THE RELATIONSHIP OF DIETARY FIBER AND HUMAN HEALTH

by

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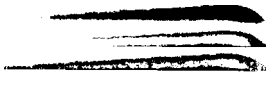

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CHAPTER I

INTRODUCTION

Recent epidemiological observations have led to the suggestion that fiber plays an essential role in the gut and in maintaining man's health.(1-8) However, Cleave over twenty years ago paved the way for the current surge of fiber interest with his "Master Disease" in "The Neglect of Natural Principles in Current Medical Practice," in which he discusses the problems of natural roughage removal from the diet.(9) Cleave is considered responsible for illustrating that fiber depletion through refinement of carbo-hydrates not only slows transit time, but also greatly increases caloric density along with resultant overconsumption of energy.(10)

Some investigators see an effective relationship between insufficient dietary fiber and a group of diseases related to increased transit time, reduced fecal mass, and increased intra-luminal pressures. The major diseases resulting from these characteristics are believed to be diverticula^ disease, appendicitis, hiatus hernia, varicose veins, hemorrhoids, and cancer of the colon and rectum.{!!-17)

Other research indicates possible direct ar.d/or indirect relationships of fiber deficiency and cholelithiasis, (17,18) blood lipid levels, (18-27) increased fecal bile lipids, (28-30) fecal steroids and lipid excretion, (31) constipation, (17,32-34) coronary heart disease, (35) diabetes, (36-38) obesity, (10,39-42,

43-45) intestinal flora and fauna, (46-49) and protection from toxic substances in the diet.(50-56)

The literature on the implications of food fiber and health is extensive. The ramifications of food fiber's importance are diverse. In view of the importance of the topic and the numerous sources of pertinent information it would be helpful to compile the major concepts of the relationships and through such a synthesis produce a professional reference work for the worker in nutritional research, education, and allied health fields.

Modern nutritional science has advanced to its present state by the designed and/or accidental demonstration that certain constituents of foodstuffs eaten by man and animals are required for maintenance of health. Soon recognition of disease resultant from deficiency or excess of nutrients led to knowledge of safe levels. The idea that something eaten in addition to these nutrients is needed to assure optimal health is relatively new, based largely on observed differences in the global distribution of chronic disorders.(57) Epidemiological investigations are studies of the distribution and dynamics of diseases or conditions affecting population groups.(58) These studies have raised questions that may be tested in controlled experiments. However, one must be cautious in that to prove on the basis of epidemio-logical studies alone that separate observations are causally related is often difficult if not impossible. Resultant hypotheses may be *very* useful in guiding future research, but they must not

be mistaken for facts.

Fiber and health interrelationships developed from epidemiological studies have resulted in an hypothesis,(59) Most of the studies compared Western nations with lesser developed countries of Africa. Perhaps the most publicised of these studies were by Burkitt, et a!., who pointed out that ischemic heart disease, appendicitis, diverticular disease, gallstones, varicose veins, hiatus hernia, hemorrhoids, and colon cancer were very rarely seen in rural areas of Africa.(60) Consumption of a traditional diet high in fiber was the basis for this "fiber theory." Other investigations have produced data supportive of this theory, including Cleave, (9,19,61) Trowel!, (62-66) Walker, (67-73) and Eastwood, (74-76) whose combined work has provided a focal point for the expanding interest in fiber.

CHAPTER II

EPIDEMIOLOGICAL STUDIES

The epidemiological evidence now available upon those diseases listed in the introduction indicates that they are either directly or indirectly related to environmental factors and directly or indirectly related to the degree of economic development. There are striking contrasts between the high prevalences of all these diseases in black and white Americans and the low prevalence of the same medical disorders in rural Africans.(77) Prevalences of intermediary levels were also found.(61,78)

According to Denis Burkitt, all the different effects of a common cause will tend to be associated with one another.(79) On the other hand associated effects (i.e. diseases) suggest a causative factor which is common to each but not necessarily the only factor in any one disorder (Figure 1). Certain diseases have been shown to be related not only in geographical distribution and historical emergence, but also in those who emigrate from less developed areas to more westernized societies as well as in those who make the change from a rural to urban environment.

Some of the diseases associated with economic development, thus having their maximum prevalence in the more affluent western nations, are rare in some nations and virtually unknown in other areas sti^l living largely in a traditional manner.(80) A hundredfold dif-ference is seen in prevalence between areas where the disease is most and least common. The average being m.ore than tenfold. (80)

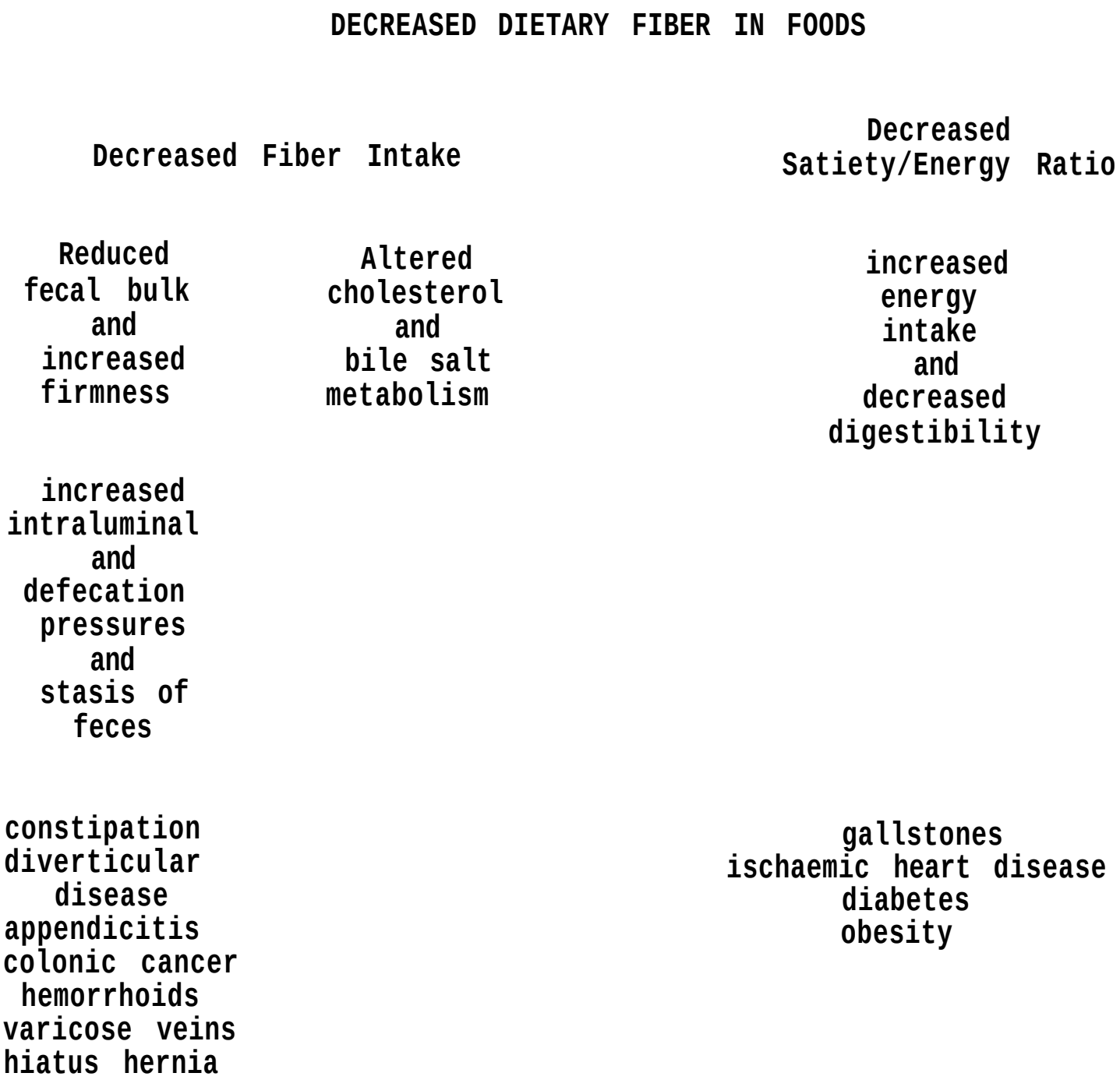


Figure 1.--Possible relationships between decreased fiber intake and certain disease states.(12)

CHAPTER III

FIBER RELATIONSHIPS TO GASTROINTESTINAL AND RELATED DISORDERS

Diverticular Disease of the Colon

Burkitt states that the most common of all gastrointestinal disorders in the western world today, diverticulosis, probably affects a third of the population over fifty years of age.(80) Yet it is either rare or unknown in indiginous Africans and in all developing countries.(81) Looking closer at rural Africa, Goulston in Ethiopia stated that diverticulosis is infrequent and diverticulitis unknown.(82) In Ghana (Accra) Dadoe saw only one case of diverticulitis in sixteen years in the medical school hospital.(83) Diggs in Liberia (Monrovia) reported two patients with diverticular disease in approximately 300 barium enema examinations, both in the highest socio-economic group.(83) Williams reported seven patients in Sierra Leone (Freetown) with the disorder over a period of twenty years, all from upper socio-economic groups,(83) In Nigeria (Lagos) Kyle, et al., recorded two cases of diverticulosis in the University Hospital over a period of three years,(84) Wapnick and Levin reported what they believed to be the only recorded case in a black Rhodesian (Salisbury).(85) In reports from South A-'rica (Johannesburg), Keeley found no diverticula in a series of 2367 autopsies between 1954 and 1956.(86) At the same hospital Solomon found six cases in approximately 1000 barium enemas in Bantu patients over a tnree-

year period while Levy at the non-European hospital saw no cases in thirteen years,(83) Higgins and Simson in 2000 consecutive autopsies found one case (87) and Bremmer and Ackermann stated the disorder practically never developed in the Bantu,(88) In South Africa (Pretoria), Simpson found only five cases in 3000 Bantu autopsies while Chapman in Durban reported only one African case in fourteen years at the King Edward teaching hospital.(83) In Kenya (Nairobi) Miller saw only one case in an African in eleven years at the Kenyatta Hospital.(83) Davies reported from Uganda (Kampala) two cases in 4000 autopsies (89) and Templeton in 300 autopsies of subjects over thirty years of age specifically looking for diverticulosis found only one case of the disorder (in a female over eighty years of age).(83) Jain observed one case in nine years in a medical school hospital in Zaire (Kinshasa) (83)

If we shift emphasis from Africa to India and the Middle East, we again find low incidence of the disorder, even among the urban areas. Bhardwaj in India (Delhi) found nine cases with 9000 barium enema examinations and Bhargava using the same technique reported twelve cases, all of which were in the more "westernized" Indians.(83) In Calcutta, Bannerjee, and Ahmed in Assam reported a similar *wery* low incidence.(83)

Zarabi and Farpour in Iran (Shiraz) saw only five cases in eight years and Abu-Tabikh in Iraq (Bahgdad) reported not more than three cases of diverticulosis in 1000 barium enema examinations,(83)

Looking at other areas of the world, diverticular disease has, until recently, been *wery* rare in Japan.(90) Kyle, et al, found a distinct difference in incidence among Europeans (three cases per 15,000) and Chinese, Indian and Malaysians (ten cases per 1,500,000) and native Fijians (one case per 137,000),(84) In Malaysia, Kutty found no cases upon autopsy in three years (83) and Kim in 500 barium enemas found no diverticula in Koreans.(91)

Diverticular disease was rare in Great Britain and in North America as late as the 1920's, but the prevalence now is in the range of five to ten percent whereas studies in Africa and India indicate a prevalence of less than one percent.(80)

Gross in 1845, (92) Cruveilhier in 1849, (93) Rokitansky in 1849, (94) Haberschon in 1857, (95) and Klebs in 1869 (96) all believed that diverticula of the colon were acquired and thought to be induced by constipation. This rare disease became relatively common in two decades.(83) In 1899 Dr. Telling first reported the disease and none of his colleagues were familiar with it but by 1908, he was describing the complications and in 1917 his classic paper on diverticulosis and diverticulitis was published.(97-99) By 1920 Sir John Bland-Sutton remarked that "in the last ten years, acute diverticulosis is recognized with the same certainty as appendicitis and is a newly discovered bane of elders."(83)

