. [Eaton, Shostak and Konner, 1988]; b) Nesse and Williams [Nesse and Williams, 1994]; c) Trevathan et al. [Trevathan et al., 2008]; d) Stearns and Koella [Stearns and Koella, 2008], in particular in the introductory chapters of c) and d).
Evolutionary Medicine is essential for a correct understanding of "primary" causes of diseases, which are well distinct from "proximate" causes, and therefore for an effective primary prevention. For example, in the case of type 1A immune-mediated diabetes, in a review of the disease [Dejkhamron et al., 2007], the weight of genetic factors in pathogenesis is well documented, but the Authors do not state that these factors are only "proximate" causes and ecological alterations are the "primary" causes of the disease (and of other autoimmune diseases), a concept that explains the extreme variation of disease frequency (from practically zero in populations living in ancestral conditions [Eaton, Shostak and Konner, 1988] up to 45 per 100,000 under the age of 15 years in Finland [Silink, 2002]) and that could indicate efficacious preventive measures.
The correct answer is clearly A that is nearly the contrary of B. Answer C and D are true without the wrong limitation to particular arguments.

Question 7) In pregnant women, especially in the first months of gestation, nausea and refusal of particular foods as vegetables and meat are frequent. This phenomenon (morning sickness) is ...:
Answers:
A) a consequence of bradykinins increment caused by raised progesterone rates produced by placenta during foetal growth;
B) a phenomenon that is advantageous and therefore favoured by natural selection;
C) a phenomenon with many supposable causes, but always without any particular advantage for mother or foetus. Analogous phenomenon is the menstrual syndrome;
D) the consequence of contrasting evolutionary exigencies between foetus and mother in the first phases of gestation. Only for the following phases evolution has been able to develop an adequate equilibrium with no trouble and fitness alteration for the mother;

Table 7 Answers obtained: A = 22 (45,83%); B = 1 (2,08%); C = 16 (33,33%); D = 7 (14,58%); No answer = 2 (4,16%); Tot. = 48 (100%); ECRA = 25%	

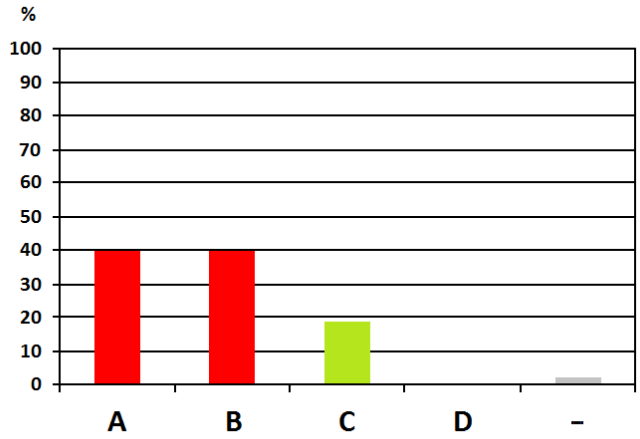
Correct answer: B
Nausea in pregnancy (morning sickness), provoked by particular foods, as strong-tasting vegetables, caffeine, alcohol, fish, meats, poultry, eggs, and in general foods with unusual smell or taste, is a defence of the mother against possible damages to the foetus deriving from potentially teratogen substances or infectious agents that could be present in particular foods [Flaxman and Sherman, 2000]. Therefore, the phenomenon is favoured by natural selection, being important for progeny safeguard (Answer B is correct). In support of this thesis, proposed by Margie Profet (1992) [Profet, 1992]: "(i) symptoms peak when embryonic organogenesis is most susceptible to chemical disruption (weeks 6-18), (ii) women who experience morning sickness are significantly less likely to miscarry than women who do not (9 of 9 studies), (iii) women who vomit suffer fewer miscarriages than those who experience nausea alone ... Animal products may be dangerous to pregnant women and their embryos because they often contain parasites and pathogens, especially when stored at room temperatures in warm climates. Avoiding foodborne microorganisms is particularly important to pregnant women because they are immunosuppressed, presumably to reduce the chances of rejecting tissues of their own offspring (Haig 1993). As a result, pregnant women are more vulnerable to serious, often deadly infections." [Flaxman and Sherman, 2000] Answers A and D are false statements that try to seem likely. Answer C could be accepted by those not accepting the strong evidence in support of B.

Question 8) In many infectious diseases, there is a condition of iron deficiency causing anemia. Such condition ...:
Answers:
A) is benign and a moderate iron supply has no consequence about possible complications and mortality rate;
B) must be cured with a suitable iron supply as to remedy the observed lack because this reduces the probability of possible complications and, consequently, disease severity and mortality;
C) must not be counterbalanced with an iron supply because this increases the probability of possible complications and, consequently, disease severity and mortality;
D) must be treated with strong doses of iron so that to pass from a state of want that weakens the organism to a state of saturation that optimises organism defensive capacities. In wild conditions, iron scarceness has been evolutionarily one of the greater tie for organism efficiency and such a scarceness manifests itself crucially in critical

circumstances when an external help is useful and sometimes indispensable for the survival;

Table 8
Answers obtained:
A = 19 (39,58%);
B = 19 (39,58%);
C = 9 (18,75%);
D = 0 (0%);
No answer = 1 (2,08%);
Tot. = 48 (100%);

