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Nutritional Assessment of Outpatients with Crohn's Disease

by

© Phyllis Ellen Hodges

A THESIS

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ABSTRACT

Crohn's disease (CD) is a chronic granulomatous inflammatory process which may affect any part of the gastrointestinal tract from the mouth to the anus. The incidence of CD is rising at an alarming rate, and the disease is associated with significant morbidity and as a result of a complex interaction of numerous pathophysiological processes, these patients with CD are at risk of developing numerous nutrient deficiencies. Unfortunately, little is known of the contribution of nutrient intake to the development of these known deficiencies; and even less is known of those nutrients which may be consumed in abnormal quanitities and which may in time lead to significant deficiencies. Accordingly, a nutrient assessment was made on 47 consecutive outpatients with CD. Anthropometric measurements, nutrient intake, and numerous hematological and biochemical tests were made on 24 females (F) and 23 males (M) with CD. The mean age of the CD patients was 31 and 32 years for males and females, respectively. Two-thirds of the patients had ileocolitis. The mean Crohn's Disease Activity Index (CDAI) was 46 in males and 118 in females. Relative body weight (RBW) was very similar in the males and females being 102% and 100%, respectively. Arm muscle circumference (AMC) was 95% of the standard in males and 98% of the standard AMC in females, with 25% of both males and females having a reduced AMC. The mean percent of standard triceps skinfold (TSF) was 120% in males, with 1/3 having a reduced TSF and 95% of the standard in females, with 1/2 having a reduced TSF.

A detailed assessment of over 20 nutrients was obtained using the 48-hour dietary recall method. The mean nutrient intake of males was

less than the recommended dietary allowance (RDA) for vitamin B_6 and folate, and in females was less than the RDA for vitamin B_6, folate, iron, calcium, and vitamin D. However, there was a wide range of intakes within each nutrient. Accordingly, the adequacy of intake was calculated according to the full RDA, 2/3 RDA, 1/2 RDA, and 1/3 RDA. Fifty percent or fewer of the male CD patients consumed the full RDA for energy (49%), vitamin A (48%), vitamin B_6 (13%), and folate (0%), while 50% or fewer of the female patients consumed the full RDA of energy (33%), calcium (38%), iron (17%), vitamin A (50%), pantothenic acid (38%), vitamin B_6 (13%), folate (8%), vitamin B_{12} (50%), and vitamin D (30%). Per 1000 kcal, males consumed significantly less vitamin A and folate than did females. The consumption of food groups by the CD patients was compared to that of Nutrition Canada, and it was found that the CD group consumed about 70% more fruit than did Nutrition Canada participants.

One-third or more of the men had values less than the lower limit of the reference value for total lymphocyte count (TLC) (50%), transferrin saturation (50%), serum iron (67%), serum carotene (38%), and serum folate (37%). One-third or more of the women had low values for TLC (55%), serum iron (60%), transferrin saturation (68%), and serum folate (50%).

Highly significant ($p < 0.01$) correlations were found between serum folate and each of dietary folate (0.59), vitamin C (0.52), vitamin B_{12} (0.58) and vitamin B_6 (0.47) in females only.

A highly significant ($p < 0.000$) correlation was found between RBW and AMC in both male (0.76) and female (0.77) patients. In females, only, the correlations between the following pairs were also

significant ($p < 0.01$): RBW vs TSF (0.63), RBW vs TLC (0.48) and AMC vs TLC (0.66).

Patients were grouped according to energy intake less than the RDA, equal to the RDA, or greater than the RDA in order to determine the value of energy intake in predicting the occurrence of low biochemical and/or anthropometric parameters. However, energy intake appeared to be of little predictive value, as the incidence of abnormal parameters was approximately equal in all categories. When patients were grouped according to RBW greater than 90% or less than 90%, female CD patients with less than 90% RBW had a higher incidence of abnormal [illegible] AMC, TLC, and total iron binding capacity.

The CDAI was correlated in [illegible]h energy (-0.38), serum albumin (-0.64), and duration of disease (0.57), and in females with hemoglobin (-0.45) and serum ferritin (0.60).

Thus, in the female CD patient, serum folate and relative body weight can be used to identify the CD patient at possible risk of nutritional deficiency and in need of nutritional counselling.

In conclusion, reduced nutrient intake is common in patients with CD, and these patients should receive a full nutritional assessment and individualized dietary counselling.

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ABBREVIATIONS

AC	arm circumference
AMC	arm muscle circumference
BEE	basal energy expenditure
CD	Crohn's disease
CDAI	Crohn's Disease Activity Index
CHI	Creatinine Height Index
CHO	carbohydrate
DF	dietary fiber
FIGLU	Formiminoglutamic acid
IBD	inflammatory bowel disease
LAA	leucocyte ascorbic acid
MBD	metabolic bone disease
MCHC	mean corpuscular hemoglobin concentration
NC	Nutrition Canada
OCA	oral contraceptive agents
PA	pantothenic acid
PCM	protein calorie malnutrition
PLE	protein losing enteropathy
RBW	relative body weight
RDA	recommended dietary allowance
SAS	salicylazosulfapyridine
TIBC	total iron binding capacity
TLC	total lymphocyte count
TPN	total parenteral nutrition
TSF	triceps skinfold

1. INTRODUCTION

Crohn's disease, first identified and described in 1932 by Crohn, Ginzberg, and Oppenheimer was once a rarity. However, several epidemiological studies have shown that it is increasing at an alarming rate. In the U.S., Miller et al observed a five-fold increase in the incidence of Crohn's disease (CD) during a 14 year period (Miller et al 1974), and in Sweden, Brahme et al noted a two-fold increase from one eight year period to the next during 1958-1973 (Brahme et al 1975).

Described as a chronic, progressive, granulomatous disorder, CD can occur anywhere in the gastrointestinal tract from mouth to anus. It is characterized by skip lesions, tendency to fistulae formation, and high incidence of recurrence after surgery. The etiology of CD is unknown, though attempts to establish an etiology have centered on genetic factors, psychogenic factors, transmissible agents, and immunological factors.

Nutritional disturbance is a common complication of Crohn's disease. The spectrum of reported nutrient deficiencies in CD ranges from vitamin A (Russell et al 1973) to zinc (McClain et al 1980), while symptoms of deficiencies range from mild symptoms such as low serum folate (Dyer et al 1972) or low leucocyte ascorbate concentrations (Hughes and Williams 1978) to severe symptoms such as scurvy (Linaker 1979) or metabolic bone disease (von Westarp et al 1978). Suggested mechanisms for these nutrient deficiencies include decreased intake, absorption, and/or utilization; increased loss and/or requirement. However, because nutrient intake is often unknown, the mecha-

nisms are sometimes speculative and the role of dietary intake in the nutrition deficiencies of CD remains undefined. Logically, then, a knowledge of dietary intake, as well as biochemical status is necessary to enable health professionals to establish the etiology of nutrient deficiencies in CD. Thus an investigative study of the dietary intake of CD patients was conducted with the following objectives:

1. To describe the nutrient intake of CD patients
2. To compare the nutrient intake of CD patients with that of Nutrition Canada and the Recommended Dietary Allowance
3. To identify the nutrients for which CD patients are at risk of consuming less-than-adequate amounts
4. To examine the relationship between dietary intake, anthropometric measurements, and biochemical parameters
5. To select factors which could identify the CD patient at risk of nutritional deficiency and in need of nutritional counselling.

2. LITERATURE REVIEW

2.1 Standard Group

2.1.1 Discussion of Nutrition Canada

Like the present study, Nutrition Canada (NC) attempted to assess nutritional status of Canadians by clinical evidence, anthropometric measurements, biochemical determinations, and dietary intake, and, therefore, would seem to be an appropriate Standard Group for comparison of nutrient intake with gastrointestinal patients. Whenever possible, comparison of the CD group was made to the Prairie population of the NC survey.

In the survey, biochemical and clinical parameters were categorized into three risk groups (high, low, moderate), indicating the probability that malnutrition exists or will develop. Similarly, dietary intakes for each nutrient were categorized into three groups. Adequate levels of intake were defined as those amounts of a particular nutrient providing a desirable margin of safety; less-than-adequate levels, above the minimum requirement, but below the desirable amount; and inadequate levels, an amount below the minimum requirement. The "adequate" classification corresponds closely to the recommended daily nutrient intake of the Canadian Dietary Standards (Canada, Department of National Health and Welfare, 1975) and the Recommended Dietary Allowances (National Research Council, Washington, D.C., 1980) (See 2.1.2 for further discussion of Recommended Dietary Allowances).

The results of the NC survey indicated the following nutritional problems in adults over 20 years of age:

(i) Fifty percent or more of adults were overweight, despite the fact that there was very little difference in caloric intake between those of normal and above normal weight.

(ii) Ten to 13% of men and 14 to 34% of women had serum cholesterol levels that placed them in the high risk categories.

(iii) In the over 65 years group, total serum protein levels indicated that 6% of men and 9% of women were at moderate and high risk. However, protein intakes indicated an even higher risk, as 27% of men and almost 38% of women had intakes of less-than-adequate or inadequate.

(iv) Poor dietary intakes of iron were indicated in 15-35% of men and 56-76% of women. Low values for hemoglobin, mean corpuscular hemoglobin concentration, and % transferrin saturation classified 6-18 % of men and 7-31% of women at risk of iron deficiency.

(v) Serum folate levels were strikingly low, indicating a moderate to high risk of developing folate deficiency in about 60% of both men and women. Dietary folate was not calculated at that time, due to the dearth of information regarding the folate content of foods.

(vi) About 20% of women were found to have inadequate calcium intakes. Serum calcium concentrations were found to be in the normal range, though this is to be expected since

serum calcium levels do not drop until very late in calcium deficiency.

(vii) Vitamin A intake was generally satisfactory in the population, but did become increasingly inadequate with age, though serum retinol levels were near or within the normal range in the general population.

(viii) Although vitamin C intakes were adequate, serum values for vitamin C indicated that 26% of adults were at high to moderate risk of vitamin C deficiency.

(ix) Thiamin intakes in relation to energy intakes indicated that 50% of women and 40% of men had less-than-adequate intakes. Urinary thiamin levels showed that over 20% of men and 10% of women were at risk of developing thiamin deficiency.

(x) Riboflavin intakes were marginal, especially among women, but urinary riboflavin levels were normal for all adults.

(xi) Moderate thyroid enlargement, particularly in women, was observed in clinical assessment by physicians. However, this finding was not interpreted to indicate iodine deficiency, as urinary iodine values were within acceptable limits.

From the foregoing results, it is obvious that even in the general population there is some evidence for nutritional deficiency and/or risk of nutritional deficiency and this should be kept in mind when considering the nutritional status of other groups.

In comparing the results of the CD study to that of the NC survey, it should be recognized that there are certain limitations which require a brief discussion.

Firstly, we are comparing the intake of a diseased group to that of a healthy group. However, increased nutrient requirement of the CD group has not been quantified and, indeed, for some nutrients an increased requirement is only speculative. Thus, at present, it is necessary to work within the limitation of comparing nutrient intake of CD patients to that of a healthy group.

Statistical comparison between any group and NC was not possible due to the manner in which the NC results were published. This was particularly limiting in comparing the intake of food groups.

It should be remembered that the NC survey commenced nine years prior to the present study. Due to a variety of factors such as increased food costs and health awareness, the potential for somewhat different food habits of Canadians now, as compared to nine years ago, is an important consideration.

There are several inconsistencies related to the biochemical interpretive standards and results of NC which require discussion. For example, a low serum folate concentration was reported in 60% of NC participants, though folate deficiency is rare in the Canadian population (Thompson and Hoppner 1979). The interpretive standards used by NC for some of the biochemical tests, including serum folate, are rather high by today's standards. Indeed, it has been recognized that in view of today's lower limit of normal serum folate concentration in healthy individuals, a considerably smaller proportion of

Canadians would be classified at risk of developing folate deficiency (Thompson and Hoppner 1979).

The report that more than twice as many women as men had high serum cholesterol concentrations is surprising and inconsistent with the current literature. For example, the well-known Framingham Study (U.S. Public Health Service, 1968) reports that serum cholesterol levels are high in more men than women, which is consistent with results of several other North American studies of heart disease.

The biochemical results relating to iron status indicated that as many as 20% of Canadian males were at risk of developing iron deficiency. In clinical practice, however, iron deficiency in males is quite rare, and when present, is almost invariably symptomatic of disease.

Finally, the reason for moderate thyroid enlargement, particularly in the Prairies, was not understood at the time of publication of the results of NC, particularly since urinary iodine values ranged from normal to high. However, re-examination of the data revealed that a change in the system of recording goiter, which was implemented during the course of the survey, had not been incorporated into the processing for the NC survey (Murray 1977). Thus, the prevalence of goiter is much lower than previously reported, and the incidence of goiter in the Prairie provinces is similar to that in other regions of Canada.

2.1.2 Recommended Dietary Allowances

Recommended dietary allowances (RDA) 1980 were used as a standard for comparison in the present study. However, the methods by which

the data were derived and the limitations of the RDA should be kept in mind. RDA are defined (page 1, RDA 1980) as,

> "the levels of intake of essential nutrients considered, in the judgement of the Committee on Dietary Allowances of the Food and Nutrition Board on the basis of available scientific knowledge, to be adequate to meet the known nutritional needs of practically all healthy persons"

The recommendations are actually estimates of nutrient requirements which are based on a number of criteria including: nutrient intake of a normal, healthy population; biochemical measurements, nutrient balance studies; the amount of a nutrient required to correct deficiency symptoms; and/or extrapolation from animal studies. The estimates of nutrient requirements derived by use of one or more of these techniques are then increased to exceed the requirements of the majority of individuals within the population. In recommending that level of a nutrient which will meet the needs of nearly all healthy individuals, it would, undoubtedly, be more scientifically valid to determine the nutrient requirements of a sample of individuals within the population, the average nutrient requirement, and the variability within that sample. While this method has been used for the estimation of some nutrient requirements of the adult, the inherent practical limitations and ethical implications make this kind of experimentation difficult. Thus, though the RDA is valid for groups within a population, the nutrient requirements of individuals are generally unknown and the RDA may exceed the nutrient intakes which many individuals require. Therefore, in an individual who consumes less than the RDA, a deficiency may not occur, but with low intakes over a period of time, the risk of developing a nutrient deficiency increases. In

addition, the body can adapt somewhat to lower levels of nutrient intakes. For example, a decrease in basal metabolic rate accompanies starvation and the percentage of a nutrient such as calcium absorbed from the gut lumen increases with lower levels of intake (Harper et al 1979). Finally, it must be stressed that the RDA apply to healthy populations and do not cover increased requirements due to the use of medication or chronic disease such as CD.

2.2 Methods to Assess Dietary Intake

There is no ideal method for assessment of dietary intakes and each method has its own advantages and disadvantages. In deciding which method to use, the purpose of the study must be clearly defined.

2.2.1 Food Records

A record of food intake can be kept by each subject for a specified period of from 1-7 days. The intake may simply be recorded, or weighed and recorded. While this method eliminates error due to memory, as may occur in the recall method, it does require greater cooperation on the part of the subject. Thus, it may introduce a bias against the less-motivated, poorly-educated, and low-intelligence people. It has been shown that as the length of the food record increases, the accuracy of recording decreases (Gersovitz et al 1978). In addition, with an increasing number of meals being eaten away from home, weighing food intakes may not be feasible.

The 7-day food record is assumed to be more representative, and therefore more valid than the 24-hour recall. However, in a group of non-institutionalized elderly subjects eating at a congregate centre,

Gersovitz et al (1978) found the 24-hour diet recall to be as accurate as the 7-day diet record, as determined by the paired t-test. Moreover, Young et al (1952) state that for groups of 50 or more where a 10% error would be acceptable, the 24-hour recall provides a convenient substitute for the 7-day record. Indeed, Marr (1971) reports greater than a 10% error with only a four-day record. When classifying the range of individual intakes into thirds, Marr found that not more than 1% would be grossly misclassified (i.e. actually in the top third, but classified in the bottom third and vice versa), but that only 80% would be correctly classified, when compared to their actual intakes. Thus, validity of this technique remains a concern. Moreover, it has been suggested that individuals may alter their food habits to fit their preconceived notion of what they should consume (Gersovitz et al 1978).

2.2.2 Twenty-four Hour Recall

The validity and reliability of the 24-hour recall have been frequently questioned (Balogh et al 1971, Beaton et al 1979) with regard to whether or not the individual can accurately remember what he ate and whether one day's intake is actually representative of an individual's habitual intake. Balogh et al (1971) showed that four recalls were necessary if in half the population, the mean caloric intake could be recorded as within $\pm$ 20% of the true mean. For other nutrients, the number of 24-hour recalls required was much higher. However, Hunt et al (1979) found very little difference in nutrient intake between 5 dietary recalls, with the exception of vitamin A. This difference in vitamin A is not surprising, as vitamin A is con-

centrated in relatively few foods, and day-to-day intake varies considerably. Other workers have reported a day-to-day variation in nutrient intake with the 24-hour recall, as well as a strong sex difference (Beaton et al 1979, Yudkin 1951). Beaton and co-workers found that women ate more on Sunday than on weekdays. However, both this day-to-day effect and the sex difference in absolute nutrient intake disappeared when expressed as nutrient concentration. Furthermore, the fact that men and women ate different quantities of food provides a strong basis for statistical analysis by sex. Two recent researchers attempting to elucidate the accuracy and limitations of the 24-hour recall have shown similar findings (Gersovitz et al 1978, Madden et al 1976). Both studies surveyed the intake of non-institutionalized elderly subjects eating at a congregate centre. To test internal validity, the 24-hour recalled intake was compared with the actual intake of nutrients. In the paired t-test, no significant differences were found between mean recalled intake and mean actual intake, with the exception of energy and protein in Madden's and Gersovitz's studies, respectively. In both of these former studies, regression analysis demonstrated the "flat-slope syndrome", in which recalled intakes tend to overestimate intakes below the mean and underestimate those above the mean. Thus the 24-hour recall would seldom indicate a difference where none exists. For group comparison, however, there is a danger of false negative, that is, failing to detect an actual difference between groups.

Thus, for large groups, the 24-hour recall is the most practical because of its wide applicability to population groups, regardless of

age, education, and intelligence. Because an interview generally takes only about one hour, this method attains a high participation rate. Moreover, bias of intake by the patient is often avoided if there is no prior knowledge of the interview. It was the method chosen for both the Ten-State Nutrition Survey (1969-70) and the Nutrition Canada Survey (1970-72).

The 48-hour recall, an extrapolation of the 24-hour recall has been used by at least one other group of researchers (Smith and Gee 1979). It was suggested that this method minimizes the error due to day-to-day variation in nutrient intake and obtains a more representative intake, while not taxing the memory much more than the 24-hour recall. However, research has not been conducted to confirm whether the 48-hour recall is more representative than one 24-hour intake, or indeed, two 24-hour intakes.

The recall method was the method chosen in the present study for assessment of dietary intake, partly because of the size of the group. Although the CD group totalled only 47, it was selected from a larger group of 154 gastrointestinal outpatients, all of whom had assessments of dietary intake. Another consideration was that by using the recall method, nutrient intake could be assessed by means of a one-hour interview at the time of the patient's visit to the clinic. Thus, participation rate was essentially 100%. Moreover, the patient had no prior knowledge of the interview, and therefore, could not change his food intake to comply with his preconceived idea of a "good diet".

The 48-hour recall was chosen over the 24-hour recall, partly to achieve some representation from both weekends and weekdays. Also,

since some patients were from out-of-town and travelled as much as a full day prior to the clinic visit, food intake during the preceding 24 hours might not be representative of their usual intake.

2.2.3 Food Frequency

Frequency of consumption of various food groups is sometimes used to assess the quality of diet. Because this method does not define portions, it is only an estimate, and as such, is useful to describe the eating habits of a population, but cannot be used to predict nutrient intakes. Hunt et al (1979) compared results of a food frequency questionnaire with mean nutrient intakes from 5, 24-hour recalls. These two methods gave similar mean estimates of carbohydrate and calorie intake, but the data on other nutrients were from 6-88% greater with the food frequency questionnaire. While the food frequency method may not be useful in estimating the nutrient intake of an individual, it may serve as a useful adjunct to other methods, and if used to supplement a 24-hour recall, would partly overcome the common criticism that the 24-hour recalled intake may not represent a typical day's intake. However, like other methods, this method does depend on the recollective skills of the subject.

2.2.4 Dietary History

This method, first described by Burke in 1947, attempts to establish the "usual consumption" of a subject by interview. Like the 24-hour recall and food frequency methods, it depends heavily upon the memory and cooperation of the subject. Being relatively time-consuming, as well, renders this method unsuitable for a large number of subjects. Many researchers feel that the diet history tends to

overestimate intakes (Young et al 1952). However, this may depend on the relative weight of a subject, as another researcher found that fat people claim to eat less than thin people (Lincoln 1972). The most limiting aspect of this method, however, is the degree of training required to obtain repeatable results. Indeed, Burke (1947) estimated that even qualified nutritionists would require several months training to accurately estimate an individual's habitual intake by the dietary history method.

2.3 Use of Laboratory Parameters for Assessment of Nutritional Status

Laboratory indices are indicators of body metabolism at a given point in time, and as such provide the biochemical basis necessary for objective assessment of nutritional status.

Laboratory measurements used to evaluate nutritional status include: levels in blood and urine, abnormal metabolic products in blood or urine, alterations in activities of certain blood enzymes, metabolites in urine, and saturation or load tests. However, it is important to recognize that there are certain limitations to all biochemical measurements, and the following points should be kept in mind. Firstly, urinary excretion levels vary more than plasma levels and, therefore, are less definitive (Christakis 1973). Biological levels fluctuate from time to time, giving rise to a variation within individuals and between individuals, which may be within normal "limits". Moreover, variations in biochemical measurements of some nutrients exist between sex, age, and race. Although the "limits" themselves, which are selected as cut-off points for certain degrees

of risk of deficiency are based on current, scientific knowledge, such knowledge is never complete in the scientific sense. Thus, decisions regarding critical levels will be somewhat arbitrary. Finally, it must be remembered that the finding of an abnormal biochemical test does not define the mechanism of nutrient deficiency, and the altered nutritional state may be due to a primary deficiency or may be secondary to pathological conditions or a deficiency of a metabolically-related nutrient. This section (2.3) will discuss the use of laboratory parameters in normal individuals, while the pathogenesis of nutritional deficiency in CD will be discussed in a later section (2.6).

2.3.1 Folate

Significant reserves of body folate are contained in the liver: 5-10 ng/g wet liver (Sauberlich et al 1974). Studies indicate that serum folate levels correlate reasonably well with liver biopsy and, therefore, that serum folate levels do provide an indication of body stores (Leevy et al 1965). However, though serum folate is an easy, early, and sensitive measurement, it is thought to indicate recent dietary intake, while red cell folate is considered to reflect long term tissue folate stores. In considering the biochemical and hematological changes that take place during dietary deprivation of folate (Herbert 1962) one notes that low serum folate levels occur as early as 22 days after folate deprivation. Low red cell folate levels occur after approximately 123 days, indicating folate deficiency at the time of erythrocyte formation, some four months previous, and megaloblastic anemia occurs shortly there[illegible] about 134 days. However, a low red cell folate does no[illegible]tween megaloblastic anemia due

to folate deficiency or vitamin B_{12} deficiency. Because vitamin B_{12} is a cofactor in the synthesis of methionine from homocysteine, in which folate functions to transfer the methyl group, a vitamin B_{12} deficiency traps folate in the methyltetrahydrofolate form (Herbert and Zalusky 1962). This may result in low red cell folate, but elevated or normal serum folate (Herbert 1967). However, a low serum folate, in addition to a low red cell folate provides strong evidence of a primary folate deficiency.

2.3.2 Vitamin B_{12}

Vitamin B_{12} is widely distributed in animal products and a primary deficiency is rare. Even in strict vegetarians who eat no animal protein, vitamin B_{12} deficiency takes 10-20 years to develop due to enterohepatic circulation of vitamin B_{12} and slow loss of body stores (Herbert 1968). However, a deficiency can be measured by serum B_{12} levels, which have been associated with low body vitamin B_{12} (Boddy and Adams 1972).

For reasons explained in 2.3.1, if vitamin B_{12} deficiency is suspected, it is essential to rule out folate deficiency. In folate deficiency, serum B_{12} levels may be low, but are generally still higher than in patients with pernicious anemia or a mixed deficiency. Both a low serum folate and a low red cell folate would be suggestive of folate deficiency or a mixed deficiency. If a vitamin B_{12} deficiency is thought to exist, the Schilling's test can indicate whether the deficiency is due to impaired absorption, bacterial metabolism, or dietary deficiency. In the Schilling's test, if absorption is normal when vitamin B_{12} is given without intrinsic factor, then the defi-

ciency is dietary. If absorption is not normal, then testing with intrinsic factor will indicate whether malabsorption is due to lack of intrinsic factor or other reasons, such as bacterial metabolism of vitamin B_{12}, ileitis, or ileal resection. In addition, incomplete urine collection could give false negative results. Comparison with urinary creatinine will serve as a check for complete urine collection.

2.3.3 Iron

There are many tests for predicting the presence of iron deficiency, and the best results are obtained by using more than one measurement, since an iron deficiency can be caused by a number of nutritional and non-nutritional factors.

Hematocrit is useful in suspecting the diagnosis of iron deficiency, but is not conclusive, as deficiencies of folate, vitamin B_{12}, and vitamin B_6 can also cause decreased hematocrit values (Sauberlich 1979). Measurement of hemoglobin gives a more direct measurement of anemia. However, hemoglobin falls in megaloblastic anemia as well as iron deficiency, and can vary according to sex, age, and nonnutritional diseases, especially those involving blood loss and inflammation. The measurement of both serum iron and the % saturation of transferrin will give more clinical significance. Low serum iron, increased total iron binding capacity (TIBC), and a low % saturation of transferrin indicate iron deficiency. However, in hemorrhage or hemolysis, serum iron might remain low for some time after iron supplementation or blood transfusion (Munro and Linder 1978). Furthermore, abnormalities in the former biochemical parameters occur as frequently in CD

patients with anemia due to chronic disease as in CD patients with iron-deficiency anemia (Dyer et al 1972, Thomson et al 1978). Thus, hematocrit, hemoglobin, serum iron, TIBC, and % transferrin saturation are unreliable in the diagnosis of iron deficiency in CD patients.

Body iron stores are reflected by bone marrow hemosiderin, though measurement is subjective and semiquantitative. Serum ferritin has been shown to correlate closely with hemosiderin, and to have a high predictive value in detecting IBD patients with iron deficiency (Thomson et al 1978). Low serum ferritin is generally associated with iron-depleted stores, but false high ferritin levels can occur with rapid turnover of cells, liver disease (Eastham et al 1976), inflammation, hemolysis secondary to SAS therapy (Thomson et al 1978), Hodgkins disease and other malignancies (Jones et al 1973), fever (Elin et al 1977), and rheumatoid arthritis (Bentley and Williams 1974).

2.3.4 Vitamin A

Total vitamin A activity is determined mainly by its two forms in foods: preformed retinol and the pro-vitamin B-carotene. Excess vitamin A is stored in the liver as retinol (Hume and Krebs 1949) and thus measurement of liver retinol is a direct measure of vitamin A reserves. However, as liver biopsy is impractical for routine use, serum levels of retinol and carotene are used, which have been shown to be related to dietary intake of these nutrients (Patwardhan 1969).