Available evidence indicates that divertitular disease of the colon was a rarity at the beginning of this century, but has risen in incidence dramatically to become the com.monest disease of

the colon in westernized countries.(100-105) In striking contrast the disease is almost unknown in those communities only recently affected by customs and habits characteristic of modern western civilization.(83)

Diverticular disease among North Americans and Europeans always affects the sigmoid colon.(106) Alterations, of the longitudinal muscles, in the form of thickening and shortening, is believed to be secondary to increased intraluminal pressures. (77,107-109) It has been suggested by Edwards that the changes responsible for diverticulosis of the intestine are due to forces from the bowel wall.(110) Burkitt postulated a hypothetical pathogenesis dependent upon diets containing too little fiber with resultant firm stools of diminished bulk.(77) It is believed the increased transit time and additional mechanical force needed for propulsion and expulsion of the feces through the colon and from the rectum raises pressures not only within the lumen of the bowel but also within the whole abdominal area.(4,16,57,77,83,110-113) If muscular weakness occurs between areas of hypersegmentation as is believed occurs with a long history of a diet poor in fiber, the lumenal pressure may cause a herniation of the mucosa with the resultant production of small cul-de-sacs referred to as diverticula. (77,114-116) Roentgenograms taken after barium m,eals reveal these diverticula as sacculations along the intestinal wal1.(114) It is believed that fecal material may become entrapped in these sacculations and with time may produce the condition known as diverticulitis. Experimental evidence supporting

these views is not abundant but Carlson and Hoelsel in an early study reported that rats maintained on low fiber diets developed diverticulosis of the colon but not on diets providing appreciable roughage.(117) The clear relationship between diet and colonic diverticulosis as proposed by Painter and Burkitt would be difficult to substantiate or refute in that a possible development period of forty years is suggested.(12,16)

Other researchers have suggested an alternative theory based upon observations of Africans eating high-fiber diets who rarely exhibited diverticulosis in direct contrast to whites in Europe and North America eating diets deficient in fiber who have a much higher incidence of the disease.(3,76,118,119) This association is strengthened by the relief of symptoms by ingestion of cereal bran.(75) Many patients suffering from the disease have been shown to have increased rectal pressures and upon treatment with cereal bran the pressure in the bowel is reduced.(2) It was such work as this that lead to the postulations in regard to diverticular development, high intraluminal pressures and low fiber diets. Eastwood, et a 1. do point out that therapeutic value is not necessarily an indicator of a previous true deficiency.(74)

A *wery* positive aspect of these considerations is the possibility that diverticular disease is not inevitable and they point out that numerous considerations may assist in the eradication of the disorder.(13) Future research needs to expand the basic knowledge of rectosigmoid pressures among healthy as well as diseased individuals, among various age and racial groups.

Further studies as those relating disease prevalence and difference in fruit and vegetable intake need to be undertaken.(75)

1. Appendicitis

Appendicitis is the most common indication for emergency abdominal surgery (4) and occurs most frequently among the young. (120,121) The prevalence of this disorder is *wery* small among Africans.(122) Burkitt believes it is found only in those Africans who have adopted a westernized life style,(118) Walker gathered information on appendectomy prevalence from 15,317 sixteen to twenty year old pupils among four ethnic groups.(73) Data revealed that among students eighteen to twenty years, appendectomy was *wery* rare in rural Negroes (0,5%), slightly more common in urban Negroes (l,4/o) but much more common in whites (16.5'0- The same research revealed that defecation frequency increases and transit time decreases among rural Negroes with large fiber intakes. Similar results, indicating appendectomy incidence was only 23 percent of the appropriate control group, were found on 1325 white pupils in institutional homes serving less refined diets as compared to the general population. Short found similar results. (123) In considering the validity of such findings, appendicitis data from the United States Navy (124) and comparable probability data from New Zealand (125) should be looked at. When such data are used to predict appendicitis among 100,000 Negro laborers living in mining camps fed diets of highly refined foods one would expect to find approximately 850 appendectomies, yet in 1970 the data revealed only twenty-two surgical procedures

performed.(126)

South African whites reveal an incidence of 17 percent, whites in England 14 percent, (120) and New Zealand about 16 percent (125) as compared to much lower ranges reported earlier among Negroes.

It is of interest to look at "found dietary changes" and their relationship to appendicitis incidence. Conditions were such after World War I that Russian diets affected by severe privations became more coarse at the same time appendicitis almost disappeared. (123) Similar findings were observed during World War II among the Swiss, (127) the residents of the Channel Islands during German occupation, and the Dutch.(128)

Earlier studies of asylums, prisons and similar institutions reveal a very low incidence of appendicitis.(73,129,130) Institutional diets consisted of simpler and higher bulk-forming capacity foods. Miller in Nairobi, Kenya, (131) Wilkie in Rumania, (132) Clark in China, (131) Harrison in Southern Arabia, (131) all reported upward trends, sometimes quite dramatic, in appendicitis with introduction of "roller" mills and finely ground flours.

According to Burkitt, clinical and pathological evidence suggests that a possible causative mechanism of the development of appendicitis results from pressure changes leading to devitilization of the mucosa with secondary bacterial invasion.(131) The structure of the appendix does not allow for ready drainage, its blood supply is limited and its circulation is easily interferred with because the vessels anastomose to a *very* limited

extent.(133) Considering the blood supply and small luminal diameter one might suggest that obstruction, plus increased pressures lowering circulation lead to the inflamatory change in the mucosa.(134-136) Barium meal studies have shown that addition of bran to the diet increases the exchange of materials in and out of the appendix lumen, (134) while high fiber meals with resultant soft feces rarely obstruct the lumen.(131)

Hiatus Hernia

The protrusion of the stomach upward into the mediastinal cavity through the esophageal hiatus of the diaphragm results in the disorder known as hiatus hernia. This condition is usually believed to be the result of congenital weakness. Repeated increases in intra-abdominal pressures due to low fecal bulk might tend to force the gastroesophageal junction upward through the hiatus either aggravating or initiating the disorder.(77)

It is suggested by Painter (115) and Burkitt (49,137) that fecal arrest (which is associated with fiber depleted diets) and increased oressures during defecation are largely responsible for hiatus hernia. These pressures often exceed 100 torr and can exceed 200 torr.(131)

Varicose Veins

The valves of the veins are arranged so that blood flows only in a heartward direction.(138,139) When skeletal muscle is constricted it exerts pressure in the nearby veins and propel Is blood toward the heart. This pumping mechanism is known as the

"venous pump" or "muscle pump." When no movement occurs the venous pump does not operate and venous pressure can rise to the full hydrostatic pressure of 90 torr. Capillary pressure also increases dramatically and fluid begins to leak from the systemic circulation into the interstitial spaces. This loss may account for as much as fifteen to twenty percent of the blood volume. This loss accompanied with the pooling of blood in the leg veins reduces venous return with resultant lowering of cardiac output and possible fainting.

The valves of the veins are sometimes destroyed or become incompetent. Destruction of the valves occurs particularly after prolonged stretching due to high venous pressure. The veins have stretched without a compensating increase in valve size, resulting in an inability to restrict reverse blood flow. As more blood pools, stretching or increase cross-sectional diameter occurs with further increase in blood pooling and final destruction of valve function. Venous and capillary pressures become *wery* high with resultant constant edema. The clinical picture is worsened by lowered diffusion of nutritional requirements due to the edema. Muscle and skin weakness soon appears and the skin often atrophies and finally ulcerates.

Varicose veins are among the most common medical problems in the western world, affecting ten to seventeen percent of adults in England and North America.(140) Varicose veins have their lowest incidence in those areas of the world that have deviated least from their traditional way of life.

Many ideas have been suggested as the cause of varicose veins. Early suggestions included that this problem reflected a failure in man to adapt to erect posture. Such supposition is now held untenable in that in those areas where women stand the most erect and carrying heavy loads on their heads, we find the least incidence of the problem.(5) Studies on hereditary factors seem to refute genetic makeup as a primary causative factor although it may be contributory.(141) Prolonged standing and pregnancy have both been taken into consideration as well as constrictive clothing, but differences in occurrence were not significant,(142,143) It is now suggested that in those areas of the world where lower fiber diets are ingested that there is a higher incidence of the problem,040) It is believed that abdominal straining associated with constipation and evacuation of small compact feces causes raised intra-abdominal pressures that are transmitted to the vena cava and its associated veins of the lower limb. Straining has been found to raise these pressures to over 200 torr.

Present knowledge of venous pressures would make one suspect that veins repeatedly subjected to these abnormal pressures may become partially or completely ineffective, followed by the blood pooling and its complicating problems discussed earlier.(49) Apparently it is not a histological change in the valves, but the fundamental problem is the dilatation of the lumen of the vein with resultant separation and incompetence of the valves.(144)

Incompetence is not always an "all or none" proposition in that visible varicosities are not always accompanied by clinically detectable cough impulses.(140)

Burkitt summarizes the relationship of varicose veins and factors raising intraluminal pressures (i.e. low dietary fiber). (140) He states that varicose veins implies reverse blood flow and in turn,valve incompetence. No histological changes in valve cusps seem to occur but rather vascular stretching and separation of cusD edges. He therefore believes that the problem is a result of raised intraluminal pressures.

Hemorrhoids

Hemorrhoids seem to be extremely rare in the undeveloped areas of the world and much more prevalent in those peoples associated with western civilization.(89,145) As with varicose veins it is believed that the vessels of the rectal column become enlarged over a period of time due to abdominal straining and result in the condition known as hemorrhoids. Straining in the defecation process is inevitably associated with constipation or low bulk feces.(5,141,146) Increased straining via abdominal muscles and diaphragm accompanies attempted evacuation of firm feces with resultant increase in transmitted pressure to vessels in the anal canal. Whatever the precise mechanism a prominent role is likely played by constipation, (140) with a mechanism similar to hemorrhoid production observed in childbirth.

Cancer

In the United States cancer is the second major cause of death; one third of these cancers arise in the digestive organs, mostly in the large intestine.(147-149) In recent years over 350,000 people died annually from various forms of this disease. Preliminary data indicate that cancer will account for more than 650,000 new patients each year.

Three major influences which are believed to influence carcinogenesis receiving increasing attention are environmental, (including dietary factors) genetics, and hormonal influences. Epidemiological research suggests that environmental factors are considered to have a much greater influence on cancer incidence than do genetic traits (150) and contributes directly or indirectly to as much as seventy-five percent of human cancer.(151) Two recent symposia bringing together world wide data relative to nutrition and cancer should adequately illustrate the importance of nutrition in modifying susceptibility to neoplasm.(152-153)

The genetics of carcinogenesis in man is a relatively new discipline which has made significant progress in recent years. (154) Genetic studies in man are seriously hampered by the nature of the subject, evidence for advances in the important area of research is supported by the large number of cancer and precancer-ous disorders in which familial or genetic etiology has been determined.(151) Clearly, progress in the search for causes of cancer and its preventions will be greatly augmented as genetics

of cancer assumes an increasingly important role along with the more complete elucidation of th.e influence of environment.

A considerable body of evidence has also accumulated indicating hormonal factors significantly influence some forms of cancer. This is particularly true for liver neoplasia (155); hypophysectomy, thyroidectomy or adrenalectomy, completely inhibit the induction of liver tumors by the azo dyes and by amino fluorenes.(156-158) Breast cancer has been convincingly associated with hormonal and nutritional imbalances in women (159) and in experimental animals.(160)

A possible involvement of diet and cancer was first directly reported at the turn of the century.(161) Although both clinical and experimental investigations were abundant during the past forty years, the subject has received special impetus during the past ten to fifteen years.