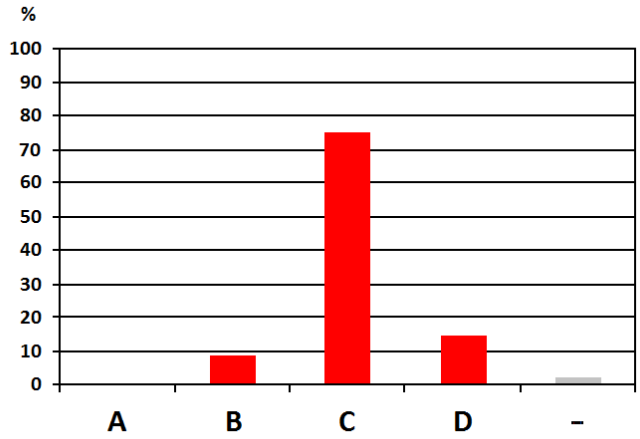
ECRA = 25%



Correct answer: C
"Acquiring iron is a fundamental step in the development of a pathogen, and the complexity and redundancy of both host and pathogen mechanisms to acquire iron and control flux and availability illustrate the longstanding and ongoing battle for iron." [Doherty, 2007]
"There is convincing evidence that iron deficiency protects against many infectious diseases such as malaria, plague, and tuberculosis as shown by diverse medical, historical, and anthropologic studies." [Denic and Agarwal, 2007]
Iron administration in Polynesian infants increased dramatically gram-negative neonatal sepsis cases and when iron administration was stopped sepses decreased [Barry and Reeve, 1977].
"In a malaria-endemic population of Zanzibar, significant increases in serious adverse events were associated with iron supplementation" [Iannotti et al., 2006]
"Recent evidence from a large, randomized, controlled trial has suggested that the universal administration of iron to children in malaria-endemic areas is associated with an increase in adverse health outcomes." [Prentice et al., 2007]
"In northeastern Tanzania, where malaria and iron deficiency are common, we found that placental malaria was less prevalent (8.5% vs. 47.3% of women; P< .0001) and less severe (median parasite density, 4.2% vs. 6.3% of placental red blood cells; P< .04) among women with iron deficiency than among women with sufficient iron stores, especially during the first pregnancy. Multivariate analysis revealed that iron deficiency (P< .0001) and multigravidity (P< .002) significantly decreased the risk of placental malaria." [Kabyemela et al., 2008]
"Oral iron has been associated with increased rates of clinical malaria (5 of 9 studies) and increased morbidity from other infectious disease (4 of 8 studies). In most instances, therapeutic doses of oral iron were used. No studies in malarial regions showed benefits ... Experimental studies in laboratory animals uniformly show reversible deleterious effects of iron administration on tests of functional immunity. These may occur even in mild deficiency. ... Experimental and in vitro animal studies suggest that organisms that spend part of their life cycle intracellularly, such as plasmodia, mycobacteria and invasive salmonellae, may be enhanced by iron therapy. " [Oppenheimer, 2001]
In a large prospective, randomized, double-blind, placebo-controlled trial in the early 1980s, iron supplementation in Papua New Guinea infants was correlated with more

frequent clinical malaria, severe lower respiratory infections, acute otitis media, measles [Oppenheimer, 2001]
"Unless the host immune response is impaired by severe iron deficiency, there is rarely an urgency to supplement iron and it is likely to contribute little to host iron status due to the block on absorption associated with inflammation. In the presence of intracellular infections such as tuberculosis or chronic inflammatory or immunosuppressive diseases (e.g. HIV), the decision to supplement iron must be considered on an individual basis, because the potential exists to benefit a pathogen rather than the host." [Doherty, 2007]
"Our bodies have a related defense mechanism, of which most people are unaware and which physicians sometimes unwittingly attempt to frustrate. Here are some clues about how it works. A patient with chronic tuberculosis is found to have a low level of iron in his blood. A physician concludes that correcting the anemia may increase the patient's resistance, so she gives him an iron supplement. The patient's infection gets worse." [Nesse and Williams, 1994]
In shorts, iron availability is a limiting factor for the growth of pathogens. Host organism tries to protect itself from the infections reducing iron quantity that is available by pathogens and, consequently, blood iron levels are actively reduced in the case of infections. It follows that the answer C is correct and that the actions described in the other answers, which are unfortunately habitual for medical practice, increase the risks for treated subjects.

Question 9) The synthesis of the sulphamides, the discovery and/or the synthesis of penicillins, cephalosporins and of many other powerful antibiotics are a series of fundamental events in the history of medicine. The USA statistics show that ...:
Answers:
A) sulphamides and antibiotics have barely influenced mortality rates for infective diseases. Moreover, bacterial antibiotic-resistance phenomena are reducing their effectiveness and even causing an increasing number of undue deaths, especially in hospital;
B) only penicillins and cephalosporins have influenced in a drastic way the mortality reduction for infective diseases. On the contrary, for sulphamides no important effect is documented for their limited effectiveness. For other categories of antibiotics (macrolides, streptomycin, rifampicin, quinolones, etc.), the beneficial effect on mortality reduction results important but inferior to that observed for penicillins and cephalosporins;
C) sulphamides and antibiotics have enormously reduced the mortality for infective diseases. Their use is by far the most important progress in the history of medicine and without them we would still be victims of the dreadful infective epidemics of the past centuries. Unfortunately, bacterial antibiotic-resistance phenomena are reducing their effectiveness and even causing an increasing number of undue deaths, especially in hospital;
D) only antibiotics, and not sulphamides, have enormously reduced the mortality for infective diseases. Their use is by far the most important progress in the history of medicine and without them we would still be victims of the dreadful infective epidemics of the past centuries. Unfortunately, bacterial antibiotic-resistance phenomena are reducing their effectiveness and even causing an increasing number of undue deaths, especially in hospital;

Table 9 Answers obtained: A = 0 (0%); B = 4 (8,33%); C = 36 (75%); D = 7 (14,58%); No answer = 1 (2,08%); Tot. = 48 (100%); ECRA = 25%	

Correct answer: A

Everyone would be ready to maintain that the use of penicillins, and of other antibiotics afterwards developed, has saved the life to an enormous number of people. The USA statistics from the beginnings of '900 up to our days show a very different picture (fig. 3 and fig. 4) [Armstrong et al., 1999]. Mortality for infectious diseases was very high at the beginning of the past century because of very poor social, economic, house, alimentary, etc. conditions. In the next years, mortality has fallen with a strong annual rate that is not at all changed with the use neither of sulphamides nor of penicillins nor of more modern antibiotics. In spite of the availability of the best modern antibiotics, "In the United States, mortality due to infectious diseases increased 58% from 1980 to 1992, a trend that was unforeseen." a phenomenon "mainly due to the emergence of the acquired immunodeficiency syndrome (AIDS)" [Armstrong et al., 1999], favoured by particular harmful habits (AIDS is partially opposed by antivirals and better checked by preventive measures).

Statistics indicate that factors of social, economic, alimentary, etc. advance and lifestyle have a very strong and decisive action, whereas the effects of antibiotics are not evident and, no matter how, they are much small in comparison with these factors. Likely, most of the decline in mortality in the nineteenth century was caused by improved condition of life and not by direct medical actions [Generaux and Bergstrom, 2005].

Moreover, it is true too that the improper use of antibiotics, especially in hospital, has caused and causes the selection of mutant stocks of pathogens with greater virulence and often practically not treatable with antibiotics. As an example of how substances developed to fight the diseases caused by pathogens can provoke considerable damages: "In the United States alone, at least 200,000 people and probably far more suffer from a hospital-acquired infection every year. The associated mortality is considerable; the Center for Disease Control has estimated that 90,000 U.S. residents die each year from nosocomial infections. To place this number in context, AIDS/HIV kills approximately 17,000 per year in the United States, influenza 37,000 per year, and breast cancer roughly 40,000 per year. As large as these numbers are, some estimates suggest that the actual magnitude of the problem could be up to tenfold higher." [Bergstrom and Feldgarden, 2008].

These data prove that the correct answer is A. The mechanisms that are behind this seemingly paradoxical answer will not be comprehensible if a correct use of evolution knowledge is not applied.

