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"the pluses & minuses of:

THE SYNDROME OF SICKNESS"

by

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Introduction

The expanding interest in the ecology of health and disease has brought a renaissance to the subject of host *resistance* and *susceptibility*. The multiplying efforts in the detection of early disease and even in the anticipation of illness has led to a rebirth of thinking regarding the *syndrome of sickness*. This report will attempt to analyze the relationship between these two variables. The first responsibility is to define what is meant by *resistance* and *susceptibility* and how one should regard the *syndrome of sickness*.

Resistance-Susceptibility

The terms resistance and susceptibility may be viewed in two different connotations[1]. From a *descriptive* standpoint, the labels are simple antonyms. Hence, there is little to be gained by viewing an individual succumbing to disease because of lowered resistance or increased susceptibility.

The designations resistance and susceptibility may be viewed in an *analytic* frame. In this sense, the tags have distinctly different meanings and practical implications. By definition, a *resistance* agent is one which, when *added*, tends to *discourage* disease and, when *eliminated*, tends to *invite* disease. A classical example would be vitamin C. Its addition tends to discourage the appearance of scurvy; its elimination invites scurvy. In contrast, a *susceptibility* agent is one which, when administered, *invites* disease and, when *eliminated*, *discourages* illness. An excellent example is sugar. Sugar in contact with the teeth tends to invite dental caries; its elimination discourages the development of dental decay. For purposes of this report, the *analytic* approach to resistance and susceptibility will be utilized.

The Syndrome of Sickness

All disease is preceded by an incubation period[2-4]. In the instance of acute mechanical trauma (e.g., an automobile accident), the incubation period is very brief and not particularly helpful in the diagnosis of disease. In the case of acute infectious disorders (i.e., measles), the incubation period is somewhat longer (approximately ten days) and may be significant from a diagnostic and prognostic standpoint. With the chronic disorders such as myocardial infarction, cerebrovascular accident, rheumatoid arthritis, periodontal disease, the incubation time extends over months and frequently several years or decades. Clearly, the longer the period, the greater the opportunity to anticipate the end problem and, hopefully, abort the process.

Initially, the patient notes only few and seemingly unrelated findings. There may be irritability, for example, associated with leg cramps. Because these apparently unrelated symptoms and signs do not fit any textbook picture of a particular disease, the complaints may either be ignored, assigned a meaningless label, or regarded as a minor psychic problem and treated symptomatically. The latter diagnosis is frequently made by exclusion. In other words, a failure to relate the signs and symptoms to classical disease nomenclature frequently results in the decision to assign an emotional tag. Hence, at this stage, the clinical picture is shown by the box on the left (Figure 1).

If the clinical situation just pictured continues, as is so often the case, then the number of symptoms and signs progressively multiplies. Sooner or later, the findings begin to crystallize in systems, organs, or localized sites. For instance, the subject may find himself with several gastrointestional complaints such as indigestion, anorexia, and hemorrhoids. At this stage, the constellation is still not classifiable

with textbook disease terminology. Hence, treatment is usually symptomatic and/or the patient is advised that the problem should be under observation. When many organ systems and/or anatomic sites are involved, the syndrome might be ascribed a psychologic etiology. This is the story shown in the middle box (Figure 1).

Finally, when the syndrome is clearly pigeon-holed in terms of its classical description, then the illness is assigned a label. In conventional medicine, it is only at this point that a diagnosis is deemed justifiable. This is pictorially portrayed in the box on the right (Figure 1).

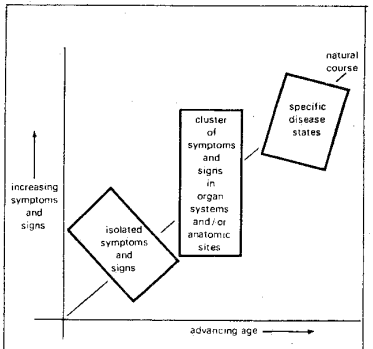
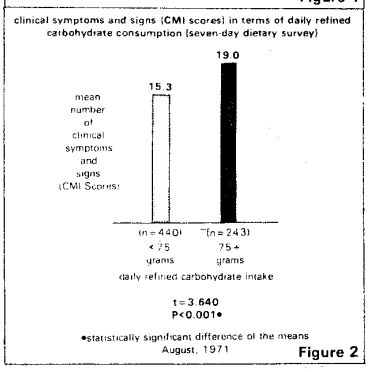


Figure 1



August, 1971

Figure 2

Method of Investigation

Five hundred seventy-nine subjects (the overwhelming majority dentists and their wives) participated one or more times in this experiment. These individuals are presently part of a multiple testing program in Florida under the auspices of the Southern Academy of Clinical Nutrition, in Los Angeles under the aegis of the Southern California Academy of Nutritional Research, in Columbus under the sponsorship of the Ohio Academy of Clinical Nutrition and in Connecticut in the framework of the Northeast Academy of Clinical Nutrition.