Three types of data are used to substantiate current evidence of the involvement of diet in cancer etiology: a) indirect relationships between the consumption of selected food constituents and cancer incidence or mortality, b) case control studies in humans, and c) experimental data,(162) Indirect relationships consist of observed relationships between the consumption of selected nutritional constituents and cancer incidence or mortality, in different countries, regions, or religious groups include the following: 1) Quantified correlations, e,g., fat consumption and breast or colon cancer, (163) and, to a lesser extent, certain

starchy foods and gastric cancer,(164,165) 2) Nonquantified reported associations between specific nutritional patterns or availability of specific food ingredients and cancer in high or low risk areas, e.g., high intake of salty food (166) and low intake of fat (167-168) in Japan in relation to gastric and colorectal cancer, respectively; vegetarian diet among Seventh Day Adventist; (167) or aflatoxin contamination of staple food in Africa.(169,170) 3) Time trends in disease incidence, e.g., the overall decrease of gastic cancer paralleled by major changes in nutritional patterns.(171 ,172) 4) Comparison of food patterns among samples of healthy individuals belonging to high and low risk populations (173,174) and observed changes in disease incidence among migrants,(175-179)

Each of the above mentioned types of study are hindered by the fact that human diet does not consist of isolated food components. A high intake of animal protein is usually associated with a high intake of fat and a relatively low intake of carbo-hydrates and fiber. Therefore attempts at isolating any one factor as a factor in carcinogenesis may be useless unless confirmed by experimental data or case control studies. Implications drawn from such studies should be handled cautiously.

Case Control Studies

Dietary case control studies are often criticized for producing inaccurate information due to poor dietary recall, quantification inaccuracies, relationships of diet at onset of the

disease as compared to present diet, and problems in selecting adequate control groups,(180)

If recent dietary habits are not representative of an individual's long term nutritional patterns, and there is no guarantee of continuing those habits, then long term orospective studies do not provide a good avenue of research. Thus obtaining dietary information at one point in time may not reveal the dietary pattern involved in the carcinogenic process. This is not to say that retrospective studies will not provide leads to subsequent more comprehensive studies.

One recent study reviewing thirty such case control studies focused primarily on gastrointestinal cancer resulted in vague, scattered, and inconsistent conclusions.(8) Nevertheless, some consistency does occur suggesting an association, in this case, of lowered dietary fiber and colon cancer.(181-183)

Laboratory animal experimentation orobably offers the most definite data, but caution must be used in relating these findings to humans. Important considerations are threshold levels, dosage, tissue response and immune mechanisms, which all may vary from species to species.

Three areas are of prime importance in animal experimental studies: 1) identification of carcinogenic agents, 2) identification of metabolic pathways which modify or activate the known carcinogens, and 3) identification of protective mechanisms or states.

Experimental work has revealed that carcinogenic agents include food additives, (184) plant toxicants, (185-188) aflatoxins, (189-190) polycyclic hydrocarbons, (191,192) nitrosamines or their precursors, (193) as well as certain normal major food constituents. (194-199)

Recent studies have enhanced the knowledge of carcinogenic and dietary relationships in that it has been revealed that dietary constituents play a direct or indirect role in determining intestinal flora and the state of bile acid metabolism.(200-205) Most efforts have been related to colonic carcinogenesis, but expanding research is looking into associations with other forms of cancer such as breast (206) and gastric,(207)

Recent work indicates that carcinogenesis may need both an initiator as well as promoter substance,(208) Environmental contact with the initiator or promoter alone produces no cancer whereas initiator contact followed by promoter contact immediately or after a time interval of even twenty to thirty years promotes the carcinogenesis. Reversing the sequence seems to not promote cancer development.

Cancer of the colon and rectum is one of the most common forms of malignancies.(76,209,210) Adenocarcinoma is the most common tumor,(106) The highest incident rate for colon cancer is in English-speaking countries (211) and is relatively more common among whites and blacks in the United States than am.ong indigenous Africans who rarely exhibit the disease.(212-214) Among European

Dorn Jews there is a higher incidence than those born in Asia or Africa.(76) It is also more common among Japanese living in the United States as compared to those living in Japan.(14,215,216) World incidence of carcinoma of the colon is illustrated as follows black people in the United States 70/100,000; Caucasians living in Hawaii, 68/100,000; Japanese living in Hawaii, 66/100,000; Japanese living in Japan 12/100,000; black Rhodesians 18/100,000; black South Africans 11/100,000; Nigerians 6/100,000.(76) Racial characters seem to be outweighed by environmental influences.(209) Black Americans have a carcinoma rate five times greater than Ugandans, because black Americans generally live longer.(217) Black Africans do have a shorter life expectancy, (218) but the disease occurs largely in the young.(214,219)

The highest correlation in developing colonic cancer is between where the individual resides rather than where he was born,(220,221) The high incidence of the disease in Europeans and North Americans, the *wery* low incidence among black Africans, and the dramatic incidence changes associated with migration, urged many researchers to look at dietary variables.

In discussing such dietary and nutritional variables, one must remember that different types of cancer are not necessarily affected in similar ways by similar dietary components.(222) Tumors develop from living cells and grow by assimilating nutrients from the host, therefore the nutritional status of the host might be critical to neoplastic growth.(150) Chronic caloric

restrictions have been shown to inhibit development of many types of tumors and lower the incidence of neoplasm.(184,222-227) An association between body weight and tumor incidence seems to exist.(222,224) Neoplasm development studies in rats have shown that the incidence of tumors were consistently higher in heavy rats than lean rats.(227) Epidemiological studies indicate that a correlation exists between obesity and cancers of the intestinal tract, genitourinary tract and liver, (222) uterus, (224,228) gall bladder, (159,222) breast, (159,228) and large bowel in men.(13,14, 224,228-232) Dietary fat seems to have a direct correlation with breast neoplasia.(233-234) Other researchers have noted an association among certain cancers of the large bowel, gall bladder, pancreas, breast, ovary, endometrium and prostate with increased dietary fat consumption in the "westernization" of the diet.(14,228) It should be noted that studies indicate that it is not only the amount of fat but the type.(235-244) Dietary protein ef*ects on tumor development is not clear.(150,245) A wide variety of responses to differing levels of dietary protein have been observed. (243) Extremely low levels predisposing rats to an early occurence and high morbidity of adrenal and lymphoid tumors, while high protein intake increased susceptibility to urinary bladder papil- lomas and adequate diets, showed the highest incidence of carcinomas occurring in the thyroid, pancreas, and pituitary. Various amino acid deficiencies seem to depress some tumors (222,246) and has been attributed to the differences in eel 1-mediated immunity,

believed to be a major defense against cancer, and humoral immunity which may enhance tumor development.(247-249) Vitamin deficiencies and excesses can enhance or suppress tumor development,(150) A deficiency of vitamin A has been related to certain cancers and precancerous lesions, (184,224,239,250,251) susceptibility to chemical carcinogens, (168,208,252) increased carcinogenic potency. (253) On the other hand, high intakes of vitamin A have been reported to increase respiratory tract tumors,(254,255) Studies have shown that riboflavin deficiency retards growth of certain tumors, (184,256,257) and a deficiency of lipotropic agents -- vitamin B12, folic acid, choline and the amino acid methionine -- enhances chemically induced tumorigenesis,(258) Ascorbic acid is believed to be important in protection from the harmful effects of nitrosamines and nitrosamides,(259-262) It is also postulated by others that vitamin C may suppress tumorigenesis by maintaining a hyaluronidase inhibitor.(263-265)

Many inorganic substances have been shown to increase tumor incidence. Among these are arsenic, beryllium, chromates, radium, lead, nickel and cadmium.(150,184,222,266,267) Deficiencies of some trace minerals have increased tumor incidence (222,224) while animal studies have shown tumor inhibition with copper.(268) Disagreement exists in the influence of zinc, sodium, potassium, calcium, magnesium and selenium in whether they act as promoters or inhibitors of carcinogenesis.(150,184,269,270) Relative hardness of water and carcinogenesis seems to have no correlation. (271)

One aspect of the diet, fiber, is receiving increasing attention. This interest originated with demographic findings correlating large bowel cancer and low intake of dietary fiber,(150, 156,167,168,182,210,220,272-274) Later research supported this hypothesis and led to fairly general acceptance that the high incidence of colon and rectal cancers in certain areas of the world are the result of dietary changes,(150,162,182,205,254,275-277) Low dietary fiber, high fat and high protein intakes coexist with increased incidence of colonic cancer.(57,76,212,278) Research into the low fiber-colonic cancer relationship is centering around: 1) fecal microflora and 2) alterations in transit time. It appears likely that fecal bacteria play a role in the origination of large bowel tumors.(279) Chemicals that normally produce bowel tumors in animals living normally did not evoke the same response in rats raised in sterile environments.(14) Similar findings were reported in other germ-free animals.(280) The feces of the latter lacked the enzyme to split the precursor to form the ultimate carcinogens. Disagreement exists as to whether microflora is altered greatly by diet or an alteration in adaptive enzymes occurs. Some researchers have indicated a difference in bacterial flora among low and high prevalence bowel cancer population,(281) An increased amount of anaerobes capable of degrading bile acids to potential carcinogens existed in the stools from high-incidence areas. Others believe that bacterial flora of the colon is *very* resistant to dietary manipulation, but propose that the differences arise in

adaptive enzyme levels from bacteria whose species classification remains unchanged.(57,282-284) Whether or not either of these postulated mechanisms of bowel carcinogenesis is correct, it is significant that even though the mucosal surface area of the small intestine is over one hundred times greater than the colon, malignant tumors occur with an incidence more than one hundred times higher in the latter than in the former.(285) Even considering histological differences among the two mucosa, the observations suggest that formation or activation of carcinogenic factors is most likely to occur in the large bowel.

In support of altered microflora and subsequent changes in produced metabolites, Beher states that intestinal microflora metabolize primary bile salts to a number of products and it is therefore reasonable to expect properties of the fecal bile pool to vary with alterations in bacterial population of the intestines, (.286) He continues that microorganisms might play a notable role in the rate of bile salt metabolism. Bile salt excretion rates were shown to be higher in conventional rats as compared to germ-free rats (287) and bile salt pools contents varied as well,(288) Drasar and Jenkins state that bacteria in the bowel could convert these bile salts or steroids in the diet into carcinogens,(282) They continue that dietary components (i.e.both nutritive and non-nutritive), and thus substrates for bacterial metabolism must be *wery* different in the largely agricultural, non-industrialized areas as compared to the high industrialized, high incidence areas.

The second major aspect being looked at in the relationship of low fiber and high colonic cancer incidence is the alteration of transit time. Studies have shown that increased fiber content in the diet was associated with bulkier stools (1,3,8,32,74,289-291) which contained appreciably larger amounts of sterols and bile acids (292,293) In regard to transit time many researchers have reported a relationship between increased dietary fiber and decreased transit time.(2,3,33,61,76,77,131 ,279,294-296) Burkitt states that the feces associated with populations with high incidence of bowel cancer is small, hard and slowly-passing (285) while Walker suggests that feces associated with populations of low incidence are more likely to be unformed, voluminous, soft and passed with ease.(291)

In conclusion it seems that a relationship between dietary fiber and cancer is indicated but not yet proven. Colonic-rectal cancer seems the most closely associated form of cancer.(297) Factors appear to support the dietary fiber-cancer relationship hypothesis but do not negate the fat-cancer hypothesis. It has been suggested that as a possible prophylactic measure against colon cancer that 1) dietary fat intake should be lowered, or 2) intake of dietary fiber be increased.(291) It is also indicated that fiber alters bacterial abilities to metabolize various chemicals (283) especially bile salts or steroids in the diet to possible carcinogens,(282,298) This alteration of fecal contents, in combination with dietary fiber's ability to mechanically dilute feces thus decreasing exposure to gut mucosa, is the basis for much of the interest in dietary fiber.

CHAPTER IV

ENERGY RELATIONSHIPS

Caloric Density

Fiber depleted food is calorically more concentrated than fiber-intact food.(299) If one looks for instance at a 100 gram serving of fresh apple with approximately 58 kilocalories (kcal) and 100 grams of caramels at 415 kcal, we see a striking difference in caloric content of two carbohydrate sources,(300) Even white bread at 275 kcal as compared to whole wheat at 240 kcal is significantly different in caloric content.