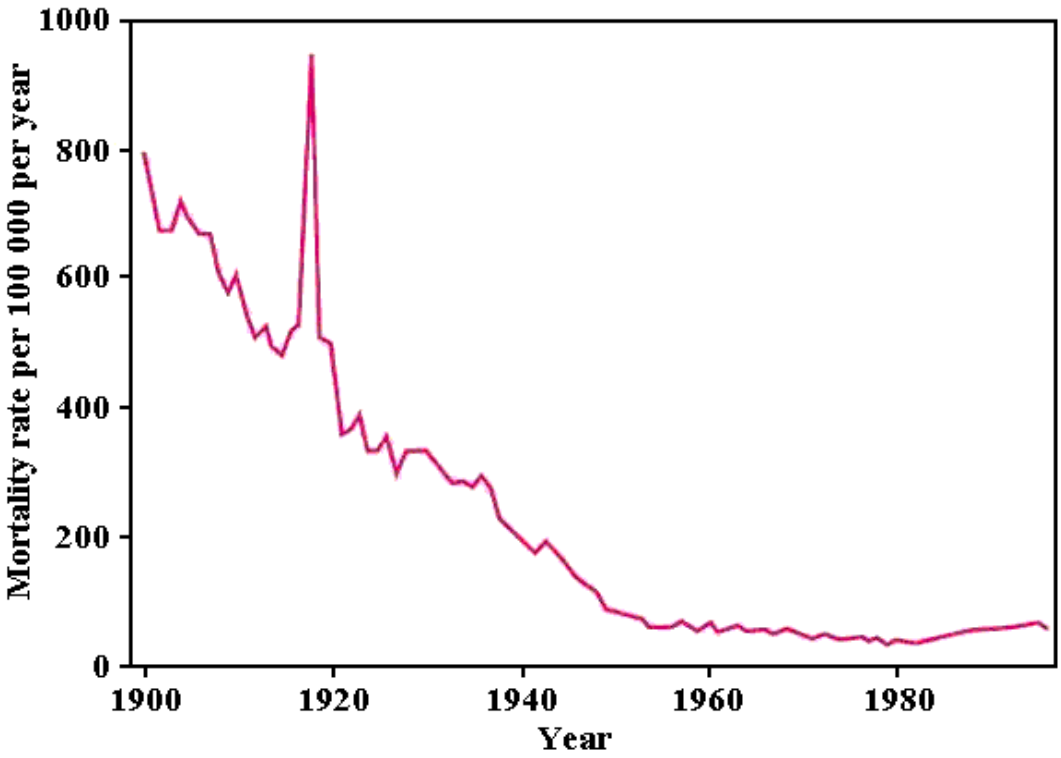


Figure 3 - Crude infectious disease mortality rate in the USA from 1900 through 1996 [Armstrong et al., 1999].

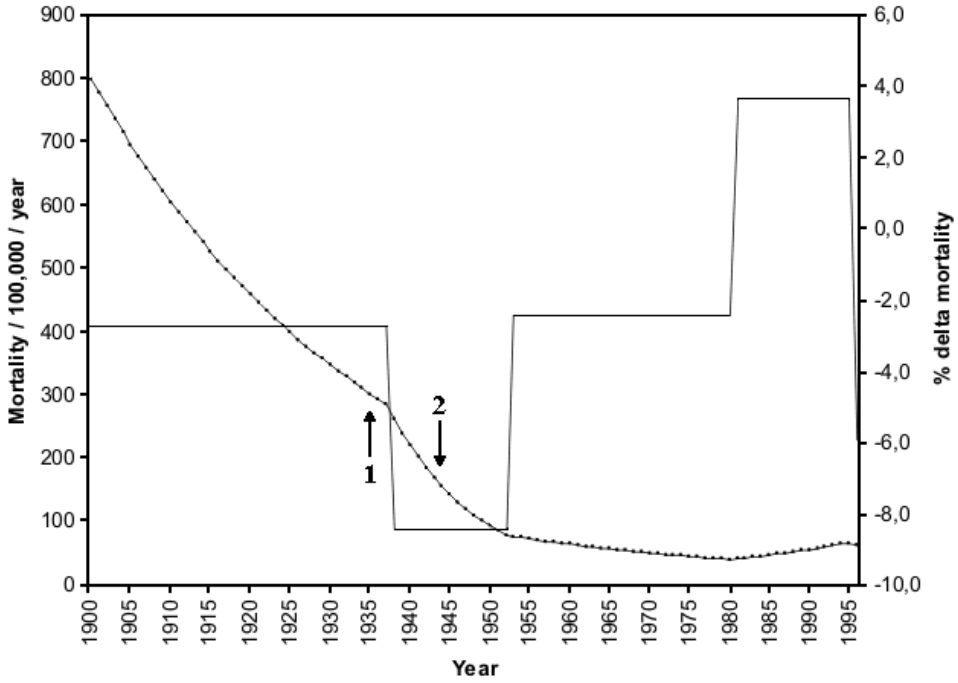
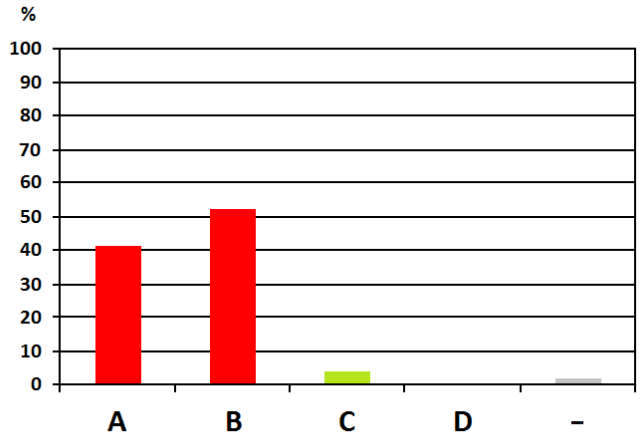


Figure 4 - Overall trends in infectious disease mortality rate and per cent variation of mortality rate in the USA from 1900 to 1996 [Armstrong et al., 1999]. The episodic strong increase of mortality due to 1918 influenza pandemic has been disregarded. Sulphonamides were released in 1935 (arrow 1) and the beginning of clinical use of penicillin was in 1943 (arrow 2) but there is no clear effect of their use on mortality rates.

Question 10) About 300 species of worms parasite for the man are known and there are many diseases caused by them. Worm infestations ...:
Answers:
A) are opposed effectively by appropriate antibiotics (vancomycin, macrolides and spiramycin, in particular) together with appropriate dietetic measures and, in some cases, laxatives and surgical remedies (e.g., in the case of hydatid cysts);
B) must be always opposed as causes of dangerous diseases and because compromise normal somatic and psychic development;
C) only in some cases must be opposed as they are useful for normal somatic development and for health;
D) are effectively opposed with drastic laxatives together with strong doses of orally administered sulphamides;

Table 10
Answers obtained:
A = 20 (41,66%);
B = 25 (52,08%);
C = 2 (4,16%);
D = 0 (0%);
No answer = 1 (2,08%);
Tot. = 48 (100%);