Each subject, on a more-or-less annual basis, completed three health questionnaires: the Cornell Medical Index Health Questionnaire, the Cornell Word Form-2, and the Oral Health Index Questionnaire.

The Cornell Medical Index Health Questionnaire (CMI)[5] is a list of 195 questions, each followed by two possible responses, yes or no. The subject is asked to choose the appropriate response and to guess if in doubt. *The questions are so structured that an affirmative response suggests pathosis.* The total number of affirmative answers is referred to as the CMI score.

Additionally, the CMI includes questions regarding social habits (tobacco, alcohol, coffee/tea consumption, exercise) which have proved useful in the evaluation of resistance and susceptibility variables. These questions also are designed so that a positive answer denotes increased susceptibility or decreased resistance to pathosis.

The Cornell Word Form-2 (CWF-2) is a modification of the ordinary type of individually administered word association technique in that it is a forced choice method. The subject is presented with a list of stimulus words, each followed by two other response words, and is asked to select the response word which better relates to the stimulus word. Thus, the CWF-2 makes a quick descriptive sketch of the individual's attitude, feeling states, and emotions or bodily reactions for clinical interpretation. It does this in a manner not readily discernable to the subject in order to enhance the degree of objectivity. The abnormal responses are revealed with a keyed grading stencil. The total pathologic number is the CWF-2 score.

The Oral Health Index Questionnaire (OHI)[7] consists of 270 questions designed for yes or no responses. The subject is encouraged to guess if uncertain. Each question is phrased so that an affirmative answer suggests a pathologic state. Also, questions regarding tobacco, alcohol, coffee/tea, vitamin-mineral supplements, and exercise are stated so that a positive response indicates an increased susceptibility or decreased resistance to pathosis. This questionnaire provides information in seven categories: (1) present oral symptoms and signs, (2) present dietary habits, (3) present emotional state, (4) present general health, (5) past oral symptoms and signs, (6) past general health, and (7) family history. Percentage scores can be calculated for each category and for the composite health of the subject.

Each subject, on an annual basis, completed two dietary questionnaires: a seven-day dietary record and the Dietronics Dietary Analysis.

A seven-day record of dietary intake was submitted by each subject and analyzed by Doctor Michael Walsh, Consultant Nutritionist, Beverly Hills, California. The intake of the major foodstuffs as well as the common vitamins and minerals was calculated from food tables[8] by computer and a printout furnished.

The Dietronics Dietary Analysis[9] is a technique based upon significant observations in Israel[10] and England[11] which suggest that the most practical method for deriving data is by means of a food frequency questionnaire. The completed Dietronics form is submitted for computer analysis and a printout is returned showing the daily intake of the major foodstuffs and most common vitamins and minerals.

Table 1
the syndrome of sickness profile (CMI scores)
(dietary analysis)*

dietary parameter	CMI scores low	CMI scores high	per centage differ ence	t	P
refined carbohydrate	15.3	19.0	24	3.640	< 0.001**
fat	18.1	15.1	20	3.177	< 0.005**
iodine	17.9	15.0	19	3.056	< 0.005**
acid	19.0	15.9	19	2.945	< 0.005**
total protein	17.6	15.3	15	2.705	< 0.010**
base	17.5	15.1	16	2.614	< 0.010**
phosphorus	17.4	14.8	18	2.515	< 0.025**
vitamin B_1	17.0	12.9	32	2.511	< 0.025**
unrefined carbohydrate	16.2	15.8	15	2.386	< 0.025**
animal protein	17.8	15.6	14	2.317	< 0.025**
calories	17.5	15.6	12	2.029	< 0.050**
vitamin B_2	17.7	15.8	12	2.006	< 0.050**
iron	17.7	15.9	11	1.871	0.050
total carbohydrate	15.7	17.5	11	1.845	0.050
vegetable protein	17.1	15.3	12	1.744	0.050
niacin	17.9	16.2	10	1.702	0.050
vitamin C	17.7	16.1	10	1.697	0.050
vitamin D	17.1	15.4	11	1.651	0.050
calcium	17.0	16.0	6	0.969	0.200
vitamin A	16.8	16.1	4	0.688	0.400