One of the major nutritional problems of developed countries is over nutrition, i,e, the amount of energy required to maintain human life (that amount needed to satisfy requirements of basal metabolism, specific dynamic action of food, growth, repair and physical activity) is exceeded,(300) Obesity has become a public health problem of great magnitude. In the United States 35 percent of all adults over forty years of age, and 20 percent of all adults, are overweight to a degree that may interfere with optimal health and longevity. Increasing life span is also placing more people into an age when fat is more easily acquired, harder to lose, and increases susceptibility to chronic degenerative diseases. Obesity aggravates cardiovascular disease, osteoarthritis, increases incidence of hypertension, atherosclerious, hernia and gall bladder disease.(300) Adult onset diabetes is commonly associ-

ated with overweight conditions. Actuarial statistics reveal that those overweight will not meet the life expectancies of the lean person. The overweight person will be considered to be ten percent or more above the desirable body weight (based on height and build) and the term obesity refers to an excess of twenty percent or more over the desirable body weight.

How might fiber content affect control of desirable body weight? It has already been stated that food fiber reduces caloric density; therefore we have already reduced the available kcal per serving. Higher amounts of fiber are also found in those foods which naturally require more chewing, thereby increasing the effort required to eat and at the same time retarding the rate of food ingestion. How quickly can you eat 100 grams of baked potato as compared to 100 grams of caramel? It is believed by some researchers that chewing is part of the satiety factor. The slower eating rate gives control mechanisms (satiety) more time to respond and prevent over consumption of nutrients.(299) Dietary fiber also tends to reduce the efficiency of intestinal absorption of certain nutrients, notably fat and protein, therefore reducing caloric intake. Foods high in fiber also *are* tradtionally considered "bulk" foods which produce a high degree of satiety relative to their caloric density.(41) A sense of "fullness" results much earlier with the higher fiber foods.

Obesity is rare among groups consuming traditional diets, normally high in fiber, even when abundant food supplies are

present.(80) Even considering their life style, which one might say requires much higher energy expenditures than the relatively inactive western life style, one can get some strong indicators of needed changes to improved health conditions. If greater energy is exerted to gather or even prepare foods the total energy utilization and storage tends toward a negative energy balance. Our present western life way makes energy so readily available, we are not often required to exert much energy to acquire large amounts of energy. It has been shown that certain animals that normally eat high-fiber diets become obese on diets reduced in fiber content,(299) Thus, the fiber content of foods as illustrated in the preceding information suggests some *wery* valuable protective measures related to dietary fiber.

Nutrient Absorption

The indigestibility of fiber, nutritionally, provides a space occupying material in foods and in predigested gastrointestinal contents. It is therefore a source of fullness and satiety but not of calories.(301) During periods of food scarcity, dietary fiber is an unwanted item, but during times of plenty it provides a level of satiety without the disadvantage of high caloric density. It takes a determined eater to ingest calorically equal amounts of certain nutrients in low and high fiber foods.

Increase in fiber intake increases the fecal output of fatty acids and a significant reduction in digestibility of dietary fat. (299,302) Fat digestibility approximates 96 to 97 percent in

normal subjects, whereas those on controlled high-fiber diets had fat digestibility reduced to 93 to 95 percent depending upon amount of fiber added to the diet. Energy utilization was also reported to be as low as 94 percent on diets with 21.5 grams of fiber per day as compared to 97 percent when the diet consisted of nine grams of fiber per day.

Earlier studies in England in which subjects were fed low-fiber diets containing five grams per day of crude fiber revealed that the low-fiber diet subjects were able to absorb 93 percent of the total energy intake (kcal) while subjects on a high-fiber diet (crude fiber approximately doubled) energy absorption decreased to 91 percent.(303) Other research showed that dietary fiber of wholemeal bread, fruit and vegetables apparently decreased the absorption of energy two percent, while energy absorption from fat was reduced similarly with energy absorption from protein being reduced at a level of three percent.

Foods having a high E/F ratio (i.e. energy/fiber ratio) are considered to be fattening.(304) Examples of high E/F foods are sugar, refined starchy carbohydrate foods, fats, milk and alcohol- Foods exhibiting low E/F ratios would be leafy vegetables, fruits and whole cereal breads.

Many factors influence body weight, but studies of diets consumed ad libitum suggest that the E/F ratio of any diet is an Important factor in man and in animals.(305-307)

Obesity

Hypothalamic regulation of appetite for food depends primarily upon the interaction of two areas of the hypothalamus: a lateral "feeding center" and a medial "satiety center."(139) Feeding center stimulation evokes an eating behavior in conscious animals whereas destruction of that area results in a fatal anorexia. On the other hand stimulation of the medial "satiety center" causes a cessation of eating, whereas lesions of the same area results in hyperphagia. In the latter case, if food is abundant, the resulting syndrome is known as hypothalamic obesity.

It is not certain that the feeding center and the satiety center simply control the desire for food. It has been suggested that it is the setpoint for body weight rather than food intake per se which is regulated by the hypothalamic centers.

In addition to the hypothalamic centers the cerebral cortex and the amygeloid nuclei also play a part in the regulation of food intake. These areas are probably not as important in total food intake as much as specific choice of foods. Memories of prior food experiences are stored in these areas and such memories play a part in the adjustment of appetite.(308)

Regulation of food intake depends upon two different types of mechanisms. Long term regulation which indicates regulation of food intake in regard to nutritive stores in the body is believed to be influenced by blood levels of certain nutrients. The precise mechanism by which these nutrient stores affect satiety

is not known. Some investigators believe that the arteriovenous glucose difference affects the hypothalamus while others feel that too much importance has been placed upon the glucostatic explanation and feel that blood levels of amino acids and fats are probably equally important.(300,309)

Short term regulation on the other hand means regulation of dietary intake in relation to the amount of food that can be processed by the gastrointestinal system in a given period.(308) It is believed that in the process of ingesting food, two principal mechanisms come into play. The first involves the "metering" of food as it passes through the mouth, and secondly, reflexes caused by increased distention of the upper gastrointestinal tract. Thus the detection of the amount of chewing, salivation, swallowing, and tasting quantitates the amount of food passing through the mouth. This sensation in some yet to be discovered mechanism inhibits the hypothalamic feeding center for up to an hour. Similarly the filling and resultant distention of the stomach and upper gastrointestinal tract via visceral sensory impulses signals the feeding center and inhibits it. In such fashion over filling of the gastrointestinal tract is avoided until food previously eaten has been digested.

A multiplicity of additional factors is probably involved in the regulation of food intake. These factors no doubt revolve around one's environment, habits, and social customs as well as conscious and unconscious emotional drives.(300)

Appetite and hunger are often confused. We often continue to eat after the hunger sensation is suppressed. Our early training seems to be *wery* important in the amounts and types of foods we consume as adults. A problem often cited by researchers is the separation of physical hunger for food and an emotional hunger for love and affection.(300) Food often becomes a substitution mechanism for love and acceptance. Many individuals who are striving for acceptance and recognition often fall into a compensatory eating habit in which eating of good food entails sensory pleasure through which tension is diminished and anxiety levels are lowered. Such habits are critical to a weight reduction program.

Overingestion of food is usually blamed on endocrine factors, body fluid, or heredity rather than food intake. Endocrine dysfunction resulting in obesity is exceptionally rare as is true "familial" obesity which is most often an environmental factor rather than a truly hereditary problem.(300)

Obesity results when the intake of energy has exceeded the expenditure, and the excess remaining in the body has been deposited as fat in the subcutaneous tissues and around the internal organs.(310)

It is this deposition of excess calories as fat that has become a major concern in the United States where an abundant food supply in conjunction with a multitude of energy-conserving devices has made obesity a major health problem.(311)

Much research has been done on the obesity problem in relation to cell types, numbers, and age of development. It appears that the identification of an adipose cell depends upon a minimum amount of lipid and may eliminate potential adipose cells or preadipocytes and mature adipose cells depleted of lipid. Calculations of total adipose cells may be innaccurate due to assumptions of mean cell diameter being the same for all portions of the body.(312) Another concern in obesity studies is the accurate determination of total body fat.

Research of adipose tissue development in early life may reveal important information in regard to obesity development. Recent work has often centered around the idea that adult obesity could be prevented through dietary regulation during infancy.(310) It has been suggested that the first year after birth is a sensitive period for adipocyte replication, and, that once these cells are produced they are permanent.(313) If this is correct, an adult who was obese as an infant would have more difficulty maintaining an optimum weight. On the other hand, other research indicates that only one-third of the obese adults in one study were obese as children.(31 4)

It seems that successful maintenance of optimum weight after obesity is low without regard to numbers of adipocytes or onset time of obesity. Prevention is indicated as the best measure and should be employed throughout childhood and more specifically during those physiological stages of development when fat increases occur.(310)

It is now believed that the number of adipose cells in adults is not fixed. In vitro experiments indicate that preadipocytes from obese adults show an increased potential of multiplication than do those from lean individuals.(315)

In summary, prevention of obesity is indicated as a critical factor in maintenance of health. Historically, it has been noted that those populations who consume the majority of their dietary calories in the form of traditional diets consisting of vegetables, whole grains and other non-fiber depleted foods do not commonly exhibit obesity.(316,317) Points considered in the hypothesis of low-fiber diets and obesity relationships are: 1) food depleted of fiber is calorically more dense than fiber containing foods, 2) fiber promotes the mechanical chewing of food thus reducing the rate of consumption, 3) intestinal absorption is reduced in regard to certain nutrients, and 4) the higher the fiber content, the higher the satiety factor of bulk.(299)

Diabetes

There are about six million diagnosed diabetics in the United States and another four million who do not realize that they are diabetic.(318) At the current rate of increase, the number of Americans with diabetes will double *ewery* fifteen years. The National Commission on Diabetes has stated that when diabetes and its complications are considered together, it emerges as the third leading cause of death in the United States.(319) The increase of diabetes is partly due to an increase in life expectancy,

better diagnosis opportunities and techniques. The incidence of diabetes is related to heredity, viruses, histocompatibility antigens, and autoimmunity factors.(320)

Two hormones, insulin and glucogon, among others, are secreted by the pancreas. Both hormones are involved in glucose, lipid and protein metabolism. The pancreas consists of two major types of tissues of which the acini secrete digestive juices into the duodenum and the islets of Langerhans which produce insulin and glucogon. Both hormones are emptied directly into the blood. The islets of Langerhans are composed of two different types of cells, the alpha and beta cells. The islets are approximately seventyfive percent insulin secreting B cells and approximately twenty percent glucogon secreting A cells.(139)

Control of glucose metabolism is the basic function of insulin. The single basic effect of insulin is enhanced diffusion of glucose through cellular membranes of most cells of the body.(308) In the absence of insulin the entrance of glucose into the cells is greatly reduced, and there is an increased liberation of glucose into the circulation from the liver via hepatic gluconeogenesis. There is thus an excess of extracellular glucose and a deficiency of intracellular glucose. A resultant "starvation in the midst of plenty."(139) The presence of insulin increases the transfer rate of glucose into the tissue as much as three to five fold with even higher glucose clearance (fifteen to twenty fold) with large amounts of insulin.

The acceleration of glucose transfer from the extracellular fluids to the interiors of cells corresponds with a decrease in blood glucose levels. The converse is true with lowered or absent insulin. The fasting blood glucose level in the early morning, at least eight hours after any previous meal, is normally 80 to 90 milligram percent, and 120 milligram percent is generally considered to be the upper limit of normal. A fasting blood glucose level above this value usually is indicative of diabetes millitus. Complete lack of insulin activity usually produces a rise in blood glucose concentration up to about 350 milligram percent.

The kidney also plays a part in glucose metabolism in that glucose is removed from urine by active transport. In the normal state reabsorption occurs in the proximal tubule and no more than a few milligrams appear in the urine per 24 hours. The renal threshold for glucose is the plasma level at which glucose first appears in the urine in more than the normal minute amounts. The actual threshold is approximately 180 milligram percent glucose in the blood.

