Rheumatoid Arthritis: put down the steak.

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Liberal Arts

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Abstract

A study of the differences of prevalence rates for rheumatoid arthritis in different countries which may reveal that there is an environmental factor that causes it. Data shows that there is a difference in prevalence rate from rural to urban populations. An urban population of a similar genetic background shows an increase in the prevalence rate of rheumatoid arthritis from its rural counterpart. Examples of this are shown among the Pakistanis, Spaniards, and Africans. Although many factors differ between rural and urban populations that could affect the prevalence rate of rheumatoid arthritis, diet may be a leading factor. A change in diet to a more westernized diet may be the environmental factor that increases an individual's susceptibility to rheumatoid arthritis. This study seeks to suggest that there is correlation between diet and rheumatoid arthritis.

I.Introduction

A diagnosis of rheumatoid arthritis is life altering, especially if it is severe. Rheumatoid arthritis impacts people all around the globe differently. It affects both men and women, children and adults. Life becomes defined by intermittent pain and possibility of disability. Rheumatoid arthritis can be the cause of giving up dreams and ambitions or of changing those dreams and ambitions to accommodate the disease.

Lack of mobility and weakness, stiffness and inflammation, all of the precursors to the joint deterioration that helps to define the disease, soon start to define the lives of the patients who fall ill from rheumatoid arthritis. The change in the health of the people who fall ill is dramatic. One man tells of pain so severe that he went to an emergency room only to be referred to a rheumatologist. Once at the rheumatologist's office, he was told he had to give up his dream, his hobby, and his career of being a discus player ("Patient Voices: Rheumatoid Arthritis." 2009). Rheumatoid arthritis has no cure; it is a disease of management. Medical intervention does not stop the disease; one just simply has it for life. Rheumatoid arthritis is of unknown origin and since we do not know specifically how it manifests, prevention is not an option. The accepted hypothesis behind the manifestation of Rheumatoid arthritis, RA, is that one must be genetically predisposed to it and come into contact with an environmental factor for the disease to manifest. The main risk factor is thought to be the HLA DRB1 alleles in combination with some environmental trigger. Infection, viruses, hormones, or bacteria are some of the identified potential triggers, but this hypothesis is still inconclusive (Silman & Pearson, 2002).

The HLA DRB1 alleles are thought to be the main risk factor of RA; these alleles are also linked to Sporadic Parkinson's in the Chinese population, leprosy in the Indonesian population,

recurrent unexplained abortion in Japanese populations, among other diseases (Sun et al., 2012, Takakuwa et al., 2003). Some of the DRB alleles are thought to play a key role in susceptibility to rheumatoid arthritis while other DRB alleles may provide protection against the disease (Sandoughi, Fazaeli; Bardestani, & Hashemi, 2011). The strongest support for an association between genes and RA comes from the major histocompatibility complex region, the MHC region. A certain sequence of the HLA-DRB1 alleles including 0101, 0102, 0401, 0404, 0405, and 0408 is observed in disease populations; this is referred to as the 'shared epitope hypothesis' (Silman, 1994). This sequence is found in nearly 50% of European populations. Silman (1994) states that "Clearly this sequence on its own is not sufficient for the development of Rheumatoid Arthritis. Further, depending on the series between 15% and 20% of confirmed patients do not possess this sequence, and thus it is not necessary for disease development." This makes it evident that the disease has a multifactorial nature and possibly that genetics and rheumatoid arthritis have a spurious relationship.

Prevalence rates of rheumatoid arthritis are different among the same genetic populations living in different areas and in different sub-cultures. By looking at populations of similar genetic make-up, genetic variance can be made an independent variable and other factors can be researched and measured. As populations move from less-developed nations to more developed, or from rural populations to urban, diet starts to differ from a culturally traditional diet to a more protein-heavy westernized diet (Silman & Pearson 2002). Diet may be linked to the increase in the incidence and prevalence rates of rheumatoid arthritis in urban populations and therefore may be key to its manifestation.