Interpretation of the significance of the measurement of serum retinol, however, is complicated by the uncertainty of the magnitude of hepatic reserves (Hodges and Kolder 1971). When dietary intake of

vitamin A is inadequate, the stored retinol in the liver is mobilized to maintain serum retinol concentrations. Generally, however, this level is somewhat lower than the range of 45-65 ug/dl observed in adults with adequate intakes of vitamin A (Hume and Krebs 1949, Sauberlich et al 1974). However, when prolonged low intakes draw upon the liver reserve, a considerably lower serum retinol level (less than 20 ug/dl) indicates depleted or depleting liver stores as well as a low dietary intake. This relationship was shown in experimental vitamin A deficiency of adult men (Hodges and Kolder 1971). A daily intake of 75 ug of retinol in vitamin A depleted men resulted in serum retinol less than 10 ug/dl, being indicative of depleted liver resources. When the dietary intake was increased to 300 ug, the serum retinol level rose only slightly to 19 ug/dl, indicating that intake of vitamin A was still inadequate and that liver stores of vitamin A were probably not being repleted. However, at a vitamin A intake of 2400 ug/day, the serum retinol rose to 60 ug/dl, indicating adequacy of vitamin A intake and probable repletion of liver vitamin A. Skin lesions associated with vitamin A deficiency disappeared and serum retinol levels increased with an intake of 600 ug/day retinol, further supporting the relationship between dietary and serum retinol, and serum retinol and hepatic stores. However, serum retinol can also be reduced in febrile state, chronic inflammation, and liver disease (Sauberlich et al 1974), all of which can occur in CD.

Serum carotene is considered to reflect recent dietary carotene intake (Patwardhan 1969) and is used as an initial screening test for malabsorption. However, a low serum carotene concentration should be

interpreted with caution. For one thing, a low serum carotene could simply indicate a low carotene consumption. Moreover, in Patwardhan's study, about 60-100% of the vitamin A consumption was said to come from the precursor forms, while in Canada considerably less of the vitamin A (32%) comes from carotenoids (Dietary Standard for Canada 1975). Also, the main site of B-carotene conversion to retinol is the intestinal mucosa and the percentage of B-carotene that is absorbed unchanged varies from 1.7-46.9% (Blomstrand and Werner 1967, Goodman et al 1966). Thus, a low serum carotene could merely reflect an increased efficiency of conversion of B-carotene to retinol. Yet, this does not explain why retinol and carotenoid levels in serum have been shown to be related to one another and serum retinol is related to total vitamin A activity (Patwardhan 1969). Furthermore, in diseases characterized by fat malabsorption, such as celiac sprue (Moore 1960) and cystic fibrosis (Underwood and Denning 1972), both low serum carotene and low serum retinol are found. Yet in adults with cystic fibrosis, there was no correlation between stool fat and serum carotene concentrations (Brown et al, unpublished observations 1980). However, since serum retinol levels are maintained for some months by hepatic stores, if malabsorption of fats and fat-soluble nutrients is suspected from low serum carotene, it can be confirmed by other tests, such as fecal fat determination.

2.3.5 Protein-Calorie Malnutrition

Protein and calorie malnutrition often occur together, since a reduction in calories almost invariably involves a reduction in

protein. Furthermore, when calorie supply is inadequate, protein is used for energy.

Evidence of dietary protein-calorie deficiency can be found in both anthropometric and biochemical measurements and when taken together can be very useful, diagnostically (also discussed in 2.4).

In assessment of almost 400 patients, Blackburn and Bistrian (in Schneider et al, Nutritional Support of Medical Practice, 1977) have identified three common types of PCM. These include visceral attrition state, adult marasmus or cachexia, and intermediate state, each of which is characterized by various anthropometric and biochemical parameters.

Visceral attrition is an acute state, which occurs in well-nourished or even over-nourished patients whose intake is largely carbohydrate. The classic example is the hospital patient receiving dextrose infusion. The insulin produced due to the dextrose and catabolic stress reduces the release of amino acids from the muscle. Thus serum albumin and transferrin are depressed, indicating decreased availability of amino acids for protein synthesis, though anthropometric measurements may be preserved due to rapid onset. A study of malnutrition in surgical patients more than one week after surgery, found depressed plasma transferrin and albumin levels in 73% and 52%, respectively (Hill et al 1977b). Depressed lymphocyte counts are generally associated with reduced serum transferrin and albumin levels (Bistrian 1975, Young and Hill 1978), and are considered to indicate protein malnutrition.

Adult marasmus or cachexia indicates chronic inadequate ingestion of both calories and protein. Because there is a supply of protein, even though it may be minimal, serum transferrin and albumin are preserved until quite late in a deficiency. Anthropometric measurements decrease as lean and fat tissue are sacrificed for preservation of visceral proteins.

The above states are, to a greater or lesser extent, indicative of primary PCM. However, they are not always so easily discernable, and may overlap with the intermediate state, which can occur in moderate to severe stress of major surgery, trauma or heart failure. In the patient who is already somewhat depleted, the additional insult of major surgery can rapidly produce visceral protein attrition, as well as depleted anthropometric measurements. Thus, it is difficult to separate the effects of catabolic stress from those of PCM.

Decreased serum protein may also occur as a result of decreased protein synthesis, carcinoma, infection, or increased losses as in hemorrhage, exudates through fistulae, diseases of the kidney and skin, or protein-losing enteropathy (Ravel 1969). Moreover, transferrin levels are increased in iron deficiency, and thus could mask low transferrin levels due to PCM.

Nutritional depletion often results in decreased immunocompetence in the malnourished individual. Depressed cellular immunity (as measured by the Candida skin test and DNCB) and decreased lymphocyte counts have been associated with PCM in adults (Bistrian 1975). Skin tests assess the cell-mediated function in vivo, by observing the body's reaction to injected antigens. However, like all clinical

tests, there are multiple limitations to the skin test. Anergy can result from conditions such as infection, liver disease, uremia, immunotherapy, and malignancy. Even in healthy individuals, the immune mechanism may not function optimally at all times. As well as PCM, a low concentration of zinc or vitamin A could also result in a negative skin test (Sauberlich et al 1979).

Urinary constituents can be used to assess protein status. Creatinine excretion corresponds to lean tissue mass (Arroyave and Wilson 1961), and thus can be used to assess metabolically active tissue by means of the creatinine height index (CHI). CHI is defined as the 24-hour urinary creatinine excretion divided by the expected 24-hour urinary creatinine excretion of a normal male and female of the same height (Scrimshaw et al 1972). The obvious limitation is that it requires a 24-hour urine collection. Moreover, accurate timing is essential, as even a 15 minute error in voiding time over a 24-hour collection period will result in a 1% error (Forbes and Bruining 1976). While it does not distinguish protein deficiency due to malnutrition, from other causes of protein deficiency, CHI is a sensitive indicator of inadequacy, and thus may be an earlier indicator of PCM than some other measurements.

2.3.6 Vitamin C

Vitamin C is not stored in appreciable amounts in body tissue, and, therefore, biochemical determination of serum vitamin C is a measure of tissue saturation, which reflects recent dietary intake (Hodges et al 1971). A decrease in dietary intake of vitamin C will be rapidly reflected in serum ascorbate concentration. Hodges et al

(1971) reported that with a diet free of vitamin C, serum ascorbate levels fell to one-half of the initial concentration within 10 days, and low levels within 40 days, with symptoms of scurvy occurring shortly thereafter in most patients. Although serum ascorbate levels are related to leucocyte ascorbate levels (Sauberlich et al 1974), the latter measurement is considered to be a better reflection of tissue stores of vitamin C (Burns 1975), while the former measurement is thought to be more closely related to recent dietary intake (Hodges et al 1971). In vitamin C deprivation, leucocyte ascorbate levels fall more slowly and are not pronounced until clinical manifestation of scurvy (Herman et al 1976). Thus, while a depressed level of leucocyte ascorbic acid may be indicative of long-term dietary deficiency, it is not a very sensitive test.

2.3.7 Calcium/Vitamin D

About 99% of body calcium is in the skeleton, with the remaining 1% distributed in the serum and other body fluids (Harper et al 1979). Although skeletal calcium as measured by bone biopsy, hand x-ray, bone densitometry, and other measurements is a reflection of long-term calcium nutriture, serum calcium is closely regulated by homeostatic mechanisms. Thus, inadequate dietary intake of calcium will not be reflected by changes in serum calcium (DeLuca 1977), as serum calcium will be maintained at the expense of skeletal calcium. Low serum calcium concentrations do occur in hypoparathyroidism, renal disease (Harper et al 1979), hypomagnesia (Gerlach et al 1970), hypoproteinemia (Schneider et al 1977), and disease characterized by malabsorption (Hahn et al 1979).

Urinary calcium excretion remains relatively constant for a given individual, regardless of intake, but varies widely between individuals. As well, increased urinary excretion of calcium occurs with increased protein intake (Allen et al 1979a), making it an impractical choice for assessment of dietary calcium intake.

Most of the dietary calcium (70-90%, Harper et al 1979) is excreted in the feces and is positively correlated with calcium intake. Therefore, the measurement of fecal calcium can be used to assess malabsorption. However, due to variation in fecal flow, fecal calcium can be incorrectly estimated, particularly without the use of a fecal marker (Allen et al 1979b). Furthermore, in gastrointestinal diseases such as CD, where protein-losing enteropathy is known to occur (Beeken et al 1972), it is possible that endogenous calcium loss, as well, could contribute to fecal calcium, thus leading to an overestimation of calcium malabsorption.

Vitamin D, under the control of parathyroid hormone, is a major factor in control of calcium metabolism (DeLuca 1977). Thus, calcium deficiency can also occur secondary to vitamin D deficiency. For example, in two studies of osteomalacia (Hahn et al 1979, Pittet et al 1979), though calcium intakes were similar in osteomalacia patients and controls, vitamin D intake and/or exposure to sunlight differed and serum vitamin D levels were significantly lower in patients. It should be noted that serum vitamin D is not necessarily related to vitamin D intake, since exposure to sunlight as well as dietary vitamin D will affect serum vitamin D activity, and there will be some seasonal variation in serum vitamin D due to variation in hours of

daylight (Stamp and Round 1974). Serum vitamin D levels are also reduced in hypoparathyroidism, renal disease (DeLuca 1977), and liver disease.

2.4 Use of Anthropometric Measurements for Assessment of Nutritional Status

Anthropometric measurements have been widely used, for some time, in assessment of nutritional status of the community (Jelliffe 1966). While no single tool can characterize nutritional status, anthropometric measurements provide sensitive indices of both present and changing states of muscle mass and body fat. Being both practical and easily interpreted, anthropometric measurements are valuable complements to dietary information and are part of the nutritional status profile for many nutritional assessment programs (Bistrian et al 1974, Blackburn et al 1977).

2.4.1 Rationale for Use of Anthropometric Measurements

Height is the most basic of the anthropometric measurements, as it is used to determine ideal body weight, basal energy expenditure, and CHI. Body weight, while a useful tool, is a composite measure of its various tissue components: fat, skeletal muscle, skin and skeleton, viscera, plasma protein, and extracellular skeleton (Blackburn et al 1977). A change in body weight does not reflect a change in individual tissues, and, therefore, cannot detect abnormalities in body composition that often accompany disease, such as depletion of muscle mass and changes in fluid retention (Moore et al 1963, Ryan et al 1957). In a study of 13 hospitalized men (Ryan et al 1957), 9 men

with muscle wasting disease had a higher percentage of body fat than healthy controls, even though their percent of standard weight was 78% as compared to 96% in controls. Lean body mass was dramatically decreased in these 9 patients. In the remaining 4 thyrotoxicosis patients who were at 81% of their standard weight, % body fat was even greater than in the muscle-wasted patients. They had a marked loss of body cell mass which was partly masked by increased retention of extracellular fluid. Thus, it is clear that there is a need to measure body fat and muscle mass separately.

2.4.2 Measurement of Body Fat

There is a wide variety of procedures which can be used to measure body fat, including: cadaver analysis, densitometry, total body water, gaseous uptake of fat-soluble gases, ^{40}K counting, and radiological anthropometry. However, the need for a practical and rapid method to regularly assess caloric reserve eliminates the above methods. The technique of relating skinfold thickness to body fat was first described by Matiegka in 1921 and has since been the subject of extensive investigation. An investigation of 19 subjects at 55 sites showed a correlation of 0.82 between actual measurement of subcutaneous fat by surgical incision and measurement of skinfold (Fry 1961). In another study, the measurement of the outer fat shadow on roentgenograms was highly correlated with skinfold measurements of the lower thoracic site (0.85-0.88, Garn 1962). As well, the sum of the biceps, triceps, subscapular, and suprailiac skinfold correlate highly with body density, being 0.835 in men and 0.778 in women (Durnin and Rahaman 1967).

From the above investigations, it can be seen that skinfold measurements are a valid measure of body fat stores. In nutritional asessment, the TSF is generally used because it is the most practical (Jelliffe 1966).

2.5 Pathogenesis of Nutritional Deficiencies in Crohn's Disease

In examining the pathogenesis of nutritional deficiencies in CD, it is important to realize that all nutrient deficiencies result from one or more of five basic causes, summarized on the next page: inadequate ingestion, absorption, or utilization; and increased requirement or excretion (Herbert 1973).

Summary of Causes of Nutrient Deficiencies in CD

Mechanism	Cause
Inadequate Ingestion	Self-induced, iatrogenic, lactase deficiency
Inadequate Absorption	Reduced intestinal length, decreased enterohepatic circulation, bacterial overgrowth, drug therapy, intestinal atrophy, secondary to other nutrient deficiencies
Inadequate Utilization	Secondary to other nutrient deficiencies, cholestyramine
Increased Requirement	Drug therapy, oral contraceptive agents, increased hematopoiesis, inflammatory response
Increased Excretion	Impaired enterohepatic circulation, protein-losing enteropathy, drainage through fistulae and ileostomies, cholestyramine, diarrhea.

The cause that should be considered first and foremost in nutritional deficiency is inadequate dietary intake. During illness, a spontaneous reduction in food intake may occur due to anorexia, or pain and diarrhea, associated with eating. Over the long term, patients may selectively eliminate certain food groups due to their

misconceptions about low-residue diets. If fruits and vegetables are eliminated, there is a danger of inadequate intake of vitamin C, folate, fiber and possibly vitamin A. Furthermore, physicians may inadvertently encourage deficiencies by prescribing a low residue diet, which is now known to be unncessary from a patho-physiological point of view, except where there is a tendency to repeated small intestinal obstruction (Heaton et al 1979). Lactase deficiency, either primary or secondary to altered mucosal integrity, can occur in Crohn's disease. Elimination of diary products will result in reduced intake of calcium, riboflavin, and possibly protein and vitamin D, unless appropriate dietary changes and supplements are effected.

A most obvious source of inadequate absorption in IBD is loss of intestinal length through resection. While the majority of nutrient absorption takes place from the small bowel, Smith and Balfour (1972) state that resection of one-third of the small bowel is still compatible with normal nutrition. Resection beyond this results in decreased absorption of all nutrients, known as "short-bowel syndrome", and poses a threat to general nutriture. Indeed, weight loss in the presence of high caloric intake, may well indicate malabsorption (Dawson 1972). "Short-bowel syndrome" is identified as one of the causes of mineral deficiencies such as magnesium and zinc (Sitrin et al 1980).

Absorption of iron is impaired by upper intestinal disease (Brooke et al 1977), as is folate (Hoffbrand et al 1968). With ileal involvement, selective malabsorption of bile acids and vitamin B_{12} occurs. Unabsorbed bile salts pass into the colon where they block water and electrolyte absorption (Brooke et al 1977), further adding

to the risk of depletion of magnesium, zinc, sodium, potassium, and water. In addition, bile salts may alter colonic permeability and allow absorption of oxalate; a partial explanation for the hyperoxaluria that is seen as a complication of Crohn's disease (Earnest 1977). Continuous excretion of bile acids will ultimately lead to depletion of the bile acid pool and interruption of the enterohepatic circulation, with ensuing malabsorption of fats and fat-soluble vitamins. Malabsorption of vitamin D interferes with absorption and utilization of calcium. Unabsorbed fatty acids bind calcium and form insoluble soaps in the intestinal lumen, further aggravating calcium malabsorption. The solubility theory of hyperoxaluria suggests that as less calcium is available for formation of Ca oxalate, free oxalate forms soluble complexes with other salts and is increasingly absorbed (Earnest et al 1974). Not only has a positive correlation been shown by Earnest et al (1974) between steatorrhea and hyperoxaluria, but decreased dietary oxalate or increased dietary calcium both result in decreased urinary oxalate. Since the ileum is also the site of vitamin B_{12} absorption, it comes as no surprise that vitamin B_{12} absorption is inversely correlated to length of ileum resected (Dyer et al 1972). However, vitamin B_{12} deficiency also occurs in patients whose disease is not limited to the ileum (Filipsson et al 1978). If there is gastric involvement, lack of intrinsic factor will contribute to malabsorption of vitamin B_{12}, as well; a factor of some importance since the incidence of peptic ulceration in Crohn's disease is from 10-20% (Cooke 1975, Kagnoff 1979). Moreover, a primary vitamin B_{12} or folate deficiency can produce partial intestinal and/or stomach

atrophy, leading to intestinal malabsorption and generating a vicious circle of primary and secondary vitamin B_{12} deficiency if left untreated (Herbert 1973). A secondary folate deficiency may occur by this same mechanism or due to zinc deficiency (see 2.6.2). Other factors causing decreased absorption of vitamin B_{12} include pancreatic insufficiency and tying up of ionic calcium as insoluble soaps (Herbert 1973).

The presence of fistulae, blind loops and strictures may lead to bacterial overgrowth with vitamin B_{12}-greedy bacteria making even less vitamin B_{12} available for absorption (Brooke et al 1977). Bacterial synthesis of some nutrients, such as folate, may actually be increased, though the extent of this synthesis is unknown. Other effects of bacterial overgrowth include decreased synthesis of vitamin K (Brooke et al 1977) and deconjugation of bile acids (Farivar et al 1980).

The two major drugs used to treat IBD, salazopyrine and prednisone, have been shown to affect nutrient absorption. Salazopyrine affects folate absorption and utilization by competitive inhibition in the intestine and elsewhere (Dhar et al 1976), while prednisone affects calcium absorption through its antagonistic effect on vitamin D (Avioli et al 1968, see 2.7.1). Absorption of vitamin B_{12} is reduced by cholestyramine (see 2.7.4).

Decreased utilization secondary to other nutrient deficiencies is known to be one cause of folate deficiency. Both vitamin B_{12} and vitamin C are necessary for folate utilization, as described more fully in sections 2.3.1 and 2.6.4. respectively. Cholestyramine binds

bile acids in the gut lumen, preventing their utilization and absorption, and increasing excretion (see 2.7.4).

Prednisone appears to increase the requirement for protein, vitamin C, vitamin B_6, and possibly zinc (see 2.7.1). Salazopyrine induces mild hemolysis and thus places an additional demand on all hematopoietic nutrients (see 2.7.2). Moreover, hematopoiesis increases the demand for all nutrients through increased body metabolic rate (Herbert, 1973). Likewise, in CD there is a chronic inflammatory response and increased cell turnover (Brooke et al 1977). However, whether or not this response causes an increased demand for nutrients is theoretical.

The nutritional status of IBD patients receiving drug therapy, who are also using oral contraceptive agents (OCA) demands additional attention. Biochemical evidence of poor folate, vitamin B_6, vitamin B_{12}, vitamin C, riboflavin, thiamin, and zinc status has been found in OCA users (see 2.7.3).

Increased excretion of nutrients, particularly water and electrolytes occurs through fistulae and ileostomies. Additional protein excretion from the ulcerated gut contributes to protein deficiency (Beeken et al 1972). The presence of unabsorbed bile acids in the colon induces secretion of water and electrolytes (Earnest 1977). Moreover, diarrhea, from a variety of causes, is a feature in at least 70% of IBD patients (Kagnoff 11979). Regardless of the cause, prolonged excretion from the gastrointestinal tract results in sodium, potassium, magnesium, and zinc depletion (Sitrin et al 1980, Cooke 1975, Brooke et al 1977) and dehydration.

In addition to the many mechanisms already mentioned for folate and vitamin B_{12} deficiency, increased biliary loss may also interfere with enterohepatic circulation of folate and vitamin B_{12}. Both folate and vitamin B_{12} are excreted in bile and have a daily circulation of 100 ug and 0.5-5 ug, respectively (Herbert 1968).

Chronic iron loss occurs as slow, continual blood loss from ulceration (Brooke et al 1977), and is probably related to severity of disease (Dyer and Dawson 1973). Additional iron may be excreted if cholestyramine is used, as it has been shown to bind iron (Thomas et al 1971).

2.6 Nutritional Deficiencies in Crohn's Disease

2.6.1 Anemia

Anemia is one of the most common and widespread nutritional abnormalities of CD and has been associated with deficiencies of iron, folate, and vitamin B_{12} (Dyer et al 1972, Hoffbrand et al 1968, Thomson et al 1978). For example, in hospitalized CD patients, Dyer et al (1972) found 79% of males and 54% of females to be anemic. In addition, low levels of various hematopoietic parameters were found in the following percentage of patients: serum iron (65%), total iron binding capacity (TIBC) (22%), serum B_{12} (16%), serum folate (65%), and red cell folate (35%). Bone marrow aspirations for hemosiderin showed 39% of CD patients to be iron deficient. Megaloblastic anemia was found in 39% of patients, with approximately 1/3 attributed to vitamin B_{12} deficiency and 2/3 to folate deficiency.

2.6.2 Folate

Folate deficiency in CD is frequent and well-documented (Dyer et al 1972, Elsborg and Larsen 1979, Hoffbrand et al 1968). In one study (Hoffbrand et al 1968), serum folate levels less than 2.0 ng/ml were found in 28% of patients. Serum folate values were related to the severity of the illness, as were red cell values. Formiminoglutamic acid (FIGLU) excretion was similarly associated with severity of disease. Haematological changes attributable to folate deficiency included macrocytosis, hypersegmented polymorphs, and megaloblastic marrow, and were observed more frequently in severely-ill patients. Vitamin B_{12} was excluded as a cause of deficiency in all but one patient.

An attempt was made to assess the causes of folate deficiency. Folate absorption, as determined by a standard oral dose of folic acid (40 ug/kg body weight) was subnormal in 4/16 patients. Three of the four had jejunal and/or duodenal involvement, while the remaining patient had CD of the terminal ileum. Thus, as most of the patients had ileal involvement, folate deficiency in jejunal involvement was concluded to be related to malabsorption.

Dietary folate was assessed in 12 patients and was above the 50 ug daily minimum (Herbert 1962) in the 7 mildly-ill patients. Four of them had normal folate absorption, though there was biochemical and hematological evidence of folate deficiency. On the other hand, the intake of all 5 severely-ill patients was less than 50 ug. From this, Hoffbrand et al concluded that inadequate intake appeared to be the major contributory factor to folate deficiency in the severely ill,

but that neither inadequate intake, nor decreased absorption were major factors in the mildly-ill patients. However, it must be pointed out that the dietary standard of 50 ug/day free folate is the minimum daily requirement to prevent symptoms of folate deficiency in a healthy adult (Herbert 1962). This figure does not allow for variation in individual requirement, nor does it contain additional allowances as may be required in illness. Only one patient had an intake equal to the recommended dietary allowance (RDA) of 200 ug free folate. Thus, the possibility of inadequate ingestion of dietary folate appears to be understated in the study by Hoffbrand and co-workers.

Similarly, Dyer et al (1972) found biochemical evidence suggestive of folate deficiency in CD, with serum folate levels less than 3.0 ng/ml in 44% of patients and red-cell folate less than 160 ng/ml in 35%. Twenty-four percent of the patients had megaloblastic changes attributable to folate deficiency. What were the suggested mechanisms for folate deficiency in this study? Folate deficiency was not more severe or more frequent in patients with disease restricted to the jejunum, which eliminates malabsorption as a cause of folate deficiency in these CD patients. This conclusion is in contrast to that of Hoffbrand and co-workers (1968), though conclusions in the 1968 study were based on abnormal folate absorption in those patients with jejunal involvement. Moreover, xylose absorption from the jejunum was almost invariably normal in Dyer and Dawson's (1973) patients with jejunal involvement. Dyer and co-workers (1972) also found that the mean values of red-cell and serum folate concentrations decreased with more severe disease and speculated that increased requirement and

utilization of folate were the cause of folate deficiency, though increased loss and/or decreased food intake could just as well be the cause of increased folate deficiency associated with severe disease. Though decreased intake was suggested as a cause of folate deficiency, unrelated to severity of disease, Dyer and co-workers did not give any evidence that folate intake was reduced in their CD patients.

Elsborg and Larsen's findings (1979) of low serum and erythrocyte folate levels in 54% and 27%, respectively, of CD patients are similar to the findings of Hoffbrand et al (1968) and Dyer et al (1972). Slight megaloblastic changes were found in about 14% of all patients. Unlike the former studies (Dyer et al 1972, Hoffbrand et al 1968), however, there was no significant correlation between folate values and disease severity. However, the criteria for judging disease activity varied from study to study and emphasizes the need for use of a standardized activity index. Similar to Hoffbrand and co-worker's results, 21% of the patients in Elsborg and Larsen's group were found to malabsorb folate, though this malabsorption was not related to disease site, nor to maintenance dose (1-3 g/day) of SAS. Though it has been suggested that SAS therapy decreases folate absorption (Dhar et al 1976), other researchers have not substantiated this finding (Gerson and Cohen 1976, see 2.7.2). However, recent work by Lucas et al (1978) suggests that folate malabsorption could be due to a deficient acid microclimate, which alters the amount of weak acid available for non-ionic diffusion. This theory is strengthened by the finding that experimental alkalinization of the jejunum has been shown to decrease the intestinal absorption of folate and that pancreatic

insufficient patients had a higher folate absorption than did controls (Russell et al 1979).

The association of greater folate depletion with higher doses of SAS suggested that increased cell turnover due to mild hemolysis could be partly responsible for the folate deficiency (Das et al 1973).

As in the study by Hoffbrand et al (1968), only a small number of patients were consuming less than the 50 ug minimum daily requirement (Elsborg and Larsen 1979), but none consumed the RDA (1980) of 200 ug free folate. Thus, less-than-adequate intakes were likely contributing to the folate deficiency observed in these CD patients, though there was no correlation between food folate and serum or erythrocyte folate.

Folate deficiency can also occur secondary to other nutrient deficiencies (including vitamin B_{12} (Herbert 1973), vitamin C (Gerson and Fabry 1974), and possibly zinc deficiency (Tamura et al 1978)). While vitamin B_{12} deficiency was cited as a cause of folate deficiency in two patients in the preceding studies (Dyer et al 1972, Hoffbrand et al 1968), examination of other nutrients was not considered in any of the former studies.

2.6.3 Iron

Iron deficiency has been widely described in CD (Bartels et al 1978, Dyer et al 1972, Thomson et al 1978) and much discussion has revolved around the validity of various laboratory parameters in the diagnosis of iron deficiency. The traditional method for assessing body iron stores is the estimation of stainable bone marrow hemosiderin. There is remarkable agreement in the literature as to the

finding of absent bone marrow iron in CD patients: Thomson et al 25%, Bartels et al 29%, Dyer et al 39%. All of the researchers reported that abnormalities of serum iron, TIBC and percent saturation of transferrin occurred in iron deficient patients, but that these abnormalities occurred with equal frequency in those patients with anemia due to chronic inflammatory disease. Thus, serum ferritin, which has been shown to correlate with bone marrow iron in healthy individuals (Lipschitz et al 1974) was examined for its diagnostic efficacy in iron deficiency. Bartels et al (1978) reported a high correlation (0.94) between serum ferritin and body iron stores. Similarly, Thomson et al (1978) found that serum ferritin below 18 ng/ml and above 55 ng/ml had an excellent specificity and predictive value, but a low sensitivity and predictive error. However, the uncertainties of serum ferritin concentrations in the 18-55 ng/ml range in chronic inflammation and febrile illness have been reported by other workers as well (Bentley and Williams 1974, Jones et al 1973). It was speculated by Thomson et al that the sources of the increased ferritin could include the inflamed intestine, mild hemolysis secondary to SAS therapy, or a reticuloendothelial response to chronic inflammation, though lack of correlation between serum ferritin and each of disease activity, SAS therapy, and serum iron suggested that these explanations did not apply to all patients.