*seven day dietary service
**statistically significant difference of the means

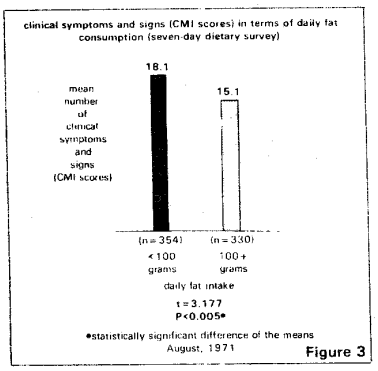


Figure 3

Through the use of these five questionnaires it was possible to analyze early illness (box on the left in Figure 1) in terms of susceptibility and resistance agents as judged by dietary and social patterns.

Results

Table 1 summarizes, in the whole group, the relationship of all of the common nutrients in terms of clinical symptoms and signs in decreasing order of statistical importance. The CMI score represents the total number of yes answers on the questionnaire. The first item is so listed because, of all of the parameters, the t value ranks the highest (3.640). An examination of Table 1 warrants analysis for five reasons. First, it is significant that the intake of relatively low versus high amounts of most of the nutrients is significantly different in terms of clinical signs and symptoms of disease. This is borne out by the number of parameters showing an asterisk connoting statistical significance. Second, even among those not significant, the majority border on being significant at the five per cent confidence level. Third, actually only two (calcium and vitamin A) show clearly no statistical significance. Fourth, in all cases where there is a significant difference in CMI score, those consuming the greater amounts show the fewer clinical symptoms and signs. Thus, according to the earlier definitions, these nutrients must be viewed as resistance agents. Finally, it is particularly noteworthy that only refined carbohydrate can be classified as a susceptibility agent. In this case, those consuming the greater amounts have more clinical symptoms and signs. There is one additional point which should be underlined. Specifically, Table 1 clearly supports those who contend that there are distinctly different clinical effects from refined versus unrefined carbohydrates[12-15]. It should be abundantly evident that various nutrients serve as resistance and susceptibility agents.

Genetic factors compose a second group of resistance-susceptibility agents which must be mentioned. Unfortunately, their control is almost impossible.

Finally, there is a third group of resistance-susceptibility factors. These factors are modifiable and represent a variety of social habits. Table 2 lists some of these variables. Several points are worthy of emphasis. First, exercise and vitamin-mineral supplementation must be viewed as resistance agents. In contrast, tobacco, coffee/tea, and alcohol fit the specifications for susceptibility agents. Next, it is noteworthy that all parameters are statistically significant when viewed as resistance and susceptibility agents.

Discussion

It should be underlined that the preceding discussion has viewed a number of dietary and nondietary variables in the light of host resistance and susceptibility. This approach to the problem is beset with a number of serious limitations which must be considered.

Single Versus Combination Variables: While it is interesting and helpful to analyze nutrients and nondietary variables *singly,* the fact of the matter is that man exists in a *multifactorial* system. Hence, all these variables are interrelated, and it is essential to view resistance and susceptibility in combined systems.

Apropos to diet, it should be recalled that refined carbohydrate foodstuffs headed the list of single variables (Table 1). Specifically, by the method employed for analysis, those consuming the relatively greater amount (75+ grams) of refined carbohydrate foods per day reported 24 per cent more clinical symptoms and signs than those subjects ingesting < 75 grams refined carbohydrates daily (Figure 2). Thus, not only is refined carbohydrate number one on the list (Table 1), it is also a *susceptibility* agent. In others words, it enhances the body's proneness to disease. Fat intake ranks second (Table 1), with those consuming the greater amount (100+ grams) per day showing 20 per cent less symptoms and signs (Figure 3). Thus, fat is a *resistance* agent since it retards or impedes the development of disease in the body.