II.Rheumatoid Arthritis

Rheumatoid arthritis is a systemic auto-immune disease that affects people around the globe with differing severity (Mathers & Pfleger, 2006). The immune system mistakenly attacks healthy tissue causing pain, swelling, and deformity as well as permanent destruction. It systematically inflames the lining of multiple joints and can also affect all the systems of the body. Rheumatoid arthritis is a chronic polyarthritis, meaning it affects five or more joints (“Rheumatoid Arthritis,” 2011). It often starts in the small joints of the hands and feet before moving on to larger joints such as hips and knees. This symmetric disease affects the right and left side simultaneously. It has many symptoms, some of them seemingly vague like malaise, fatigue, muscle soreness, weakness, fever and some more pronounced like pain, stiffness, deformity, swelling, redness, loss of mobility, and a decrease in quality and length of life (“Rheumatoid Arthritis,” 2011; Mathers & Pfleger 2006). Rheumatoid arthritis can also lead to other diseases and illnesses. Some comorbid conditions associated with RA are anemia, osteoporosis, bacterial infections, lymphoma, myocardial infarction, heart failure, cerebrovascular accident, depression, and skin cancer. This list does not include the issues, symptoms, or conditions caused by or associated with treatment of rheumatoid arthritis (Quolin III & Brent, 2010). Although, Rheumatoid arthritis has many symptoms and many associated conditions, it is difficult to diagnose because of the lack of a distinct clinical, laboratory, or radiological marker of the disease (Mathers & Pfleger, 2006).

Because it is often hard to diagnose RA because of the lack of a distinct marker, different criteria has been established by associations to help in the epidemiological study of rheumatoid arthritis. The original set of criteria is the 1987 revised American College of Rheumatology Criteria which was used prior to the newest 2010 criteria. The original criteria was made in 1958

and revised in 1987. The 1987 criteria was used before the majority of modern day technology which test certain aspects of the disease in a laboratory as well as by visible inspection. A comparison of the two tables below shows the slight differences in how RA was defined and diagnosed from 1958 until 2009 and from 2010-present. Rheumatoid arthritis was originally measured with the help of the 1958 table and/or the revisions completed in 1987. The use of different tables could have an impact on the perceived prevalence rate of RA since the criteria is more broad in the 1987 table such as the score for the amount of joint affected and CRP and ESR abnormalities (Van der Linden, Knevel, Huizinga, & van der Helm-van Mil, 2011).

Table 1.1

	1987 Criteria		**2010 Criteria**	
Criteria	Description	Score	Description	Score
Morning stiffness	In and around joints for at least one hour	1	Clinical synovitis/swelling in at least one joint not explained by another disease	NA
Joint Involvement	Physician observed soft tissue swelling or fluid in three of fourteen possible joints	1	One large joint Two to ten large joints One to three small joints(with or without large joint) Four to ten small joints (with or without large joint) >ten joints (at least one small joint)	0 1 2 3 5
Arthritis of hand joints	At least one swollen hand or wrist area	1	NA	NA

Symmetric arthritis	Simultaneous bilateral involvement	1	NA	NA
Rheumatoid Nodules	Subcutaneous nodules over bony prominences, extensor surfaces, or in juxtaarticular regions observed by physician	1	NA	NA
Serology	Positive RF serum test	1	Negative RF and negative ACPA Low positive RF and ACPA High Positive RF and ACPA	0 1 2
Radio graphic changes	Erosions or unequivocal bony decalcification in or adjacent to the involved joints, but not consistent with osteoarthritis	1	NA	NA
Acute phase reactants	CRP and ESR	NA	Normal CRP and ESR Abnormal CRP and ESR	0 1
Duration of symptoms	First for criteria must be present for more than six weeks	NA	<six weeks ≥six weeks	0 1
Criteria Score Required		≥4/7		≥6/10

ACPA stands for anti-citrullinated protein antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor; NA, not applicable

Figure: This table shows a comparison of the revised 1987 criteria on the left to the 2010 criteria on the right.