In attempting to explain the mechanism of iron deficiency in CD, Bartels et al (1978) examined iron absorption in 31 CD patients. As determined from both whole body counting and red cell ^{59}Fe incorporation following oral administration of $^{59}FeCl_3$ with a small carrier

dose, iron absorption was found to be normal in CD patients as compared to controls. Though there was a wide range of absorption, the magnitude of absorption was not related to disease activity, disease site, serum albumin, or hemoglobin. This suggested that iron deficiency was not due to malabsorption or increased loss. Yet, the presence of iron deficiency was somewhat of a paradox, as these patients were receiving oral iron medication, though the amount of the supplement was not reported. It is possible that patients were taking the supplements irregularily, or, alternatively, if the supplemental dose were small, a reduction in food intake could decrease iron stores. Furthermore, patients frequently take medication with meals and it has been shown that certain foods reduce iron absorption while other foods, especially those containing vitamin C, increase iron absorption (Rossander et al 1979). Moreover, recent findings of scurvy (Linaker 1979) and low leucocyte ascorbic acid levels in CD patients (Hughes and Williams 1978), raise the possibility that vitamin C deficiency could be contributing to iron deficiency in CD.

2.6.4 Vitamin C

In patients who adopt a low-residue diet, either self-imposed or physician-prescribed, the danger of nutrient deficiencies is very real. Restriction of fresh fruit and vegetables, specifically, can result in vitamin C deficiency. Ascorbic acid deficiencies, as determined by serum ascorbate and leucocyte ascorbate levels have been noted in CD (Gerson and Fabry 1974, Hughes and Williams 1978, Linaker 1979).

It was first reported by Gerson and Fabry (1974) that ascorbate concentrations in blood and ileal tissue were lower in CD patients than in controls. This was thought to be particularly significant, and it was suggested that the characteristic fistulae formation and poor wound healing in CD could be related to incomplete formation of collagen, which requires vitamin C.

Hughes and Williams (1978) compared leucocyte ascorbic acid (LAA) levels in 19 CD patients (161 nmol/10^8 WBC) to that of controls (233 nmol/10^8 WBC) and found a significant difference, though patients were still well above the safe antiscorbutic level of 85 nmol/10^8 WBC. Of the four patients consuming less than 30 mg of vitamin C, two had a LAA levels of less than the safe antiscorbutic level. A significant but low correlation (0.30) was found between LAA levels and dietary vitamin C. However, there was no relationship between LAA levels and surgery or drugs (SAS or azathioprine).

In another group of ten CD patients (Linaker 1979), the mean LAA level was 93 nmol/10^8 WBC as compared to 226 nmol/10^8 WBC in the control group. Scurvy was noted in one patient whose LAA level was 25 nmol/10^8 WBC, and upon assessment was found to be consuming less than 10 mg ascorbic acid per day. This patient is a classic example of one who had been on a self-imposed low residue diet because of abdominal cramps. Five of the patients had intakes of 30 mg or less, and of these, four had LAA levels below the safe antiscorbutic level. However, there was no significant difference in mean dietary intake between controls and patients.

Thus, low LAA levels in CD patients were associated with decreased vitamin C intake (Hughes and Williams 1978, Linaker 1979), but the mean vitamin C intake in CD patients was not lower than that of controls. This suggests that some aspect of the disease itself imposed upon a less than adequate intake was responsible for the subclinical vitamin C deficiency observed in CD patients.

Results of the above studies have implications for folate deficiency. Firstly, since vitamin C and folate are common to many of the same foods, a deficiency in one implies a concomittant deficiency in the other. Secondly, it is known that ascorbic acid prevents the irreversible oxidation of tetrahydrofolate to 10-formyl folic acid, thus removing it from the metabolic pool (Stokes et al 1975). It is not surprising then, that folate deficiency, as evidenced by megaloblastic anemia, does in fact occur in scurvy (Zalusky and Herbert 1961). However, the scorbutic patient in Linaker's study had a normal serum and red cell folate concentration. Though only one patient in the previous studies was reported to have scurvy (Linaker 1979), it is quite possible that subclinical ascorbic acid deficiency may be contributing to folate deficiency, particularly in view of low LAA levels in some CD patients.

2.6.5 Fiber

It is well known that over the last century, consumption of dietary fiber in North America has decreased, while consumption of refined carbohydrate has increased (Trowell 1976). This dietary alteration has been implicated in the pathogenesis of several prevalent disease states such as diverticular disease (Painter et al 1972),

cancer of the colon and rectum (Burkitt 1969), gout, ischemic heart disease (Trowell 1976), gallstones (Trowell 1976, Burkitt 1973), hiatal hernia, hemorrhoids (Burkitt 1973), and diabetes (Kiehm et al 1976). However, the basis for the suggestion that decreased fiber intake is involved in the etiology of these diseases is based on the observation that such diseases (including CD) are almost unknown in countries where dietary fiber intake is high. There are no published reports in the literature to suggest that dietary fiber manipulation can cause any of the above disease states in humans. However, there is growing evidence to show that fiber consumption in CD may differ from that of controls, and that consumption of refined sugars is substantially greater in CD patients than in controls (Kasper and Sommer 1979, Martini and Brandes 1976, Mayberry et al 1980, Thornton et al 1979).

Two reports on dietary fiber intake in CD were published in 1979 (Kasper and Sommer 1979, Thornton et al 1979). Kasper and Sommer reported that CD patients ate more dietary fiber (DF) than did controls, while Thornton et al reported that CD patients consumed slightly less DF than did controls. However, the CD patients in the former study consumed significantly more energy than did controls, and when DF was expressed per 1000 kcal the difference between CD patients and controls disappeared. Thus, the observed increase in fiber intake by CD patients was due the amount of food consumed, and when expressed per 1000 kcal, the DF consumption of CD patients and controls is the same. Both of the previous studies observed an alteration in fruit/vegetable consumption. Kasper and Sommer found that CD patients ate considerab-

ly less raw fruit and vegetables than did controls. There was no significant difference in cereal consumption (Kasper and Sommer 1979), including cornflake consumption (Thornton et al 1979) between CD patients and controls. Thus, a previous report of higher cornflake consumption at breakfast by CD patients (James 1977) was not confirmed.

Martini and Brandes (1976) were the first to report that CD patients ate significantly more refined sugar than controls, both before and after diagnosis of CD. However, this work was criticized for two reasons. Firstly, the average duration of the disease was 4-1/2 years and it is questionable whether or not patients could accurately remember dietary habits this long. However, mean sugar consumption remained higher in CD patients than in controls in post-diagnosis diet (166 g vs 74 g) as well as in pre-diagnosis diet (177 g vs 74 g). Secondly, the dietary method was criticized, as dietary intake was assessed by means of a postal questionnaire. However, two subsequent studies using the dietary history method (Thornton et al 1979) and the seven-day recall method (Kasper and Sommer 1979) confirmed Martini and Brande's finding of a significantly higher sugar consumption in CD patients. Refined sugar intake in CD patients compared to controls was reported to be 122 g vs 65 g (Thornton et al 1979) and 156 g vs 91 g (Kasper and Sommer 1979). Mayberry et al (1980) found that in addition to eating more refined sugar than controls, CD patients also ate more sugar than ulcerative colitis patients. However, he used the same (postal questionnaire) method for assessing dietary intake as Martini and Brandes (1976). Furthermore, his sugar consumption data were based on the quantity of sugar added

to beverages and cereals and, therefore, would be biased in favor of those consuming more beverages and cereals. Although the methodology of this study is suspect, the results do concur with the results of previous studies: increased sugar consumption is characteristic of the pre-diagnostic as well as the post-diagnostic diet of CD patients. Alterations in the diet for no apparent reason suggest aberrations in taste acuity. Impaired detection of sucrose has been reported in zinc-deficient CD patients (McClain et al 1980, Solomons et al 1977). Since several other characteristics of zinc deficiency also occur in CD patients, this leads one to wonder whether the observed increased sugar consumption in CD patients could be a compensatory response to the decreased taste acuity observed in zinc-deficient CD patients. If this were so, then a disproportionate consumption of sugars could signal a subclinical zinc deficiency.

Some authors have suggested that the dietary differences discussed above have etiological implications for CD. It has been postulated that habitual, excessive sugar consumption could alter the intestinal flora and milieu of the intestinal lumen, such that the mucosa may be damaged (Martini and Brandes 1976) or that the growth of an infective agent may be promoted (Thornton et al 1979). Unqualified acceptance of this theory is about as simplistic as the "reduced-fiber, increased disease" theory. While an association has been reported between increased refined sugar intake and CD, the experimental basis for suggesting refined sugar as a causal agent in CD is lacking.

2.6.6 Protein/Protein-Calorie Malnutrition

Early speculation was that hypoproteinemia in CD was due to decreased synthesis of protein. However, Steinfeld et al (1960) showed that hepatic synthesis of protein was actually greater than normal in CD patients and, while absorption of protein was somewhat decreased, it was not substantial enough to account for the observed hypoproteinemia. Steinfeld et al thus speculated that this hypoproteinemia was due to increased protein loss from the gut. Other investigators (Beeken et al 1972, Warshaw et al 1973) later confirmed Steinfeld and co-workers' speculation of protein-losing enteropathy (PLE) in patients with CD. Using ^{51}Cr albumin or ^{51}Cr chloride, Beeken et al showed that 70% of their patients with CD had excessive protein clearance, with maximal values reaching 15 times normal. However, serum protein levels were low in only eight patients. Thus, protein loss is far more extensive than suggested by serum protein levels. It is possible that increased hepatic synthesis of protein in CD patients is maintaining serum protein levels within normal in some patients, despite excessive loss. Though protein loss correlated poorly with the location of disease and malabsorption of xylose, vitamin B_{12}, or fat, it was highly correlated with the length of the diseased intestine. In contrast, the PLE in studies by Warshaw et al (1973) occurred in a patient with a comparatively short length (50 cm) of diseased intestine. It was also suggested that bacterial overgrowth was contributing to protein loss. The presence of fat malabsorption, perhaps caused by bile acid deconjugation in the presence of bacterial overgrowth, strengthened the suggestion of bacterial overgrowth.

There are few surveys which describe the incidence of protein malnutrition in inflammatory bowel disease (IBD) patients (Hill et al 1977a). However, one would expect that protein malnutrition would be highest in active disease where food intake may be low, in extensive disease where PLE may be high, and post-surgically when catabolic stress increases protein requirement. In 1977, Hill et al compared the incidence of protein malnutrition in various categories of IBD: ileostomy, remission, elective surgery, acute attack, urgent surgery, and post-surgical complications. They found that parameters indicative of poor protein status were usually associated with active disease: compared to controls and the other groups, IBD patients requiring urgent surgery had low values of plasma albumin, transferrin, pre-albumin, hemoglobin, and greater weight loss. Patients who developed major complications after surgery had even lower values for the ab parameters, and also had a lower arm muscle circumference than any other group. It is difficult to separate the effects of catabolic stress from those of protein-calorie malnutrition (PCM) in this group which closely resembles the intermediate state described by Blackburn and Bistrian (2.3.5). Increased amounts of protein and energy have been used in total parenteral nutrition (TPN) and enteral nutrition to decrease symptoms of PCM in CD patients, both presurgically and post-surgically (Elson et al 1980, Goode et al 1976, Harford and Fazio 1978, Kirschner et al 1981, Milewski and Irving 1980, Voitk et al 1973). Harford and Fazio used TPN as primary or adjunctive therapy in CD patients and reported an average weight gain of 9.5 pounds and an average increase in albumin of 0.49 g/dl. Elson et al

(1980) also reported weight gain, positive nitrogen balance and a similar increase in serum albumin in IBD patients with TPN. Though TPN is almost invariably associated with improvements in protein status, such improvements are not exclusive to TPN, and similar improvements are noted with enteral nutrition if it can be tolerated by the patient. Voitk et al (1973) reported weight gain and positive nitrogen balance in 12/13 IBD patients who were taking elemental diets, as well as few post-surgical complications in the 7 patients who ultimately required surgery. It is possible that a lack of post-surgical complications is due to increased protein intake, as protein malnutrition has been associated with delayed wound healing and immunoincompetence (Moore and Brennan 1975). As well, a relationship between duration of protein-depletion, weight loss, and serum albumin has been reported in rats (Daly et al 1972). Moreover, in these rats, as duration of protein depletion and weight loss increased, bursting strength of a standard colonic anastomosis decreased.

Goode et al (1976) reported the advantages of an elemental diet and a normal diet to be virtually the same. Lean tissue repletion, as measured by whole body ^{40}K counting was 18.5% and 19% in CD patients consuming elemental diets and normal diets, respectively. In a retrospective study, Milewski and Irving (1980) found median weight, hemoglobin, and plasma albumin to be the same in three treatment groups of CD patients: parenteral nutrition, low-residue diets, and normal diets. Oral nutrition has also been used successfully in children with CD to reverse growth failure, a sign of PCM (Kirschner et al 1981). Using TPN, Kelts et al (1979) reported a similar increase in

growth velocity in children with CD. On a regime providing 75 kcal/kg/day or greater, patients gained weight, increased lean body mass and resumed linear growth.

Finally, the catabolic effect of corticosteroid therapy on skeletal muscles is well-recognized and documented (Myles and Daly 1974, Young 1970). Negative nitrogen balance and decreased muscle mass are common in patients taking corticosteroids, regardless of the associated illness.

2.6.7 Vitamin B_{12}

Vitamin B_{12} malabsorption is a common finding in CD (Dyer et al 1972, Farivar et al 1980, Fausa 1974, Filipsson et al 1978). Because vitamin B_{12} absorption takes place in the ileum, one would expect malabsorption of vitamin B_{12} to be related to ileal involvement. However, studies have consistently shown that there is a poor correlation between malabsorption of vitamin B_{12} and extent of ileal disease (Farivar et al 1980, Fausa 1974, Filipsson et al 1978). This is likely due to several other factors in CD which can contribute to malabsorption of vitamin B_{12}: bacterial overgrowth, decreased intrinsic factor if there is gastric involvement, pancreatic insufficiency, lack of available calcium in the gut due to steatorrhea, and decreased intestinal length.

Dyer et al (1972) found low serum B_{12} and abnormal Schilling's test in 7% and 48%, respectively, of unoperated patients. However, these abnormalities occurred in a much higher percentage of resected patients: 33% had a low serum B_{12} and 83% had an abnormal Schilling's test. Moreover, the lowest levels of serum B_{12} were found in patients

who had had more than 100 cm resection of the ileum. Low serum B_{12} was not found in colonic involvement. Thus, in this study, vitamin B_{12} deficiency was usually associated with resection of the terminal ileum and was somewhat related to length of resection. In contrast, Fausa (1974) reported that malabsorption of vitamin B_{12} was unrelated to the length of ileum resected, but was found in most patients with ileocolic resection. This finding suggests bacterial overgrowth due to contamination of the ileum by colonic bacteria. Filipsson et al (1978) reported findings of vitamin B_{12} malabsorption in a much larger sample than either of the former studies. Vitamin B_{12} malabsorption and extent of diseased ileum showed a low correlation. However, urinary vitamin B_{12} excretion correlated highly (0.76) with the length of ileal resection, which confirms the earlier findings of Dyer et al (1972). Furthermore, vitamin B_{12} absorption did not improve significantly up to 3-5 years after surgery, though a significant improvement was observed in patients operated upon for disease confined to the large bowel. This finding exemplifies the decreased absorption of vitamin B_{12} that is associated with short-bowel syndrome.

Farivar et al (1980) examined vitamin B_{12} metabolism in unoperated CD patients. They found the Schilling's test to be positive in 42% of patients with ileal or ileocolonic involvement. As with the previous investigators, there was no correlation between the extent of ileal involvement and urinary vitamin B_{12}, nor between the Crohn's Disease Activity Index (CDAI) and urinary vitamin B_{12}. Moreover, a positive bile acid breath test was found in 42% of the patients. Though 19% of the patients were found to have bile acid malabsorption,

a normal bile acid absorption in the remaining 23% confirmed that elevated $^{14}CO_2$ excretion in the breath was due to bile-acid deconjugation in the presence of bacterial overgrowth. Thus, bacterial overgrowth was likely contributing to malabsorption of vitamin B_{12} in these patients with CD.

Thus, the above studies have shown that vitamin B_{12} malabsorption is not related to the extent nor the severity of ileal disease, but it related to the length of intestine resected and that bacterial overgrowth probably contributes to vitamin B_{12} malabsorption.

2.6.8 Calcium/Vitamin D

The endpoint of calcium deficiency in CD is metabolic bone disease (MBD). A recent study has shown that there was some evidence of MBD in 60% of CD patients as measured by photon densitometry, microradiological evaluation of the hands, or bone biopsy (von Westarp et al 1978). Other researchers have reported osteomalacia as measured by bone biopsy in 71% (Driscoll et al 1977) and 36% (Compston et al 1978) of patients with CD.

Abnormalities of calcium metabolism are associated with steatorrhea (Earnest et al 1974), as unabsorbed fatty acids may form insoluble soaps and inhibit absorption. Calcium absorption can also be reduced as a result of corticosteroid therapy (Avioli et al 1968, Klein et al 1977). Also, decreased intake could contribute to calcium deficiency, particularly in the case of lactose intolerance (Brooke et al 1978). In addition, increased intestinal loss of calcium has been associated with enteric protein loss (Krawitt et al 1976). Calcium deficiency can also occur secondary to vitamin D deficiency for which

there are several mechanisms: decreased dietary intake, malabsorption due to binding of vitamin D by cholestyramine (Compston and Horton 1978), or decreased absorption due to bile salt deficiency or intestinal disease (Sitrin et al 1980). It is also suggested, though unproven, that protein-bound 25-OH vitamin D_3 in PLE (Sitrin et al 1980) or excessive loss of vitamin D in decreased enterohepatic circulation (Compston and Creamer 1977, Sitrin et al 1980) could contribute to vitamin D, and thus calcium deficiency. There are several reports in the literature which illustrate many of the above mechanisms.

A classic example of osteomalacia diagnosed by bone biopsy was recently reported in a patient who had undergone two intestinal resections (Sitrin et al 1980). Biochemical abnormalities included a low serum 25-OH vitamin D_3 and calcium absorption of only 17% (normal 50%). Steroid therapy and steatorrhea in this patient were undoubtedly contributing to calcium malabsorption. Decreased dietary intake of calcium due to lactose intolerance was an additional mechanism for calcium deficiency. However, vitamin D deficiency due to decreased intake and/or malabsorption appeared to be contributing to calcium deficiency as 2000 I.U. of vitamin D/day succeeded in returning serum 25-OH vitamin D_3 levels to normal. Osteomalacia was diagnosed by means of bone biopsy and radiological evaluation 2 years post-surgically in a woman who had undergone ileal resection (Compston and Horton 1978). Biochemical, radiological and histological improvement was achieved in 6 months with 50 ug of oral 25-OH vitamin D_3/day. Intermittent cholestyramine therapy, because of its binding effect on

bile acids, was suspected of causing vitamin D malabsorption sufficient to aggravate existing mild osteomalacia.

Hypocalcaemic chorea was noted in another patient with CD (Howdle et al 1979) with elevated alkaline phosphatase and decreased bone density in the hands. Complete neurological response was seen with oral vitamin D: because only a single dose was required, malabsorption of calcium secondary to vitamin D deficiency was sited as the cause of hypocalcemic chorea and, presumably, of decreased bone density.

As mentioned previously, there are several possible mechanisms for calcium malabsorption, though information on calcium absorption in CD is sparse (Krawitt et al 1976). In a group of 31 patients with CD involving different areas of the intestine, only four were found to have calcium malabsorption resulting in negative calcium balance. Moreover, there was no evidence of increased endogenous fecal calcium or total secreted intestinal calcium. Calcium absorption was comparable in patients with or without steatorrhea. Furthermore, there was no correlation between calcium and fat excretion, which suggests that the formation of insoluble calcium salts did not play a major role in calcium absorption. However, calcium excretion did correlate with protein clearance in CD patients, which was from 3-7 times that of controls. This could indicate either that protein-drag of calcium occurs in PLE, or could simply reflect the severity of the disease. Somewhat surprisingly, there was no relationship between steroid therapy and calcium malabsorption. This findings is in conflict with

others (Avioli et al 1968, Klein et al 1977) who have found that prednisone depresses calcium absorption.

Though many researchers have reported low serum levels of 25-OH vitamin D_3 in CD patients (Compston and Creamer 1977, Compston and Horton 1978, Driscoll et al 1977), only one has examined intestinal absorption or dietary intake of vitamin D, or seasonal variation in serum 25-OH vitamin D_3 levels. In 1977, Compston and Creamer reported that absorption of orally-administered 25-OH vitamin D_3 was significantly lower in patients with small bowel resections than in controls. However, this cannot be taken to indicate unequivocal malabsorption of vitamin D, as plasma 25-OH vitamin D_3 levels after an oral dose are also affected by rate of further metabolism and of tissue-uptake of 25-OH vitamin D_3. The mean vitamin D intake of 1.75 ug/day in these patients is less than half of the RDA of 5.0 ug/day. Thus, decreased dietary intake could well be more significant in the etiology of calcium deficiency than previously recognized. This could be of even greater importance in the winter months, as it was shown that serum 25-OH vitamin D_3 levels were lower in the majority of patients in the winter months, probably due to decreased endogenous synthesis of vitamin D.

Vitamin D therapy has been used to normalize serum 25-OH vitamin D_3 levels and to treat bone disease in patients with CD (Compston and Horton 1978, Driscoll et al 1978, Sitrin et al 1980). The patient reported by Compston and Horton showed biochemical and histological improvement on 2000 I.U. vitamin D/day for 6 months. This same dosage brought about a normalization of serum OH-vitamin D_3 levels in another

patient with CD, however Sitrin and co-workers (1980) indicated that up to 10,000 I.U./day might be necessary to normalize this parameter in other patients. In a larger group of CD patients, Driscoll et al (1977) reported that 4000 I.U./day was required to maintain normal levels of serum 25-OH vitamin D_3 in most patients. Bone biopsy one year later, revealed improvement in parameters indicative of osteomalacia. However, in one patient who had severe malabsorption, 25,000 I.U./day was required to maintain a normal serum 25-OH vitamin D_3 level, but this amount did not improve existing bone disease. The variation seen in the foregoing levels of vitamin D therapy are possibly due to several factors, including use of steroids or cholestyramine, seasonal variation in serum 25-OH D_3 level, resection, decreased enterohepatic circulation, or dietary intake.

2.6.9 Vitamin A

Though fat malabsorption has been studied in CD (Dyer and Dawson 1973, Filipsson et al 1978) and is known to occur in some patients, absorption of fat-soluble vitamins (other than vitamin D) has received little attention. However, fat-soluble vitamins are subject to similar pathophysiological mechanisms as fatty acids and may very well be deficient in some patients with CD.

Russell et al (1973) reported abnormal dark-adaptation in 13 patients with small bowel disease (six with regional enteritis, six with celiac sprue, and one with jejunal diverticulosis), who otherwise had no signs of vitamin A deficiency. Although they reported that all patients had normal serum carotene and serum retinol, 12/13 had serum retinol lower than that observed in subjects with normal liver re-

serves of vitamin A (Hume and Krebs 1949, Sauberlich et al 1974). This was in spite of the fact that some subjects had been taking oral supplements of 3,500-10,000 I.U. vitamin A/day, and, this strongly suggests malabsorption, increased loss, or increased requirement. Malabsorption was confirmed as xylose excretion was found to be abnormal in nine patients and fecal fat excretion was elevated in seven patients. However, serum vitamin A or serum carotene were not correlated with degree of fat malabsorption. This is not necessarily surprising as a lack of correlation between serum carotene and fecal fat has been reported by others as well (Brown et al 1980, unpublished observations). Moreover, even in vitamin A deficiency and/or malabsorption, serum vitamin A levels are maintained somewhat below 45 ug/100 ml (Hume and Krebs 1949) but greater than 20 ug/100 ml (Hodges and Kolder 1971) until late in deficiency. Thus, absence of a correlation between serum carotene and fecal fat does not exclude malabsorption in the etiology of vitamin A deficiency. In 2/4 patients given a parenteral dose of 50,000 I.U. vitamin A and 5/5 patients given a 25,000 I.U. vitamin A orally for seven days, dark adaptation failed to return to normal. Following 30 days of 50,000 I.U. vitamin A/day, dark adaptation returned to normal in all but two. Several reasons were suggested by the authors for initial failure of the vitamin A therapy. It was suggested that this initial failure to reverse abnormal dark adaptation in most patients may have reflected individual differences in the initial degree of vitamin A depletion. Dietary inadequacy was ruled out by Russell and co-workers as a cause of vitamin A deficiency, since patients were reported to be taking

3,500-10,000 I.U./day of water-miscible vitamin A. Moreover, recent reports of vitamin A therapy for normalization of bowel function in CD used 50,000 I.U./day of retinol palmitate (Skogh et al 1980), a form which is even more efficiently absorbed. Furthermore, it was found that vitamin A normalized the altered permeability pattern seen in some patients with CD and stopped diarrhea. However, since the patient is being maintained on 100,000 I.U. retinol palmitate/day, this suggested not only decreased absorption, but increased requirement and/or utilization as well. Alternatively, Russell et al suggested that rod regeneration in vitamin A deficient animals requires 3-5 months and the time required for such regeneration may have been reflected in prolonged abnormal dark adaptation in their patients. While this explanation is sound, it suggests that dark adaptation lacks sensitivity. Indeed, the use of dark adaptation as a means of detecting subclinical vitamin A deficiency is somewhat controversial (Sauberlich et al 1974, Rodriguez and Irwin 1972). Furthermore, serum vitamin A was less than 20 ug/100 ml in four patients and less than 30 ug/100 ml in another four patients, strongly suggesting vitamin A deficiency without the need of dark adaptation determination.

2.7 The Effect of Drugs on Nutritional Status

2.7.1 Prednisone

Prednisone is a glucocorticoid, and as such will exert many of the same metabolic effects as the endogenous steroid. With increased steroid secretion or steroid therapy the body is geared toward gluconeogenesis and both appetite and protein catabolism increase. The net

catabolic effects of glucocorticoid hormones on skeletal muscle are well-recognized and documented (Young 1970), and include loss of muscle mass and negative nitrogen balance. A curious mobility of fat, from the limbs to the trunk and face eventually results in Cushing's syndrome, characterized by a "moon-face" and "buffalo-hump". In addition to this redistribution of adipose tissue, an increase in weight is also reported (Myles and Daly 1974). It is thought that this weight gain is due to improved symptoms and appetite, as well as fluid retention.

Prednisone has an antagonistic effect on vitamin D, possibly causing a lower production of the biologically active form of the vitamin (Avioli et al 1968). As a result, decreased calcium transport and absorption occur, with a corresponding increase in urinary calcium and magnesium. As calcium is resorbed from the bone to maintain serum calcium, bone density progressively decreases, eventually resulting in osteomalacia (Myles and Daly 1974).

Reports of increased need for zinc in steroid therapy are controvesial. Flynn et al (1971) reported that urinary zinc is elevated and serum zinc is decreased by high parenteral dose corticosteroids, whereas Briggs and co-workers (1971) showed that short-term oral doses have no effect on zinc nutriture. However, six patients on long-term steroid therapy presented with delayed wound healing, which was successfully treated with oral zinc sulphate (Flynn et al 1973). In yet another study, Solomons and Rosenfield (1976) failed to find a significant difference in plasma zinc between patients on and off steroids.

Furthermore, there was a poor correlation of plasma zinc with daily steroid dose.

The requirement for vitamin C appears to increase with corticosteroid therapy; McWhirter (1974) showed that ascorbic acid has the ability to reverse the inhibitory step in the formation of collagen in patients who are taking corticosteroids. Moreover, he reported that vitamin C also corrects the neutrophilic leucocytosis which has been reported to occur with prednisone therapy (Myles and Daly 1974).