Glucose metabolism is also affected by liver activity under the control of the hormone glucagon. Glucagon from the alpha cells opposes insulin in some functions and complements it in other ways. Glucagon tends to raise blood glucose levels while insulin tends to reduce it. Both pancreatic hormones increase the availability of glucose to the cells. Glucagon accomplishes

this by way of accelerating liver glycogen to glucose conversion while insulin increases transport of glucose into the cells. The breakdown of liver glycogen to glucose is the first mode of action in glucagon's attempt to elevate blood glucose. Activation of the enzyme adenylcyclase by glucagon promotes the increases of cyclic AMP in liver cells. Cyclic AMP causes glycogenolysis. Glucagon's second mode of action is the increase of gluconeo-genesis in the liver. This conversion of proteins to glucose is a result of protein mobilization from body tissues and a corresponding increase in liver uptake of amino acids for this conversion. Glucagon can produce a dramatic blood glucose elevation in a matter of minutes.

The control of glucagon secretion is almost exactly the opposite of insulin control. When blood glucose concentration falls below normal, the pancreatic secretion of glucagon increases. Starvation and severe exercise will activate the glucagon mechanis" to insure adequate blood glucose levels.

In addition to glucose metabolism the pancreatic hormone, insulin has profound effects upon fat metabolism. When glucose is readily available insulin increases the transport of this glucose into adipose tissue. Acetyl coenzyme A and alpha-glycerophosphate, both products of glucose metabolism, promote fat storage. The polymerization of acetyl coenzyme A to a fatty acid, which then reacts with glycerophosphate to form a neutral fat, results in the synthesizing of fat. The absence of insulin lowers the orovision of appropriate products for fat synthesis. The

balance between synthesis and breakdown of triglycerides depends in part on whether the supply of glycerophosphate (from glucose) is sufficient to pick up the fatty acids release by the spontaneous breakdown. Insulin normally inhibits release of free fatty acids directly. Epinephrine, adrenocorticotrophin, and somatotrophin stimulate fat mobilization directly. Thus, in the presence of insulin, carbohydrates are utilized preferentially and excess carbohydrate is stored as fat, whereas in the absence of insulin fatty acids are mobilized and utilized in the place of carbohydrates, (308)

In regard to protein deposition in cells, insulin is almost as potent an influence as somatotrophin. Insulin increases the rate at which amino acids are transported through cellular membranes, thus increasing their availability for protein synthesis, as well as increasing protein formation by the ribosomes. Less directly insulin influences protein metabolism through its promotion of glucose utilization by the cells. This increased utilization is said to be the "protein-sparing" effect in that carbohydrates are used in preference to proteins for energy production. The opposite occurs in the absence of insulin resulting in large quantities of protein and fat rather than carbohydrates being converted to energy.

Insulin's overall effect on growth is a powerful one. Its promotion of protein anabolism, as well as making large quantities of carbohydrate available for energy, makes it critical in the

normal growth processes.

A major disorder of carbohydrate metabolism, diabetes mellitus, has probably afflicted man for thousands of years. It was first clearly described in the first century A.D. by Aretaeus who described a "melting down of the flesh and limbs to urine," and named the disease "diabetes" from the Greek word for "siphon," due to the polyuria and polydipsia associated with it.(321) Susruta recognized the sweetness of the urine in the fifth century A.D., and the presence of sugar was recognized by Dodson in the eighteenth century.(321) Dogs, pancreatictomized by Von Mering and Minkowski in 1889, developed the disease.(321) Banting and Best, in 1921, produced a purified pancreatic extract capable of supporting life in pancreatectomized dogs and in humans.(321) Later modifications of the explanation of diabetes mellitus syndrome did not only include information in regard to insulin but other endocrine, immunologic and chemical interactions combining to regulate the blood glucose concentration and that diabetic individuals do not necessarily lack insulin. Even with all these interrelated factors diabetes most likely results from irregularities of insulin production.

In diabetes, glucose accumulates in the blood stream, especially after meals. If a glucose load is given to a diabetic, the rise in blood glucose is higher and returns to the baseline more slowly than it normally does. This response is utilized in the standard oral alucose tolerance test as the chemical diagnosis

of diabetes. The impaired glucose tolerance is due in part to decreased peripheral utilization of glucose. In the absence of insulin, glucose entry into skeletal muscle, cardiac and smooth muscle and other tissues is inadequate to sustain life. Intestinal absorption and renal tubule reabsorption of glucose is unaffected. Brain and red blood cell uptake of glucose is also normal.

A second and perhaps the major cause of hyperglycemia in diabetes is the alteration of liver glucostatic function. The liver normally removes glucose from the blood and stores it in the form of glycogen, but due to the presence of glucose-6-phosphase in the liver, it also discharges glucose into the blood. Insulin facilitates the synthesis of glycogen and in turn inhibits hepatic glucose output. During periods of high blood glucose, insulin secretion is normally elevated while hepatic glucogenesis is decreased. Glucose output remains elevated in the diabetic.

It is this continued elevated level of glucose that indicates the primary abnormality of diabetes in that the affected person fails to utilize adequate quantities of glucose for energy. This continual high level of glucose results in urinary loss of glucose with resultant high osmotic pressure in the renal tubules, thus diminishing the reabsorption of water. As a result the diabetic loses copious amounts of water along with the glucose. In the extreme case extracellular dehydration can be *wery* damaging.

This failure to utilize glucose deprives the diabetic of a major portion of the normal dietary energy supply. As a result

of nutrient deficiency the diabetic person usually becomes very hungry, and even though he eats in large quantities, the carbohydrate portion contributes little to his energy demands.

The shift to fat metabolism in the diabetic often increases the quantity of keto acids in the extracellular fluid to as high as 25 to 50 times normal levels. This occasionally shifts the pH of body fluids from its normal value of 7.4 to as low as 7.0, Acidosis of this nature is incompatible with life for more than a few hours.

One of the major problems resulting from prolonged diabetes is that carbohydrate metabolism, even with the best possible treatment, cannot be maintained at a sufficiently high level to prevent some excess fat metabolism. Cholesterol deposition in the walls of the blood vessels is normally an accompaniment of rapid fat metabolism. Although diabetic acidosis can be rapidly fatal and therefore a fearful complication of the disease, it is now less important than these changes in blood vessels. Diabetics are prone to develop atherosclerosis prematurely, an effect that probably reflects the elevated levels of cholesterol and plasma triglycerides when the disease is poorly controlled. In the diabetic plasma cholesterol is usually elevated, although a controversial point, it has been shown that in severe diabetics cholesterol synthesis is decreased. The rise in levels being due to an increase in cholesterol containing *wery* low density and low-density B-1apoproteins secondary to the great increase in

circulating triglycerides.(139) Another factor may be a decline in hepatic degradation of cholesterol which contributes to the rise when greater than the rate of synthesis, thus resulting in a pathogenicity essentially no different from other forms of hypertriglyceridemia. Unique, though, are the small vessel changes in the diabetic. Basement membrane thickening is seen as a result of excessive deposition of collagen and mucoproteins.(321) Many areas of the body are affected, but expecially important clinical effects are seen in the retina, kidneys, nervous system and skin.

The etiology of diabetes suggests variations in the disease. The spontaneous diabetic has a defect in secretion of insulin by the beta cells. In the obese patient who may not be overtly diabetic, and the individual treated with corticoids, the presence of high insulin levels when glucose levels are normal may indicate reduced insulin effectiveness. Thus, it becomes a question of relative or absolute deficiency of insulin.

It is known that certain hereditary patterns, chemicals and degenerative diseases alter the pancreatic ability to produce insulin. It is also known that many middle-aged or elderly persons develop a type of immunity to insulin. Apparently the immune system produces antibodies that destroy insulin before it can produce appropriate effect.(308) Another important factor relates to work done in the late fifties when a new dietary agent, glucose tolerance factor, was postulated, (322) and it was described as an enhancer of insulin's association with receptor

sites of sensitive tissue.(323) Work in the mid-sixties revealed demonstrated improvements of glucose tolerance in humans upon chromium supplementation.(324,325) Chromium in its biological form resembles a hormone. It is released in response to the physiological stimulus of insulin and is carried to peripheral tissues where it exerts a facilitating effect upon a biological action which in its absence would occur at a reduced rate. (326)

Presently, since cure of the disease is impossible, the objectives of control must be to minimize ketoacidosis and other symptoms resulting from hyperglycemia. Although such efforts are often effective, the brittle diabetic may have difficulty in achieving even these limited objectives. Avoidance of patient damage by treatment is also of prime concern. Treatment takes several forms including diet, insulin, exercise and the oral hypoglycemic drugs. Clinical assessments of glycosuria, blood glucose, the progress of complications and nutritional status are needed to adjust and monitor progress of treatment.

Early dietary control was suggested in 1675 by Thomas Willis, who recommended a high carbohydrate diet. In 1797, John Rollo suggested complete avoidance of dietary carbohydrate. A starvation diet was encouraged in the late 1800's.(327) In 1914, F.M. Allen encouraged rigorous caloric control.(327) Geyelin, in 1923, administered high carbohydrate diets to insulin-treated patients. (327) Progress in dietary considerations has revealed that in insulin-independent diabetics, the main objective is caloric

reduction, whereas in insulin-dependent diabetics (juvenile-onset) diet therapy should allow for normal growth and attainment of desirable weight.(328-331) In both types of diabetes, there is decreasing emphasis on the priority of carbohydrate restriction. (327,328-330,332,333) Although some research indicates a relationship between high carbohydrate diets and elevated triglyceride levels, (334) the former American Dietetic Association diet seemed to favor fat intake and is therefore potentially dangerous to the vascular system.(333) The new ADA diet has reduced fat and increased carbohydrates allowances. Research now encourages the ingestion of starches high in fiber.(64,335,336) Three main diet philosophies now include the weighed diet, (337) the constant carbohydrate diet, (338) and the measured diet.(339)

It has been suggested that increased consumption of fiber-depleted carbohydrate diets has played a part in the etiology of the increasing incidence of diabetes.(40,335,336) Cleave et al. based their conclusions upon the relationship of sugar consumption and diabetes.(5) They reviewed the work of Himsworth (340) and suggested the reduction of sugar consumption in the years 1941-1947 was largely responsible for the reduction in female diabetic mortality in the same period. Work by Trowel 1 examined the relationships of dietary fiber, especially the effects of the 1942-1953 period of compulsory National flour (a high fiber flour) and the return to high extraction white flour after 1953.(40,69) It was noted that during the years of the comipulsory National flour.

female diabetes mortality decreased by more than 25 percent. It was during this period that the average crude fiber content of the wheat was 5.0 g/kg. In the two periods reported it was noted that fat intake was similar and sugar intake was 5kg/person/year lower in 1942 to 1946 than in the period 1939-1941.

Kiehm et al. conducted a study similar to the study of Stone and Connor (341) in which patients were switched from a 2200 kcal diet that contained 234 gm. of carbohydrate (43 calorie percent) and containing starch to simple sugar ratio of 1.15 to a diet containing 419 gm. carbohydrate (75 calorie percent) and a starch to simple sugar ratio of 2.63.(36) Average cholesterol levels fell from 198 to 151 mg/dl.(p 0.01), triglyceride levels fell from 165 to 140 mg/dl and blood glucose fell from 183 to 136 mg/dl (p 0.05). No significant weight changes occurred and those individuals on low insulin maintenance or on oral hypoglycemic therapy were able to suspend therapy.

In a summary of twelve similar studies in which starch was substituted for sucrose on an isocaloric basis it was found that in *ewery* case there was a reduction in serum cholesterol levels (average 13 mg/dl).(20) Substituted foods consisted of bread, legumes, rice, potatoes and fruit and they clearly had more fiber components but no exact data on content was available.