(Van der Linden et al., 2011)

III. Risk factors

The etiology of RA is still unknown but it is traditionally thought that one must be genetically predisposed to the condition and then be exposed to an environmental factor. An environmental factor is anything in an individual's environment that is hypothesized to cause rheumatoid arthritis ("Rheumatoid Arthritis," 2011). Besides the earlier mentioned HLA DRB1 alleles, a number of other products of the MHC region have been linked to rheumatoid arthritis: the corticotrophin releasing hormone, oestrogen synethase, IFN-γ and other cytokines (Silman & Pearson, 2002). The environmental factors fall into broad categories of virus, infection, bacteria, and hormones. Some of the viruses that are thought to cause rheumatoid arthritis are Epstein-Barr virus, parvovirus, and bacteria such as *Proteus* and *Mycoloplasma* (Buchanan, 1990). It has even been hypothesized that when Halley's Comet circled the earth in the late eighteenth century it sprayed the earth with a more virulent strain of a virus that led to the epidemic of rheumatoid arthritis over the last few centuries (Buchanan, 1990). Although rheumatoid arthritis is among the leading conditions causing disability, little about this debilitating disease is actually known (Helmick et al., 2008).

IV. History of Rheumatoid Arthritis

Many studies have shown that, if not a new disease, rheumatoid arthritis was relatively rare before the 1800's (Buchanan 1990). Little evidence of Rheumatoid arthritis has been found in ancient skeletal remains prior to the eighteen hundreds, but a few possible examples exist, one being one skeleton found among four hundred Saxon and Romano-British skeletons and one found among the four hundred and sixteen skeletal remains in a Roman

cemetery in Britain. That is a prevalence rate of .25 percent for the Saxon and Romano-British cemetery and .24 percent for the Roman cemetery, which does not take into account that these are the only possible examples that have been found thus far in the world for this time period. A possible reason that ancient remains have little evidence of Rheumatoid arthritis could be due to soil type and burial methods which may have an impact on the erosive lesions seen in RA patients being degraded. Even taking this into consideration, the evidence of historical cases is scarce. Even early medical literature lacks definite evidence of the disease, with very few cases being described before the seventeenth century (Buchanan 1990). The first written and reasonable account of rheumatoid arthritis was written by Thomas Sydenham in the seventeenth century (Short).

The lack of evidence of rheumatoid arthritis prior to the seventeenth century leads to questions about what has changed between then and now. Two things that began around that time period was the Agriculture Revolution and another was the Industrial Revolution. The nutritional and societal changes brought on by these revolutions could have begun an epidemic (Chambers & Mingay, 1966). These revolutions changed drastically the way in which *Homo sapiens sapiens* lived. The agriculture and industrial revolutions changed the way that nutrients were acquired and the way that humans labored; they changed the societies that humans had lived in for thousands of years (Chambers & Mingay, 1966).

V. Prevalence

Rheumatoid arthritis has different prevalence rates based upon sex, lifestyle, and age and it is not equally prevalent across the globe. Rheumatoid arthritis typically affects women approximately three times more frequently than men. It is not the later in life disease that the

majority of people assume that it is. Rheumatoid arthritis typically begins in the third to fifth decade of life but the onset can occur at any time in one's life ("Rheumatoid Arthritis," 2011).

A notable finding shows that in developed countries, the prevalence of RA is approximately 0.5 to 1% of the adult population (Helmick et al., 2008). In the United States, the prevalence rate is estimated at 1.07% for the adult population 18 years and older (Helmick et al., 2008). Rural communities and non-developed nations show less prevalence of rheumatoid arthritis which implicates differences between developed and non developed nations as well as rural and urban areas as potential risk factors to developing Rheumatoid arthritis. Mathers (2006) states that "A study in Soweto showed a prevalence of RA among urban blacks equivalent to that seen in white Europeans, while rural black groups have showed much lower prevalence." The population of Soweto in comparison to rural populations within the area shows a rural-urban drift in prevalence of rheumatoid arthritis, especially after the age of 50. After the age of 50, the prevalence of rheumatoid arthritis in Soweto increases from 0.9% to 3.8% where as the prevalence in rural communities in the area only increased to 0.8%, which is a startling difference. The population in Soweto has a prevalence that is 4.75 times greater than the prevalence rates in the nearby rural communities (McGill, 1991).

Another group of people showing an interesting prevalence of RA is Pakistanis living in the UK compared to those living in Pakistan. Pakistanis living in the UK have a higher prevalence rate than those living in their home country (Silman & Pearson, 2002). The prevalence of rheumatoid arthritis in Pakistanis living in the UK is 0.3% compared to the prevalence in Pakistanis living in Pakistan which is 0.14%. The UK population has nearly double the occurrence (Hameed & Gibson, 1997). This prevalence rate is still much smaller than the prevalence of the English population which is 1.6% (Mathers & Pfleger, 2006). Another

population of startling urban to rural divergence in prevalence of rheumatoid arthritis is Spain. The overall estimation for the country as a whole is 0.5% but there is a ratio of 4:1 urban to rural divergence (Caroma et al., 2002).