The need for vitamin B_6 appears to be increased in steroid therapy, as well (Rose 1972). Pyridoxal 5-phosphate is required for biosynthesis of nicotinic acid from tryptophan. With insufficient vitamin B_6, tryptophan is not completely metabolized and intermediate metabolites, such as xanthurenic acid, are excreted in the urine. After steroid injection, higher levels of such intermediate metabolites were present in the urine than before steroids. However, administration of vitamin B_6 prevented accumulation of these metabolites.

2.7.2 Salicylazosulfapyridine (SAS)

SAS can have adverse side effects such as anorexia, nausea, and vomitting which may, in themselves, cause a reduction in food intake. Thus nutrient deficiencies may develop simply because of decreased ingestion. However, the folate deficiency often associated with SAS may be due to decreased absorption (Franklin and Rosenberg 1973), or increased loss due to mild hemolysis (Das et al 1973). Franklin and Rosenberg found serum folate levels less than 3.6 ng/ml in 63% of IBD patients. In absorption studies with tritiated pteroylmonoglutamic acid there was a 24% reduction in folate absorption when patients were

on SAS, as compared to when they were not. However, Gerson and Cohen (1976) found absorption of pteroylpolyglutamic acid to be normal in four out of five subjects who were on SAS, though serum folate was low in two of the five. They speculated that the low serum folate was due to decreased intake. Discrepancies in these two studies may have been due to the different forms of folate used, and thus, the need for stricter attention is emphasized. Recent in vitro experiments by Dhar et al (1976) suggest that SAS interferes with absorption and utilization of folate through competitive inhibition in the intestine and elsewhere, and that inhibition is related to the concentration of SAS.

The mild hemolysis observed with SAS therapy (Das et al 1973) can effect other hematopoietic nutrients. Indeed, it is thought to be a cause of increased serum ferritin concentration in CD patients with absent bone marrow hemosiderin (Thomson et al 1978), though studies have not been conducted to determine iron loss or malabsorption with SAS therapy.

2.7.3 Oral Contraceptive Agents (OCA)

OCA have many effects on nutrient requirements (Theuer 1973). Evidence suggestive of folate deficiency has been observed in women taking OCA (Shojania et al 1969, Whitehead et al 1973). Shojania et al (1969) found that OCA users had significantly lower serum folate, red cell folate, and higher FIGLU excretion than controls. However, within three months after cessation of the drug, these hematopoietic parameters and FIGLU excretion of the experimental group returned to normal. Although there was lack of agreement in several early studies of folate status in OCA users (McLean et al 1969, Shojania et al 1969,

Spray 1968), this inconsistency was subsequently shown to be due to the use of different forms of folic acid (Strieff 1970). Megaloblastic, cytologic changes reported in the cervical mucosa of about 20% of OCA users by Whitehead et al (1973) were thought to be due to folate deficiency. Moreover, others have found megaloblastic anemia in OCA users to be folate-responsive (Theuer 1973). Therefore, it would appear that about 20-30% of women using OCA have abnormally low folate status (Theuer 1973). Particularly if intake is already marginal, altered metabolism imposed by OCA may result in overt folate deficiency.

Rose (1965) was the first to report that women taking estrogen-containing contraceptives exhibited an abnormality of tryptophan metabolism similar to that present in vitamin B_6 deficiency. Others (Aly et al 1971, Price et al 1967) also observed increased excretion of xanthurenic acid and other metabolites after an oral load of tryptophan. Although it was subsequently shown that supplementation with 25 mg of pyridoxine hydrochloride (Luhby et al 1971) would prevent excretion of tryptophan metabolites after a tryptophan load, such supplementation is not necessary to maintain normal levels of metabolites derived from dietary sources of tryptophan (Leklem et al 1975). Notwithstanding the frequency with which abnormal tryptophan metabolism occurs in OCA users, there remains uncertainty as to whether OCA produce a true vitamin B_6 deficiency. Only about 15-20% of OCA users have direct biochemical evidence of vitamin B_6 deficiency as measured by a higher in vitro stimulation of alanine aminotransferase activity by pyridoxal phosphate (Lumeng et al 1974). However, pyri-

doxal phosphate concentrations returned to normal in most of OCA users within six months, suggesting that the effect of OCA on vitamin B_6 metabolism is temporary.

Evidence of poor riboflavin and thiamin status has also been reported in OCA users (Sanpitak and Chayutimonkul 1974). Serum and leucocyte ascorbic acid levels have been reported to be lower in OCA users than in controls (Rivers and Devine 1972, Theuer 1973). Also, serum B_{12} levels (Wertalik et al 1971) and serum zinc levels (Theuer 1973) are depressed in women using OCA, though serum levels of other minerals and vitamins are elevated. Levels of serum copper, vitamin A and iron are higher than normal with the use of OCA (Theuer 1973). Serum transferrin is increased as well, though hemoglobin levels are normal. The need for iron might well be reduced in OCA users, as they generally report lighter menstrual bleeding than before the use of OCA. As well, the vitamin K requirement appears to be reduced by OCA (Scrogie et al 1967), as an increased level of vitamin K dependent clotting factors has been found in the blood of women using OCA.

2.7.4 Cholestyramine

Cholestyramine is used symptomatically to treat diarrhea due to bile salt catharsis. However, cholestyramine sequesters bile acids and malabsorption of fat and fat-soluble nutrients can occur (Heaton et al 1972, Longenecker and Basu 1965, Roe 1968). Furthermore, with prolonged use of the drug, the mechanism may travel full-circle and result in bile salt deficiency, thus exacerbating malabsorption of fatty acids and fat-soluble vitamins. At least one case of osteomalacia due to vitamin D malabsorption has been documented in a woman

receiving cholestyramine (Compston 1978, Heaton et al 1972). Cholestyramine therapy may result in decreased absorption of iron and vitamin B_{12}, as well. Researchers (Greenberger 1973, Thomas et al 1971) have shown that cholestyramine binds both organic and inorganic iron, thereby reducing absorption. Work by Coranato and Glass (1973) suggests that competition by cholestyramine for the binding sites on the intrinsic factor molecule causes reduced vitamin B_{12} absorption.

3. METHODOLOGY

3.1 Selection and Diagnosis of Patients

The study group consisted of all the CD patients who were admitted to the gastroenterology teaching clinic at the University of Alberta Hospital between April and November, 1979. Of the 47 CD patients, there were 23 males and 24 females, aged 18 to 62 years.

Diagnosis of Crohn's disease was made by the attending physicians according to the following criteria:

(i) Medical history, physical findings, and clinical course compatible with Crohn's disease

(ii) no known enteric pathogens in stool cultures

(iii) radiological abnormalities characteristic or suggestive of CD

(iv) sigmoidoscopy or colonoscopy evaluation and biopsy results characteristic of CD

The Crohn's Disease Activity Index was calculated for each patient according to the criteria of Best (1976).

Data were collected from patients by means of anthropometric measurements, dietary interviews, and biochemical tests.

3.2 Anthropometric Measurements

Each patient's height, weight, mid-arm circumference (AC), and triceps skinfold thickness (TSF) was obtained at the clinic. A beam balance with a height measure was used to take height and weight data. Each patient was weighed in street clothing (without shoes and top

coat) and relative body weight was calculated (Blackburn et al 1977, Jelliffe 1966). Upper AC was measured by taking the midpoint between the acromian process of the scapula and the olecranon process of the ulna. The arm was flexed such that the ulna and humerus formed a right angle, and the midpoint was marked with a pencil. With arm extended and muscles relaxed, the AC was then measured at this midpoint, and percent of standard AC was calculated, using the standard of Bistrian 1977. The mid-arm TSF thickness was measured with the arm hanging relaxed at the side. A lengthwise skinfold was firmly grasped between the finger and thumb about one cm above the site to be measured. A Lange skinfold caliper with a constant pressure of 1 gm/square mm of jaw surface was applied to the site, at a depth equal to the skinfold and the skinfold measurement was read. The TSF was recorded as the mean value of three measurements and percent of standard TSF was calculated (Frisancho 1974).

Some controversy exists regarding which arm should be used for AC and TSF measurements. In the Nutrition Canada Survey (Dept of National Health and Welfare, Ottawa, 1973) skinfold measurements were taken on the left arm, while in the Ten-State Nutrition Survey measurements were taken on the right arm (Frisancho 1974). Bistrian (1974) reported that anthropometric measurements of hospital patients were made on the left arm. After taking several anthropometric measurements on both sides of the body, Ward et al (1975) concluded that either right or left-sided measurements will give equal precision. Anthropometric measurements of CD patients were done on the non-

dominant arm to avoid bias due to disproportionate muscle development in the dominant arm (Blackburn 1977).

Mid-arm muscle circumference was calculated from the TSF and AC as described by Jelliffe (1966) and percent of standard AMC was calculated for each patient.

3.3 Dietary Evaluation

The method used for dietary assessment was based on the method used in the Nutrition Canada Survey (Dept of National Health and Welfare, Ottawa, 1973). Dietary data were collected by four interviewers: a dietetic intern, a graduate student, and two registered dietitians, all of whom were trained in the Nutrition Canada techniques of dietary interview. The standardized interviewing techniques of the Nutrition Canada Survey were used to ensure consistent data collection. Forty-three patients were interviewed at the clinic, one patient was interviewed at home, and three patients were assessed in the hospital. The patient had no prior knowledge of the date of the interview, thereby eliminating the possibility of altering usual food intake to comply with his/her preconceived idea of what might be expected by the interviewer. Each subject was asked to recall all foods and beverages he had consumed during the 48-hour period starting at midnight three days before the interview. Food portion models, constructed according to Nutrition Canada specifications were used for estimating amounts of food consumed. The models included: 1) cups, glasses; 2) bowls, plates; 3) fish, meat, pie models; 4) papier-mache filled spoons; 5) papier-mache mounds. Each model was coded with a

letter and some models were marked to denote specific volumes. Letter and numbers representing the amounts consumed were entered on the dietary recall form. In some cases, a ruler was used to measure dimensions of specific food items. Calculation of the weight of the portion in grams was then possible using the densities of foods (gm/cubic inch) provided by Nutrition Canada. For each food item recalled by the subject, the interviewer recorded the time of consumption, an exact description of the food item and the amount consumed. Details were requested from mothers or wives when male subjects could not recall details about what food was sereved or how it was prepared. In some cases, recipes were obtained from the patients. For hospital intakes, the food was weighed in grams by the interviewer before the tray was taken to the patient. The weight was later corrected for food not eaten. Two patients (one male and one female) were taking parenteral nutrition. The nutrient contributions of the parenteral nutrition were later added to the computer calculation of nutrient intake.

Each food was subsequently coded by the interviewer, using the individual code numbers from Composition of Foods, Agricultural Handbook No 8 (Watt and Merrill 1963), and additional code numbers created by Nutrition Canada and D.A. Smith (1977). Food intake data were then keypunched and converted to nutrient intake using the tape of the computer program which was used by Nutrition Canada to calculate nutrient intakes. Daily intake was computed for the following nutrients: energy, protein, carbohydrate, fat, crude fiber, iron, vitamin A, calcium, phosphorus, thiamin, ascorbic acid, vitamin B_{12},

vitamin B_6, pantothenic acid, free folate, and total folate. Vitamin D intake was calculated by hand.

Food consumption patterns were studied by categorizing foods into the nine major food groups used to prepare the Nutrition Canada food consumption patterns report (Dept of National Health and Welfare 1978): fats and oils; fruits and fruit products; grain and grain products; nuts, soybeans and miscellaneous seeds; meat, fish, poultry, and eggs; milk and milk products; sugars and sweets; vegetables; mixed dishes; and soft drinks. The food group and subgroups are listed in the appendix (Appendix 33). The daily intake of each food group in grams was calculated by the computer for each patient.

3.4 Biochemical Tests

Laboratory determinations were performed for each patient on the day of interview or as close as possible to that day. For some patients the laboratory tests had been performed usually within the preceding three months and the tests were not repeated. All determinations were made within the Department of Laboratory Medicine, University of Alberta Hospital, Edmonton, by the standard method used there (Appendix 34).

For the biochemical tests, the reference values used by the Department of Laboratory Medicine at the University of Alberta Hospital, Edmonton were chosen for comparison to the CD group. The reference values at the University of Alberta Hospital are determined in one of two ways: either by determination of the distribution of biochemical values of 10,000 or more patients presenting to the

Hospital, and/or by reference to the current literature. Therefore, the reference values used in the present study are not necessarily the same as those for a healthy population and, thus, some values may differ slightly from those in the current literature.

3.5 Statistical Methods

The data collected - anthropometric measurements, food intake and biochemical lab values - were keypunched and transferred to computer tape for analysis. Descriptive statistics were calculated for each variable. Cumulative percentage distributions were calculated from frequency distribution tables.

Pearson correlation coefficients were calculated between nutrient intake and biochemical parameters (Dunn 1964).

The Student's T-test was used to determine whether there was a significant difference in nutrient density between male and female Crohn's disease patients (Dunn 1964).

4. RESULTS

4.1 Clinical Characteristics of Crohn's Disease Patients

The mean age of CD patients was similar in the male (31 yrs) and the female (32 yrs) groups (Table 1). The mean height and weight of the CD patients were close to that of the average North American male and female. Relative weight was close to 100% for both males and females. The triceps skinfold (TSF) and arm muscle circumference (AMC) measurements are given both in mm and percent of standard. The mean percent of standard TSF was 120% in males as compared to 95% in females, indicating that as a group, male CD patients were fatter than females. Muscle reserve was slightly depleted in both males and females, being 98% and 95%, respectively, of standard arm muscle circumference.

The number of patients on steroids was 65% for both the male and female groups. The site of disease was remarkably similar, as 14 males and 15 females had ileal-colonic involvement, 9 males and 8 females had CD of the ileum, and one female had colonic involvement only. The mean duration of disease was slightly higher in females, being 95 months (6-324), as compared to a mean duration in males of 74 months (6-216). Thus, it was interesting that the mean Crohn's Disease Activity Index was also higher in females than in males, being 118 (0-434) and 46 (0-188), respectively.

Table 1: Characteristics of Crohn's disease patients

	Males[1]		Females[2]	
	Mean[3]	Range	Mean[3]	Range
Age (yrs)	31 ± 10	(18 - 62)	32 ± 11	(19 - 56)
Height (cm)	176 ± 6	(166 - 189)	164 ± 6	(150 - 170)
Weight (kg)	72 ± 10	(55 - 90)	58 ± 11	(44 - 85)
Relative weight[4]	102 ± 15	(78 - 136)	100 ± 20	(73 - 150)
Triceps skinfold				
- mm	13.1 ± 6.2	(3.0 - 26.0)	18.1 ± 7.4	(7.0 - 35.0)
- % of standard[5]	120 ± 58	(27 - 232)	95 ± 39	(34 - 184)
Arm Muscle Circumference				
- cm	25.6 ± 3.0	(19.0 - 32.0)	20.9 ± 2.7	(18 - 29)
- % of standard[6]	95 ± 12	(70 - 119)	98 ± 13	(83 - 136)
Duration of disease (mo)	71	(6 - 216)	95	(6 - 324)
Crohn's Disease Activity Index	46	(0 - 188)	118	(0 - 434)
Site of disease (ileum, colon, ileum & colon)	9-0-14	-	8-1-15	-
Steroid therapy (%)	65	-	65	-

1 Number of subjects = 23
2 Number of subjects = 24
3 Values are means ± s.d.
4 Calculated as % ideal weight for height according to 1959 Metropolitan Standards, Jelliffe (1966).
5 Standard triceps skinfold: 11 mm for males, 19 mm for females; Frisancho (1974).
6 Standard arm muscle circumference: 27.0 cm for males, 21.3 cm for females; Bistrian (1977).

4.2 Dietary Intake

4.2.1. Nutrient Intake

The nutrient intake is reported in Tables 2 (males) and 3 (females) as the mean and the range. In the last two columns the Recommended Dietary Allowance (RDA) and nutrient intakes of Nutrition Canada (NC) participants are given for comparison. The mean nutrient intake in CD patients was less than the RDA in the male group for vitamin B_6 and folate (Table 2). In the female CD patients, the mean intake of vitamin B_6, folate, iron, calcium, and vitamin D was less than the RDA (Table 3). However, there was a wide range of intakes within each nutrient (Tables 2 and 3). Thus, the adequacy of intake according to the RDA is given in Tables 4 (males) and 5 (females). The numbers in each column indicate the cumulative percentage of patients consuming the full RDA, 2/3 RDA, 1/2 RDA, and 1/3 RDA. Less than 50% of the male CD patients were consuming the full RDA for a number of nutrients, and the percentage of patients who did consume the full RDA is given in brackets: energy (49%), vitamin A (48%), vitamin B_6 (13%), and folate (0%). Even at 1/3 RDA, less than 100% of the men had achieved this level of intake for vitamin A, vitamin C, vitamin D, and folate. The array of nutrients in which 50% or fewer of the female CD patients achieved consumption of the full RDA was greater than in the males. The percentage of females who did consume the RDA for the following nutrients is indicated in brackets: energy (33%), calcium (38%), iron (17%), vitamin A (50%), pantothenic acid (38%), vitamin B_6 (13%), folate (8%), vitamin B_{12} (50%), and vitamin D (30%). Similarly, a greater number of females than males failed to

Table 2: Mean daily nutrient intakes of male Crohn's disease patients; comparison with Recommended Allowances and Nutrition Canada

Nutrient	Daily nutrient intakes Mean[1]	Range	RDA[2]	Nutrition Canada[3]
Energy (Kcal)	2861 ± 912[4]	1312 - 4486	2300 - 3100	3349
Protein (g)	103 ± 37	56 - 200	56	124
Fat (g)	116 ± 44	39 - 215	-	155
Carbohydrate (g)	333 ± 116	182 - 699	-	337
Crude fiber (g)	4.3 ± 1.6	1.6 - 7.5	-	4.8
Calcium (mg)	1048 ± 675	295 - 3222	800	1189
Phosphorus (mg)	1679 ± 666	634 - 3343	800	-
Iron (mg)	17.6 ± 7.1	7.4 - 44	10	19
Vitamin A (RE)[5]	1133 ± 630	241 - 2834	1000	2145
Vitamin A (IU)	6353 ± 4641	957 - 19952	-	-
- Carotene (IU)	3828	59 - 15785	-	-
- Retinol (IU)	2597	524 - 4662	-	-
Thiamin (mg)	1.9 ± 1.9	0.6 - 10.0	1.4	1.7
Riboflavin (mg)	2.4 ± 1.1	0.9 - 5.2	1.6	3.0
Ascorbic acid (mg)	187 ± 181	16 - 922	60	114
Pantothenic acid (mg)	6.3 ± 3.7	2.2 - 19	4 - 7	-
Vitamin B6 (mg)	1.9 ± 1.4	0.7 - 7.7	2.2	-
Vitamin B12 (µg)	4.7 ± 3.8	1.1 - 19	3.0	-
Folate (µg)[6]	211 ± 90	77 - 386	400	226
Vitamin D (IU)	281 ± 237	0 - 911	200	-

1 Each value is the mean of two days. n = 23

2 Recommended Dietary Allowances, Revised 1980, Food and Nutrition Board, National Research Council, National Academy of Sciences, Washington, D.C.

3 Mean daily nutrient intakes of males (20 - 39 years), Prairie region

4 Values are means ± s.d.

5 RE = retinol equivalents; 1 retinol equivalent = 1 ug retinol (3.33 IU) or 6 µg B-carotene (10 IU)

6 Total folate

Table 3: Mean daily intake of female Crohn's disease patients; comparison with Recommended Allowances and Nutrition Canada

Nutrient	Daily nutrient intakes Mean[1]	Range	RDA[2]	Nutrition Canada[3]
Energy (Kcal)	1867 ± 866[4]	571 - 4303	1600 - 2400	1946
Protein (g)	68 ± 31	23 - 134	44	75
Fat (g)	74 ± 39	26 - 197	-	88
Carbohydrate (g)	232 ± 114	54 - 540	-	207
Crude fiber (g)	3.3 ± 2.2	0 - 8.6	-	3.2
Calcium (mg)	707 ± 526	103 - 2131	800	788
Phosphorus (mg)	1114 ± 562	325 - 2476	800	-
Iron (mg)	11.7 ± 6.2	0.0 - 26	18	12
Vitamin A (RE)[5]	1056 ± 806	208 - 3557	800	1134
Vitamin A (IU)	5131 ± 4422	1014 - 19423	-	-
- Carotene (IU)	3973	0 - 17719	-	-
- Retinol (IU)	2194	534 - 11308	-	-
Thiamin (mg)	1.4 ± 1.9	0.29 - 10.0	1.0	1.1
[illegible]in (mg)	1.7 ± 1.1	0.4 - 5.0	1.2	1.8
[illegible] acid (mg)	135 ± 120	11 - 500	60	90
Pantothenic acid (mg)	4.2 ± 2.6	1.7 - 13	4 - 7	-
Vitamin B6 (mg)	1.4 ± 1.3	0.4 - 6.0	2.0	-
Vitamin B12 (µg)	5.3 ± 7.1	0.5 - 33	3.0	-
Folate (µg)[6]	185 ± 122	54 - 500	400	145
Vitamin D (IU)	167 ± 133	6.5 - 500	200	-

1 Each value is the mean of two days. n = 24.
2 From Recommended Dietary Allowances, Revised 1980, Food and Nutrition Board, National Research Council, National Academy of Sciences, Washington, D.C.
3 Mean daily nutrient intakes of females (20 - 39 years), Prairie region
4 Values are means ≠ s.d.
5 RE = retinol equivalents; 1 retinol equivalent = 1 ug retinol (3.33 IU) or 6 µg B-carotene (10 IU)
6 Total folate

Table 4: Percentage of male Crohn's disease patients meeting the Recommended Allowances

Nutrient	Percentage of intakes meeting allowances[1]			
	Full RDA[2]	2/3 RDA	1/2 RDA	1/3 RDA
Energy	49	87	96	100
Protein	100	100	100	100
Calcium	52	78	91	100
Phosphorus	96	100	100	100
Iron	96	100	100	100
Vitamin A	48	83	91	96
Thiamin	61	91	100	100
Riboflavin	87	91	100	100
Ascorbic acid	87	91	91	96
Pantothenic acid	74	91	100	100
Vitamin B6	13	57	74	100
Vitamin B12	74	96	96	100
Folate	0	26	48	74
Vitamin D	57	70	83	91

[1] Percentages were calculated from mean nutrient intakes of 23 males

[2] From Recommended Dietary Allowances, Revised 1980, Food and Nutrition Board, National Research Council, National Academy of Sciences, Washington, D.C.

Table 5: Percentage of female Crohn's disease patients meeting the Recommended Allowances

Nutrient	Percentage of intakes meeting allowances[1]			
	Full RDA[2]	2/3 RDA	1/2 RDA	1/3 RDA
Energy		75	83	96
Protein		92	100	100
Calcium	38	58	67	75
Phosphorus	71	83	92	100
Iron	17	38	75	88
Vitamin A	50	71	75	96
Thiamin	54	83	92	100
Riboflavin	63	83	92	100
Ascorbic acid	67	75	88	92
Pantothenic acid	38	67	79	100
Vitamin B6	13	38	54	79
Vitamin B12	50	58	75	96
Folate	8	21	33	58
Vitamin D	30	58	71	75

[1] Percentages were calculated from mean nutrient intakes of 24 females

[2] From Recommended Dietary Allowances, Revised 1980, Food and Nutrition Board, National Research Council, National Academy of Sciences, Washington, D.C.

consume 1/3 RDA for a wider range of nutrients. Less than 100% of the females achieved consumption of 1/3 RDA for energy, calcium, iron, vitamin A, ascorbic acid, vitamin B_6, vitamin B_{12}, folate, and vitamin D.

4.2.2 Food Consumption Patterns

Table 6 describes the mean daily intake of food groups for both the CD group and NC participants, and expresses the respective intakes in grams per day. The column "Relative Intake" expresses the nutrient intake of CD patients as percent increased or decreased compared to NC intake. Consumption of food groups was similar with the following exceptions: fruit intake of the male CD patients was increased 79% and soft drink consumption was decreased 76% compared to NC. For female CD patients, fruit consumption was increased 69% compared to NC participants.

4.2.3 Nutrient Density

The nutrient intake/1000 kcal for the male and female CD patients is given in Table 7. The nutrient intake/1000 kcal was the same in the male and female groups for all nutrients, except vitamin A and folate, of which the males consumed smaller amounts than females ($p < 0.05$).

4.3 Biochemical Data for Crohn's Disease Patients

The data in Tables 8 and 9 present the results of hematological and biochemical tests for male and female CD patients, respectively. The numbers of patients in whom each test was performed varies and is given in the first column. The mean values and range of values for

Table 6a: Mean daily intake of food groups of Crohn's disease patients (males); comparison with Canadian Population

Food group	Crohn's patients[1]	Nutrition Canada[2]	Relative Intake[3]
	(grams)	(grams)	(%)
Fruit products	438 ± 327[4]	244[5]	+ 79%
Vegetables	276 ± 137	344	- 20%
Dairy Products	471 ± 482	420	+ 12%
MPFE[6]	212 ± 82	285	- 26%
Cereals	271 ± 177	282	- 4%
Foods - Sugar[7]	52 ± 45	64	- 19%
Fats and Oils	26 ± 26	33	- 19%
Nuts and Legumes	13 ± 20	15	- 13%
Mixed Dishes	87 ± 105	132	- 34%
Soft Drinks	96 ± 218	408	- 76%

1 Number of patients = 23

2 Canada Department of National Health and Welfare, Nutrition Canada. Food Consumption Patterns Report. Information Canada, 1976.

3 [Crohn's patients' intake - Nutrition Canada intake]/Nutrition Canada Intake

4 Values are means ± s.d.

5 Values for young adult males, 20 to 39 years of age. National figures

6 MPFE = meat, poultry, fish, eggs

7 Foods primarily sugar: sugars, cake icings, syrups, honey, molasses, jellies, jams, candies, chocolate syrup, gelatine dessert powders.

Table 6b: Mean daily intake of food groups of Crohn's disease patients (females); comparison with Canadian Population

Food group	Crohn's patients[1]	Nutrition Canada[2]	Relative Intake[3]
	(grams)	(grams)	(%)
Fruit products	344 ± 308[4]	204[5]	+ 69%
Vegetables	204 ± 163	233	- 12%
Dairy Products	265 ± 262	289	- 8%
MPFE[6]	138 ± 76	160	- 14%
Cereals	194 ± 132	198	- 2%
Foods - Sugar[7]	33 ± 46	44	- 25%
Fats and Oils	20 ± 18	22	- 9%
Nuts and Legumes	3 ± 7	8	- 62%
Mixed Dishes	87 ± 79	106	- 18%
Soft Drinks	138 ± 129	175	- 19%

1 Number of patients = 24

2 Canada Department of National Health and Welfare, Nutrition Canada. Food Consumption Patterns Report. Information Canada, 1976.

3 [Crohn's patients' intake - Nutrition Canada intake]/Nutrition Canada Intake

4 Values are means ≠ s.d.

5 Values for young adult females, 20 to 39 years of age, National figures

6 MPFE = meat, poultry, fish, eggs

7 Foods primarily sugar: sugars, cake icings, syrups, honey, molasses, jellies, jams, candies, chocolate syrup, gelatine dessert powders.

Table 7: Nutrient densities of intakes of Crohn's disease patients

	Nutrients per 1000 kilocalories	
	Males	Females
	(n = 23)	(n = 24)
Protein (g)	37	38
Calcium (mg)	360	367
Phosphorus (mg)	586	606
Iron (mg)	6.4	6.5
Vitamin A (RE)	392 *	601 *
Thiamin (mg)	0.61	0.75
Riboflavin (mg)	0.90	0.94
Ascorbic acid (mg)	61	76
Pantothenic acid (mg)	2.2	2.2
Vitamin B6 (mg)	0.65	0.74
Vitamin B12 (ug)	1.6	2.9
Folate (μg)	75 *	101 *
Vitamin D (I.U.)	92	85
Crude fiber (g)	1.6	1.8

* Comparison between males and females $p < 0.05$.
Statistical test used was Student's t-test.