ECRA = 25%



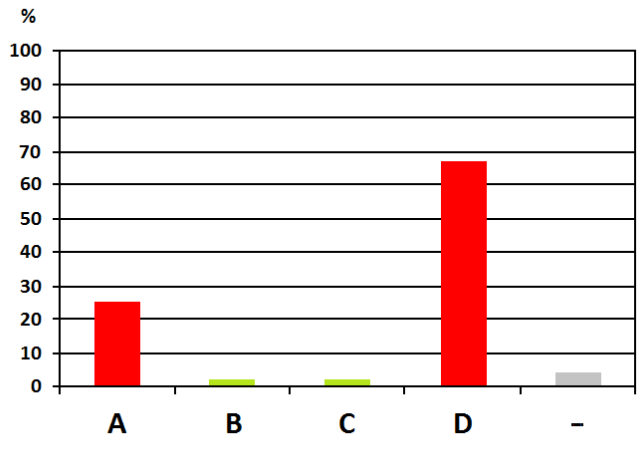
Correct answer: C
According to “hygiene hypothesis”, children exposed to viruses, bacteria and parasitic worms are protected against the onset of atopic diseases [von Mutius, 2002] and allergies [Cooper, 2004].
In general, in the western world, worm infestations do not cause severe troubles and rather result indispensable for a correct development of the immunologic system because our species has coevolved with the practically constant presence of worm infestations.
An example: “The most successful human helminth of the western world is the pinworm *Enterobius vermicularis*, and some 50% of young children in Europe and North America may have been infested around the middle of the twentieth century. Pinworms are benign, usually asymptomatic, and may have immunomodulatory properties that protect against the development of immune-mediated disorders including diabetes and asthma. Their decline in response to improved living conditions might explain a number of features of the epidemiology of childhood atopy and diabetes.” [Gale, 2002]
In particular, some intestinal worms secrete chemicals that suppress the immune system to prevent the host from attacking the parasite [Carvalho et al., 2006]. Without these substances, the immune system becomes oversensitive and unbalanced [Yazdanbakhsh et al., 2002].
Modern mass worm disinfestation has altered the delicate balance between our species and worms, causing serious autoimmune diseases. At present, some therapeutic techniques in experimentation try to treat autoimmune diseases modulating the

immunologic system with the deliberate infestation of sick subjects with a parasitic worm. “Helminthic therapy” seems a promising treatment for allergies [Falcone and Pritchard, 2005] and for several autoimmune diseases, as Crohn's disease [Hunter et al., 2004; Summers et al., 2005; Croese et al., 2006], allergic asthma [Falcone and Pritchard, 2005; Leonardi-Bee et al., 2006], multiple sclerosis [Correale and Farez, 2006], rheumatoid arthritis [Osada et al., 2008], etc., whose increasing incidence is greater in industrialised countries in comparison with developing countries with less strict hygienic habits [Leonardi-Bee et al., 2006; Zaccone et al., 2006; Rosati, 2001; Silman and Pearson, 2002; Weinstock et al., 2004].
However, it is true that many types of worm infestations cause severe and deadly diseases, but, as possible evolutionary explanation, this is caused by great alterations of our ancestral ecological niche provoked by human actions, in particular in the case of high demographic densities with polluted rivers used for drinking. This means that the primary causes of worm infestations epidemics are serious alterations of the habitats or of lifestyles and not a mere consequence of the existence of parasitic worms.
Consequently, only answer C is acceptable, but it should be supplemented with the necessity of the correction of altered habitats or lifestyles, where this is opportune.

Question 11) For the best definition of the normal parameters of the health conditions for man, which should be measured in the conditions when a population is on average in an optimal condition of health, it is necessary to consider (excluding subjects that are clinically sick or suffering from violent causes) a significant sample of the population ...:
Answers:
A) of the USA;
B) of the !Kung (Botswana);
C) of the Efé (Democratic Republic of the Congo);
D) of Todi, model town for the quality of life, and of towns similar in excellent quality of environment, food and lowest stress;

Table 11
Answers obtained:
A = 12 (25%);
B = 1 (2,08%);
C = 1 (2,08%);
D = 32 (66,66%);
No answer = 2 (4,16%);
Tot. = 48 (100%);

ECRA = 50%



Correct answers: B and C
The genes of our species are adapted to Paleolithic-like conditions of life, that is of hunter-gatherer populations, and only partially to conditions of more recent ages (e.g., use of dairy products for some populations as a consequence of cattle-breeding and use of milk; use of starchy food as a consequence of agriculture developed by Neolithic populations; etc.) [Eaton, Shostak and Konner, 1988]. Only few populations of the

modern age live according to life conditions analogous to those of the Paleolith (e.g., the !Kung of Botswana, the Efé of the Democratic Republic of Congo, and few other populations [Eaton, Konner and Shostak, 1988]). Because of evolutionary mechanisms, the best health state should be found in life conditions analogous to those for which our genes are adapted and, in fact, among the !Kung and the Efé diseases as diabetes, hypertension, atherosclerotic diseases, caries, constipation and its complications, appendicitis, myopia, astigmatism, most types of cancer and of mental diseases, etc. are exceptional or practically inexistent [Eaton, Konner and Shostak, 1988]. Consequently, in such populations the normal or optimal values of all vital parameters must be measured (Answer B and C are correct) and not in populations as those of the USA living in conditions that are largely different from those that are the best for our genes. Therefore, answer A is wrong as (although less) answer D.

Question 12) Our species is afflicted by a great number of cancer types, with an increasing morbidity in the last decades because of the greater life span, and has been defined as "especially vulnerable" to cancer (Mel Greaves, 2008) in comparison with other animal species.

Answers:

A) It is not true that our species is particularly vulnerable to cancer;

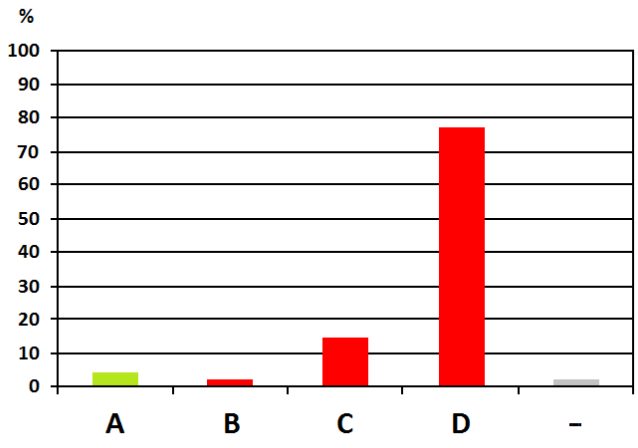
B) It is true that our species is particularly vulnerable to cancer, as widely proved by statistics beyond any reasonable doubt;

C) The vulnerability of our species to cancer is a probable consequence of our considerable longevity. Other species with considerable longevity (e.g., certain species of Rockfish that reach 100 years of age) show similar cancer frequencies in older individuals;

D) It is true that our species is particularly vulnerable to cancer, but minimising with appropriate preventive measures the cases of cancer caused by polluting substances, environmental factors, bad life habits (e.g., smoke) cancer incidence could be reduced by about 70%;