The prevalence of Rheumatoid arthritis in urban populations, in comparison to rural populations, is startling. The examples of the populations in the Soweto area, of Pakistanis, and of those in Spain show ratios of 4.75:1, 2:1, and 4:1 respectively. Such differences in prevalence rates may suggest that an environmental factor that is more often present in the urban areas causes an increase in the prevalence of rheumatoid arthritis. The chart below shows a visible representation and comparison of the differences in prevalence rates of rheumatoid arthritis by multiple countries and communities.

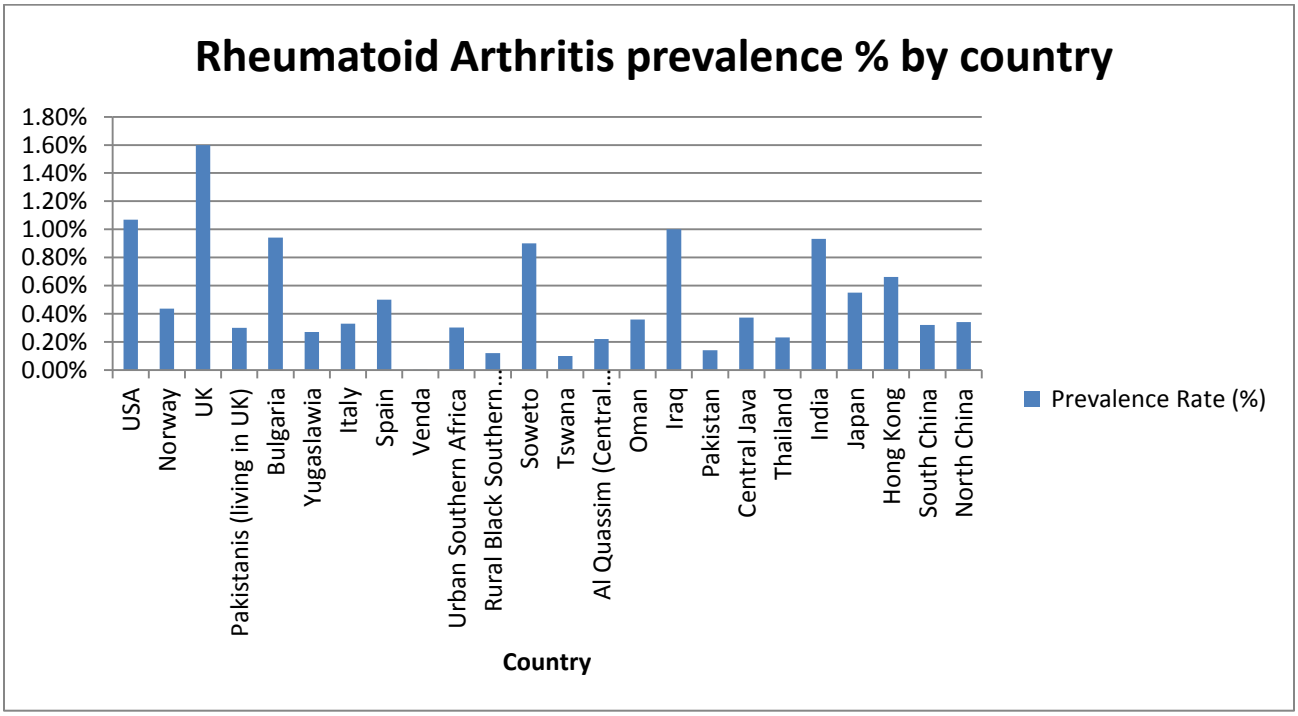

Figure 1. Rheumatoid Arthritis prevalence % by country. This figure shows countries with their corresponding prevalence percent to illustrate the differences in countries and rural/urban divides. The prevalence rate is done per 100,000 people.