Table 8: Biochemical data of male Crohn's disease patients

Parameter	Biochemical data			Reference value[2]	Percentage of patients with low values[3]
	n[1]	Mean	Range		
Serum albumin (g/dl)	19	4.1 ± 0.4[4]	3.4 - 4.9	3.0 - 4.8	0
Total lymphocyte count (/mm^3)	20	1798 ± 1045	222 - 4896	1500 - 3500	50
Hemoglobin (g/dl)	23	14.0 ± 1.6	10.3 - 16.6	13	22
Hematocrit (%)	22	41.5 ± 4.2	32.4 - 48.7	40 - 54	23
Mean corpuscular hemoglobin concentration (%)	22	34 ± 1	32 - 35	32 - 36	0
Serum iron (ug/dl)	18	61.4 ± 33.3	14 - 130	80 - 170	67
Total iron binding capacity (ug/dl)	18	319 ± 79	155 - 496	250 - 400	17
Transferrin saturation (%)	18	20 ± 11	4 - 36	20 - 55	50
Serum ferritin (ng/ml)	17	189 ± 242	16 - 999	15 - 200	0
Serum folate (ng/ml)	19	4.2 ± 3.5	0.5 - 16.9	3.0 - 15.0	37
Serum vitamin B12 (pg/ml)	18	356 ± 174	94 - 700	140 - 520	11
Serum calcium (mg/dl)	21	9.3 ± 0.4	8.8 - 9.9	8.5 - 10.5	0
Serum phosphorus (mg/dl)	21	3.5 ± 0.6	2.1 - 4.4	2.5 - 4.8	5
Serum vitamin D (ng/dl)	10	20 ± 13	6 - 43	> 10	20
Serum carotene (ug/dl)	13	63 ± 10	8 - 109	50 - 250	38
Alkaline phosphatase (IU/l)	20	127 ± 209	31 - 1092	40 - 110	10

1 n = number of patients
2 The range of normal values, from the Department of Laboratory Medicine, University of Alberta Hospital, Edmonton
3 Percentage of patients with values below the reference value, except for alkaline phosphatase which states the percentage of patients above the reference value
4 Values are means ± s.d.

Table 9: Biochemical data of female Crohn's disease patients

Parameter	Biochemical data			Reference value[2]	Percentage of patients with low values[3]
	n[1]	Mean	Range		
Serum albumin (g/dl)	24	3.9 ± 0.6[4]	2.8 - 4.8	3.0 - 4.8	13
Total lymphocyte count (/mm^3)	22	1564 ± 999	275 - 4250	1500 - 3500	55
Hemoglobin (g/dl)	24	12.6 ± 1.6	9.2 - 15.2	> 12	29
Hematocrit (%)	23	38 ± 5	30 - 40	37 - 47	30
Mean corpuscular hemoglobin concentration (%)	22	33 ± 1	31 - 35	32 - 36	9
Serum iron (ug/dl)	22	54 ± 30	9 - 132	60 - 150	60
Total iron binding capacity (ug/dl)	22	309 ± 68	164 - 430	250 - 400	15
Transferrin saturation (%)	22	18 ± 10	6 - 52	20 - 55	68
Serum ferritin (ng/ml)	17	101 ± 100	13 - 324	15 - 200	18
Serum folate (ng/ml)	22	4.2 ± 4.4	0.6 - 16.9	3.0 - 15.0	50
Serum vitamin B12 (pg/ml)	19	363 ± 239	84 - 908	140 - 520	11
Serum calcium (mg/dl)	24	9.0 ± 0.5	8.2 - 10.1	8.5 - 10.5	17
Serum phosphorus (mg/dl)	23	3.5 ± 0.7	2.5 - 5.0	2.5 - 4.8	0
Serum vitamin D (ng/dl)	9	23 ± 10	9 - 38	> 10	11
Serum carotene (ug/dl)	15	76.5 ± 6	37 - 121	50 - 250	13
Alkaline phosphatase (IU/l)	23	72 ± 23	32 - 110	40 - 110	0

1 n = number of patients
2 The range of normal values, from the Department of Laboratory Medicine, University of Alberta Hospital, Edmonton
3 Percentage of patients with values below the reference value, except for alkaline phosphatase which states the percentage of patients above the reference value
4 Values are means ± s.d.

each parameter is indicated. The reference values used by the Department of Laboratory Medicine at the University of Alberta Hospital are given in the second column from the right and percentage of patients with values less than the reference values is given in the last column. One-third or more of the men had values less than the lower limit of the reference value for the following parameters: total lymphocyte count (50%), transferrin saturation (50%), serum iron (67%), serum carotene (38%), and serum folate (37%) (Table 8). One-third or more of the women had values less than the lower limit of the reference value for total lymphocyte count (55%), serum iron (60%), transferrin saturation (68%), and serum folate (50%) (Table 9).

4.4 Correlations Between Selected Nutrients and Biochemical Tests

Pearson correlation coefficients between selected nutrients and biochemical parameters are shown in Tables 10-13, inclusive.

4.4.1 Correlations between dietary folate, iron, protein, vitamin B_6, vitamin B_{12}, vitamin C, and biochemical parameters

In males, correlations were found mainly between dietary parameters: highly significant correlations were found between dietary protein and each of dietary folate, iron, vitamin B_6 and vitamin B_{12}; dietary iron and dietary vitamin B_{12}; dietary iron and dietary folate; dietary vitamin C and each of dietary vitamin B_6 and serum ferritin (Table 10). In females, dietary folate showed a highly significant correlation with a number of dietary parameters, including dietary vitamin B_{12}, vitamin C, protein, and vitamin B_6 (Table 11). Serum

Table 10: Pearson correlation coefficients between intakes of selected nutrients and hematological data of male Crohn's disease patients

	Dietary parameter						Hematological parameter			
Variable	Folate[1]	Iron[1]	Vitamin C[1]	Protein[1]	Vitamin B12[1]	Vitamin B6[1]	Serum Folate[2]	Serum Ferritin[2]	Serum B12[2]	Total Lymphocyte Count[2]
Dietary parameter										
folate	1.0	0.60**	0.14	0.55**	0.27	0.12	-0.01	-0.21	-0.03	-0.23
iron	0.60**	1.0	-0.05	0.75**	0.41*	0.12	0.06	-0.32	0.23	-0.34
Vitamin C	0.14	-0.05	1.0	0.27	0.25	0.85**	0.07	0.74**	-0.21	-0.35
protein	0.55**	0.75**	0.27	1.0	0.73**	0.41*	0.02	0.09	0.39	-0.38*
Vitamin B12	0.27	0.41*	0.25	0.73**	1.0	0.22	-0.20	0.09	0.43*	-0.40*
Vitamin B6	0.12	0.12	0.85**	0.41*	0.22	1.0	0.18	0.74**	-0.25	-0.44*
Hematological parameter										
Serum folate	-0.01	0.06	0.07	0.02	-0.20	0.18	1.0	-0.11	-0.10	0.03
Serum ferritin	-0.21	-0.32	0.74**	0.09	0.09	0.74**	-0.11	1.0	-0.24	-0.65**
Serum B12	-0.03	0.23	-0.21	0.39	0.43*	-0.25	-0.10	-0.24	1.0	0.04
Total lymphocyte count	-0.23	-0.34	-0.35	-0.38*	-0.40*	-0.44*	0.03	-0.65**	0.04	1.0

[1] Number of patients for correlations between nutrients was 23
[2] Number of patients for correlations between nutrients and hematological data varied from 17 to 20; see Table 8 for hematological data

* Correlation coefficient significant ($p < 0.05$)
** Correlation coefficient significant ($p < 0.01$)

Table 11: Pearson correlation coefficients between intakes of selected nutrients and hematological data of female Crohn's disease patients

	Dietary parameter						Hematological parameter			
Variable	Folate[1]	Iron[1]	Vitamin C[1]	Protein[1]	Vitamin B12[1]	Vitamin B6[1]	Serum Folate[2]	Serum Ferritin[2]	Serum B12[2]	Total Lymphocyte Count[2]
Dietary parameter										
folate	1.0	0.41*	0.82**	0.60**	0.70**	0.74**	0.59**	-0.10	0.26	-0.17
iron	0.41*	1.0	0.12	0.81**	-0.22	0.09	-0.20	-0.27	-0.01	0.13
Vitamin C	0.82**	0.12	1.0	0.34*	0.70**	0.66**	0.52**	-0.09	0.22	-0.04
protein	0.60**	0.81**	0.34*	1.0	0.13	0.37*	-0.05	-0.16	-0.06	-0.08
Vitamin B12	0.70**	-0.22	0.70**	0.13	1.0	0.78**	0.58**	0.05	0.15	-0.35
Vitamin B6	0.74**	0.09	0.66**	0.37*	0.78**	1.0	0.47**	-0.07	0.58*	-0.34
Hematological parameter										
Serum folate	0.59**	-0.20	0.52**	-0.05	0.58**	0.47**	1.0	-0.01	0.14	-0.24
Serum ferritin	-0.10	-0.27	-0.09	-0.16	0.05	-0.07	-0.01	1.0	0.58*	0.33
Serum B12	0.26	-0.01	0.22	-0.06	0.15	0.58*	0.14	0.58*	1.0	0.17
Total lymphocyte count	-0.17	0.13	-0.04	-0.08	-0,35	-0.34	-0.24	0.33	0.17'	1.0

1 Number of patients for correlations between nutrients was 24
2 Number of patients for correlations between nutrients and hematological data varied from 17 to 22; see Table 9 for hematological data

* Correlation coefficient significant ($p < 0.05$)
** Correlation coefficient significant ($p < 0.01$)

folate was the only laboratory parameters which correlated with nutrient intake, and it was correlated with dietary folate, vitamin B_{12}, vitamin B_6, and vitamin C (Table 11). Other pairs in which correlations were observed were dietary iron vs dietary protein, and dietary vitamin B_{12} vs dietary vitamin C.

4.4.2 Correlations between dietary calcium, phosphorus, protein, vitamin D, and biochemical parameters

As in the previous section, correlations were found mainly between dietary parameters. In Table 12, significant correlations were found between the following pairs of dietary intake in males: calcium and vitamin D, calcium and protein, calcium and phosphorus, phosphorus and protein, phosphorus and vitamin D, protein and vitamin D. Significant correlations ($p < 0.05$) were also observed between serum calcium and each of dietary calcium, dietary phosphorus, dietary protein, and dietary vitamin D. However, the correlations were low and since all of the serum calcium concentrations in the male CD patients were normal, clinical application of this finding is limited. Table 13 shows highly significant correlations in females between all the possible pairs of dietary calcium, phosphorus and vitamin D. As well, serum vitamin D was correlated with serum calcium.

4.5 Correlations Between Anthropometric and Biochemical Parameters

Table 14 shows Pearson correlation coefficients between anthropometric and selected biochemical parameters. A highly significant correlation was found between relative body weight and arm muscle circumference in both male and female CD patients. In females, correlations

Table 12: Pearson correlation coefficients between selected nutrients and hematological data of male Crohn's disease patients

	Dietary parameter				Hematological parameter				
Variable	Calcium[1]	Phosphorus[1]	Protein[1]	Vitamin D[1]	Serum Calcium[2]	Serum Phosphorus[2]	Serum Vitamin D[2]	Serum Alkaline Phosphatase[2]	Total Lymphocyte Count[2]
Dietary parameter									
Calcium	1.0	0.87**	0.77**	0.86**	0.37*	0.15	0.08	-0.19	-0.40*
Phosphorus	0.87**	1.0	0.94**	0.78**	0.38*	0.12	0.09	-0.17	-0.44*
Protein	0.77**	0.94**	1.0	0.66**	0.40*	0.02	0.29	-0.14	-0.38*
Vitamin D	0.86**	0.78**	0.66**	1.0	0.41*	0.10	-0.35	-0.10	-0.38
Hematological parameter									
Serum calcium	0.37*	0.38*	0.40*	0.41*	1.0	0.00	0.30	0.06	-0.01
Serum phosphorus	0.15	0.12	0.02	0.10	0.00	1.0	-0.30	-0.07	0.27
Serum vitamin D	0.08	0.09	0.29	-0.35	0.30	-0.30	1.0	-0.50	-0.05
Alkaline phosphatase	-0.19	-0.17	-0.14	-0.10	0.06	-0.07	-0.50	1.0	-0.05
Total lymphocyte count	-0.40*	-0.44*	-0.38*	-0.38*	-0.01	0.27	-0.05	-0.05	1.0

[1] Number of patients for correlations between nutrients was 23
[2] Number of patients for correlations between hematological data and nutrients varied from 10 to 21; see Table 8 for hematological data

* Correlation coefficient significant ($p < 0.05$)
** Correlation coefficient significant ($p < 0.01$)

Table 13: Pearson correlation coefficients between selected nutrients and hematological data of female Crohn's disease patients

	Dietary parameter				Hematological parameter				
Variable	Calcium[1]	Phosphorus[1]	Protein[1]	Vitamin D[1]	Serum Calcium[2]	Serum Phosphorus[2]	Serum Vitamin D[2]	Serum Alkaline Phosphatase[2]	Total Lymphocyte Count[2]
Dietary parameter									
Calcium	1.0	0.94**	0.84**	0.38*	0.16	0.05	0.01	-0.09	-0.14
Phosphorus	0.94**	1.0	0.94**	0.48**	0.05	-0.08	-0.03	-0.06	-0.06
Protein	0.84**	0.94**	1.0	0.37*	-0.07	-0.10	0.13	-0.15	-0.08
Vitamin D	0.38*	0.48**	0.37*	1.0	-0.37*	-0.05	-0.72**	0.06	-0.24
Hematological parameter									
Serum calcium	0.16	0.05	-0.07	-0.37*	1.0	0.17	0.76**	0.13	0.16
Serum phosphorus	0.05	-0.08	-0.10	-0.05	0.17	1.0	-0.26	0.14	-0.16
Serum vitamin D	0.01	-0.03	0.13	-0.72**	0.76**	-0.26	1.0	-0.62	0.39
Alkaline phosphatase	-0.09	-0.06	-0.15	0.06	0.13	0.14	-0.62	1.0	0.38
Total lymphocyte count	-0.14	-0.06	-0.08	-0.24	0.16	-0.16	0.39	0.38	1.0

[1] Number of patients for correlations between nutrients was 24
[2] Number of patients for correlations between hematological data and nutrients varied from 9 to 24; see Table 9 for hematological data

* Correlation coefficient significant ($p < 0.05$)
** Correlation coefficient significant ($p < 0.01$)

Table 14: Pearson correlation coefficients between anthropometric and biochemical data in Crohn's disease patients

	Relative weight[1]		Arm muscle circumference (% of standard)[2]		Triceps skinfold[3] (% of standard)	
	Male	Female	Male	Female	Male	Female
Arm muscle circumference (% of standard)	0.76**[4]	0.77**	1.0	1.0	-0.10	0.18
Triceps skinfold (% of standard)	0.29	0.63*	-0.10	0.18	1.0	1.0
Serum albumin	-0.11	-0.02	-0.02	0.01	0.10	-0.07
Total lymphocyte count	0.06	0.48*	0.19	0.66*	0.06	-0.03
Total iron binding capacity	-0.32	0.14	-0.27	0.04	-0.19	-0.26

[1] Calculated as % ideal weight for height according to 1959 Metropolitan Standards, Jelliffe (1966).
[2] Standard arm muscle circumference: 27.0 cm for males, 21.3 cm for females; Bistrian (1977).
[3] Standard triceps skinfold: 11 mm for males, 19 mm for females; Frisancho (1974).
[4] Number of patients for each pair of correlations varied from 18 to 24

* Correlation coefficient significant ($p < 0.01$)
** Correlation coefficient significant ($p < 0.001$)

between the following pairs were also significant: relative weight vs triceps skinfold, relative weight vs total lymphocyte count, arm muscle circumference vs total lymphocyte count.

4.6 Predictive Value of Grouping Crohn's Disease Patients According to Energy Intake or Relative Body Weight

Tables 15 and 16 show the percentage of male and female CD patients who have low anthropometric and biochemical values when grouped according to energy intake less than the RDA, equal to the RDA, or greater than the RDA. Energy intake appears to be of little value in predicting the presence of low biochemical or anthropometric parameters, as the incidence of low parameters occurs with equal frequency at all levels of energy intake.

Table 17 shows the percentage of male and female CD patients who have low anthropometric and biochemical values when grouped according to greater than 90% of relative body weight and less than 90% of relative body weight. Relative body weight appears to be of little value in predicting the presence of low anthropometric or biochemical values in male CD patients. However, female CD patients with less than 90% of relative body weight have a greater incidence of abnormal biochemical and anthropometric values than do female CD patients with greater than 90% of relative body weight.

Table 15: Percentage of male Crohn's disease patients with low values for selected parameters when grouped according to energy intake

Parameter	Energy Intake (Kcal)		
	< 2300 (N = 7)	2300 - 3100 (N = 8)	> 3100 (N = 8)
Triceps skinfold (≤ 75% of standard)	29 (7)[1]	0 (7)	57 (7)
Arm muscle circumference (≤ 90% of standard)	14 (7)	43 (7)	14 (7)
Serum albumin (≤ 3.0 g/dl)	0 (7)	0 (6)	0 (6)
Total lymphocyte count (< 1500 /mm^3)	43 (7)	63 (8)	40 (5)
Total iron binding capacity (< 250 mg/dl)	0 (5)	50 (6)	0 (7)

[1] Number of patients for whom selected variable was available.

Table 16: Percentage of female Crohn's disease patients with low values for selected parameters when grouped according to energy intake

Parameter	Energy Intake (Kcal)		
	< 1600 (N = 10)	1600 - 2400 (N = 9)	> 2400 (N = 5)
Triceps skinfold (≤ 75% of standard)	10 (10)[1]	43 (7)	100 (3)
Arm muscle circumference (≤ 90% of standard)	30 (10)	29 (7)	0 (3)
Serum albumin (≤ 3.0 g/dl)	30 (10)	11 (9)	0 (5)
Total lymphocyte count (< 1500 /mm^3)	44 (9)	67 (9)	60 (5)
Total iron binding capacity (< 250 mg/dl)	29 (7)	11 (9)	0 (4)

[1] Number of patients for whom selected variable was available.

Table 17: Percentage of Crohn's disease patients with low values for selected parameters, when grouped according to relative weight[1]

Parameter	Relative Weight[1] ≥ 90%		Relative Weight[1] < 90%	
	Males (N = 19)	Females (N = 15)	Males (N = 4)	Females (N = 8)
Triceps skinfold (≤ 75% of standard)	22 (18)[2]	17 (12)	67 (3)	63 (8)
Arm muscle circumference (≤ 90% of standard)	17 (18)	8 (12)	67 (3)	50 (8)
Serum albumin (< 3.0 g/dl)	0 (15)	13 (15)	0 (4)	13 (8)
Total lymphocyte count (< 1500 /mm^3)	53 (17)	36 (14)	33 (3)	86 (7)
Total iron binding capacity (< 250 mg/dl)	21 (14)	10 (15)	0 (4)	25 (8)

[1] Calculated as % ideal weight for height according to 1959 Metropolitan Standards, Jelliffe (1966).

[2] Number of patients for whom selected variable was available.

4.7 Correlations Between the Crohn's Disease Activity Index (CDAI) and Selected Variables

Pearson correlation coefficients between the CDAI and nutrient intake, biochemical tests, and anthropometric measurements is reported in Table 18.

Correlations were calculated between the CDAI and four nutrients - energy, protein, carbohydrate, and folate - but the only significant correlation was a negative one between the CDAI and energy intake in male CD patients. However, the correlation was quite low (-0.38, $p < 0.05$). In addition, there was no correlation between the CDAI and the number of nutrients consumed in amounts less than the RDA.

In males, the CDAI was negatively correlated with serum albumin (-0.64). However, since all the serum albumin concentrations were within the normal range, clinical usefulness of these results is limited. In female CD patients, the CDAI was negatively correlated with hemoglobin, though the correlation was somewhat low (-0.45), and positively correlated with serum ferritin (0.60).

The CDAI was not correlated with either of the anthropometric measurements of percent relative body weight or percent of standard arm muscle circumference.

The CDAI was correlated with duration of disease in male CD patients (0.57), but not in female CD patients.

Table 18: Pearson correlation coefficients between the Crohn's Disease Activity Index and selected variables

Variable	Crohn's Disease Activity Index	
	Male [1]	Female [2]
Energy intake	- 0.38*	- 0.12
Protein intake	- 0.21	0.01
Carbohydrate intake	- 0.26	- 0.11
Dietary folate	- 0.07	- 0.19
Nutrients < RDA	0.29	0.21
Serum albumin	- 0.64**	- 0.09
Hemoglobin	- 0.24	- 0.45*
Serum folate	- 0.12	0.07
Serum ferritin	- 0.23	0.60**
Total lymphocyte count	- 0.29	- 0.21
% Relative body weight [3]	0.11	- 0.06
% Standard arm muscle circumference [4]	0.07	- 0.22
Duration of disease	0.57*	- 0.46

1 Number of pairs for each correlation varies between 17 and 23.
2 Number of pairs for each correlation varies between 17 and 24.
3 Calculated as % ideal weight for height according to 1959 Metropolitan Standardss, Jelliffe (1966).
4 Standard arm muscle circumference: 27.0 cm for males, 21.3 cm for females; Bistrian (1977).

* Correlation coefficient significant ($p < 0.05$)
** Correlation coefficient significant ($p < 0.01$)

5. DISCUSSION

5.1 Protein

Evidence of protein malnutrition was apparent in a significant proportion of patients with CD: arm muscle circumference (AMC) of less than 90% of the standard was observed in one-quarter of the males and females with CD (Appendix 1) and half of all the CD patients had low total lymphocyte counts (TLC, Tables 8 and 9). These abnormal TLC occurred despite 80% of the males and 58% of the females with low TLC being on steroids. However, the incidence of abnormal serum albumin was not consistent with the incidence of abnormal AMC and TLC, as none of the males and only 13% of the females had a low serum albumin concentration. Other researchers, as well (Beeken et al 1972), have reported an unexpectedly low incidence of abnormal serum protein despite evidence suggesting the potential of protein deficiency. However, a normal serum albumin despite a decreased AMC and TLC may be due to increased hepatic synthesis of protein (Steinfeld et al 1960), and/or could reflect the adult marasmus described by Blackburn and Bistrian (2.3.5).

Impaired dietary intake of protein was unlikely to be the major explanation for this high prevalence of protein malnutrition since protein intake in CD patients was similar to that of NC (Tables 2 and 3) and exceeded the RDA in all men (Table 4) and 83% of the women (Table 5). However, 30% of the females were consuming less than the RDA for protein of 0.8 g/kg body weight (Appendix 3a). Reduced energy intake in over half of the male and female CD patients (Tables 4 and

5) could have contributed to protein malnutrition, as it is well documented (Inoue et al 1973, Munro and Naismith 1953) that efficiency of nitrogen utilization decreases with reduced energy intakes. Furthermore, the work of several researchers (Garza et al 1977, Hegsted 1976) has cast some doubt on the metabolic balance approach to establishing protein requirement and suggests that the RDA for protein may be inadequate for some individuals. Moreover, the RDA of all nutrients, including protein, is for healthy individuals. In CD, a number of factors increase the risk of protein malnutrition: these include enteric protein loss, catabolic effects of the inflammatory process, and catabolism of protein in conjunction with steroid therapy. Indeed, 9 out of 10 patients with reduced AMC, 80% of males and 58% of females with reduced TLC, and 65% of all patients were taking steroids. These results suggest, therefore, that it may be necessary for CD patients receiving corticosteroids to consume greater than the RDA for protein.

5.2 Energy Intake

Energy malnutrition was evident in CD patients, as 17% of males and 33% of females had relative body weight less than 90% (Appendix one). It should be cautioned, however, that a decreased body weight indicates that energy intake may be low at present, but alternatively, could indicate that energy intake was low at some unknown previous time. Thus, present caloric intake must also be considered in assessment of adequacy of energy consumption. A sizeable number of patients with CD consumed low intakes of energy, but the exact proportion of

patients judged to be at risk depends upon the definition of normal or adequate energy intakes. In female CD patients, the mean energy intake was less than the median value of the RDA, but was comparable with that of NC (Table 3) and greater than the lower limit of the RDA for energy intake. For male GD patients, the mean energy intake was greater than the median value of the RDA, but was certainly less than the mean energy intake of NC (Table 2) and above the lower limit of the RDA for energy intake. However, 46% of the female patients with CD consumed less than 1600 kcal/day, and 67% consumed less than 2000 kcal/day; the comparable figures for male CD patients were 30% less than 2300 kcal/day and 51% less than 2700 kcal/day. However, these figures do not take individual energy requirements into account. Energy intake with respect to individual energy requirements will be discussed shortly.

The assessment of the adequacy of energy intake for an individual patient depends upon their energy requirements. There are numerous factors which influence energy requirements: body weight, physical activity, age, sex, and state of health. Crohn's disease may modify an individual's energy requirements due to the presence of an inflammatory process, malabsorption, enteropathy, and the use of certain medications. There are only a limited number of ways in which energy requirements may be estimated. There are no previous reports of determination of energy requirement by direct or indirect calorimetry in patients with inflammatory bowel disease. In the long term, changes in body weight suggest alterations in energy requirements, but such changes in body weight may only reflect a change in body composi-

tion. Indeed, weight change frequently occurs in conjunction with active CD (Best 1976) and may reflect alterations in energy requirement due to the disease process. The calculation of basal energy expenditure (BEE) using the Harris-Benedict standards (Rutten et al 1975) has been applied to the estimation of energy requirements of healthy individuals. The BEE is then multiplied by a coefficient which varies with disease state; coefficients have been calculated for surgical or burn patients (Rutten et al 1975, Wilmore et al 1974), and the value of this coefficient may vary from 1.54 BEE to 2.5 BEE. The BEE for our patients with CD was 1361 kcal/day for women and 1698 kcal/day for men, but no coefficient has been calculated for CD patients, and thus we are only able to approximate the energy requirements of CD patients using this technique. However, a study of children with CD found basal metabolic rate to be normal (Kelts et al 1979). Therefore, using a coefficient of 1.5 BEE (Rutten et al 1975) to calculate energy requirement, 52% of the males and 62.5% of the females were consuming less energy than they required. This is similar to the percentages of males and females consuming less than the median value of the range of the RDA.

Accordingly, it is difficult to confidently agree upon the optimal energy intake for patients with CD. Other studies have suggested that energy intake by CD patients is either normal (Martini et al 1976; Thornton et al 1979) or high (Kasper et al 1979), and all of these former studies demonstrated a greater energy intake than did the present investigation. In these other studies the energy intakes were not analyzed separately for males and females, and as the proportion

of men and women with CD varied from study to study, this clearly would have influenced the mean energy intake of a combined group. The duration and site of the disease was not detailed in the previous work and may have influenced energy intake as well. In addition, these previous studies were conducted in England and West Germany, and energy intake in normal healthy individuals may vary with location, even within regions of a given country (Canada, Dept of National Health and Welfare, Ottawa, 1973). Finally, energy intake may be influenced by the activity of the underlying disease process, and the activity of the CD was not reported in the previous studies. The mean Crohn's Disease Activity Index (CDAI) in our patients was 46 (0-188) and 118 (0-434) for males and females, respectively. This indicates that our patients had mild to moderate disease activity, but there was no correlation between disease activity and energy intake. Thus energy intake did not appear to simply reflect underlying disease activity, and some other factor(s) must be sought to explain the wide variation of energy intake in patients with CD.