Figure 4 examines the *combination* of findings with regard to daily refined carbohydrate *and* fat intake. It will be observed that the *lowest* number of clinical findings (13.2) is found in the group characterized by a high fat (high resistance) and low refined-carbohydrate (low susceptibility) diet. Conversely, the *greatest* number of clinical findings (20.8) is noted in the group with the low fat (low resistance) and high refined-carbohydrate (high susceptibility) diet. Two additional points deserve special mention. First, the difference in these two groups is 58 per cent, clearly much more than in the case of the single variables (refined carbohydrates 24 per cent; fats 20 per cent), as listed in Table 1. Second, the intermediate groups in terms of refined carbohydrates and fat (Figure 4) occupy intermediate positions in terms of clinical problems (16.9 and 17.7).

The observations noted with single and combined *nutrients* also prevail in the case of *nondietary* parameters. For example, mention was made earlier (Table 2) of exercise and tobacco consumption. It will be observed that exercise is to be viewed as a resistance agent (Figure 5). In contrast (Figure 6), the use of tobacco must be regarded as a susceptibility agent. Once again, the *combination* of exercise *and* tobacco consumption is more delineating than these variables singly (Figure 7). It will be observed that the *lowest* number of clinical findings (13.3) is found in the group characterized by daily exercise (high resistance) and no tobacco consumption (low susceptibility). Conversely, the *greatest* number of clinical findings (24.1) is noted in the group with no daily exercise (low resistance) and with tobacco intake (high susceptibility). Two additional points warrant particular mention. First, the difference in these two groups is 81 per cent, surely much more than in the case of the single variables (exercise 51 per cent; tobacco 27 per cent), as listed in Table 2. Second, the intermediate groups in terms of exercise and tobacco (Figure 7) occupy intermediate positions with regard to clinical problems (16.5 and 20.0).

The point has been made that many *single* variables (e.g., refined carbohydrates, fats, exercise, tobacco) may be viewed as significant resistance or susceptibility agents. It was underscored that these same variables gain in significance when viewed in

Table 2
the syndrome of sickness profile
(social habits) *

social parameter	CMI scores negative	CMI scores positive	percentage difference		P
exercise	13.5	20.4	51	7.446	< 0.001 **
tobacco	15.3	19.4	27	3.394	< 0.001 **
coffee-tea	15.3	19.6	28	3.197	< 0.005 **
vitamin-mineral supplement	15.4	18.9	23	2.854	< 0.005 **
alcohol	15.3	18.3	20	2.526	< 0.025 **

*questions obtained from the Cornell Medical Index Health Questionnaire
**statistically significant difference of the means

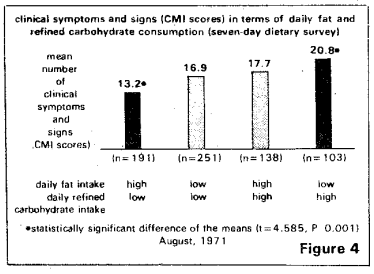


Figure 4

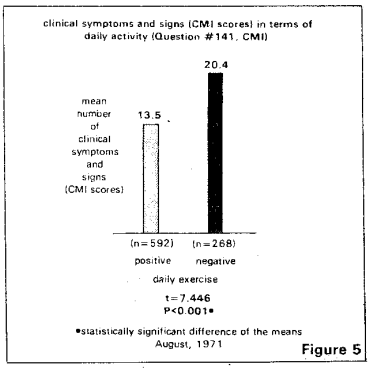


Figure 5

combinations. Several nutrients were noted in Table 1 to either border on being significant as resistance-susceptibility agents (the P value is not quite significant at the five per cent confidence level) or to be, unequivocally, not significant. It might prove profitable to examine some of these seemingly nonsignificant *single* variables in combinations to determine whether this type of analysis alters their possible significance.

Table 1 shows that iron and vitamin C show lower, and therefore more desirable, *mean* clinical scores in those consuming the greater amounts of these nutrients. However, by the usual statistical techniques, the differences are not statistically significantly different. Figure 8 is a pictorial portrayal of the mean number of clinical symptoms and signs (on the ordinate) in terms of the daily intake of *both* iron and vitamin C. By this technique, it is abundantly evident that there are significant differences. For example, viewing clinical state and the individual nutrients (Table 1), the percentage differences are about 10 per cent. Figure 8 shows that the mean clinical scores between the groups characterized by high iron and vitamin C intake (high resistance) versus low iron and vitamin C consumption (low resistance) is 21 per cent. More importantly, this difference is clearly statistically significant.