Table 12
Answers obtained:
A = 2 (4,16%);
B = 1 (2,08%);
C = 7 (14,58%);
D = 37 (77,08%);
No answer = 1 (2,08%);
Tot. = 48 (100%);

ECRA = 25%



Correct answer: A

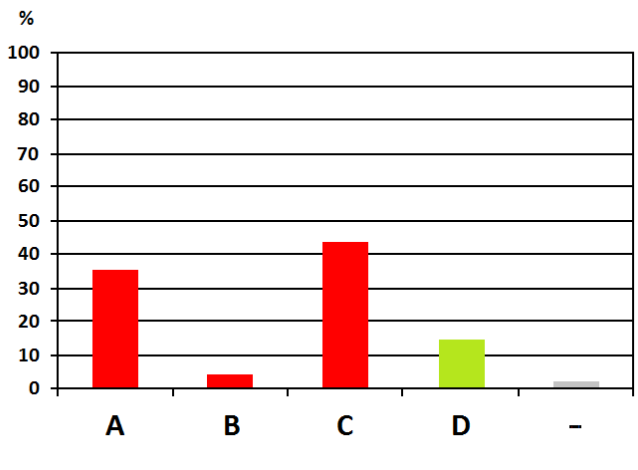
There are species with considerable longevity in natural conditions that show mortality rates not increasing with age ("animals with negligible senescence", e.g., some species of Rockfish with a longevity in wild of 100 years [Finch, 1990; Finch and Austad, 2001]) and therefore cannot have an age-related increment of mortality rate for cancer

[Libertini, 2008]. This demonstrates that cancer mortality is not necessarily in function of age (Answer C is wrong).
In the comparison of human populations living in modern conditions with populations of animal species that live in natural (or natural-like) conditions, the documented result is that our species is afflicted by many types of cancer while wild animal species seem to be almost exempt [Greaves, 2008]. This can create the impression that our species is particularly vulnerable to cancer [Greaves, 2008]. But, in the comparison of human populations living in Paleolithic-like conditions (e.g., !Kung of Botswana, Hadza in Tanzania, etc. [Trevathan et al., 2008, introduction]) with animal species reared in particular conditions, analogous to those of our species in civilised conditions, the opposite is documented: the above-said human populations are nearly exempt from cancer [Eaton, Konner and Shostak, 1988], a phenomenon not due to short life expectancy as more than 8% of individuals exceed 60 years of age [Blurton Jones et al., 2002], whereas reared animals show many cancer types [Greaves, 2008]. Greaves observes that for our species at least 90% of the cancers are caused not by genetic inheritance but by deliberate choices about diet and lifestyle [Greaves, 2000]. Populations living in Paleolithic-like conditions for which our genes are adapted and showing "near-absence of cancer" [Trevathan et al., 2008, introduction] demonstrate that cancers are caused almost exclusively by diets and lifestyles modified in comparison with those to which our genes are adapted.
All this proves that alterations of the ecological niche to which the species is not adapted is the primary condition causing cancer and not a specific genetic vulnerability to cancer of our (or of other) species. Therefore, the answer B is false and the answer D underestimates the importance of the alterations of our ecological niche, while the right answer is A.

Question 13) An accurate hygiene and a careful and continuous cleaning of all the rooms of daily life is ...:
Answers:
A) one of the few achievements of the civilisation that has determined only advantages for the health;
B) a sure way to cause many diseases, without any advantage;
C) a sure way to prevent many diseases, without any disadvantage;
D) a sure way to cause many diseases and to prevent many other diseases;

Table 13
Answers obtained:
A = 17 (35,41%);
B = 2 (4,16%);
C = 21 (43,75%);
D = 7 (14,58%);
No answer = 1 (2,08%);
Tot. = 48 (100%);

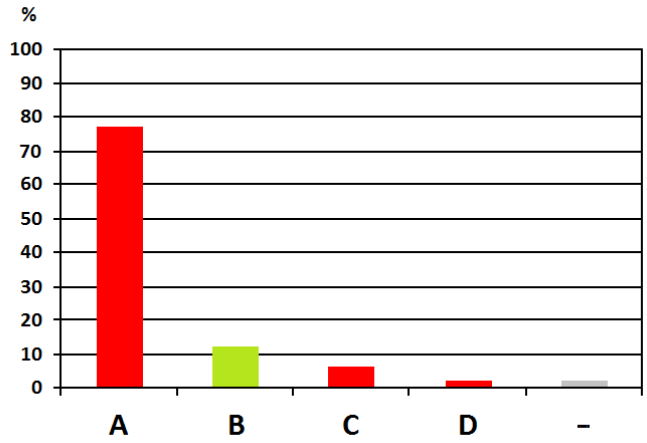
ECRA = 25%



Correct answer: D

Comparing modern hygienic conditions with those of the previous last centuries, a huge improvement with consequent reduction of mortality due to infectious diseases is unquestionable. However, the correct term of comparison is not the dreadful urban conditions of the seventeenth or eighteenth centuries but the Paleolithic conditions to which our genes are adapted [Eaton, Shostak and Konner, 1988; Williams and Nesse, 1991; Nesse and Williams, 1994].
According to "hygiene hypothesis", alterations of exposure modalities, especially in childhood, to infectious agents, symbiotic microorganisms, as gut and skin flora, and parasites, jeopardize the correct development and modulation of the immune system [Strachan, 2000; Gale, 2002; Bach, 2002; Bufford and Gern, 2005].
"Epidemiologic data provide strong evidence of a steady rise in the incidence of allergic and autoimmune diseases in developed countries over the past three decades. The incidence of many diseases of these two general types has increased: asthma, rhinitis, and atopic dermatitis, representing allergic diseases, and multiple sclerosis, insulin-dependent diabetes mellitus (type 1 diabetes) - particularly in young children - and Crohn's disease, representing autoimmune diseases." [Bach, 2002]
"Western countries are being confronted with a disturbing increase in the incidence of most immune disorders, including autoimmune and allergic diseases, inflammatory bowel diseases, and some lymphocyte malignancies. Converging epidemiological evidence indicates that this increase is linked to improvement of the socio-economic level of these countries, posing the question of the causal relationship and more precisely the nature of the link. Epidemiological and clinical data support the hygiene hypothesis according to which the decrease of infections observed over the last three decades is the main cause of the incessant increase in immune disorders." [Bach, 2005]
The modern extreme hygiene does not allow a correct development of the immunologic system and provokes an increasing incidence of allergic [Leonardi-Bee et al., 2006] and autoimmune diseases, sometimes severe and deadly as type 1 diabetes or juvenile diabetes [Silink, 2002], rheumatoid arthritis [Silman and Pearson, 2002], ulcerative colitis and Crohn's disease [Weinstock et al., 2004], multiple sclerosis [Rosati, 2001], etc., which are practically nonexistent in ancestral conditions [Eaton, Shostak and Konner, 1988] while in modern populations are often combined (e.g., thyroiditis and type 1 diabetes [Huber et al., 2008]; celiac disease and autoimmune thyroiditis, type 1 diabetes, autoimmune liver diseases, inflammatory bowel disease [Ch'ng et al., 2007]; type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and Crohn's disease [Zaccone et al., 2006]).
Consequently, answer D is correct, while B and C are incomplete and A is surely false and misleading.