A further question to consider is the potential relationship between energy intake and body weight. In this study there was no significant correlation between relative body weight and either energy intake or energy intake/BEE. This lack of correlation persisted even when patients with less than 80% relative weight and greater than 120% relative weight were excluded. What are the possible explanations for this surprising finding? A change in energy intake will require time to be reflected as a change in relative weight. Some CD patients may purposely gain weight during periods of quiescent disease activity, or

may inadvertently gain weight from fluid retention or increased appetite due to steroid therapy. This lack of correlation between energy intake and relative weight may also reflect changes in energy requirement: the expected positive correlation between relative weight and energy intake or energy intake/BEE assumes a constant energy requirement. The energy requirement of individual patients with CD is likely changing over time as a result of malabsorption or enteropathy, and thus the ratio between energy intake and requirement would also change, thereby preventing the demonstration of the expected correlation between intake and relative weight. The practical clinical implication of this finding must be stressed: the relative weight of a patient with CD is not a good reflection of the adequacy of their energy intake.

The percentage of energy intake comprised of protein was similar in male and female CD patients and those healthy individuals studied in the NC survey (Appendix 32). Both male and female CD patients consumed about 5% more of their energy as carbohydrates (CHO), and about 5% less of their energy as fat (Appendix 32). It is not possible to determine whether this was statistically different from the results of NC. However, other dietary studies have suggested a higher CHO consumption by CD patients (Kasper et al 1979, Martini et al 1976, Mayberry et al 1980, Thornton et al 1979), and specifically a higher intake of refined sugar. We were not able to specifically analyze our patients' intake of refined sugar, but their intake of "Foods primarily sugar" was actually slightly less than that consumed by NC participants. However, a striking difference was present in the greater

fruit consumption by our CD patients (Table 6). It is likely that the increased carbohydrate intake in our CD patients was due to their greater intake of fruit. This greater intake of fruit was largely comprised of fruit drinks which contain relatively large amounts of refined sugar.

Unfortunately, fruit drink consumption of NC participants was not available, and it was not possible to determine whether CD patients consumed more fruit drinks and/or more refined sugar than did NC. However, we have confirmed that CD patients consumed increased amounts of CHO, and, clearly, future studies must attempt to determine if a larger intake of refined sugar is responsible for the increased CHO consumption.

5.3 Iron

The mean daily iron intake of male patients with Crohn's disease (CD) was well above the recommended daily allowance (RDA), and almost 100% of these patients consumed the full RDA of iron. However, in the female patients with CD, the mean daily iron intake was considerably lower than the RDA (Table 3), with only 17% of the women consuming the full RDA and a full 25% consuming less than half the RDA (Table 5). By comparison, the mean daily iron intake of Nutrition Canada (NC) participants was similar to that of the CD group for both males and females. However, the iron deficiency which occurs in some patients with CD (Thomson et al 1978, Bartels et al 1978) may still be on the basis of this observed reduction in iron intake. This point is substantiated from the NC survey in which iron intake was less than the

RDA in some participants who were also found to have abnormal hemoglobin concentration, mean corpuscular hemoglobin concentration (MCHC), and % transferrin saturation. These hematological abnormalities were taken as evidence for iron deficiency in the NC survey, and while this assumption may be valid in healthy individuals, it may not necessarily apply in CD. For example, although abnormalities in serum iron concentration, iron binding capacity, % transferrin saturation, and hemoglobin concentration are known to occur in CD patients with iron deficiency, such abnormalities occur with equal frequency in patients with anemia secondary to the chronic inflammatory disease process (Child et al 1973, Thomson et al 1978). Indeed, the most reliable method of assessing body iron stores is still the estimation of bone marrow hemosiderin. This study was not designed to test specifically for iron deficiency and did not include bone marrow smears. However, this study did include the measurement of serum ferritin concentrations, which correlate closely with reticuloendothelial iron in healthy persons. In the present study, serum ferritin concentrations were above the reference value in all male patients (Table 8) and were within the range diagnostic of iron deficiency in only 18% of the female patients (Table 9). Other studies vary considerably in the reported prevalence of low serum ferritin concentrations. Bartels et al (1978) found low serum ferritin in 29% of males and 44% of females with CD. In a comparable Canadian study (Thomson et al 1978), serum ferritin was low in only 10% of CD patients. In the present study, dietary iron intake was greater than the RDA in nearly all the males (Table 4), so it was expected to find the serum ferritin values in the

normal range. However, there was a poor correlation between dietary iron and serum ferritin concentration (Table 10). In females, iron intake was less than the RDA in 83% (Table 4), but the serum ferritin concentration was low in only 18% (Table 9), and there was once again a poor correlation between serum ferritin concentration and iron intake (Table 11). Thus serum ferritin concentration is not a useful parameter for prediction of iron intake. Furthermore, the serum ferritin may also be of limited value to predict the presence of established iron deficiency in patients with CD (Thomson et al 1978). Why is the serum ferritin concentration a poor indicator of the presence of inadequate iron intake? While a good correlation is present between body iron stores and serum ferritin concentration in healthy individuals (Valberg et al 1976), the serum ferritin concentration may be inappropriately elevated in a host of diseases (Jacobs et al 1976, Bentley and Williams 1974), including CD (Thomson et al 1978). The inappropriately elevated serum ferritin in some patients with CD may be due to reticuloendothelial dysfunction or mild hemolysis secondary to the use of Salazopyrine (Das et al 1973). Finally, the body iron stores may be adequate to maintain a normal serum ferritin for several months after the patient begins to consume a diet containing inadequate iron, and therefore the lower prevalence of proven iron deficiency than the prevalence of low iron intake may simply reflect the time required for inadequate intake to be translated into established iron deficiency. Of even greater interest, however, is to speculate on the pathophysiology of the known iron deficiency in some patients with CD. This study convincingly demonstrates that the daily

iron intake is low in a large proportion of female patients with CD (Table 5). Furthermore, some malabsorption of dietary iron may have occurred as a result of the inadequate intake of ascorbic acid by these patients (Table 5). Malabsorption of iron has been demonstrated previously in a small number of children with ulcerative colitis (Ormerod 1967), but there is no comparable data for CD. Finally, the requirement for iron may be increased in these patients due to their loss of excessive iron and blood as a result of their enteropathy (Beeken et al 1972).

5.4 Folate

An alarmingly large proportion of patients with CD were consuming low amounts of folate (Tables 4 and 5). For example, none of the male CD patients consumed the RDA for folate, and less than 50% consumed half the RDA. Only eight percent of the female patients with CD were consuming the full RDA for folate, and only slightly more than half the patients were consuming one-third of the RDA. In comparison, the mean folate intake of males from the NC survey was 221 ug versus 211 ug in the CD group. Females from the NC survey actually consumed slightly less folate per day than did the female CD patients: 146 ug and 185 ug, respectively. Thus, the mean daily folate intake of the CD group was very similar to that of NC, although the folate intakes of both groups were less than the RDA. On the basis of the lack of biochemical evidence of folate deficiency in NC participants, it has been suggested that the RDA for folate is, in fact, too high (Thompson and Hoppner 1979). However, not even 50% of the CD patients were

consuming half the RDA for folate, which, even by liberal standards places them at risk of developing folate deficiency (Herbert 1962). Moreover, low serum folate levels were found in 37% and 50% of the male and female CD patients, respectively (Tables 8 and 9). Therefore, a large proportion of patients with CD who consume only half the RDA are likely to develop low serum folate concentrations. If the RDA for folate is too high, as suggested from the results of the NC survey (Thompson and Hoppner 1979), then half the RDA is clearly too low for CD patients to maintain normal folate balance.

The occurrence of low serum folate concentrations in CD patients, as well as low red cell folate and megaloblastic anemia is well-documented (Hoffbrand et al 1968, Dyer et al 1972, Cooke 1975). Various speculations of folate deficiency include decreased folate intake, malabsorption, increased loss from the inflamed gut, and increased requirement due to rapid red cell turnover due to the use of SAS. None of the above investigators, however, examined dietary folate intake in patients with CD. Thus, it is significant that the present study first demonstrated evidence of low dietary intakes of folate, and second, demonstrated a highly significant correlation between serum folate concentration and dietary folate intakes in female CD patients (Table 11). In a recent study of elderly people in Sweden, a low correlation was found between dietary folate intake and serum folate concentrations in women, but the correlation was not significant (Borgstrom et al 1979).

While it is tempting to speculate that a low serum folate concentration represents folate deficiency, it must be remembered that serum

folate is not a valid reflection of long-term folate deficiency or of body folate stores (Herbert 1962). SAS is thought to alter the absorption of dietary folate (Dhar et al 1976). While it might be suggested that the lack of a significant correlation between dietary folate and serum folate concentration in male CD patients might be due to their ingestion of SAS, similar proportions of male and female CD patients were consuming SAS, and yet there was a significant correlation between dietary folate and serum folate in female CD patients. Notwithstanding the fact that the presence of a low red cell folate concentration, megaloblastic anemia, and the exclusion of vitamin B_{12} are needed to confirm the existence of established folate deficiency, a low serum folate concentration may be the first sign in the biochemical spectrum of the development of folate deficiency. Thus the demonstration of a low serum folate concentration in a patient with CD must signal the likelihood of a low folate intake, and the patient's potential risk of developing folate deficiency.

5.5 Vitamin B_{12}

Unlike many of the other nutrients, the mean intake of vitamin B_{12} (B_{12}) was well above the RDA in both male and female CD patients (Tables 2 and 3, respectively). These mean intakes are at the low end of the range of estimated average U.S. intake of 5-15 ug/day (U.S. RDA 1980), though the range may be as low as 1 ug or as high as 100 ug. However, B_{12} intakes of the CD group were slightly higher than the estimated average of 3.1 ug/day in Great Britain (Adams et al 1973). Although the RDA for B_{12} of 3.0 ug/day is probably greater than needed

by many adults, it has been set high to allow for variation in hematopoietic response and ileal absorption. It has been suggested that a B_{12} intake of one ug/day is probably adequate in the healthy adult (Herbert 1968). For one thing, as intake of vitamin B_{12} decreases, absorption increases (RDA 1980). Moreover, the enterohepatic circulation of bile supplies 0.5-5.0 ug/day of B_{12} (Herbert 1968). Thus intakes of less than the RDA might be quite adequate in the healthy adult. However, in CD, this normal process may be interrupted in several ways: malabsorption of B_{12} due to ileal dysfunction or resection, lack of gastric intrinsic factor, or bacterial overgrowth. Thus, it would be unwise to condone B_{12} intake of less than 3.0 ug/day in the CD patient. While the mean intakes of B_{12} were normal in patients with CD, the prevalence of adequate intakes was abnormal. In Tables 4 and 5, it is shown that 74% of males and only 50% of females were consuming the RDA of vitamin B_{12}. Examination at the level of 2/3 RDA again points out the consistently poorer intakes of females, with only 58% consuming this level as compared to 96% of males. It must be stressed that deficiency of vitamin B_{12} takes years to develop (Herbert 1968). However, 11% of the CD patients had serum B_{12} concentrations less than the reference value (Tables 8 and 9). Other investigators have found low serum B_{12} concentrations in 16-20% of CD patients (Dyer 1973, Cooke 1975). In this study, both of the males with a low serum concentration of B_{12} were consuming less than the RDA of B_{12}. A Shillings test without added intrinsic factor was normal in one of these male patients, so it can be concluded that low serum B_{12} was due to inadequate dietary B_{12}. In contrast, B_{12} intake in both

female patients with low serum B_{12} was normal. Biochemical parameters for assessment of malabsorption were not available in either case. However, both females, as well as both males with a reduced serum B_{12} concentration had ileal involvement or resection, and it is likely that they suffered from B_{12} malabsorption. How is the low serum B_{12} concentration explained in the two women with normal B_{12} intake? Both females had folate intakes less than the RDA and low serum folate concentrations. A primary deficiency of either (B_{12} or of folate) will have a facilitative effect on a secondary deficiency of the other vitamin (Herbert 1973). Because folate intake was low and B_{12} intake was not, folate deficiency in these two females might be suspected as the primary nutritional defect. In addition, these patients had ileal involvement. Thus, it appears that a mixed deficiency exists in these women.

Though the other CD patients consuming less than the RDA for B_{12} did not have biochemical evidence of B_{12} deficiency, it is likely that in time there would be progressive depletion of B_{12} body stores, especially in the presence of malabsorption. Thus, the presence of B_{12} malabsorption must be suspected, since over 90% of the CD patients had involvement of the ileum. Therefore, those patients consuming less than the RDA of B_{12} would be at additional risk of developing B_{12} deficiency.

5.6 Vitamin C

The mean vitamin C intake of CD patients was one and a half times greater than that of NC participants, and both means were well above

the RDA (Tables 2 and 3). It should be cautioned, though, that this does not preclude underconsumption of vitamin C, as 13% of male CD patients (Table 4) and 33% of female CD patients (Table 5) were consuming less than the full RDA. Other studies have shown that significant percentages of CD patients are consuming less than the RDA of vitamin C, as well (Hughes & Williams 1978, Linaker 1979). For example, Linaker showed that 50% of patients with CD were consuming less than the RDA of vitamin C. Although there was no significant difference in vitamin C intake between controls and CD patients in Linaker's study, 7 out of 10 CD patients had low leucocyte ascorbic acid (LAA) levels. Likewise, Hughes and Williams (1978) found LAA levels to be lower in CD patients than in controls. Indeed, in Hughes' study, 63% of the CD group were consuming less than the RDA of vitamin C. Unfortunately, we were not able to perform measurements of LAA levels in our patients. It must be pointed out that the RDA of vitamin C is far in excess of that needed to prevent scurvy (Bartley 1953). In fact, only one patient who did consume less than 10 mg vitamin C/day (the minimum necessary to prevent scurvy) showed clinical signs of scurvy (Linaker 1979). All of the patients in the present study were consuming greater than 10 mg of vitamin C/day (Appendix 10), and thus it was to be expected that none of our patients demonstrated clinical signs of ascorbate deficiency.

Scurvy is a late indicator of vitamin C deficiency and the above studies show that low vitamin C intake is associated with low LAA levels, which may be an earlier indicator of vitamin C deficiency and clinical disease, i.e. scurvy. Moreover, it is possible that vitamin

C intakes greater than scorbutic levels could be affecting utilization of other nutrients, such as folate and iron. It is well known that vitamin C facilitates absorption of food iron (Rossander et al 1979). In addition, vitamin C is believed to be necessary for the prevention of irreversible oxidation of tetrahydrofolate and thus, removal from the folate metabolic pool (Stokes et al 1975). Thus a decreased vitamin C intake could cause secondary iron and folate deficiencies, both of which are known to occur in CD. In the present study, a highly significant correlation was found between dietary vitamin C and serum folate (Table 11), which possibly reflects the relationship suggested by Stokes et al (1975). However, an even higher correlation between dietary vitamin C and dietary folate (Table 11) is undoubtedly reflecting the extent to which vitamin C and folate occur in common foods, as well as the general quality of the diet. Thus, due to either decreased utilization of folate in vitamin C deficiency, or concomittant reduction of dietary intake of vitamin C, deficiencies of these two nutrients (folate and vitamin C) could and do occur simultaneously (Tables 4 and 5). In view of the highly significant correlations between vitamin C intake and folate intake, folate intake and serum folate, and vitamin C intake and serum folate (Table 11), patients with a low serum folate concentration might also be at risk of developing or having vitamin C deficiency. It may be concluded that CD patients who are consuming less than the RDA of vitamin C are at risk of developing deficiencies of either vitamin C and/or other nutrients.

5.7 Vitamin B_6

The mean vitamin B_6 consumption in CD patients was less than the RDA (Tables 2 and 3) and only a small number of patients consumed the RDA of vitamin B_6 (Tables 4 and 5). There is a paucity of data describing the vitamin B_6 requirements of the human, there are inconsistencies in the determination of the vitamin B_6 content of foods, and vitamin B_6 intakes of populations have not been widely described. Thus, it is not surprising that data were not available for comparison to NC. However, occurrence of vitamin B_6 deficiency is rare and has previously been reported in alcoholics (Li 1978) and in the elderly (Driskell 1978), thus suggesting that the RDA for vitamin B_6 is too high. Since vitamin B_6 requirement is increased as protein intake increases (Baker et al 1964), an alternate way to assess vitamin B_6 adequacy involves examining the relation of vitamin B_6 to the amount of protein consumed (Donald 1978): using a ratio of 0.02 mg of vitamin B_6/gram of protein, the vitamin B_6 requirements of male and female CD patients would be 2.0 mg and 1.5 mg, respectively, which coincides with the vitamin B_6 allowance of the Dietary Standard for Canada (Bureau of Nutritional Sciences 1975). However, even the lower Canadian allowance is met by only 26% of the men and 21% of the women in the present study. It should be kept in mind that many CD patients had protein intakes less than the mean protein intake for the CD group, but more than the RDA for protein, and at protein intakes equal to the RDA, vitamin B_6 requirements would be 1.1 mg/day and 0.8 mg/day for males and females, respectively. However, even assuming this lowest acceptable protein consumption, intake of vitamin B_6 would

still be low for 26% of male and 46% of female CD patients. Thus, although the adequacy of vitamin B_6 will vary with protein consumption, clearly a significant number of CD patients are consuming levels of vitamin B_6 which places them at risk of developing vitamin B_6 deficiency. Furthermore, steroid therapy appears to increase vitamin B_6 requirement, placing those patients on steroid therapy at additional risk of developing dietary deficiency of vitamin B_6 (Rose 1972). The present study did not include biochemical parameters such as pyridoxal phosphate and xanthurenic acid to establish vitamin B_6 deficiency, and thus it was not possible to confirm suspected inadequacy of dietary vitamin B_6 intakes. However, pyridoxine deficiency may give rise to cutaneous lesions such as aphthous ulcers, as well as anemia, both of which occur in patients with CD. It should also be pointed out that there is considerable overlap in the clinical deficiency symptoms of the B-vitamins, and thus, distinguishing one B-vitamin deficiency from another is often difficult. Furthermore, a decreased intake of several B-vitamins may occur simultaneously. Thus, when a deficiency of one B-vitamin is suspected, deficiencies of the other B-vitamins should also be suspected.

5.8 Anemia

Anemia is common in patients with CD (Brooke et al 1977). Numerous nutrients are essential for the maintenance of a normal hemoglobin concentration, and these include iron, folate vitamin B_{12}, ascorbic acid, protein, vitamin B_6, and trace elements such as copper. Established deficiencies or low dietary intakes of most of these substances

have been observed in patients with CD (Tables 4 and 5), and often the anemia may be multifactorial in origin. This study was not specifically designed to establish the role of vitamin B_6, protein, or trace elements in the etiology of the anemia. In some patients, the anemia was due to deficiencies of iron, and possibly folate or vitamin B_{12}. The majority of patients with anemia and CD are thought to have the anemia of chronic disease (Child et al 1973, Dyer et al 1972, Thomson et al 1978). Clearly, however, future studies must focus on the potential role of correction of deficiencies of pyridoxine, protein or trace elements and the reversal of the anemia.

5.9 Thiamin

The mean thiamin intake of male and female CD patients was greater than both the RDA and that of NC (Tables 2 and 3). Thus, it was somewhat surprising that almost half of the patients in both the male and female groups consumed less than the RDA for thiamin (Tables 4 and 5). Does thiamin consumption less than the RDA place individuals at risk of deficiency? Thiamin deficiency was once considered to be rare in spite of low thiamin intakes. However, the NC Survey (Canada, Dept of National Health and Welfare, 1973) observed decreased urinary thiamin excretion and clinical signs suggestive of thiamin deficiency in some individuals with thiamin intakes considerably less than RDA. A thiamin intake less than the full RDA, however, does not necessarily place an individual at risk of deficiency. The RDA is based on a high level of energy intake and since thiamin requirement varies with caloric intake (RDA 1980), the RDA for thiamin involves a

certain margin of safety. Thus, thiamin intakes of less than 2/3 RDA which were generally associated with energy intakes less than the lower range of the RDA, in both male and female CD patients, were within the recommended ratio of 0.5 mg thiamin/1000 kcal, except for 1 male and 2 female patients. In contrast, almost half of the men and women in NC had low thiamin intakes in relation to energy intake. This is not to say that a thiamin intake in CD patients less than the RDA should be condoned on the basis that energy intake is less than the RDA, but simply recognizes that thiamin intake in the present study is in proportion to energy intake, and on this basis may be adequate. However, two female patients and one male patient consumed very close to the daily minimum thiamin requirement of 0.3 mg/1000 kcal that is necessary to prevent signs of thiamin deficiency (Dietary Standard for Canada 1975), and these patients are thus definitely at risk of developing thiamin deficiency. Beriberi was not present in any of the CD patients, but this is a very late indicator of thiamin deficiency. Early biochemical indicators of thiamin deficiency such as erythrocyte transketolase activity were not assessed in this study to confirm the suspicion of thiamin deficiency in these three patients with potentially low intakes of thiamin. It may be of even greater importance that several of the earliest symptoms of decreased thiamin intake are depression and irritability, loss of appetite, and loss of weight (Briggs and Calloway 1979), and these symptoms are frequently experienced by CD patients. Thus, these symptoms could be subclinical indicators of thiamin deficiency and could signal a need to assess thiamin adequacy in the CD patient.

5.10 Riboflavin

The mean riboflavin intake of both male and female CD patients was greater than the RDA (Tables 2 and 3). Although the mean riboflavin consumption of male CD patients was less than that of NC (Table 2) and the corresponding intake of female CD patients was equal to that of NC (Table 3), a considerably higher percentage of female (39%) than male (17%) CD patients consumed less than the RDA of riboflavin (Tables 4 and 5). Does riboflavin consumption of less than the RDA place individuals at risk of developing riboflavin deficiency? The answer is not clear. Almost half of the male and female NC participants consumed less than the RDA of riboflavin, but urinary riboflavin excretion was normal and clinical signs of riboflavin deficiency were absent (Canada, Dept of National Health and Welfare 1973). However, erythrocyte glutathione reductase activity is probably a more sensitive indicator of riboflavin deficiency than urinary riboflavin excretion (Bamji 1969) and had it been determined in the NC study would have been more conclusive of dietary adequacy or inadequacy. Although the RDA for riboflavin has been related to energy intake (RDA 1980), a total daily riboflavin intake of approximately 1.2 mg regardless of total caloric intake allows a safety margin of 20%, based on evidence that intakes of 1.0 mg riboflavin/day increase urinary riboflavin excretion and erythrocyte riboflavin in deficient subjects (Pargaonkar and Srikantia 1964). Riboflavin consumption in all male CD patients exceeded or was very close to 1.0 mg/day (Appendix 9). However, several females had riboflavin intakes of 0.5-1.0 mg/day (Appendix 9). While a minimum riboflavin intake of 0.5-0.6 mg/1000 kcal has been

shown to maintain erythrocyte glutathione reductase activity within the normal range (Bamji 1969), and all females in the present study exceeded this ratio, it is not clear whether the total daily riboflavin intakes of 0.5-0.7 mg in female CD patients consuming less than 1000 kcal will produce a riboflavin deficiency. Thus, although all female CD patients exceeded the ratio (of 0.5 mg riboflavin/1000 kcal), those 17% whose total riboflavin intakes were 0.5-0.7 mg are at risk of developing riboflavin deficiency. However, biochemical parameters for the assessment of riboflavin status were not part of the experimental design, so it was not possible to confirm riboflavin deficiency.

Milk supplies about 40% of all the riboflavin in the food supply (Briggs and Calloway 1979), and some CD patients may restrict milk due to lactose intolerance (Sitrin et al 1980). Thus, it was somewhat surprising that more patients did not have a low riboflavin consumption. Indeed, the mean consumption of dairy products in the CD group did not really differ from that of NC (Table 6). Only three patients in the present study (one male and two females) stated they had lactose intolerance, though their respective riboflavin intakes were well above the RDA and they consumed moderate amounts of dairy products. However, of the three male patients whose riboflavin intakes were 0.9-1.1 mg/day and the four female patients whose riboflavin intakes were 0.5-0.7 mg/day, milk was not consumed at all or was consumed in small amounts in tea or coffee. This percentage is similar to the estimated 15-25% of people in the general population who use milk sparingly or not at all (Briggs and Calloway 1979). Thus, in the

present study, the low riboflavin intakes did not occur in those patients who were purportedly lactose intolerant, but rather in those patients who had an apparent dislike for dairy products and this dislike occured not more frequently in CD patients than in the general population.

5.11 Pantothenic Acid

As with most other nutrient intakes in the present study, the female CD patients fared worse than the male CD patients, with almost 2/3 of the women and 1/2 of the men consuming less than the lower limit of the RDA for pantothenic acid (PA) (Tables 4 and 5). Pantothenic acid intake is generally in proportion to the intake of the other B-vitamins, and thus in view of the prevalence of low intakes of some of the other B-vitamins in the present study such as thiamin, riboflavin, vitamin B_6, vitamin B_{12}, and folate, it was not surprising to find intakes of PA less than the RDA. How does the intake of PA in the present study compare with other intakes of PA? The average U.S. diet provides about 7 mg/day PA, ranging between 5 and 20 mg/day (Fry et al 1976). While the mean PA intake for male CD patients (Table 2) falls within this range, that of the female CD patients is somewhat below this range (Table 3). However, on the basis of similar intakes of other nutrients (Tables 2 and 3), the mean PA intake of CD patients is likely similar to that of NC participants. Therefore, the question is whether intakes of PA less than the RDA will place individuals at risk of deficiency. While the essentiality for PA is well established (Denko et al 1947, Fry et al 1976), the amount of requirement is not

well established and thus there are little data available on which to base predictions of the effect of PA intakes less than the RDA. Indeed, in the absence of enough scientific evidence to establish a recommended allowance, a provisional allowance for nutrient intakes, such as PA, is based on normal intakes of that nutrient by a population without signs of deficiency (RDA 1980). However, diets as low as 1 mg/day of PA for several months have not resulted in clinical deficiency (Denko et al 1947), and clinical deficiency symptoms have only been produced in man by feeding metabolic antagonists (Hodges et al 1959) or a purified diet (Fry et al 1976). On the basis of lack of clinical evidence, however, it could be premature to assume adequacy of low PA intakes, as subclinical deficiency could be present, but unrecognized. Unfortunately, the biochemical standards for PA are not well defined and therefore are not conclusive for PA deficiency. It could be of some importance to CD patients that included in the spectrum of deficiencies in experimental animals are gastrointestinal disturbances - gastritis with enteritis and diarrhea (Ellestad-Sayed 1976). It is possible that a subclinical deficiency of PA could be contributing to these symptoms in CD.

In the absence of biochemical standards for PA it is not possible to determine whether or not PA consumption less than the RDA will place an individual at risk of deficiency. However, since PA is provided in proportion to other B-vitamins (Cohenour and Calloway 1972), a diet which focuses on adequacy of B-vitamins in general should ensure adequate PA.

5.12 Calcium Homeostasis

The mean calcium intake in CD patients was well above the RDA for men (Table 2), but the mean was less than the RDA for women (Table 3). Both mean calcium intakes were consistent with those of NC participants (Tables 2 and 3). However, of CD patients, almost half the men and two-thirds of the women were consuming less than the RDA of calcium (Tables 4 and 5). In the healthy individual, without CD, consuming a calcium intake of considerably less than the RDA probably does not place the individual at risk of developing calcium deficiency, since calcium balance can be maintained in men and women on 200-400 mg/day (FAO/WHO 1962) a FAO/WHO (Food and Agriculture Organization/World Health Organization) recommends calcium intakes of only 400-500 mg/day. Therefore, the extent of the impaired calcium intake in the patient with CD may be more fully appreciated by the finding that only 33% of the females and only 9% of the males consumed less than half the RDA for calcium.