(Brighton, de la Harpe, van Staden, Badenhorst, & Myers, 1988; Carmona et al., 2002; Hameed & Gibson, 1997; Mathers & Pfleger, 2006; McGill, 1991)

VI. The Effects of Nutrition on Auto-immune disease and specifically Rheumatoid Arthritis

Nutrition has been shown to adversely affect auto-immune diseases and the changes in diet occurring in the last few hundred years may be the cause of the seeming "outbreak" of rheumatoid arthritis (Buchanan, 1990). Buchanan (1990) also states that "Nutrition profoundly influences auto-immune diseases in animals, and a more nutritious diet, especially in terms of protein content, could conceivably modify the immune response to allow for the development of chronic arthritis. In pigs, a protein rich diet can lead to rheumatoid-like arthritis." Rabbits fed cow's milk also exhibit rheumatoid arthritis like symptoms (Buchanan, 1990). Westernized diets are very protein- and diary- centered. The change in diet as seen with these animals, between protein heavy and the control, between cow's milk and the control may suggest diet having an effect on the manifestation of rheumatoid arthritis in human beings.

It is possible that besides protein, saturated fatty acids might also play a role because they favor the production of prostaglandins of the 2 series and the leukotriene B_4 which are both inflammatory hormones (Buchanan, 1990). Arachidonic acids, also known as omega-6 fatty acids, are also involved with inflammation (Silman & Pearson 2002; "Paracrines Derived

from Polyunsaturated Fatty Acids”). It is essential that human beings have an equal ratio of omega-3 to omega-6 fatty acids for good health (Simopoulos, 2002).

Many studies have shown that fasting improves RA in human patients which either happens by reducing production of chemical mediators of inflammation, changing bowel flora or gut permeability, or affecting cellular immunity (Buchanan, 1990). Omega-3 fatty acids have been shown to have a positive effect on RA; it could possibly be because fatty acids such as eicosapentaenoic acid compete with arachidonic acids, which are involved in inflammation. A healthy diet has a balance between the omega-3 and omega-6 fatty acids, the ideal ratio of the fatty acids is one to one (Silman & Pearson, 2002;“Paracrines Derived”).

In today’s western diets, there is an excessively high ratio of omega-6 fatty acids to omega-3 fatty acids, usually between 15:1-16.7:1. The western diet is deficient in omega-3 fatty acids and over abundant in omega-6 fatty acids. A diet with an unequal ratio of omega-6 to omega-3 fatty acids can be extremely harmful. Diets high in omega-6 fatty acids can promote the pathogenesis of many diseases, including auto-immune diseases as well as inflammatory diseases (Simopoulos, 2002). Meyer et al. (2003) explains that “Eicosanoids produced from the n-6 PUFA AA have mainly vasoconstrictor, pro-aggregatory, and pro-inflammatory actions, whereas eicosanoids produced from n-3 PUFA EPA result in primarily vasodilation and anti-inflammatory actions. Hence, there is a necessity to balance these fatty acids in our cell membranes, which can be achieved by modifying dietary intakes.” In clinical trials, an increase of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in the form of fish oils, an omega-3 fatty acid, even improves joint pain (Simopoulus, 2002). Omega fatty acids are also linked to the production of prostaglandin, a hormone-like substance. Prostaglandins are

important in many physiological functions including the inflammatory and allergic responses (“Omega-3 Fatty Acids, 2013).

It is important to understand the sources of omega-6 and omega-3 fatty acids so that the differences in diets can be observed. Sources of Omega 6-fatty acids include: baked goods, brazil nuts, cereals, corn oil, cottonseed oil, eggs, hemp oil, meats from grass fed animals, pecans, pine nuts, pumpkin oil, safflower oil, sesame oil, soybean oil, sunflower oil, sunflower seeds, wheat germ oil, and certain whole grains. Sources of Omega 3 fatty acids include: whole grains, legumes, certain nuts and seeds, fresh fruits and vegetables, and wild fish/seafood (Longe, 2008). These sources have food products that are similar but the source of the oils and many of the seeds and nuts differ. This list is not inclusive of every source and does not give examples the types of foods that help to release some hormones that may have a negative effect on rheumatoid arthritis. By looking at this list, a trend can be noticed in the sources in which a westernized diet may get many of its omega-6 fatty acids. Corn oil, eggs, cereals, baked goods, and meats from grass fed animals are staples of the westernized diet which all are omega-6 fatty acids. It can also be seen that there is a deficiency in the westernized diet of food products that contain omega-3 fatty acids. Westernized diets typically have a decrease in carbohydrates and fiber and an increase in fat (Bourne, Lambert, & Steyn, 2002).