Techniques for Data Acquisition: Mention was made earlier that the parameters listed in Table 1 were derived from a seven-day dietary record. Clearly, other dietary surveys as well as other avenues are available which provide information regarding resistance and susceptibility agents. Two illustrations will be offered at this time.

A relatively new and exciting method for deriving dietary state has recently been reported[9,11]. It is essentially based upon the frequency with which certain foods are consumed. The computer printout provides the daily intake of the major nutrients as well as many vitamins and minerals. For instance, the output includes an analysis of daily vitamin E consumption, an item not reported in the seven-day dietary.

Figure 9 analyzes the relationship of daily vitamin E intake in terms of CMI scores. It is clear that the difference is of a magnitude of about 18 per cent. If one were to interpose this information into Table 1, vitamin E must be regarded as one of the most significant resistance agents.

Each of the subjects completed the Oral Health Index Questionnaire (OHI). One of the questions deals with the daily vitamin-mineral supplementation. Figure 10 portrays the results. It will be noted that the clinical picture is significantly different in those with and without daily supplementation. Hence, in view of these findings, it is fair to regard daily vitamin-mineral supplementation as a significant resistance agent.

The significance of a single resistance or susceptibility agent can vary widely depending upon how questions are posed. For example, one of the items in

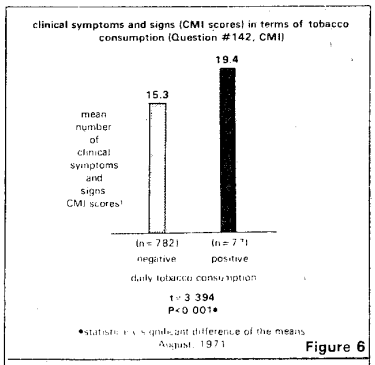


Figure 6

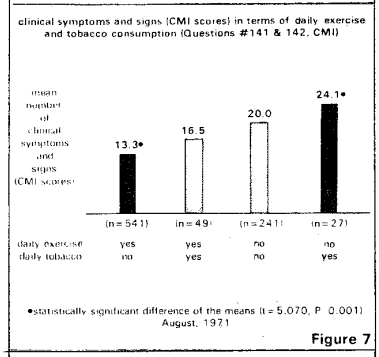


Figure 7

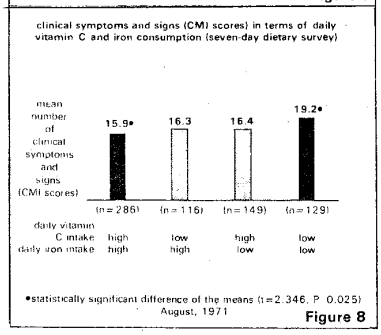


Figure 8

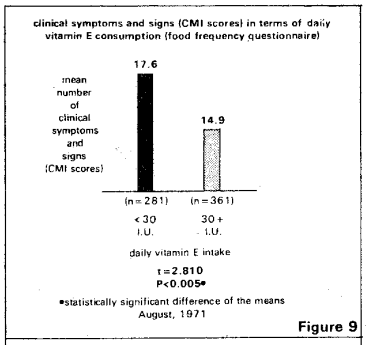


Figure 9

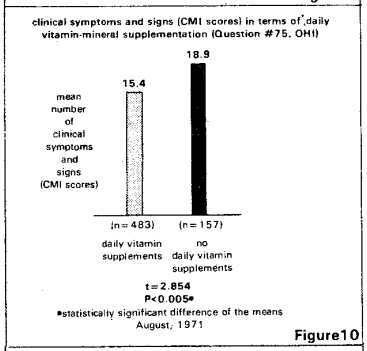


Figure10

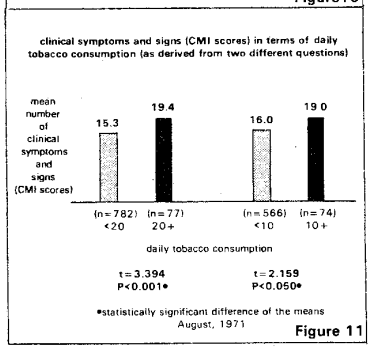


Figure 11

the Cornell Medical Index Health Questionnaire is phrased in such a way as to discriminate between those smoking more than twenty cigarettes versus less than twenty cigarettes daily. In contrast, in the Oral Health Index Questionnaire the question delineates those smoking more than ten cigarettes per day versus less than ten cigarettes daily. Figure 11 shows that the phraseology of a question may influence the results. In this particular instance, the findings are more sharply demarcated on the basis of the greater cigarette consumption.