It must be stressed that in patients with CD there is the additional risk of their having vitamin D or protein deficiency on the basis of impaired intake. Indeed, in this ~~study~~ it was found that only 57% of men and 30% of women consumed the RDA for vitamin D (Tables 4 and 5). Similar to the case for calcium intake, 17% of males and 29% of females consumed less than half the RDA for this vitamin. Furthermore, evidence for protein malnutrition, based on abnormal AMC, was found in one-quarter of patients with CD, whereas over half these patients had a reduced total lymphocyte count (Tables 8 and 9). Thus, patients with CD are at risk of developing multiple

deficiencies of calcium, vitamin D and protein, and any CD patient consuming less than half the RDA for calcium is potentially at risk for developing impaired calcium balance.

Impaired calcium balance may develop after only a prolonged period of impaired intake of calcium, vitamin D, and protein (Tietz 1976). Were there any signs of calcium deficiency in these patients with CD? There are a host of parameters used to suspect or diagnose the presence of calcium deficiency and bone disease. These include serum calcium concentration, calcium absorption, urinary calcium, serum concentrations of the vitamin D analogues, serum and urinary phosphate concentrations, serum alkaline phosphatase activity, measurement of cortical thickness or X-ray of the hands, bone densitometry, Singh index of the trabecular pattern of the femoral head, and bone biopsy. We had measurements of serum calcium, phosphate, and alkaline phosphatase in most of our patients, and total vitamin D activity in some of our patients. All the male CD patients had serum calcium concentrations greater than 8.5 mg/dl, but the serum calcium was between 8.2 and 8.4 mg/dl in four female patients (Table 9 and Appendix 27), and these values remained slightly below the lower limit of normal calcium concentration even after correcting for the serum albumin concentration. The serum phosphate concentrations were normal in all patients, and although the serum alkaline phosphatase activity was increased in two patients (Table 8), their serum calcium concentrations were normal (Table 8). The serum magnesium concentrations were normal in all but one patient, (G.K.), and his value of 1.3 mg/dl normalized after supplementation and correction of his ileostomy dys-

function; his serum calcium was normal (Table 8). In contrast to the report of Sitrin et al (1980), the serum total vitamin D activity was reduced in only 2 of the 10 men and one of the 9 women in whom this assay was performed (Tables 8 and 9). It is of interest that only one of the women with a slightly reduced serum calcium concentration also had reduced serum vitamin D activity, and yet, the serum calcium concentration was normal in the two men with reduced serum vitamin D activity. Thus, there is no agreement qualitatively or quantitatively between these four indirect measurements of calcium balance: serum calcium, phosphate, alkaline phosphatase, and vitamin D.

On the other hand, is there any relationship between dietary intakes and these laboratory parameters? There was no correlation between calcium intake and serum calcium concentrations in women, or between vitamin D intake and serum vitamin D activity in men (Tables 12 and 13). While there was a weak, but statistically significant correlation between calcium intake and serum calcium concentrations in men, and between vitamin D intake and serum vitamin D acitivity in women (T[redacted] 12 and 13), the clinical application of these correlations is doubtful since the serum calcium concentrations were normal in the men, and the serum vitamin D was reduced in only one female CD patient. Indeed, the lack of correlation between dietary intakes of calcium and serum calcium concentrations is not surprising since serum calcium levels are regulated by complex homeostatic mechanisms, and impaired calcium intakes would not be expected to be reflected by low serum calcium concentrations until late in the development of calcium deficiency. In addition, the intake of vitamin D would not neces-

sarily be reflected by serum levels of vitamin D since the serum vitamin D activity may be influenced by exposure to sunlight. Thus, these indirect parameters of calcium homeostasis are of limited value for the prediction of calcium or vitamin D intake. However, the finding of a low value of either serum calcium concentration or vitamin D activity does suggest that a specific patient may be at risk of developing a dietary deficiency of calcium or vitamin D. For example, three of the four women with low serum calcium concentrations had a reduced intake of both calcium and vitamin D, and one woman had a low intake of just vitamin D (Table 5). In addition, the one female with a low serum vitamin D activity and one of the two males with low serum vitamin D activity also had a low vitamin D intake. Therefore, the finding of a low serum calcium concentration or vitamin D activity clearly does not exclude the potential for a serious deficiency in the intake of these nutrients, but the finding of such abnormal serum values must raise the index of suspicion for the potential presence of nutrient risk. Moreover, one group of researchers (Bell et al 1977) has shown that a diet rich in foods containing phosphate additives may contribute to a low serum calcium. Experimental feeding of foods high in phosphate additives significantly reduced the serum calcium concentrations in 8 adults. Phosphates are added to a wide variety of processed foods including meats, cheese, carbonated beverages, dressings, and refrigerated bakery products (Deman and Melnychyn 1971).

How useful are the measurements of serum calcium, phosphate, alkaline phosphatase, or vitamin D activity to establish the presence of calcium imbalance? Unpublished observations by von Westarp et al

(1981) have indicated a poor correlation between these serum values and the presence of metabolic bone disease, diagnosed on the basis of bone biopsy or hand bone X-ray. Using these end-points, approximately one-third of female patients with CD have established metabolic bone disease (MBD). It is of interest to point out that the same percentage of women consumed less than half the RDA for calcium and only 30% of the women consumed the RDA for vitamin D (Table 5). Thus, one of the mechanisms responsible for the development of MBD is impaired dietary intake. Additional factors potentially producing or accelerating the development of calcium imbalance must include corticosteroid therapy, steatorrhea, and lactase deficiency (Sitrin et al 1980). While this study was not specifically designed to establish the pathophysiological factors important for the development of bone disease, our limited data provided courtesy of Dr. C. von Westarp (1981) indicate that over half the patients with CD had calcium malabsorption, and a further but different half had steatorrhea. The extent of calcium loss into the stool of patients with CD was not assessed. In this study, three of the four female patients with low serum calcium concentrations and the two men with low serum vitamin D were consuming corticosteroids, and over 50% of the patients ingesting inadequate amounts of calcium or vitamin D were receiving this medication. Therefore, there are several potential and real factors which may be responsible for the development of MBD in patients with CD, and future studies must examine the role of dietary supplementation in the prevention of calcium deficiency.

5.13 Vitamin A

Mean vitamin A intake was greater than the RDA in both male and female CD patients (Table 2 and 3). While the female intake was close to that of NC, male CD patients consumed slightly more than half the vitamin A of NC participants. However, vitamin A is highly concentrated in relatively few food sources and daily intake varies considerably. For example, mean daily intake for the nationwide male NC group was much closer to that of the male CD group. Despite an adequate mean daily intake of vitamin A in CD patients, only half the male and female CD patients were consuming the RDA of vitamin A (Tables 4 and 5). Although vitamin A is stored in appreciable amounts in the liver (Hodges et al 1971), daily consumption of insufficient amounts of vitamin A can eventually deplete the liver stores. Serum vitamin A (retinol) concentrations were not assessed in the present study. Serum carotene concentrations are used clinically to obtain an assessment of recent vitamin A intake, and an evaluation of the possible presence of steatorrhea. Serum carotene concentrations were performed in a small number of our patients: 38% of the males and 13% of the females were below the lower limit of normal, but there was no significant correlation between serum carotene concentrations and vitamin A intake nor between serum carotene and carotene intake. It must be stessed that such comparisons were possibly in only 28/47 patients, and a larger sample must be evaluated before any conclusions may be drawn.

5.14 Fiber

The crude fiber (CF) intake of patients with CD was similar to the results obtained in NC (Tables 2 and 3). The cereal intake of CD patients is similar to NC, but the fruit intake of the CD group was greatly increased above NC (Table 7). The male CD patients consumed 76% less soft drinks than NC, and it is possible, though unproven, that fruit drinks were substituted for the soft drinks. If this were the case, then the greater intake of fruit would be due to a greater intake of fruit drinks. These juices contain little or no fiber and would thus make an insignificant contribution to total fiber, while at the same time would contribute to the total carbohydrate intake.

Dietary fiber (DF) may be 5-10 times higher than CF (Trowell 1973). Dietary fiber in CD patients has been reported to be increased (Kasper et al 1979) or decreased (Thornton et al 1979), as compared with controls. The DF intakes in these studies were 27 gm/day and 17 gm/day, respectively (Kasper et al 1979, Thornton et al 1979) and this compared with a figure of 12.7 gm/day in our patients with CD.

5.15 Nutrient Density

In the present study, we found that, in general, women were at greater risk than men for developing nutrient deficiency. Is this sex-related discrepancy due to an inadequate intake of food by female patients with CD, or was the quality of their diets suboptimal? To answer this question, it was necessary to examine the nutrient density of the diets consumed by CD patients. This qualitative comparison is given in Table 7 which shows that the only statistically significant

difference in the nutrient intake of male and female CD patients per 1000 kcal was in vitamin A and folate, of which males consumed less than females. Not surprisingly, these same nutrients were the only two nutrients in which fewer males than females met the RDA (Tables 4 and 5). Vitamin A is concentrated in relatively few foods, some of them being vegetables and fruits. Thus, it is possible that fruit/vegetables comprised a proportionately larger portion of female than male diets in patients with CD. Therefore, the quality of the diets consumed by male and female CD patients was generally comparable, but men generally require and consume more energy than women. The RDA for nutrients other than energy is the same or only slightly higher for men than women, and thus men are more likely to achieve their RDA for nutrients simply because they eat more.

5.16 Specific Factors Which Could Identify the Crohn's Disease Patient at Risk of Nutritional Deficiency

Recent advancements in biochemical analyses and increased understanding of metabolic processes have resulted in a proliferation of tests for assessment of nutritional status. However, it is costly and often impractical to perform a wide battery of tests in all patients, particularily when chronic disease states such as CD make it necessary to evaluate biochemical status at regular intervals. Therefore, there is a need for a few selected predictive parameters to identify those patients at risk of nutritional deficiency and in need of further nutritional assessment and or counselling.

What were the correlations between biochemical, dietary, and anthropometric parameters? From Tables 10-14 (inclusive) were chosen the biochemical, dietary, and anthropometric parameters which correlated with the greatest number of variables. In female CD patients, serum folate concentration correlated with four dietary parameters: folate, vitamin C, vitamin B_{12}, and vitamin B_6 (Table 11). In male CD patients, analyses of the same variables showed a correlation between dietary parameters only: protein vs folate, iron, vitamin B_6, and vitamin B_{12} (Table 10). A difference between males and females is not to be expected, and it is not clear why these differences in correlations existed. It was observed that fewer men had low nutrient intakes and abnormal biochemical parameters and possibly the relationship between nutrient intakes and biochemical parameters within the normal range is not linear, and thus is not reflected in a simple correlation. In addition, some patients had taken or were taking supplements of iron, vitamin B_{12}, and/or folate at the time of the dietary assessment. It was difficult to control for this in determining correlation, as length of time on supplements, amount of supplement, and multi-vitamin vs a single vitamin supplement were varied. However, correlations between dietary folate and serum folate in the present study were the same whether the folate supplemented group was included or not. Thus, in female CD patients, serum folate concentration could be used as a relative indicator of dietary folate, vitamin C, vitamin B_{12}, and vitamin B_6. It should be cautioned that despite a significant correlation with several nutrients, a low serum folate concentration does not necessarily indicate a low intake of these

nutrients, but simply indicates the likelihood of lower nutrient intake relative to an individual with a higher serum folate concentration.

In both male and female CD patients, significant correlations were observed between dietary intakes of calcium, phosphorus, protein and vitamin D (Tables 12 and 13). This is not surprising, as it is probably reflecting the extent to which these nutrients occur together in dairy products. Thus, in male CD patients dietary protein was correlated with each of dietary calcium, phosphorus, vitamin D, folate, iron, vitamin B_{12}, and vitamin B_6 (Tables 10 and 12). At this time, however, the practical significance of the relationship is unclear, since all protein intakes in the male CD group were greater than the RDA (Table 4). However, there was evidence of protein malnutrition and thus optimal protein intake in male CD patients, especially those on steroids, must be determined. Thus, there is no single parameter in male CD patients which will predict the risk of nutrient deficiency. Likewise, in females, the practical implication of the correlations between dietary calcium, phosphorus, protein, and vitamin D are limited, since the majority had protein and phosphorus intakes greater than the RDA (Table 5), and dietary calcium and vitamin D showed only a low correlation with one another (Table 13).

Body weight is generally considered to obscure disproportionate changes in body fat and muscle mass that occur in disease states and therefore is not a sensitive indicator of nutritional status. However, arm muscle circumference (AMC) is reported to specifically reflect protein status and not to correlate particularly well with

body weight (Section 2.4). Thus, it was somewhat surprising that in the present study AMC correlated only with total lymphocyte count (TLC) and that relative body weight (RBW) showed a similar correlation with TLC (Table 14). Furthermore, RBW was highly correlated with AMC in both male and female CD patients and with triceps skinfold (TSF) in females (Table 14). Therefore, RBW was as good or a better indicator of biochemical and/or anthropometric parameters in CD patients as was AMC. The practical significance of this finding is that RBW is easier to determine and does not require the same skill as determination of AMC or TSF. As a predictive factor RBW can be used to assess muscle reserve, TSF, and TLC in female CD patients.

5.16.1 Crohn's Disease Activity Index (CDAI) and Relationship to Nutrient Intake

The CDAI was not correlated with intake of energy, protein, carbohydrate, or folate in females (Table 18). In males, there was a significant negative correlation between the CDAI and energy intake, but the correlation was quite low (-0.38, Table 18). Thus, if the CDAI was used as an indicator of energy intake in males, the interpretation could result in a false positive, that is, the assumption of high energy intake associated with a low CDAI. The danger of an erroneous assumption such as this is obvious. Therefore, it can be concluded that the CDAI is not reliable as a predictive parameter of poor nutrient intake.

5.16.2 Crohn's Disease Activity Index and Relationship to Biochemical Tests

In females, the CDAI was negatively correlated with hemoglobin and positively correlated with serum ferritin. Nutritionally speaking, the correlation between hemoglobin and the CDAI is of little predictive value, since the anemia of CD can be due to one of several nutrient deficiencies or the chronic inflammatory disease process. However, it could be used as a screening device to signal a possible deficiency of iron, folate, vitamin C, vitamin B_{12}, or vitamin B_6. The positive correlation between serum ferritin and the CDAI was somewhat surprising. However, the interpretation of serum ferritin concentrations within the normal range is difficult. The several factors which may inappropriately elevate serum ferritin, including mild hemolysis secondary to the use of SAS and/or reticuloendothelial dysfunction could well be affecting this relationship between serum ferritin and the CDAI.

Serum albumin was negatively correlated with the CDAI in males (Table 18). However, since all the serum albumin concentrations were above normal in males, the practical significance of this relationship is limited. It should be noted, however, that the upper range of the CDAI in the male group, with the exception of one patient, was well within the range indicative of mild disease. Thus, if the observed relationship (between the CDAI and serum albumin) continued as disease activity increased, there is potential for a clinically significant relationship between the CDAI and serum albumin in a group of CD patients with a wider range of disease severity.

The CDAI was correlated with duration of disease in males, but not in females (Table 18). Since chronic disease imposes a chronic demand on nutrients, a potential exists for increased nutrient deficiency as duration of disease increases. However, as suggested by the former correlations, this may or may not be related to the CDAI. Again, the range of disease severity was not wide, and with a wider range of the CDAI, the correlation may exist in both males and females.

5.17 Male/Female Differences in Crohn's Disease Patients

Female nutrient intakes were generally poorer than that of males. The mean nutrient intake of female CD patients was less than the RDA for more nutrients (Table 3) than that of male patients (Table 2). Seventy-five % of the females consumed less than the RDA of 6 or more nutrients, compared to only 36% of the males. Consumption of quantitatively poorer diets by females are not necessarily surprising. Women require less energy and consume less food than men, though they require the same amount or more of many nutrients than do men. Qualitatively, however, female diets are usually equal and often superior to that of men, and the present study showed that the nutrient consumption per 1000 kcal was the same in men and women, except for vitamin A and folate, of which men consumed significantly less (Table 7).

It has been suggested, that food intake may be reduced in response to the pain, diarrhea, and anorexia associated with CD. Although the CDAI was higher in females, there was no correlation

between the CDAI and nutrient intake (Table 18). In contrast, in the male group there was a negative, though low (-0.38) correlation between the CDAI and energy intake. Thus, it appears that males with a higher CDAI tend to reduce their food intake, but females do not.

A greater number of females than males had abnormal values for serum albumin, TLC, hemoglobin, MCHC, % transferrin saturation, serum ferritin, serum folate, and serum calcium. This is not surprising in view of their poorer nutrient intakes. However, there were several inconsistencies between the male and female groups in relationships between biochemical parameters and nutrient intakes. For example, the incidence of low serum B_{12} was identical in males and females, though the males with low serum B_{12} concentrations had consumed less than the RDA and the females with low serum B_{12} concentrations had consumed more than the RDA. It was subsequently noted that these females also had low serum folate concentrations and thus a mixed deficiency was suggested. It is possible that the use of OCA among the women was placing increased demands on their body folate stores and was thus responsible for the greater proportion of low serum folate concentrations in women, despite poor folate intakes in both men and women. As well, use of OCA has been associated with low serum B_{12}, serum and leucocyte ascorbic acid, and serum zinc (2.7.3). Also, serum levels of vitamin A and iron are higher than normal in OCA users (2.7.3). Indeed, this may have contributed to a lower incidence of abnormal serum iron concentrations in women than men, despite high iron intakes in all the men and low iron intakes in all the women.

Dietary folate in females was highly correlated with dietary vitamin B_6, vitamin B_{12}, vitamin C, iron, and protein, but in males was only correlated with the latter two nutrient intakes. Moreover, serum folate was correlated with dietary folate, vitamin B_6, vitamin B_{12}, and vitamin C in females, but not in males. The correlation between nutrients in the female CD patients could simply be indicating consistent quality of diet in females. Though similar proportions of the males and females failed to achieve the full RDA for folate, a consistently larger number of males consumed 2/3, 1/2, and 1/3 RDA. Indeed, 74% of males, but only 58% of females consumed 1/3 RDA for folate. It is possible that the relationship between dietary folate and serum folate does not become linear until folate intake drops below a minimal level.

Male/female differences were observed in the CDAI and its relationship to other parameters. The CDAI and duration of disease were both higher in females than in males and the demands of chronic disease could contribute to poor nutritional status, though correlations between biochemical parameters and the CDAI were not conclusive for nutritional deficiencies. The CDAI was negatively correlated with hemoglobin and positively correlated with serum ferritin in females and negatively correlated with serum albumin in males (Table 18). This lack of agreement in correlations could reflect a difference in the effects of varying disease severity.

Some of the inconsistencies reported in the present study could also have been due to taking of supplements. As previously mentioned (5.16), the amounts and kinds of supplements varied considerably, and

some patients could not remember brand names or amounts of a supplement taken, so it was difficult to control for supplements. However, the correlation between serum folate and dietary folate was very similar when calculated for the whole group or when calculated for those who did not take a folate supplement.

Finally, the two patients taking total parenteral nutrition could have added to the male/female differences. Although one male and one female were taking total parenteral nutrition, the nutrients provided can vary in both kind and amount. In this case, the female was supplemented with amounts of thiamin, pantothenic acid, vitamin B_6, vitamin B_{12}, riboflavin, and folate which in some instances provided more than 10 times the RDA.

5.18 Nutrient Supplements Taken by Crohn's Disease Patients

Several CD patients took one or more nutrient supplements, including folate, iron, vitamin C, vitamin A, vitamin D and calcium. As well, as few patients had vitamin B_{12} injections. However, information on nutrient supplementation was not included in the discussion of individual nutrients for several reasons:

1) information on supplements was not collected during the initial phase of the study.

2) from information found in patient charts, it became evident that several patients routinely took supplements, but did not report them at the time of the dietary interview.

3) the length of time patients had been on supplements, as well as the daily dosage of supplements, varied greatly.

In the present study, because of the problems noted, a decision was made not to use the supplement information at all. Notwithstanding the above concerns, however, it was noted that the correlation between serum folate and dietary folate was almost identical, regardless of whether or not the folate-supplemented patients were included. This is not to say that nutrient supplements have no effect on the relationships between dietary and biochemical parameters, but emphasizes the need for complete information regarding nutrient supplementation.

5.19 Comparison of Nutrient Intake in Steroid vs Nonsteroid Groups

Steroid therapy was associated with signs of protein malnutrition in CD patients: 9/10 patients with reduced AMC were on steroids, and 6/11 females and 8/10 males with reduced TLC were on steroids. Comparison of mean protein intake in the steroid vs nonsteroid groups (Appendix 35), however, indicates that there was little difference in intake for either the male or female groups. Comparison of intakes of other nutrients which are particularly important in steroid therapy (energy, calcium, and vitamin D), showed that the female steroid group consumed more energy that did the nonsteroid group. The male steroid group consumed more calcium than did the non-steroid group. The signs of protein malnutrition associated with steroid therapy do not appear to be related to differences in dietary intake, but may be due to the catabolic effects of steroid therapy.

6. SUMMARY OF FINDINGS

1. Nutritional assessment of 23 male and 24 female Crohn's disease (CD) outpatients was made by means of 48-hour dietary recall, anthropometric measurements, and biochemical tests.

2. The mean age of the CD patients was 31 years for males and 32 years for females. Male CD patients had a mean height and weight of 176 cm and 72 kg, respectively, while comparable figures for female CD patients were 164 cm and 58 kg. Triceps skinfold was 120% of the standard triceps skinfold in men, but only 95% of the standard in women. Percent of standard arm muscle circumference was quite comparable in the male and female groups, being 95% and 98% for males and females, respectively.

3. The mean duration of disease was shorter in males, being 71 months as opposed to 95 months in females. The Crohn's Disease Activity Index was also lower in males (46) than in females (118). Fourteen males and 15 females had CD of the ileum and colon, 9 males and 8 females had CD of the ileum, and one female had colonic involvement.

4. It was found that the mean intake of vitamin B_6 and folate in male and female CD patients, as well as the mean intake of calcium, vitamin D, and iron in female patients was less than the recommended dietary allowance (RDA). However, there was wide variation in food

intake between patients, which was masked by the mean nutrient intake. Thus, the percentage of individuals consuming various fractions of the RDA was calculated, and it was found that some patients consumed less than 1/3 of the RDA for some nutrients. Some males consumed less than 1/3 of the RDA for vitamin A, ascorbic acid, folate and vitamin D, whereas some females consumed less than 1/3 of the RDA for energy, calcium, iron, vitamin A, ascorbic acid, vitamin B_6, vitamin B_{12}, folate and vitamin D.

5. The mean daily intake of food groups of CD patients was compared to that of NC participants. Fruit intake of CD patients was found to be 79% higher in males and 69% higher in females than that of Nutrition Canada, but was thought to be largely attributable to fruit drink intake in CD patients. Soft drink intake in male CD patients was 76% less than that of NC.

6. Quality of diet was compared in male and female CD patients by expressing nutrient intake per 1000 kcal. It was found that males consumed significantly less folate and vitamin A per 1000 kcal than did females.

7. More than 30% of the male and female CD patients had abnormal values for total lymphocyte count, serum iron, % transferrin saturation, serum folate, and in males only, serum carotene.

8. Significant correlations were found between several dietary parameters in males and females. The correlations between serum folate and each of dietary folate, vitamin C, vitamin B_6 and vitamin B_{12} were also significant ($p < 0.01$) in females only. As well, a significant correlation ($p < 0.05$) was also found between serum calcium and each of dietary calcium, phosphorus, protein and vitamin D in males. However, the correlations observed in males were of little practical significance, since all serum calcium concentrations were within the range of normal in the male CD patients.

9. Relative weight was found to be correlated with % standard arm muscle circumference in males and females, and with total lymphocyte count and % standard triceps skinfold in females only. Thus, it appears that relative weight can be used as a predictor of protein status in CD patients and of adipose tissue reserve in female patients only.

10. The percent of male and female CD patients who had low anthropometric and biochemical values when grouped according to energy intake less than the RDA, equal to the RDA, or greater than the RDA was calculated. However, energy intake appeared to be of little value in predicting the presence of selected low biochemical and/or anthropometric parameters, as the incidence of low parameters occurred with equal frequency at all levels of energy intake.

11. The value of weight as a predictor of selected low anthropometric and/or biochemical parameters was also investigated by grouping patients according to greater than or equal to 90% of relative body weight or less than 90% of relative body weight. In male CD patients, relative body weight appeared to be of little predictive value. However, female patients with less than 90% relative body weight had a greater incidence of abnormal triceps skinfold, arm muscle circumference, total lymphocyte count, and total iron binding capacity than did females with greater than or equal to 90% relative body weight.

12. The Crohn's Disease Activity Index (CDAI) was calculated for each patient and was then correlated with selected dietary, biochemical, and anthropometric parameters. In males, the CDAI was negatively correlated with energy intake and serum albumin and positively correlated with the duration of the disease. However, the usefulness of these correlations is questionable, since the correlation with energy was quite low (-0.38) and all serum albumin concentrations were within the normal range in the male CD patients. In females, the CDAI was negatively correlated with hemoglobin and positively correlated with serum ferritin.

13. It was concluded that serum folate, relative body weight, arm muscle circumference, and total lymphocyte count could be used as predictive parameters to identify the CD patient at risk and in need of nutritional counselling.

7. RECOMMENDATIONS

7.1 Energy Intake

Low energy intake was reported in a sizeable number of CD patients, but there was no correlation between energy intake and body weight. Factors contributing to this lack of correlation are suggested to include: altered energy requirement due to the disease process, malabsorption, protein-losing enteropathy, and the use of certain medications. For this reason, it is recommended that future studies be designed to examine the presence and extent of steatorrhea and creatorrhea in CD and that these be correlated with the Crohn's Disease Activity Index and gastrointestinal protein loss. The determination of O_2 consumption and estimation of basal energy expenditure should be examined to determine if the basal requirement in CD is increased with respect to that of a normal individual, and if the basal energy expenditure is related to the Crohn's Disease Activity Index. Such studies would provide a better understanding of the energy requirements of patients with CD.

7.2 Carbohydrate Consumption

Carbohydrate consumption in the present study was slightly higher than that of Nutrition Canada, but it was not possible to determine whether or not this difference was statistically significant, nor whether it was due to an increase in simple and/or complex carbohydrate. Future studies should assess the intake of refined sugar and fiber in CD patients, and these values should be compared with the

intake of a well-matched control group. Finally, the potential role of dietary fiber in the prognosis of CD should be assessed by a well-designed prospective long-term clinical trial.

7.3 Protein

Although protein intake was generally normal when assessed at one point in time, signs of protein deficiency included decreased arm muscle circumference, and depressed total lymphocyte count. CD involves a number of factors which could increase protein requirements including protein-losing enteropathy, the catabolic effects of the inflammatory process and of steroid therapy. Therefore, the extent of protein loss and its relation to the Crohn's Disease Activity Index should be examined in future studies, and the assessment of protein intake and signs of protein deficiency should be examined prospectively over a suitably prolonged interval. Such studies would establish the relative importance of these postulated mechanisms contributing to protein deficiency.

7.4 Iron

The intake of iron was reduced in the majority of females with CD and anemia was common. However, in CD, anemia is not necessarily a sign of iron deficiency. The discrepancy between abnormal intakes of iron and the tentative diagnosis of iron deficiency accomplished using the serum ferritin concentration emphasizes the need for future studies to develop a simple, yet more reliable test for the diagnosis of iron deficiency in CD patients. Future studies should also focus on

the potential mechanisms for the development of anemia in these patients: what is the role of the low intake of vitamin C in iron absorption, is the absorption of food and elemental iron impaired, is the gastrointestinal loss of iron excessive, and do these patients respond normally to iron supplementation?