Another study in which diabetics were fed a fat free, high carbohydrate diet with 85 percent of its calories derived from carbohydrates, it was found by Brunzell et al. that in individuals

with mild diabetes (i.e. those with normal fasting blood glucose but elevated levels two hours after a meal), an improvement in glucose tolerance was observed after ten days on the test diet. (342) When Brunzell et al. fed the same diet to moderate and severe diabetics (those with fasting hyperglycemia) a reduced glucose tolerance and increased urinary glucose loss was seen in patients controlled solely by diet. Some improvement was noted in drug sensitivity by the diet, (343)

Crapo et al, using whole foods as carbohydrate sources found test meals of potato, bread, rice, or corn produced lower plasma insulin peaks than glucose in non-diabetics.(344) Corn and rice gave lowest results while bread and potato were higher in insulin response. Digestable carbohydrates were maintained at the same level in all meals. Results such as these indicate that not only the amount of carbohydrate but also the source can be influential in tolerance of carbohydrates. Although these researchers attributed the changes to the type of starch, the results of other workers indicate that the type and amount of indigestable components may make the difference.(345,346)

Such responses with diabetic patients should encourage further investigations to identify what alterations or components of diet are responsible for improved glucose tolerance. In one such investigation Haber et al. using raw apples, raw apple puree or depectinized apple juice looked at the effects of dietary fiber on glucose tolerance.(347,348) The subjects ingested in one phase of

the experiment, one of the three sources of sugars over a specified time span to minimize the effects of the ability to consume the product (juice faster than puree, puree faster than whole apple). In another phase of the experiment an ingestion time span was not specified, blood glucose and insulin levels were recorded for three hours following the meals. Blood glucose levels were similar in both timing and amplitude for all the test meals. An interesting difference was seen in that by one and one half hours after "fast and slow" test meals of juice and puree, blood glucose had fallen significantly lower than fasting levels, although less of a drop was seen with the puree than with the juice, Raw apple on the otherhand, produced no hypoglycemia, but rather produced a curve with maintenance of fasting levels after one and one-half hours. Amplitude of the insulin response was greatest with juice and lowest for raw apples. Correspondingly the lowest insulin rise accompanied the most favorable blood glucose picture.

Thus in addition to the known correlation between obesity and diabetes, high-fiber, high-carbohydrate diets have been shown to have beneficial effects on glucose tolerance and insulin dependency of diabetics. (299) In individuals with mild diabetes there was an improvement in glucose tolerance explained on the basis of increased sensitivity to insulin.(36) Moderate and severe diabetics (with fasting hyperglycemia) were also helped by the diet. Of the thirteen patients in the experiment, three who required forty or more units of insulin per day, showed no response

Nine others, using insulin or sulfonylurease were able to discontinue use of the medication while one other was able to reduce daily medication by nearly fifty percent. Perhaps another positive response to the diet was indicated in that all patients reduced their serum cholesterol while some also had reduced levels of serum triglycerides.

Other studies suggest that dietary fiber may reduce post-prandial hyperglycemia by reducing the rate of food emptying from the stomach into the intestine, (349,350) while some workers report that animals on high fat diets with the complex carbohydrate starch as the carbohydrate source had significantly lower insulin and glucose levels after glucose load than those fed the less complex carbohydrate sucrose. The effects of dietary fiber or the more complex carbohydrates upon insulin response and serum glucose levels is far from clear, but it is suggested that the effect may be from increasing the time required for ingestion (345) or limiting energy intake.(8,25,26,112,351)

CHAPTER V

CURRENT CONCEPTS OF THE INFLUENCE OF DIETARY FIBER ON TRANSIT TIME

The time taken for the passage of material from the mouth to anus is known as transit time and varies from person to person, and even in an individual, transit time is variable.(13) Various techniques have been devised to more accurately measure and hopefully standardize transit time measurements. These techniques have ranged from the ingestion of colored glass beads (352) to sophisticated radioisotope methods.(113)

It has long been known that certain unabsorbable portions of food have laxative effects. The effects of fiber on transit time was known by Hippocrates (353) as well as others. In the present century, Cowgill and Anderson (353) and Fantus et al. (134) brought attention to the effects of bran on bowel function and content. Dimock stated a relation between cellulose fiber and prevention of constipation.(354) During the same period, Williams and Olmstead studied laxative properties of other foods.(355) Many workers have since reported decreased transit time and increased fecal bulk in relation to cell wall contents of various foods.(70, 72,113,356-359) Connell stated, ". . . only one point is definitely known about fiber and colonic activity, namely that fiber produces a rather larger stool," and it is proposed that ". . . stool weight may be related exponentially, to the transit

time . . ."(356)

Not all subjects decrease transit time when given bran. When some individuals possessing rapid transit times (<24 hr) are given bran, there is an increase in transit time,(351) Mitchell and Eastwood state that such findings suggest that there is some regulating mechanism or that there is an ideal transit time varying with the source of dietary plant fiber,(13) The mechanism by which fiber alters the transit time is not adequately elucidated but it has been suggested that the filling of the colon with a more bulky, moisture laden stool results in a more easily passed stool requiring less straining.

Kirwin and Smith concluded that specific gravity is quite important in transit time measurement. Using pellets of various specific gravity, they found that those with specific gravity similar to that of gut contents were propelled at the same rate as gut contents while those heavier and lighter pellets moved to the periphery of the gut contents and were expelled more rapidly, (360) These findings paralleled similar results obtained by Hoelzel in a much earlier experiment.(361) Such work raises the possibility of specific gravity alterations due to fiber contents of the feces.(13) It is also suggested that small intestinal transit time is relatively constant in normal persons or those with constipation, or those with diarrhea whereas the differences often seen *are* due to colonic transit changes.(360,362) It is known that the small intestine contents are high in water relative

to colonic contents. The functions of the colon are (1) absorption of water and electrolytes from chyme and (2) storage of fecal matter until it can be expelled. Ordinarily 500 to 800 ml. of chyme is emptied into the colon each day, and of this, most of the water and electrolytes are reabsorbed, leaving an average volume of feces of 100 to 200 ml. each day.(308) It is thus suggested that with this normal physiological withdrawal of water the presence of solid dietary fiber will alter the specific gravity of the colonic contents and therefore the colonic transit time.(13) Burkitt (13,212) did find rapid transit time (25-40 hrs.) in native African school children eating high fiber diets, but found much slower transit time (over 70 hrs.) in English boarding school boys consuming low fiber diets. Decreased transit time and increased fecal bulk relative to fiber in the diet has been reported by other workers. (70,72,356,363-366) Eastwood et al. reported a doubling in fecal weight with the addition of sixteen grams of bran per day to human diets for three weeks. Both wet and dry weights increased.(33) Wyman et al. found that raw bran increased wet and dry weight of feces but they did not find a similar value with cooked bran.(367) Harvey et al. reported a "normalization" or convergence of transit times in individuals given thirty grams of bran per day over a four week period.(368)

It seems appropriate in a discussion of transit time to include pertinent points involved in the pharmacology of laxatives. Many individuals exist who cannot produce a bowel movement without taking

some form of purgative or colon stimulant and it is estimated that one person in three over the age of sixty takes a laxative at least once a week.(34) Effective laxative action results in an increase in fecal water excretion, and increased fecal water excretion is usually secondary to altered intestinal fluid and electrolyte movement.(32) The exact role of motility in the production of alterations of fluid and electrolyte movement is ill defined and requires further study. There is at present no direct evidence that changes in motility, motor function, or transit time alter intestinal electrolyte absorption, and a decrease in transit time alone should never result in fluid and electrolyte accumulation.(32) Pharmacological agents, such as codeine, increase transit time and may decrease fecal water excretion, but probably do so by increasing the time that the absorbing surface is exposed to luminal contents.

Traditionally laxatives have been classified into groupings that neither reflect pathophysiological considerations nor possess any logical basis to explain laxative action.(369) Those classed as stimulants (irritants) were believed to act by "stimulation" of peristalsis by "irritation" of colonic mucosa. Recent works indicate that these "stimulants" probably act by altering fluid and electrolyte absorption. Another major class is the "stool softener," a classification which could apply to all laxatives for, if effective, all laxatives should result in "stool softening." The saline or osmotic laxatives make up another major category. Their laxative effect is attributed to their poor absorbability

with resulting hyperosmolarity. Magnesium salts as a representative of the group may act in a way mediated by cholecystokinin, and recent works show that magnesium salts decrease both circular smooth muscle contractility of the ileum and decrease transit time.(370,371) The final major class of laxatives is that which is grouped under the heading "bulk." Several different materials are classified as bulk laxatives, and the recent interest in dietary fiber has brought increased attention to this group. These agents are the brans, the semi-synthetic cellulose esters (methylcellulose), mucilaginous seeds and seed coats (e.g. "metamucil"), or the mucilaginous gums (e,g, "normacol"). Data does not suggest that bulk products directly affect mucosal electrolyte transport, but the general assumption is that they provide laxative action by virtue of their ability to absorb fluid resulting in less fluid available for absorption. Other possible explanations may be suggested in that certain "bulky" agents alter fecal bile acid composition,(50)

Laxative action in general should be considered in terms of increases in fecal water excretion in spite of prior emphasis on mobility abnormalities.(32) Most studies indicate that laxative action is a result of altered intestinal fluid and electrolyte movement often associated with net fluid and electrolyte accumulation. It is this alteration of fluid and electrolyte movement that is central to effective laxative action.

CHAPTER VI

FECAL NUTRIENTS/TRACE MINERALS: ALTERATIONS IN RELATION TO FIBER CONSUMPTION

Fiber with its ion-exchange and water-holding capacity can interact with other nutrients in the diet and alter their utilization,(299,372-375) Some researchers have reported that fiber can cause a decrease in the capacity of the body to utilize several nutrients while others report no adverse effects (376,377) or even a beneficial role,(378) Evaluation of any such work must consider (1) quantitative and qualitative dietary fiber and (2) test period duration.

It has been shown that subjects on various high whole wheat diets show evidence of negative calcium balance.(379-381) This effect of whole grain products on calcium absorption has been ascribed to the phytic acid content of these foods.(76,382) One of the advantages of white flour is that the removal of the bran means a great reduction in the phytate (inositol hexophosphate). A possible harmful aspect of phytate is that it plays a role in the forming of insoluble calcium compounds and, hence, leading to a possibly reduced absorption of calcium. There are indications that these changes in calcium balance are only short term, and that over longer periods man has shown an ability to adapt to the higher fiber intake and return to normal calcium balance, while others believe these adaptations are too selective and incomplete.

(383) Perhaps as important is the observation that yeast leavened whole wheat bread does not produce a decrease in mineral balance due to fermentation of phytate.(301)

Studies involving other trace minerals are also in conflict. (380) Zinc, iron and copper studies have also shown lessened availability in those diets high in fiber.(299,373,384-389) Binding of a portion of dietary trace minerals, especially zinc, iron and calcium by wheat fiber may help explain why deficiencies of these metals are prevalent in rural areas of the middle East where high fiber, high phytate diets exist. It is now believed that a viscious circle begins in the diets that limit the availability of zinc, in that the enzyme responsible for the destruction of phytic acid in the gut appears to be a zinc-enzyme whose activity depends upon dietary zinc availability.(390)

From a nutritional perspective, it would be advisable to monitor the nutritional status of subjects altering fiber intake to any great extent, especially those considered to be in a marginal state of balance in regard to these minerals.(299)

In addition to the classically recognized diseases associated with inadequate intakes of iron and iodine and the beneficial effects of fluorine in preventing tooth decay, several recent studies have brought considerable attention to trace elements deficiencies and imbalances in a number of clinical disorders. Protein-calorie malnutrition studies in infants whose diets were based on dairy products revealed hypocupraemia with a

range of copper-responsive symptoms including demineralization of bone, defective erythrocyte production and poor iron absorption. (391) It has also been suggested that a high zn:cu ratio in the diet predisposes one to coronary heart disease.(392) Zinc deficiency is suggested to be at least partially responsible for growth retardation and arrested sexual development in adolescent boys,(393) Clinical abnormalities of taste and smell have been reversed by zinc supplementation (394) Zinc supplementation of patients has also been shown to improve wound healing after surgery (395) although, possibly, only when the patients are initially zinc-depleted,(394) Some workers have reported marked improvement in glucose tolerance in patients suffering from maturity-onset diabetes after chromium treatment.(323,324) It has also been postulated that silicon may be involved in the evolvement of arthritic conditions and atherosclerosis.(396,397) In light of the growing body of knowledge on trace elements, it would seem clear that one should not ignore these nutrients when considering the adequacy of diets in the future. If trace elements play such an important and widespread role in human health, it would also seem important that any aspect of the diet (fiber, etc) should be thoroughly researched to more completely elucidate any possible interactions.