Question 14) The great infective epidemics of the previous centuries were ...:
Answers:
A) a consequence of the almost total absence of medical cures and by the inexistence of antibiotics, antiviral drugs and vaccines;
B) an indirect consequence of the introduction of agriculture and of craftsmanlike and industrial technologies;
C) caused mainly by the arrival of deadly infections from America;
D) caused by the increasing pollution determined by craftsmanlike and industrial activities;

Table 14 Answers obtained: A = 37 (77,08%); B = 6 (12,5%); C = 3 (6,25%); D = 1 (2,08%); No answer = 1 (2,08%); Tot. = 48 (100%); ECRA = 25%	

Correct answer: B

Changes in human demographics and society, contamination of food sources or water supplies, changes in land use or agricultural practices are indicated among the main causes of infections and epidemics [Woolhouse and Gowtage-Sequeria, 2005].

The great epidemics of the previous centuries were caused by a huge increase of demographic density and by population gathering in urban centres without sewer systems and with water frequently infected. Frequency and harshness of the epidemics of the previous centuries fell drastically with the construction of sewer and water supply systems and with the improvement of economic and alimentary conditions before the discovery and the use of sulphamides and antibiotics. For example, in the USA, the mortality deriving from infectious diseases has fallen before the introduction of sulphamides and antibiotics [Armstrong et al., 1999]. Smallpox vaccine has been one of the few great exceptions of a medical treatment that has had effectiveness and importance before the origin of modern medicine [Hopkins, 2002]. Consequently, answer A is false. With the discovery of America many dangerous infections (e.g., smallpox, measles, influenza, pertussis, parotitis, diphtheria, etc.) were transferred from the populations of the Old World (which were partially adapted to them for the dreadful epidemics endured in the previous centuries) to the populations of the New World that had no evolutionary experience about them and so sustained devastating and mortal epidemics [McNeill, 1976; Meltzer, 1992]. The opposite happened only for syphilis that became after Colombo a heavy scourge for European populations [McNeill, 1976] (Answer C is false).

The increasing pollution caused by craftsmanlike and industrial activities may have contributed somehow to historically more recent epidemics, but cannot have caused preceding epidemics (Answer D is false).

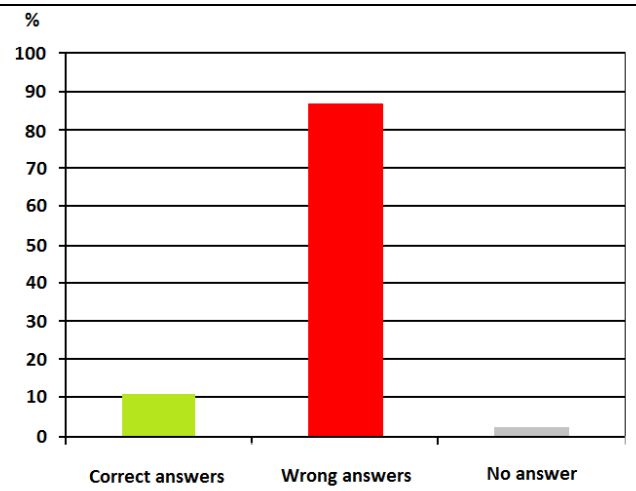
The introduction of agriculture and of craftsmanlike and industrial technologies, from Neolithic age on, has allowed an increasing demographic growth and, in parallel, the origin of greater and greater urban centres. These conditions are the requirement and the real or primary cause of infective epidemics of the past and present time. Therefore, the correct answer is B.

Overall results

The correct answers were only 11,16% and this low result should be assessed by considering that the value of the expected correct random answers (30,36%) was almost triple!

Answers obtained:
Correct answers = 75 (11,16%)
Wrong answers = 582 (86,61%)
No answer = 15 (2,23%)
Tot. = 672 (100%)

ECRA = 30,36%



Only for two questions (1 and 6) the percentage of correct answers was greater than ECRA (29,16% and 45,83%, respectively). But, the relatively high number of correct answers to question 6 (Is evolutionism useful to practical medicine?) was in contradiction with the other answers expressed where possible indications of Evolutionary Medicine were disregarded or contradicted.
The small number of correct answers to most question (3, 4, 5, 7, 9, 10, 11, 12) was outstanding, in particular for the two questions (3 and 11) were two or more answers were correct.

Conclusion

The percentage of correct answers, which was greatly lower than ECRA, indicates not only that in the medical field there is crass ignorance of Evolutionary Medicine, but also that there are deep-rooted prejudices against its basic concepts.
The confusion between primary and secondary or proximate causes of diseases, the ignorance of the concept of mismatch between our adaptation and current lifestyles and ecological conditions, the thaumaturgic qualities attributed to antibiotics and similar substances are some examples of this ignorance and of the related prejudices.
Unfortunately, the ignorance of the principles of Evolutionary Medicine is not just a problem of insufficient scientific knowledge, but something that has very serious consequences for the organization of health systems and for the prevention and treatment of diseases. The difference between knowing and not knowing Evolutionary Medicine is not a problem of higher or lower academic scores for health professionals, but a difference that is measured in a countless number of preventable diseases and deaths.
It is absurd that malpractice cases, in which single individuals die or get worse, arouse a great deal of interest while there is a news blackout about the ignorance of the medical world of the principles of Evolutionary Medicine, a giant malpractice case with serious consequences for the health of billion people.

References

Armstrong, G.L., Conn, L.A. and Pinner, R.W., 1999. Trends in infectious disease mortality in the United States during the 20th century. *JAMA* 281, 61-6.

Bach, J.F., 2002. The effect of infections on susceptibility to autoimmune and allergic diseases. *N. Engl. J. Med.* 347, 911-20.

Bach, J.F., 2005. Infections and autoimmune diseases. *J Autoimmun.* 25, S74-80.

Barry, D.M. and Reeve, A.W., 1977. Increased incidence of gram-negative neonatal sepsis with intramuscula iron administration. *Pediatrics*. 60, 908-12.

Bergstrom, C.T. and Feldgarden, M., 2008. The ecology and evolution of antibiotic-resistant bacteria. In: Stearns, SC & Koella, JC (eds) *Evolution in health and disease* (2nd ed.). Oxford University Press, Oxford (UK).

Blurton Jones, N.G., Hawkes, K. and O'Connell, J.F., 2002. Antiquity of postreproductive life: are there modern impacts on hunter-gatherer postreproductive life spans? *Am. J. Hum. Biol.* 14, 184-205.

Bufford, J.D. and Gern, J.E., 2005. The hygiene hypothesis revisited. *Immunol. Allergy Clin. North Am.* 25, 247-62.