7.5 Folate

Both folate intake and serum folate were reduced in male and female CD patients. A significant correlation was noted between dietary folate and vitamin B_{12}, vitamin C, vitamin B_6, iron, and protein in females; between dietary folate and the latter two nutrient intakes in males; and between serum folate and dietary folate, vitamin C, vitamin B_6, and vitamin B_{12} in females. It is not known why the latter correlations occurred in females only. It is recommended that future studies include the more definitive sign of folate deficiency, red cell folate, and that the correlation between megaloblastic anemia, red cell folate, and serum folate be determined to establish the efficacy of serum folate as a predictor of folate deficiency. Furthermore, folate absorption and ^{51}Cr protein loss from the gut should be determined, and related to folate status. Supplementation with folate, its effect on serum folate, and determination of red cell turnover should be determined to establish ideal duration of therapy.

7.6 Vitamin B_{12}

Vitamin B_{12} intakes were low in about 1/4 of the males and 1/2 of the females, but low serum B_{12} concentrations occurred in only a small

proportion of patients with CD and megaloblastic anemia was not present in any of the patients. However, in time, a reduced intake of vitamin B_{12} will result in a low serum B_{12} concentration. In addition, malabsorption of vitamin B_{12} due to ileal dysfunction or bacterial overgrowth may also contribute to a vitamin B_{12} deficiency. Thus, an annual serum B_{12} will identify the patient with a vitamin B_{12} deficiency and the Schilling's test will identify those patients with malabsorption. Future studies should be designed to determine if malabsorption is due to ileal dysfunction and/or bacterial overgrowth. In order to determine if vitamin B_{12} malabsorption is due to ileal disease, it is necessary to examine the relationship between the Schilling's test and extent of ileal disease, and the Schilling's test and stool bile acids. The ^{14}C breath test can be used to identify malabsorption due to the presence of bacterial overgrowth. Response to antibiotics will confirm and ameliorate vitamin B_{12} malabsorption due to bacterial overgrowth. In the case of ileal dysfunction, regular B_{12} injections should be considered to avoid vitamin B_{12} deficiency.

7.7 Vitamin C

Low vitamin C intake was reported in a modest proportion of CD patients. However, the biochemical significance of this finding could not be determined in these CD patients. Lack of vitamin C has been implicated in iron and folate deficiency. Indeed, the correlatioin between dietary vitamin C and dietary folate, and between dietary vitamin C and serum folate strongly supports the need for the deter-

mination in future studies of serum and leucocyte ascorbic acid concentrations, and their relation to serum folate and red cell folate, as well as to the patients' iron status.

7.8 Vitamin B_6

Vitamin B_6 consumption was reduced in almost all of male and female CD patients. However, biochemical parameters of vitamin B_6 nutriture were not assessed in the present study. Future studies should include the measurement of such parameters as serum pyridoxal phosphate, intermediary metabolites such as xanthurenic acid, and alanine aminotransferase activity. As well, vitamin B_6 status should be related to steroid therapy and anemia. Moreover, because there is considerable overlap in the clinical deficiency symptoms of the B-vitamins, when a deficiency of one B-vitamin is suspected, deficiencies of the other B-vitamins should be suspected and screened for with appropriate biochemical tests (7.9-7.11).

7.9 Thiamin

Almost half of the CD patients had low thiamin intakes, though biochemical measurements for assessment of thiamin deficiency were not determined. However, several of the earliest symptoms of decreased thiamin intake are experienced by patients with CD, and include depression and irritability, loss of appetite and loss of weight. Thus, there is a need for future studies to assess thiamin status with such measurements as erythrocyte transketolase activity.

7.10 Riboflavin

Low riboflavin consumption was reported in a small number of male CD patients and a moderate number of the female CD patients, though biochemical parameters for the assessment of riboflavin deficiency were not determined. Though some patients with CD have lactose intolerance and thus might restrict dairy products which are a primary source of riboflavin, the patients who reported lactose intolerance in the present study consumed adequate amounts of riboflavin. However, future studies to examine consumption of riboflavin, calcium, and vitamin D in CD patients with lactose intolerance should be conducted. As well, biochemical assessment of riboflavin intake should include determination of erythrocyte glutathione reductase activity.

7.11 Pantothenic Acid

Almost 1/2 of the male and 2/3 of the female CD patients consumed less than the lower limit of the RDA for pantothenic acid. However, diets providing much less pantothenic acid than the RDA have not resulted in clinical deficiency. Clinical deficiencies of pantothenic acid in animal studies, though, include gastr[illegible] with enteritis and diarrhea, and it is possible that a deficiency of pantothenic acid could be contributing to these symptoms in CD patients. Thus future studies should include assessment of adequacy of pantothenic acid intake. Because biochemical standards for pantothenic acid are not well-defined and, therefore, are not conclusive for pantothenic acid deficiency, future studies must also include determination of biochemical standards for pantothenic acid.

7.12 Calcium/Vitamin D

Calcium and vitamin D intake was markedly reduced in female CD patients, and moderately reduced in male CD patients. However, there are no reliable standard biochemical methods of assessing calcium nutriture. Thus, it is recommended that calcium deficiency be identified by the parameters used to clinically identify metabolic bone disease, and these include: bone biopsy, measurement of cortical thickness of hand bone, Singh index of the trabecular pattern of the femoral head, bone densitometry, parathyroid hormone, and serum vitamin D. It is suggested that research tools used to assess abnormal calcium metabolism be performed in CD and correlated with the presence of metabolic bone disease diagnosed from bone biopsy. If a defect in calcium metabolism is found to be common in CD, then the mechanism of this defect should be assessed measuring calcium absorption and loss from the bowel, and correlating this with magnesium status, steatorrhea, bile salt wastage, protein balance, consumption of drugs, and the Crohn's Disease Activity Index. Finally, the patients should receive appropriate supplements of calcium and/or vitamin D, and their response assessed by following the possible changes in the indirect measures of bone metabolism listed above.

7.13 Vitamin A

Half of the male and female patients in the present study were reported to be consuming low amounts of vitamin A. However, as vitamin A is concentrated in relatively few foods and daily intake varies, vitamin A consumption in CD patients should be determined over a

longer period of time. Serum retinol concentrations should be determined as well, and related to steatorrhea, fecal bile acids, serum carotene, and the presence of abnormalities in dark adaptation.

7.14 Zinc

Dietary zinc was not assessed in the present study. However, clinical evidence of zinc deficiency in CD patients has been reported by several groups and may be contributing to retarded growth, anorexia, malabsorption of folate, and depressed serum albumin. Thus, it is important for future studies to assess zinc intake in CD patients, to seek (a) more reliable way(s) of determining zinc status.

7.15 Patient Management

Initially, it is recommended that all patients with CD be assessed for height, weight, change in weight, total lymphocyte count, serum folic acid concentration, and arm muscle circumference, in addition to any other clinically indicated and appropriate tests. If these parameters are normal, they should be repeated in 6-12 months. If these parameters are abnormal, however, the patient should be referred to a dietitian for individual counselling, in addition to having serum iron, total iron binding capacity, serum ferritin, serum B_{12}, SMA_{12}, and CBC. Findings in the literature have identified and/or suggested several nutrient deficiencies by means of several biochemical parameters not performed in the present study, and it is recommended that future studies be designed to confirm the usefulness

of serum and leucocyte ascorbic acid, red cell folate, serum retinol, stool bile acids, ^{14}C breath test, and parameters used to assess the status of thiamin, riboflavin, pantothenic acid, copper, and zinc.

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Appendix 1: Height, Weight, Triceps Skinfold, Mid-Arm Circumference and Arm Muscle Circumference for Crohn's Disease Patients

Males

Patient#	Height (cm)	Weight (kg)	Triceps Skinfold (mm)	Mid-Arm Circum-ference (cm)	Arm Muscle Circum-ference
1012	182	69	-	-	-
1014	188	78	15	28.0	23
1044	175	55	03	22.3	21
1034	177	62	-	-	-
1004	180	71	20	29.0	23
1030	168	63	13	30.5	26
1002	168	83	12	32.5	29
1045	178	65	08	28.0	26
1017	183	79	15	30.5	26
1028	179	86	16	34.5	30
1029	175	64	06	26.8	25
1013	170	68	11	28.5	25
1047	166	59	05	26.5	25
1038	178	85	14	31.5	27
1022	170	76	20	32.5	26
1019	169	60	05	28.5	27
1007	189	83	18	31.0	25
1023	175	84	05	31.0	29
1035	168	69	17	32.1	27
1008	173	65	10	28.0	25
1009	171	70	26	30.0	22
1025	173	90	18	37.5	32
1037	180	61	19	24.8	19

Females

Patient#	Height (cm)	Weight (kg)	Triceps Skinfold (mm)	Mid-Arm Circum-ference (cm)	Arm Muscle Circum-ference
1042	167	47	18	24.0	18
1024	166	-	-	-	-
1018	164	52	13	23.8	20
1031	168	46	04	21.5	20
1010	157	44	12	25.0	21
1006	170	62	19	27.5	22
1032	164	61	-	-	-
1036	170	70	-	-	-
1026	164	51	12	21.5	18
1041	154	66	-	-	-
1046	170	57	09	24.5	22
1020	167	49	10	22.0	19
1011	161	85	35	37.0	26
1016	170	62	23	28.0	21
1027	160	78	16	34.0	29
1001	163	71	23	28.6	21
1040	168	69	24	30.0	22
1043	160	54	07	22.5	21
1021	166	52	22	26.0	19
1033	150	47	26	26.7	19
1048	150	54	22	28.0	21
1005	170	53	21	25.0	18
1003	166	50	09	25.1	22
1039	160	56	27	27.8	19

Appendix 2: Cumulative Percent Distribution of Energy Intake[1] in Crohn's Disease Patients

	Males		Females	
Calories/day	n	%	n	%
< 500	0	0	0	0
500 - 749	0	0	3	13
750 - 999	0	0	1	17
1000 - 1249	0	0	3	29
1250 - 1499	1	4	0	29
1500 - 1749	2	13	4	46
1750 - 1999	0	13	5	67
2000 - 2249	4	30	2	75
2250 - 2499	3	43	2	83
2500 - 2749	4	61	1	88
2750 - 2999	0	61	1	92
3000 - 3249	2	70	0	92
3250 - 3499	0	70	1	96
3500 - 3749	2	78	0	96
3750 - 3999	3	91	0	96
4000+	2	100	1	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 3: Cumulative Percentage Distribution of Protein Intake[1] in Crohn's Disease Patients

g/day	Males		Females	
	n	%	n	%
0 - 24	0	0	2	8
25 - 49	0	0	4	25
50 - 74	5	22	12	75
75 - 99	8	57	2	83
100 - 124	6	83	2	92
125 - 149	0	83	2	100
150 - 174	3	96	-	-
175 - 200	1	100	-	-

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 3a: Cumulative Percentage Distribution of Protein Intake in Crohn's Disease Patients

	Males		Females	
g/kg body weight/day	n	%	n	%
0.4 - 0.5	0	0	3	13
0.6 - 0.7	0	0	4	30
0.8 - 0.9	2	9	2	39
1.0 - 1.1	8	43	2	43
1.2 - 1.3	3	57	4	65
1.4 - 1.5	2	65	4	83
1.6 +	8	100	4	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 4: Cumulative Percentage Distribution of Calcium Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
0 - 99	0	0	0	0
100 - 199	0	0	6	25
200 - 299	2	9	0	25
300 - 399	0	9	2	33
400 - 499	3	22	1	38
500 - 599	2	30	2	46
600 - 699	3	43	2	54
700 - 799	1	48	2	63
800 - 899	0	48	3	75
900 - 999	1	52	1	79
1000 - 1099	3	65	0	79
1100 - 1199	0	65	2	88
1200 - 1299	2	74	1	92
1300 - 1399	1	78	0	92
1400 - 1499	1	82	0	92
1500 - 1599	1	87	0	92
1600 - 1699	1	91	0	92
1700 +	2	100	2	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 5: Cumulative Percentage Distribution of Phosphorus Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
0 - 499	0	0	3	13
500 - 999	4	17	8	46
1000 - 1499	5	39	8	79
1500 - 1999	8	74	3	92
2000 - 2499	4	91	2	100
2500 - 2999	0	91	-	-
3000 - 3499	2	100	-	-

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 6: Cumulative Percentage Distribution of Vitamin A Intake[1] in Crohn's Disease Patients

	Males		Females	
Retinol Equivalents/day	n	%	n	%
0 - 250	1	4	1	4
251 - 500	1	9	6	30
501 - 750	4	26	5	50
751 - 1000	6	52	2	58
1001 - 1250	5	74	1	63
1251 - 1500	13	87	2	71
1501 - 1750	0	87	4	88
1751 - 2000	1	91	0	88
2001 - 2250	0	91	1	92
2251 - 2500	0	91	1	96
2501 - 2750	1	95	0	96
2750 - 3000	1	100	0	96
3000 +	-	-	1	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 7: Cumulative Percentage Distribution of Iron Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
0.0 - 5.9	0	0	4	17
6.0 - 7.9	1	4	2	25
8.0 - 9.9	0	4	6	50
10.0 - 11.9	1	9	3	63
12.0 - 13.9	5	30	1	67
14.0 - 15.9	4	48	1	75
16.0 - 17.9	3	61	3	83
18.0 - 19.9	2	69	2	92
20.0 - 21.9	3	82	0	92
22.0 - 23.9	2	91	1	96
24.0 - 25.9	1	95	0	96
26.0 - 27.9	0	95	1	100
28.0 - 29.9	0	95	-	-
30.0 +	1	100	-	-

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 8: Cumulative Percentage Distribution of Thiamin Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
< 0.5	0	0	2	8
0.5 - 0.9	4	17	9	46
1.0 - 1.4	9	57	7	75
1.5 - 1.9	5	78	4	92
2.0 - 2.4	3	91	1	96
2.5 - 2.9	1	96	0	96
3.0 +	1	100	1	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 9: Cumulative Percentage Distribution of Riboflavin Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
0 - 0.4	0	0	1	4
0.5 - 0.7	0	0	3	17
0.8 - 1.0	2	9	3	30
1.1 - 1.3	1	13	4	46
1.4 - 1.6	1	17	1	50
1.7 - 1.9	4	35	2	58
2.0 - 2.2	5	57	4	75
2.3 - 2.5	3	70	2	83
2.6 - 2.8	1	74	1	88
2.9 - 3.1	0	74	1	92
3.2 +	6	100	2	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 10: Cumulative Percentage Distribution of Ascorbic Acid Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
0 - 19	1	4	2	8
20 - 39	1	9	4	25
40 - 59	1	13	2	33
60 - 79	2	22	3	46
80 - 99	2	30	2	54
100 - 119	1	35	1	58
120 - 139	4	52	1	63
140 - 159	0	52	0	63
160 - 179	1	56	3	75
180 - 199	1	61	2	83
200 - 219	2	69	0	83
220 - 239	2	78	0	83
240 - 259	1	82	0	83
260 - 279	2	91	0	83
280 - 299	0	91	1	88
300 +	2	100	3	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 11: Cumulative Percentage Distribution of Pantothenic Acid Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
< 1.0	0	0	0	0
1.0 - 1.9	0	0	5	21
2.0 - 2.9	3	13	3	33
3.0 - 3.9	3	26	7	63
4.0 - 4.9	3	39	3	75
5.0 - 5.9	6	65	2	83
6.0 - 6.9	3	78	2	92
7.0 - 7.9	0	78	0	92
8.0 - 8.9	3	91	1	96
9.0 - 9.9	0	91	0	96
10.0 +	2	100	1	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 12: Cumulative Percentage Distribution of Vitamin B6 Intake[1] in Crohn's Disease Patients

	Males		Females	
mg/day	n	%	n	%
0.0 - 0.49	0	0	3	13
0.50 - 0.99	5	17	8	46
1.0 - 1.49	6	44	8	79
1.5 - 1.99	7	74	1	83
2.0 - 2.49	3	87	1	88
2.5 - 2.99	2	96	2	96
3.0 +	1	100	1	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 13: Cumulative Percentage Distribution of Vitamin B12 Intake[1] in Crohn's Disease Patients

	Males		Females	
ug/day	n	%	n	%
< 1.0	0	0	1	4
1.0 - 1.9	1	4	9	42
2.0 - 2.9	5	26	2	50
3.0 - 3.9	5	48	4	67
4.0 - 4.9	5	70	1	71
5.0 - 5.9	1	74	1	75
6.0 - 6.9	2	83	1	79
7.0 +	4	100	5	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 14: Cumulative Percentage Distribution of Folate Intake[1,2] in Crohn's Disease Patients

	Males		Females	
ug/day	n	%	n	%
0 - 99	1	4	6	29
100 - 199	11	52	10	67
200 - 299	6	78	4	83
300 - 399	5	100	2	92
400 - 499	-	-	2	100

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.
2. Total folate

Appendix 15: Cumulative Percentage Distribution of Vitamin D Intake[1] in Crohn's Disease Patients

	Males		Females	
I.U./day	n	%	n	%
0 - 49	2	9	6	25
50 - 99	2	17	2	33
100 - 149	4	35	5	54
150 - 199	2	44	5	75
200 - 249	4	61	2	83
250 - 299	1	65	1	87
300 - 349	2	74	0	87
350 - 399	0	74	3	100
400 - 449	3	87	-	-
450 - 549	2	96	-	-
550 +	1	100	-	-

1. Values were calculated as the means of two, consecutive 24-hour dietary recalls.

Appendix 16: Cumulative Percentage Distribution of Serum Albumin in Crohn's Disease Patients

	Males		Females	
g/dl	n	%	n	%
2.5 - 2.9	0	0	3	13
3.0	0	0	0	13
3.1	0	0	0	13
3.2	0	0	0	13
3.3	0	0	2	21
3.4	1	5	2	29
3.5 - 3.9	6	37	5	50
4.0 - 4.4	7	74	6	75
4.5+	5	100	6	100

Appendix 17: Cumulative Percentage Distribution of Total Lymphocyte Count in Crohn's Disease Patients

	Males		Females	
thousand/mm^3	n	cumulative %	n	cumulative%
< 1000	3	15	7	32
1000 - 1199	2	25	0	32
1200 - 1499	5	50	5	55
1500 - 1799	2	60	2	64
1799 - 1999	1	65	1	68
2000 - 2499	3	80	5	91
2500 - 2999	3	95	0	91
3000 - 3499	0	95	0	91
3500 +	1	100	2	100

Appendix 18: Cumulative Percentage Distribution of Hemoglobin in Crohn's Disease Patients

	Males		Females	
g/dl	n	%	n	%
< 11	2	9	5	21
11.0 - 11.9	0	0	3	33
12.0 - 12.9	3	22	4	50
13.0 - 13.9	5	43	8	83
14.0 - 14.9	7	74	2	92
15.0 +	6	100	2	100

Appendix 19: Cumulative Percentage Distribution of Hematocrit in Crohn's Disease Patients

	Males		Females	
%	n	%	n	%
< 30	0	0	1	4
30 - 34	2	9	5	26
35 - 39	3	23	7	57
40 - 44	11	73	8	91
45 - 49	6	100	2	100

Appendix 20: Cumulative Percentage Distribution of Mean Corpuscular Hemoglobin Concentration in Crohn's Disease Patients

	Males		Females	
%	n	%	n	%
< 32	0	0	2	9
32 - 33	8	35	5	32
34 - 35	15	100	15	100

Appendix 21: Cumulative Percentage Distribution of Serum Iron in Crohn's Disease Patients

	Males		Females	
ug/dl	n	%	n	%
< 60	9	50	13	59
60 - 79	3	67	6	86
80 - 99	4	89	1	91
100 - 119	1	94	1	95
120 - 139	1	100	1	100

Appendix 22: Cumulative Percentage Distribution of Total Iron Binding Capacity in Crohn's Disease Patients

	Males		Females	
ug/dl	n	%	n	%
< 200	2	11	1	5
200 - 249	1	17	2	14
250 - 299	1	22	7	45
300 - 349	10	78	6	73
350 - 399	3	94	3	86
400 - 449	0	94	3	100
450 - 499	1	100	-	-

Appendix 23: Cumulative Percentage Distribution of Transferrin Saturation in Crohn's Disease Patients

	Males		Females	
%	n	%	n	%
< 10	4	22	5	23
10 - 19	5	50	10	68
20 - 29	5	78	5	91
30 - 39	4	100	1	95
40 - 49	-	-	0	95
50 +	-	-	1	100

Appendix 24: Cumulative Percentage Distribution of Serum Ferritin in Crohn's Disease Patients

	Males		Females	
ng/ml	n	%	n	%
< 15	0	0	3	18
15 - 49	3	18	3	36
50 - 99	6	53	6	71
100 - 149	1	59	1	77
150 - 199	3	76	1	83
200 +	4	100	3	100

Appendix 25: Cumulative Percentage Distribution of Serum Folate in Crohn's Disease Patients

	Males		Females	
ng/ml	n	%	n	%
< 3.0	7	37	11	50
3.0 - 5.9	9	84	7	82
6.0 - 8.9	2	95	2	91
9.0 - 11.9	0	95	0	91
12.0 - 14.9	0	95	0	91
15.0 +	1	100	2	100

Appendix 26: Cumulative Percentage Distribution of Serum Vitamin B12 in Crohn's Disease Patients

	Males		Females	
pg/ml	n	%	n	%
< 140	2	11	2	11
140 - 199	2	22	5	37
200 - 299	3	39	2	48
300 - 399	5	67	4	68
400 - 499	3	83	1	74
500 - 599	1	88	0	74
600 +	2	100	5	100

Appendix 27: Cumulative Percentage Distribution of Serum Calcium in Crohn's Disease Patients

	Males		Females	
mg/dl	n	%	n	%
< 8.5	0	0	4	17
8.5 - 8.9	6	29	5	38
9.0 - 9.4	9	71	10	71
9.5 - 9.9	6	100	4	96
10.0 +	-	-	1	100

Appendix 28: Cumulative Percentage Distribution of Serum Phosphorus in Crohn's Disease Patients

	Males		Females	
mg/dl	n	%	n	%
< 2.5	1	5	0	0
2.5 - 3.4	10	52	13	57
3.5 - 4.4	10	100	8	91
4.5 +	0	-	2	100

Appendix 29: Cumulative Percentage Distribution of Serum Vitamin D in Crohn's Disease Patients

	Males		Females	
ng/dl	n	%	n	%
< 10	2	20	1	11
10 - 19	3	50	3	44
20 - 29	3	80	3	77
30 - 39	1	90	2	100
40 +	1	100	-	-

Appendix 30: Cumulative Percentage Distribution of Serum Carotene in Crohn's Disease Patients

	Males		Females	
ug/dl	n	%	n	%
< 30	3	23	0	0
30 - 49	2	38	2	13
50 - 69	2	54	4	40
70 - 89	2	69	3	60
90 - 119	4	100	5	93
120 +	-	-	1	100

Appendix 31: Cumulative Percentage Distribution of Alkaline Phosphatase in Crohn's Disease Patients

	Males		Females	
I.U./l	n	%	n	%
< 40	1	5	2	9
40 - 80	13	70	13	63
81 - 110	4	90	9	100
111 - 139	0	90	-	
140 +	2	100	-	-

Appendix 32: Percent Distribution of Energy Intake as Protein, Fat, and Carbohydrate in Crohn's Disease Patients and Nutrition Canada

	Crohn's Disease				Nutrition Canada[1]	
	Males (N = 23)		Females (N = 23)		Males	Females
	Mean ± SD	Range	Mean ± SD	Range	Mean	Mean
Protein	15 ± 3.6	(10-23)	15 ± 4.6	(0-22)	15	16
Fat	39 ± 7.1	(27-53)	35 ± 12.5	(0-55)	43	41
Carbohydrate	46 ± 7.9	(36-62)	50 ± 15.4	(25-99)	42	43

1. Prairie population, aged 20-39 years.

Appendix 33: Food Groups and Subgroups[1]

1. Fats and oils (excluding bacon and salt pork)
   - Butter
   - Other fats and oils (lard, margarine, vegetable shortening, salad and cooking oils, salad dressings, suet, tartar sauce)

2. Fruits and fruit products (excluding baby foods)
   - Citrus fruits (excluding juices)
   - Fruits other than citrus (excluding juices)
   - Fruit juices, ades, nectars
   - Fruit mixtures

3. Grain and grain products

4. Nuts, soybeans, and miscellaneous needs
   - Soybeans, and miscellaneous seeds and their products (excluding dried beans and peas)
   - Nuts (including peanuts and coconuts)

5. Meat, poultry, fish and eggs (excluding soup and baby foods)
   - Beef
   - Pork
   - Veal
   - Lamb
   - Wild game (including domestic rabbit)
   - Eggs
   - Poultry (including wild fowl)
   - Fish (including frog legs, roe and caviar)
   - Shellfish and turtles
   - Miscellaneous (sausage, cold cuts, luncheon meats and animal organs)

6. Milk and milk products
   - Fluid and dried milk (including buttermilk, skim milk, whole and canned milk; milk drinks such as hot chocolate and cocoa; whey and yoghurt)
   - Cream, half and half, and milk desserts such as custard, ice cream, ice milk, sherbert
   - Cheese and cheese products

7. Sugars and sweets
   - Sugars, cake icings, cake icing mixes
   - Syrups, honey, molasses
   - Jellies, jams
   - Candies
   - Chocolate, chocolate syrup, dry cocoa, gelatin dessert powders

8. Vegetables (including dried beans, lentils and peas, but excluding soups and baby foods)

9. Mixed dishes
   - Baby foods
   - Soups
   - Mixtures of major food groups
   - Miscellaneous items not classified elsewhere (baking powder, bouillon cubes, carob flour, chewing gum, condiments, plain gelatin, water ices, pudding mixes and puddings, seaweeds and yeast)

10. Soft drinks

1. Food groups and subgroups used to prepare the Nutrition Canada food consumption patterns report. Department of National Health and Welfare, 1977.

Appendix 34: Methodology for Laboratory Tests

Hemoglobin, Hematocrit, Lymphocytes:

- Dacie, J.V. and S.M. Lewis. Practical Hematology, 5th edition, 1975.

Serum Ferritin

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Appendix 35: Comparison of Mean Nutrient Intake in Crohn's Disease Patients: Steroid and Non Steroid Groups

	Males		Females	
	Steroid (n = 15)	Non Steroid (n = 8)	Steroid (n = 15)	Non Steroid (n = 8)
Energy (Kcal)	2787	2861	2011	1619
Protein (g)	111	102	70	64
Vitamin D (I.U.)	276	225	151	147
Calcium (mg)	1095	910	700	756

1. Values were calculated as the means of two, 24-hour dietary recalls.

10. CURRICULUM VITAE

Phyllis Hodges

Personal

1.	Nationality	Canadian
2.	Birthplace	Mayerthorpe, Alberta
3.	Birthdate	June 4, 1947
4.	Marital Status	Married, four children
5.	Interests	Soccer, alpine skiing, nordic skiing, cycling, Beta Sigma Phi Sorority, music (Grade VIII piano and Grade III theory, University of Toronto, Royal Conservatory of Music)

Academic

6. Secondary School Education:

   Mayerthorpe High School, Mayerthorpe, Alberta

7. University Education:

   a) University of Alberta, Edmonton. Faculty of Home Economics, B.Sc. (H.Ec.), 1965-1968.

   b) University of Alberta, Edmonton. Faculty of Education, P.D. (A.D.) 1968-1969.

Professional Experience

8. Edmonton Separate School Board, Teacher; Junior High Home Economics; Grade V; High School Clothing and Textiles, Food Science; 1969-1976. Supervisor: Ms. S. Pisesky.
9. University of Alberta, Teaching Assistant, Academic Year 1978-1979, September-December, 1980. Supervisor: Dr. E. Donald.
10. Local Board of Health, Edmonton; Project Director, Stage III of the Adolescent Nutrition Survey, 1981.

Honors and Awards

11. Government of Alberta, bursary for Summer Program in French, Universite Laval, 1978.

Publications

12. Hodges, P.E., and J.E. Edwards. A Nutrition Needs Assessment of Edmonton Adolescents, Stage III. Edmonton Local Board of Health, June 1981.

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