The Anatomy of the Syndrome of Sickness: Thus far, an attempt has been made to develop a profile of resistance and susceptibility agents utilizing the total number of reported symptoms and signs as derived from the Cornell Medical Index Health Questionnaire as an experimental model for the syndrome of sickness. It is noteworthy to observe that profiles of specific disorders can be developed in the same way. Two illustrations are offered.

According to all studies, the incidence and prevalence of mental illness ranks it among the most critical medical problems in the United States. For this and other reasons, increasing attention is being given to its proneness profile with the hope that this approach might abort the devastating effect of psychiatric problems. In this latter regard, principal attention is being given to the role of early childhood trauma and other emotional scars. Relatively little attention has, until recently, been accorded the possible role of diet.

Figure 12 pictorially summarizes the relationship of daily refined carbohydrate consumption to the mean psychologic scores as derived from the Cornell Word Form-2 test. Several points deserve special attention. First, the psychologic score is higher, on a mean basis, in the group characterized by the higher refined carbohydrate intake. Second, the difference is statistically significant ($t=2.507$, $P < 0.025$). Third, according to earlier definitions, refined carbohydrate foodstuffs must be viewed as a potential susceptibility agent in the genesis of psychopathy. Fourth, it was earlier shown that refined carbohydrate foods can be regarded as a susceptibility agent in the syndrome of sickness as judged by total CMI scores.

According to all health statistics, the incidence of oral disease (dental caries and periodontal pathosis) exceeds that of any other single medicodental problem. Diet is recognized as a factor in the genesis of these stomatologic problems. However, the implication is that the effects are mediated locally.

Figure 13 pictorially portrays the relationship of daily physical activity to the mean oral symptom and sign score, called PRESOREX (present oral health index) derived from the Oral Health Index Questionnaire. A number of items requires elaboration. First, the mean number of oral findings is higher in the group reporting no daily exercise. Second, there is a statistically significant difference in oral state in terms of physical activity ($t=3.108$, $P < 0.005$).

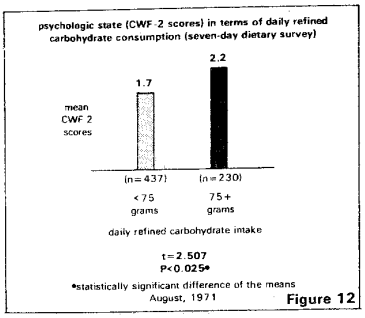


Figure 12

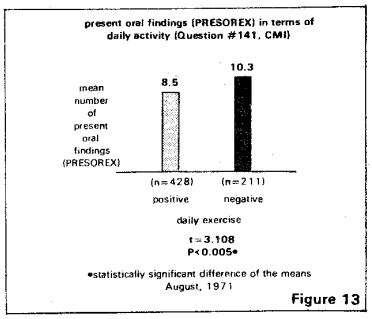


Figure 13

Third, these findings brand exercise as a resistance agent. Fourth, it was shown earlier that exercise serves as a resistance agent in the development of the syndrome of sickness by means of CMI scores.

Summary

The evidence seems clear that chronic disease begins with few and seemingly unrelated symptoms and signs. With time, the clinical picture becomes more complex and, finally, the constellation of findings is adequate to assign a textbook label. The evidence is abundant that disease is of multifactorial origin and that host and local influences are operational in almost all instances. This is true of both oral and extraoral pathosis.

There is increasing information to suggest that host state can be viewed as the net result of interaction among a number of resistance and susceptibility agents. By definition, a resistance agent is one which, when added, tends to discourage the development of disease. In contrast, a susceptibility agent is one which invites the development of disease.

A study of the syndrome of sickness, utilizing all early symptoms and signs (CMI scores) suggests that refined carbohydrate foods, tobacco, alcohol, and coffee/tea must be considered as susceptibility factors. On the other hand, unrefined carbohydrates, proteins, fats, calories, the vitamins and minerals are generally to be viewed as resistance agents along with exercise.

What is particularly exciting is the fact that other proneness profiles can be identified utilizing diet and nondietary variables. Examples are offered to show the possibility of developing a mental illness proneness profile and an oral health proneness profile.•

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