Carvalho, E.M., Bastos, L.S. and Araújo, M.I., 2006. Worms and allergy. *Parasite Immunol.* 28, 525-34.

Chow, Y.C., Dhillon, B., Chew, P.T. and Chew, S.J., 1990. Refractive errors in Singapore medical students. *Singapore Med. J.* 31, 472–3.

Ch'ng, C.L., Jones, M.K. and Kingham, J.G.C., 2007. Celiac disease and autoimmune thyroid disease. *Clin. Med. Res.* 5, 184-92.

Cooper, P.J., 2004. Intestinal worms and human allergy. *Parasite Immunol.* 26, 455–67.

Correale, J. and Farez, M., 2007. Association between parasite infection and immune responses in multiple sclerosis. *Ann. Neurol.* 61, 97–108.

Croese, J., O'Neil, J., Masson, J., Cooke, S., Melrose, W., Pritchard, D. and Speare, R., 2006. A proof of concept study establishing *Necator americanus* in Crohn's patients and reservoir donors. *Gut* 55, 136–7.

Davison, F. and Nair, V., 2004. *Marek's disease. An evolving problem.* Elsevier Academic Press, London (UK).

Davison, F. and Nair, V., 2005. Use of Marek's disease vaccines: could they be driving the virus to increasing virulence? *Expert Rev. Vaccines* 4, 77-88.

Dejkhamron, P., Menon, R.K. and Sperling, M.A., 2007. Childhood diabetes mellitus: Recent advances & future prospects. *Indian J. Med. Res.* 125, 231-50.

Denic, S. and Agarwal, M.M., 2007. Nutritional iron deficiency: an evolutionary perspective. *Nutrition* 23, 603-14.

Devendra, D., Liu, E. and Eisenbarth, G.S., 2004. Type 1 diabetes: recent developments, *BMJ* 328, 750-4.

Dirani, M., Tong, L., Gazzard, G., Zhang, X., Chia, A., Young, T.L., Rose, K.A., Mitchell, P. and Saw, S.M., 2009. Outdoor activity and myopia in Singapore teenage children. *Br. J. Ophthalmol*. 93, 997-1000.

Dobzhansky, T., 1973. Nothing in biology makes sense except in the light of evolution. *Am. Biol. Teach.* 35, 125-9.

Doherty, C.P., 2007. Host-pathogen interactions: the role of iron. *J. Nutr.* 137, 1341-4.

Eaton, S.B., Konner, M. and Shostak, M, 1988. Stone agers in the fast lane: chronic degenerative diseases in evolutionary perspective. *Am. J. Med.* 84, 739-49.

Eaton, S.B., Shostak, M. and Konner, M., 1988. The paleolithic prescription: a program of diet & exercise and a design for living. Harper & Row, New York (USA).

Falcone, F.H. and Pritchard, D.I., 2005. Parasite role reversal: worms on trial. *Trends Parasitol.* 21, 157-60.

Feillet, H. and Bach, J.F., 2004. On the mechanisms of the protective effect of infections on type 1 diabetes. *Clin. Devel. Immun.* 11, 191–4.

Finch, C.E., 1990. *Longevity, Senescence, and the Genome*. The University of Chicago Press, Chicago (USA).

Finch, C.E. and Austad, S.N., 2001. History and prospects: symposium on organisms with slow aging. *Exp. Gerontol.* 36, 593-7.

Fitzsimons, D., François, G., Hall, A., McMahon, B., Meheus, A., Zanetti, A., Duval, B., Jilg, W., Böcher, W.O., Lu, S.N., Akarca, U., Lavanchy, D., Goldstein, S., Banatvala, J. and Damme, P.V., 2005. Long-term efficacy of hepatitis B vaccine, booster policy, and impact of hepatitis B virus mutants. *Vaccine* 23, 4158-66.

Flaxman, S.M. and Sherman, P.W., 2000. Morning sickness: a mechanism for protecting mother and embryo. *Q. Rev. Biol.* 75, 113-48.

François, G., Kew, M., Van Damme, P., Mphahlele, M.J. and Meheus A., 2001. Mutant hepatitis B viruses: a matter of academic interest only or a problem with far-reaching implications? *Vaccine* 19, 3799-815.

Fredrick, D.R., 2001. Myopia: was mother right about reading in the dark? *Br. J. Ophthalmol*. 85, 509-10.

Fredrick, D.R., 2002. Myopia. *BMJ*. 324, 1195-99.

Gale, E.A.M., 2002. A missing link in the hygiene hypothesis? *Diabetologia* 45, 588–94.

Generaux, D. and Bergstrom, C.T., 2005. Evolution in action: understanding antibiotic resistance. In: Cracraft, J. and Bybee, R.W. (eds) *Evolutionary Science and Society: Educating a New Generation*. AIBS/BCSC, Washington, DC.

Greaves, M.F., 2000. *Cancer: The Evolutionary Legacy*. Oxford University Press, Oxford (UK).

Greaves, M., 2008. Cancer: evolutionary origins of vulnerability. In: Stearns, C.S. and Koella, J.C. (eds) *Evolution in health and disease* (2nd ed.). Oxford University Press, Oxford (UK).

Hopkins, D.R., 2002. *The Greatest Killer: Smallpox in History*. The University of Chicago Press, Chicago (USA).

Hsu, H.Y., Chang, M.H., Ni, Y.H. and Chen H.L., 2004. Survey of hepatitis B surface variant infection in children 15 years after a nationwide vaccination programme in Taiwan. *Gut* 53, 1499-503.

Huber, A., Menconi, F., Corathers, S., Jacobson, E.M. and Tomer, Y., 2008. Joint genetic susceptibility to type 1 diabetes and autoimmune thyroiditis: from epidemiology to mechanisms. *Endocr. Rev.* 29, 697-725.

Hunter, M.M. and McKay, D.M., 2004. Review article: helminths as therapeutic agents for inflammatory bowel disease. *Aliment. Pharmacol. Ther.* 19, 167-77.

Iannotti, L.L., Tielsch, J.M., Black, M.M. and Black, R.E., 2006. Iron supplementation in early childhood: health benefits and risks. *Am. J. Clin. Nutr*. 84, 1261-76.

Kabyemela, E.R., Fried, M., Kurtis, J.D., Mutabingwa, T.K. and Duffy, P.E., 2008. Decreased susceptibility to *Plasmodium falciparum* infection in pregnant women with iron deficiency. *J. Infect. Dis.* 198, 163-6.

Kee, C.S. and Deng, L., 2008. Astigmatism associated with experimentally induced myopia or hyperopia in chickens. *Invest. Ophthalmol. Vis. Sci*. 49, 858-67.

Leonardi-Bee, J., Pritchard, D. and Britton, J., 2006. Asthma and current intestinal parasite infection: systematic review and meta-analysis. *Amer. J. Resp. Crit. Care Med.* 174, 512–23.