CHAPTER VII

TOXICITY PROTECTION

The antitoxic properties of fiber in rat and mouse rations were reviewed by Ershoff in 1974.(50) Fiber has been shown to reduce the toxic effects of Tween 60 and Tween 20, glucoascorbic acid, sodium cyclamate, and Red Dye #2, cyclamate, yellow #5 and yellow #6.(51-56,76,299,330,398) It seems that the protective effect of the plant fiber-containing materials are greater than could be accounted for on the basis of their cellulose content per se,(51) Studies related to fiber component antitoxic effects were initiated by Wooley and Krampitz in 1943.(399) Their work indicated that immature mice fed a purified ration containing 5-10 percent glucoascorbic acid failed to grow and eventually died. These symptoms did not occur in mice fed similar doses of glucoascorbic acid in conjunction with a natural food stock ration, nor did they in mice fed purified diet supplemented with dried grass. Later studies indicated that alfalfa meal at a ten percent level provided similar protection as did dehydrated *rye,* orchard, wheat, fescue, and oat grasses, (51) Cellulose per se when incorporated into the purified diet had a moderate effect in mice and rats, but its protective effect was considerably less than that obtained from the plant-fiber containing materials indicated above. (51,400,401)

The concurrent administration of bulk-forming substances

counteracted adverse effects of such nonionic surface-active agents as polyoxyethylene sorbitan monostearate (Tween 60) in weanling rats.(402) These investigators suggested that the toxic effects of Tween 60, when fed with the purified, low-fiber diet were due to the lack of sufficient residues in the diet to absorb the surface active agent. It was also observed that the addition of celluflour or agar to the diet prevented intestinal irritation but did note that marked differences exist in the toxicity protection among varying bulk-forming substances.

The protective action of alfalfa meal has been demonstrated in rats fed a purified, low-fiber diet containing toxic levels of chlorazanil hydrochloride.(398) Findings indicated that the levels of chlorazanil hydrochloride used in the experiments caused a highly significant retardation in weight increment and an increase in serum nonprotein nitrogen, urea nitrogen, and creatinine. These effects were largely alleviated by the inclusion of 20 percent alfalfa meal level in the diet. Purified cellulose at the ten percent level or supplements of the known nutrients provided no protection.

Sodium cyclamate, when incorporated at the five percent level in a purified, low-fiber diet for immature rats produced a marked retardation in growth, hair alterations and diarrhea.(53) Various levels of alfalfa meal incorporated into the diet had a protective influence. A distinct growth-promoting effect was seen at the 15 percent and 20 percent levels. The animals receiving alfalfa

supplementation appeared healthy and exhibited normal hair but had a mild diarrhea with soft but well-formed stools. Dessicated kelp and wheat bran fed at ten percent level also had a protective effect. Purified cellulose at a five or ten percent level was effective in counteracting the sodium cyclamate diet, but was less effective than the other supplements already mentioned. Blond psyllium seed powder, blond psyllium husk powder, guar gum, watercress powder, carrot root powder, sugar cane bagasse, rice straw and pectin incorporated at the ten percent level all showed significant protective activity against cyclamate toxicity exceeding that of a ten percent cellulose supplement.(51)

Immature rats fed amaranth (FD&C Red No. 2) at a five percent level in a purified, low-fiber diet exhibited a greatly decreased growth rate, an unthrifty appearance and resultant death within two weeks of first feeding. (54) Known nutrient supplementation, either alone or in combination, produced little if any protective effect. Ten percent levels of alfalfa meal, alfalfa residue, watercress powder or parsley powder incorporated into the above diet counteracted the toxic effects. In tnis case purified cellulose when incorporated at the ten percent level produced similar effects, although no or little protection was exhibited when the level was reduced to the two percent level which corresponded to a crude fiber content of ten percent alfalfa meal supplementation. Pectin fed at the ten percent level in the ration was also active but less so than the ten percent cellulose supplement.

Thus, it can be seen that a number of chemicals when incorporated in a purified, low-fiber diet induce toxic effects in rats and mice at dosages which have little if any adverse effect when fed with a natural food-stock ration.(299) Supplementation of the purified diets with known nutrients, either alone or in combination, was without protective effect. In most cases the amounts of these various chemical additives were given in massive doses, but the toxic effects were largely counteracted by supplementation with various types of fiber.

The postulated mechanisms for such protective effects by dietary fiber include:

1. The bulk in the intestines is increased by the addition of fiber resulting in an effective dilution of toxicant concentration.

2. The toxicant and fiber bind preventing (a) its absorption or direct effect on the animal tissue or (b) its modification (activation) by the intestinal environment.

3. Increases in fiber content of the diet decreases transit time, thus lowering the time for incubation of non-absorbed toxins or intestinal carcinogens.(299)

CHAPTER VIII

THE INFLUENCE OF FIBER ON INTESTINAL FLORA

Anaerobic culture methods have revealed that well-known intestinal species such as Escherichia coli,, Lactobacillus acidophilus, or Streptococcus faecal is are greatly outnumbered by anaerobic bacteria including many species not previously characterized or described,(403) It is estimated that between 400 and 500 species, with a wide range of metabolic activities, occur in numbers of 200 to 400 billion per gram of colonic contents and approximates half the fecal mass of the contents of the colon.

Intestinal flora probably represents one of the most complex interrelationships of organisms and environment found in the natural world. Research has yielded preliminary analysis of this ecosystem, but much work needs to be done in order to more accurately describe the interplay among bacterial species and their effects upon host physiology.

The effects of diet per se, in altering intestinal flora remain unclear because of conflicting evidence. Some researchers have reported increased numbers of certain anaerobes, notably bacteroides, and lower counts of streptococci and other aerobic microorganisms in intestinal contents of individuals consuming high fat, high meat, low fiber diets.(284,404) Another report indicates that certain aerobic organisms were significantly higher among subjects on a Japanese diet than those on an American diet.(405)

Others have found no significant differences in intestinal bacterial flora in those subjects consuming different diets, i.e. high meat versus no meat diet, vegetarians versus omnivores, etc. (49,57) One study indicates that a liquid diet containing no fiber and virtually no fat caused an increase in fecal enterobacteria and a reduction in Enterococci and other lactic acid bacteria. (406) Others have reported that bacterial flora of the colon are *wery* resistant to dietary manipulation but suggest that changes in adaptive enzymes occur in bacteria whose species classification does not appear to be altered.(57) Studies with gnotobiotic rats in which diets were altered produced no practical guide to relationships of diet, numbers of bacteria or bacterial interaction,(407) In one study where the diet was supplemented with fiber the total anaerobic counts increased significantly while the subjects were on the high fiber diet.(46) Another study in which foods relatively rich in dietary fiber were added to the normal diets of the subjects produced no alteration in the fecal flora.(282)

Although findings have often been inconsistent in demonstrating changes in bacterial species and genera with dietary changes it has been shown that dietary components do effect changes in the metabolic properties of the flora.(408-410)

Several difficulties arise when one attempts to determine exact host-gut microflora interactions. The nature of dietary fiber will vary from plant to plant; with the age, tyoe and variety of plant and also the anatomical source of the fiber.(411)

Substantial amounts of pectins and hemicelluloses can be found in rapidly growing plants whereas the more mature plant will contain a preponderance of lignin and cellulose, Lignins seem not to be modified by bacteria whereas it has been reported that polysaccharides are subject to bacterial degradation in the colon,(1) The alignment of bacteria on dietary fiber in the gut has not been clearly elucidated. We do not know whether absorption to the fiber occurs or if a random distribution in the heterogenous phase is present. The production of bacterial extracellular enzymes which could permeate the gut contents may provide extracellular as well as intracellular metabolism.(411)

In summary, fiber, bacteria, digestive secretions, and nutrients have a *wery* complex interrelationship. The physical characteristics of fiber as discussed earlier indicate that a combination of wettability, ion exchange capabilities, and bile acid absorption exist. Both fiber and bile are metabolizable by bacteria and bile and its resultant metabolites influence bacterial metabolism. To add to the complexity, one must also consider fiber's influence on water distribution and amounts, surface configuration, spaces, time, redox potentials, concentration and pH alterations.

CHAPTER IX

FIBER'S RELATIONSHIP TO LIPID METABOLISM

Fiber and Coronary Heart Disease

In the United States and other technologically developed countries coronary heart disease accounts for a large proportion of disabilities and death,(412) United States mortality attributed to atherosclerosis is estimated to be 165,000 persons under 65 years of age and 625,000 persons of all ages annually. It is the largest component of cardiovascular diseases that are reported to account for 50 percent of United States mortality. It is expected that a middle aged male of the United States has about a 25 percent chance of developing some form of coronary heart disease during the fourth decade to seventh decade of life. (412)

One aspect of coronary heart disease (CHD) is coronary occlusion. In this disease process a coronary vessel becomes totally or partially blocked. If this occurs, all area beyond the stenosis or occlusion is not adequately supplied with nutrients and stops contraction, with the resultant pathological condition commonly referred to as a "heart attack,"(308) If a major portion of coronary muscle is affected, stroke volume and rate are greatly depressed resulting in an ineffective pump which will no longer sustain life. Occlusion may occur rapidly or slowly, and in the majority of cases it results from atherosclerosis.(412)

Atherosclerosis is a disease of fatty deposition in the walls of the arteries. The deposition products include a high cholesterol content, with smaller amounts of phospholipids and neutral fat.(413) Fibrous tissue gradually grows around and infiltrates the fatty deposits. As the condition progresses there is often calcium incorporated into the deposits with resultant solid calcium compounds. Eventually, in many instances the vessels become extremely fibrotic, constricted and even *wery* hard in consistency, a condition referred to as arteriosclerosis or "hardening of the arteries."

Acute occlusion of the coronary vessels may occur as a result of atherosclerosis in one of two ways: (1) clotting of the blood may occur due to fatty deposits breaking through the inside surface of the vessel, or (2) the fatty deposits may actually break free of their point of origin and be carried to an area where its passage may be physically impeded due to a decrease in the lumen size.(308) Either situation may result in diminished coronary function. Unfortunately, in about twenty-five percent of the cases death occurs within the first few hours. About one-third of those that survive the initial symptoms die within a year.(414) In those cases where only small vessels are involved the heart is often only temporarily weakened for one to three months while collateral circulation attempts to replace lost or lessened blood flow.(308)

Coronary occlusion is believed to occur in everyone if they

live long enough.(308,415)

The lipid hypothesis of coronary heart disease proposes that plasma lipids, particularly cholesterol, are involved in the development of atherosclerosis.(416-419) It has been proposed that the accumulation of lipid in the arterial wall involves at least three processes: (1) the transfer of plasma lipids or lipoproteins from blood to the artery (2) the binding and sequestration of lipids in the arterial wall, and (3) the metabolism and removal of lipids or lipoproteins from the artery. (413,420) Genetic factors alone, or in conjunction with, hyperlipidemia may participate in the development of atherosclerosis. (418) Genetic factors may include hypertension, abnormality in the structure and function of platelets, endothelial cells, and arterial smooth muscle cells.(421,422). Almost everything imaginable has been implicated. The various factors that have been related to arteriosclerosis and heart disease are illustrated in Figure 2.