VII.Diets Compared

Rural populations of South Africa obtain less of their energy from protein than do urban populations. Their fat intake is also far lower. There has been a shift in the diet of black Africans from their traditional diet which is high in omega-3 fatty acids, and low on protein

consumption to a more westernized diet that is high in omega-6 fatty acids and also high in protein. A traditional diet delivers more than 60% of its energy from carbohydrates and less than 25% of its energy from fat. A typical westernized diet delivers less than 50% of its energy from carbohydrates and more than .35% of its energy from fat (Bourne, Lambert, & Steyn, 2002).

The same can be seen in the populations of Pakistanis living in the UK compared to Pakistanis living in Pakistan. Pakistanis living in Pakistan have a more traditional Mediterranean-style diet than their Pakistanis counterparts in the UK. The traditional Pakistanis diet differs from the traditional diet of rural populations of Africa but also is a diet with a proper balance of omega-3 fatty acids to omega-6 fatty acids, and has a lower protein consumption, especially protein obtained from animals (Longe, 2008).

People in Spain, an European Mediterranean country, in the past had a traditional Mediterranean diet but has become a more westernized diet from the 1960s t today. Spainards'' intake of omega-3 fatty acids were cut by fifty percent or more, and its omega-6 fatty acids intake and its protein intake from meat, poultry, and their products (including diary) have increased by roughly fifty percent over the past 50 years (Moreno, Sarria, & Popkin, 2002). These findings are similar to the findings for the South African populations as well as the Pakistanis. This data shows changes in diet from a diet consisting of high omega-3 fatty acids and low animal protein consumption to one that is more westernized with high protein and fat consumption from animals and their products.

Populations with more westernized diets, those in developed countries in general, have a much higher a prevalence rate of rheumatoid arthritis. An exception is China which has a relatively low prevalence rate but also does not have a truly westernized diet. China's diet

instead has a balance of Omega-3 and -6 fatty acids and low animal protein consumption (Meyer et al., 2003).

IIX.Discussion

The data on prevalence rate and diet suggests that what occurred around the seventeenth century that caused an outbreak of rheumatoid arthritis is not the presence of Halley's Comet circling the earth and spaying it with virulent virus stains (Buchanan, 1990). Nor is it necessary for one to carry the correct sequence of HLA DRB1 alleles because if it were the prevalence rates would be similar across nations and across centuries (Buchanan, 1990).

What occurred around the seventeenth century was the agriculture revolution as well as the industrial revolution. The agriculture revolution allowed for farmers to farm large amounts of crops and animals to be consumed by the general public as well as preserved. These revolutions allowed for many people to move from the rural country side to the cities and to substantially changed populations' diets.

The change in diet and in prevalence rate of RA is seen globally. The increase in prevalence rate can be seen in the modern day by observing the recent changes from traditional diets to westernized diets. By accounting in general for genetic factors and limiting the discussion to populations of similar genetic make compared across the rural and urban divide, one can see that there is a substantial difference in rates between rural and urban populations. This difference can be correlated with the shift in diets from traditional diets heavy in certain grains and vegetables to those heavy in fats and proteins. It appears that the change in diet is causal to the increase of Rheumatoid arthritis, but more research is necessary.

IX.Conclusion

Extensive research needs to be done on the change of diet from rural to urban, or traditional to western. Technology can now measure exact dietary intakes and what these nutrients do within the human body. Diet affects the entire human body. Rheumatoid arthritis may be directly or indirectly related to diet. Diet affects hormone production, which has been noted as a potential risk factor for RA. Certain fatty acids have been shown to produce the hormone like prostaglandin produces an inflammatory response in the body which may show a link between diet, hormones, and RA.

More research on diet as a contributing factor to rheumatoid arthritis is needed. In general, though, the public needs to be made aware of the dangers of an unbalanced diet can actually be. The risk of a diet high in fat and protein is possibly no longer just obesity and high cholesterol, which are very curable conditions, but RA, which is presently incurable. Developed nations have something to learn from tradition and underdeveloped nations. Our diet is relatively new and our Paleolithic ancestors possibly had it right when it came to diet. It is time to accept that not all new things are good things.

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