Libertini, G., 1983. *Ragionamenti Evoluzionistici*, Società Editrice Napoletana, Naples (Italy); [English edition:] 2011. *Evolutionary Arguments on Aging, Disease and Other Topics*, Azinet Press (USA).

Libertini, G., 2008. Empirical evidence for various evolutionary hypotheses on species demonstrating increasing mortality with increasing chronological age in the wild. *TheScientificWorldJOURNAL* 8, 182-93 DOI 10.1100/tsw.2008.36.

McNeill, W.H., 1976. *Plagues and Peoples*. Garden City, New York (USA).

Meltzer, D.J., 1992. How Columbus sickened the New World. *New Scientist* 136, 38-41.

Nesse, R.M. and Williams, G.C., 1994. *Why we get sick*. Times Books, New York (USA).

Oppenheimer, S.J., 2001. Iron and its relation to immunity and infectious disease. *J. Nutr.* 131, S616-33.

Osada, Y., Shimizu, S., Kumagai, T., Yamada, S. and Kanazawa, T., 2009. *Schistosoma mansoni* infection reduces severity of collagen-induced arthritis via down-regulation of pro-inflammatory mediators. *Int. J. Parasitol.* 39, 457-64.

Prentice, A.M., Ghattas, H., Doherty, C. and Cox, S.E., 2007. Iron metabolism and malaria. *Food Nutr. Bull*. 28, S524-39.

Price, W.A., 1939. *Nutrition and Physical Degeneration*. Paul B. Hoeber, New York – London.

Profet, M., 1992. Pregnancy sickness as adaptation: A deterrent to maternal ingestion of teratogens. In Barkow, J., Cosmides, L. and Tooby, J. (eds.), *The adapted mind*. Oxford University Press, Oxford (UK).

Read, A.F. and Mackinnon, M.J., 2008. Pathogen evolution in a vaccinated world. In: Stearns, S.C. and Koella, J.C. (eds) *Evolution in health and disease* (2nd ed.). Oxford University Press, Oxford (UK).

Richards, M.P., 2002. A brief review of the archaeological evidence for Palaeolithic and Neolithic subsistence. *Europ. J. Clin. Nutr.*, 56, 1262-78.

Rogers, A.H. (ed.), 2008. *Molecular Oral Microbiology*. Caister Academic Press, Adelaide (Australia).
Rosati, G., 2001. The prevalence of multiple sclerosis in the world: an update. *Neurol. Sci.* 22, 117-39.
Rose, K.A., Morgan, I.G., Ip, J., Kifley, A., Huynh, S., Smith, W., and Mitchell, P., 2008a. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmol.* 115, 1279-85.
Rose, K.A., Morgan, I.G., Smith, W., Burlutsky, G., Mitchell, P., and Saw, S.M., 2008b. Myopia, lifestyle, and schooling in students of Chinese ethnicity in Singapore and Sydney. *Arch. Ophthalmol.* 126, 527-30.
Saw, S.M., Katz, J., Schein, O.D., Chew, S.J. and Chan, T.K., 1996. Epidemiology of myopia. *Epidemiol. Rev.* 18, 175-87.
Silink, M., 2002. Childhood diabetes: a global perspective. *Horm. Res.* 57, S1-5.
Silman, A.J. and Pearson J.E., 2002. Epidemiology and genetics of rheumatoid arthritis. *Arthritis Res.* 4, S265-72.
Stearns, S.C. and Koella, J.C. (eds), 2008. *Evolution in health and disease* (2nd ed.). Oxford University Press, Oxford (UK,.
Strachan, D.P., 2000. Family size, infection and atopy: the first decade of the "hygiene hypothesis". *Thorax* 55, S2-10.
Summers, R.W., Elliott, D.E., Urban, J.F. Jr, Thompson, R. and Weinstock, J.V., 2005. *Trichuris suis* therapy in Crohn's disease. *Gut* 54, 87–90.
Trevathan, W.R., Smith, E.O. and McKenna, J.J. (eds), 1999. *Evolutionary Medicine.* Oxford University Press, New York (USA).
Trevathan, W.R., Smith, E.O. and McKenna, J.J. (eds), 2008. Evolutionary Medicine: new perspectives. Oxford University Press, New York (USA).
Trevathan, W.R., Smith, E.O. and McKenna, J.J., 2008. Introduction and overview of Evolutionary Medicine. In: Trevathan, W.R., Smith, E.O. and McKenna, J.J. (eds) Evolutionary Medicine: new perspectives. Oxford University Press, New York (USA).
Truswell, A.S., Kennelly, B.M., Hansen, J.D. and Lee, R.B., 1972. Blood pressure of !Kung bushmen in northern Botswana. *Am. Heart J.* 84, 5-12.
Verlee, D.L., 1968. Ophthalmic survey in the Solomon Islands. *Am. J. Ophthalmol.* 66, 304-19.
Virally, M., Blicklé, J.F., Girard, J., Halimi, S., Simon, D. and Guillausseau, P.J., 2007. Type 2 diabetes mellitus: epidemiology, pathophysiology, unmet needs and therapeutical perspectives. *Diabetes Metab*. 33, 231-44.
von Mutius, E., 2002. Environmental factors influencing the development and progression of pediatric asthma. *J. Allergy Clin. Immunol.* 109, S525–32.
Weinstock, J.V., Summers, R. and Elliott, D.E., 2004. Helminths and harmony. *Gut* 53, 7-9.
Wild, S., Roglic, G., Green, A., Sicree, R. and King, H., 2004. Global prevalence of diabetes estimates for the year 2000 and projections for 2030. *Diabetes Care* 27, 1047-53.
Williams, G.C. and Nesse, R.M., 1991. The dawn of Darwinian medicine. *Quart. Rev. Biol*. 66, 1-22.
Witter, R.L., 2001. Protective efficacy of Marek's disease vaccines. *Curr. Top. Microbiol. Immunol.* 255, 57-90.
Wong, T.Y., Foster, P.J., Hee, J., Ng, T.P., Tielsch, J.M., Chew, S.J., Johnson, G.J. and Seah, S.K., 2000. Prevalence and risk factors for refractive errors in an adult Chinese population in Singapore. *Invest. Ophthalmol. Vis. Sci*. 41, 2486-94.
Woolhouse, M.E.J. and Gowtage-Sequeria, S.G., 2005. Host range and emerging and reemerging pathogens *Emerg. Infect. Dis.* 11, 1842-7.
Yazdanbakhsh, M., Kremsner, P.G. and van Ree, R., 2002. Allergy, parasites, and the hygiene hypothesis. *Science* 296, 490-4.
Young, F.A., Leary, G.A. and Baldwin, G.R., 1969. The transmission of refractive errors within Eskimo families. *Am. J. Optom. Physiol. Optics* 46, 676-85.
Zaccone, P., Fehervari, Z., Phillips, J.M., Dunne, D.W. and Cooke, A., 2006. Parasitic worms and inflammatory diseases. *Parasite Immunol.* 28, 515-23.