Although exact mechanisms of hyperlipidemia's effects on the rate of atherosclerosis are not known, a considerable amount of epidemiological data suggests that hyperlipidemia is associated with the premature development of atherosclerosis.(423-425) Familial hyperlipidemia studies indicate that those members with genetically determined hyperlipidemia have a higher correlation with atherosclerosis which lends support to the lipid hypothesis. (426-423) Lipoprotein importance in the lipid hypothesis ^:s o^

Influencing Factor	Perceived Risk
Homogenized milk	0.2
Cholesterol in diet, refined sugar, hydrogenated fats, degree of water hardness	0.5
Zinc/copper ratio in diet	0.6
Lack of fiber, obesity, lack of exercise	0.7
Saturated fatty acids, hypertension, cigarette smoking	0.8
Stress of society	0.9
Heredity factors	1.0

Figure 2.—Perceived risk levels of possible influencing factors on coronary heart disease, (35)

current interest. It has been suggested that increased amounts of plasma high-density lipoproteins (HDL) have a "protective" role in lipid metabolism.(377,429-431)

Plasma lipoproteins are necessary for the transport of cholesterol.(432) These complex particles consist of a membranous coat of specific apoproteins, phospholipids, free cholesterol, and a non-protein core containing lipids.(433) Ultracentrifugation and electrophoresis have provided major classes of lipoproteins. Listed in order of decreasing density, protein and phospholipid concentration, and increasing triglyceride concentration, these include: (1) high density lipoproteins (HDL), (2) low density lipoproteins (LDL), (3) intermediate density lipoproteins (IDL), (4) *wery* low density lipoproteins, (VLDL), and (5) chylomicrons. Dietary and recycled cholestrol are transported initially after absorption in chylomicrons and VLDL fractions and eventually secreted via the thoracic duct into the bloodstream.(432) VLDL's contain about 15 percent of blood cholesterol with LDL's accounting for about 65 percent.(434) The ready uptake of LDL's by many tissues appears to be mediated by cell surface LDL binding receptors.(435-437)

Following release of LDL cholesterol in tissues, any excess not utilized by the tissue must be released into the extra cellular fluid for return to the liver where it may be incorporated into bile acid synthesis or may be excreted into the plasma. HDL may incorporate unesterified membrane cholesterol which is either

transferred to VLDL through the action of lecithin-cholesterol acyltransferase (LCAT) or directly returned to the liver.(434-436, 437) It is also suggested that HDL may directly block LDL cholesterol uptake by cell receptors and thus prevent cholesterol accumulation.(438) Approximately twenty percent of the plasma cholesterol is carried by the HDL and it has been suggested that the relative concentrations of plasma LDL and HDL could vary the balance of tissue cholesterol uptake and removal. Diet has been reported to have little effect on HDL as compared to LDL. HDL concentration is higher after puberty in females than males, is increased by physical activity, moderate alcohol ingestion and estrogens.(434)

Cholesterol's degradation and excretion from the body is achieved mainly through the conversion of cholesterol to bile acids, but is also converted to steroid hormones and by losses in feces and from the skin surface.(432,437)

The lowering of cholesterol levels in the plasma has been attributed to several factors.(433,439) Among various dietary components, fiber has been suggested as having an effect upon plasma lipids and cholesterol.(440) One reviewer found apparent disagreement in regard to the effects of dietary saturated fat on lipid metabolism. Hyperlipidemic or atherogenic effects were not seen with any of the fats when fed to rats with commercial laboratory rations.(440) However, when saturated fat was fed as part of a semipurified diet, it was definitely atherogenic and cholesteremic.(441 ,442) It was concluded that since the diets

had only saturated fats in common some other dietary component, most likely fiber, was accountable for the differences.(440)

Fiber's possible implication in influencing lipid metabolism has led to extensive research that has provided relevant data in the problems of coronary heart disease.(443)

It is believed that fiber, by binding bile salts, prevents the absorption of cholesterol and reabsorption of bile acids. Bile is secreted by the liver and is made up of a large quantity of bile salts, a moderate quantity of cholesterol, a small amount of the green pigment biliverdin and a number of other less important substances.(139) The bile salts are not enzymes, but act as a powerful detergent.(308) The detergent action aids in the intestine in mixing and breaking the large fat globules of the food into small globules. The smaller globules with their larger surface area allow the lipases of the intestinal tract to act more effectively. Without this action of bile *wery* little dietary fat would be absorbed. Bile secretion is a continuous process but the flow of bile into the intestinal tract is not continuous. A circular muscle, the sphincter of Oddi , around the outlet of the common bile duct prevents flow into the duodenum causing the bile to flow into the gallbladder. The gallbladder mucosa reabsorbs much of the fluid and electrolytes of the bile.(139,308) Concentration of bile may be as great as twelve-fold allowing the gallbladder with a maximum volume of approximately 50 ml, to accomodate the active components of the approximate 600 ml. daily

production by the liver.(308) Two simultaneously occurring mechanisms are believed to cause the gallbladder to empty into the small intestine. First, the presence of food (particularly fats) causes the release of cholecystokinin from the tissues of the duodenum, the hormone passes via the blood to the smooth muscle of the gallbladder and causes muscular contraction thus a release of the bile into the intestinal tract. Second, the presence of food in the duodenum increases peristalsis which causes inhibitory nervous stimuli to the sphincter of Oddi.(139,308)

Ninety to 95 percent of the bile salts that are ejected into the lumen of the duodenum are absorbed from the terminal ileum by an extremely efficient active transport system.(139) The resorbed bile salts are transported back to the liver via the portal vein and are eventually reexcreted in the bile. This system of excretion, reabsorption and excretion, is known as the enterohepatic circulation. The total bile salt pool of approximately 3.5g is repeatedly recycled in this manner. It has been estimated that the bile salt pool may recycle as many as six to eight times per day.(139) The bile salts not reabsorbed are eventually converted to the salts of deoxycholic acid and lithocholic acid,(286)

It has been proposed that fiber interferes with this enterohepatic circulation, thus increasing the rate of catabolism of cholesterol to bile acids.(299,444) This interruption in conjunction with the possibility that fiber could prevent micellar formation essential for cholesterol absorption could lower

cholesterol pools in the body.(443)

The effects of various forms of dietary bulk on serum lipids are not clearly understood but it is known that individuals on high vegetable content diets tend to have lower serum cholesterol levels than individuals on lower fiber diets.(68,445) True vegetarians whose cholesterol levels are about twenty-eight percent lower than those of the standard population ingest 125 percent more fiber. Lacto-ovo vegetarians ingest fifty percent more fiber and have cholesterol levels that are eleven percent lower.(299) These reports have been supported by others indicating that certain foods high in fiber influence blood lipid levels and atheroma formation.(446,447) Trowel l extensively reviewed the relationships and concluded that natural dietary fiber, which is a structural heterogenous mixture of celluloses, lignins and pectic substances could differ in their effects upon cholesterol.(81) Several investigators began to evaluate various fiber components effects on blood lipid values.

Bran and cellulose have little effect on lowering serum cholesterol in humans and other animals although they might increase fecal bile acids excretion.(19,29,446,448-454) Earlier animal studies indicated that certain dietary fiber components did affect serum cholesterol.(455,456) In one such study New Zealand white rabbits were fed a purified ration of 30 percent casein, 15 percent beef tallow, 15 percent ground cellulose, six percent salt mixture and other essential vitamins and minerals.

During the first five weeks of the experiment the purified rations were fed without added cholesterol, and during the second five weeks, cholesterol was added to the ration at the rate of 0.5 percent. The experimental data revealed that serum cholesterol concentrations in rabbits fed purified ration containing fifteen percent beef tallow were lowered with the addition of either five percent pectin or 0.5 percent cholestyramine to the ration during the five week period. The effects of the addition of both pectin and cholestyramine were additive in lowering the serum cholesterol values. During the second five week period of feeding, the same ration but with 0.5 percent cholesterol added, the pectin and cholestyramine, singly or in combination, slowed the increase in serum cholesterol.(457) Similar research in rabbits and other animals have shown a hypocholesterolemic action of pectin.(458-474)

Experimentation on human subjects have shown that pectin, guar gum, lignin, and mixed complex carbohydrates reduce serum cholesterol levels and increase fecal acidic and neutral steroids excretion.(19,21,299,475-478)

One report indicated that 15 grams of pectin per day resulted in a 15 percent drop in serum cholesterol, a 16 percent increase in fecal excretion of neutral steroids and a 40 percent increase in excretion of bile acids.(479) Another report showed no hypocholesterolemic effect by pectin.(480) Subsequently it was reported that the cholesterol-lowering effect of pectin was dose-related. (481) A plasma cholesterol decrease by two to six percent

was seen in 16 subjects when two to ten grams of pectin were administered. Another investigator found a twelve percent reduction in plasma cholesterol in seven men after two weeks of administration of 36 grams of pectin per day.(25)

Although no effect was seen on serum triglycerides the administration of 40 to 50 grams per day of pectin over a two week period to nine normolipidemic and hyperlipidemic patients showed a significant decrease in serum total and unesterified cholesterol. (482)

In addition to pectin, guar gum and psyllium seed celloid have been reported to yield an hypocholesteremic effect in man. (21,25,29,480) The substances are chemically dissimilar and it is suggested that their physical state in the intestine may determine their action. The presence of a gel in the intestine could cause interference with the equilibrium between the micellar phase and the molecular phase which- passes into the layer on the brush border and might reduce lipid absorption.(479)

The interrelationship of diet and lipemia is neither simple nor direct. One would hope that a simple nutrient ingestion and dose-response situation would exist, but unfortunately this is not so. The complexity of the modern diet and the interactions among dietary components are far from being completely clarified.

One dietary component, complex carbohydrates are generally found to reduce serum lipid levels, although it may be some time before assessment of what component and what quantity is needed

to produce the desired response.(21,483)

Gallstones and Cholecystitis

Disease of the gallbladder is secondary to gallstones in nearly all cases.(484) It has been reported that 98 percent of cholecystectomies in England and America are the result of stone formation.(485,486) In western societies 85 percent of the stones are cholesterol stones.(139) Minor components are made up of calcium carbonate, calcium palmitate and calcium phosphate.(487) Therefore, gallstones are caused mainly by the precipitation of the fatty product cholesterol which is excreted in the bile.(308, 484)

Formation of stones occurs in the gallbladder or bile ducts, either when an atypical material appears in the bile or the relative composition of the bile is altered in such a way that a normal constituent precipitates. Calcium billirubinate stones form if certain bacteria containing a glucuronidase deconjugate bilirubin in the bile. Calcium combines with the free bilirubin to form the highly insoluble calcium bilirubinate.(139) The ratio of cholesterol and bile acids normally is such that cholesterol remains in solution and stones do not form. If that ratio is altered with resultant super-saturated bile, precipitation and formation of stones occurs.(488-490)

Epidemiological studies have indicated gallstones are rare among primitive peoples, even though their diets are greatly varied.(50,449,491) Gallstone incidence is reported to increase

with urbanization and westernization.(423,484,492) Diseases associated with cholesterol-rich gallstones include obesity and diabetes.(493-498)

Gallstone patients have been reported to have bile salt pools reduced by as much as 40 to 50 percent of normal size.(499-501) In animals it has been shown repeatedly that liver synthesis of bile salts is inhibited when refined carbohydrates are added to the diet.(484) It has also been shown that in experiments with bile fistula, dogs in which there is a constant drainage of bile salts, the liver is stimulated to synthesize new bile salt at a maximal rate. In fasting dogs, synthesis could be increased when protein was fed, but this result could be reduced by pre-feeding high calorie semi-synthetic diets and completely abolished with the addition of sucrose,(502) Other animal studies indicate that bile salt synthesis is reduced on diets high in refined carbohydrates and little or no fiber,(293,434,503) Further studies have confirmed these findings, and have shown that dietary fiber markedly increases the intestinal bile salt pool,(286)

CHAPTER X

PHYSICAL ASPECTS OF DIETARY FIBER

Fiber as a Food Additive or Ingredient

Fiber materials such as polysaccharides have been used as functional ingredients in the food industry for many years. Among the primary fiber materials used are the "gums" which are used as gelling agents or stabilizers. Gums in this sense are considered to be polysaccharides that are dispersible in either hot or cold water to produce viscous mixtures or solutions.(299)

The structural and textural properties of plants are largely determined by the gum constituents present in almost all natural foods.(504) Gums are often used as food additives in prepared foods to impart desirable texture and functional properties to finished products.(505) Commercially gums are normally used as water soluble or water-dispersible hydrocolloids. Their properties usually consist of suspending, dispersion, and stabilization in aqueous dispersions. Gums may act as emulsifiers, adhesives, coagulants, binders, lubricants or film formers.(506)

Commonly used commercially available gums are shown in Figure 3.

Fiber Analysis

The quantitative and qualitative analysis of dietary fiber is a complex process. A mixture of various substances arising from the cell wall of plants and an array of polysaccharides occurring

Seaweed Extracts

- Agar
- Alginates
- Carrageenan
- Furcellaran

Plant Exudates

- Gum Acacia (Arabic)
- Gum Tragacanth
- Gum Ghatti
- Gum Karaya

Seed Gums

- Locust Bean Gums
- Guar Gum

Plant Extracts

- Pectin

Biosynthetic Gums

- Xanthan

Cellulose Derivatives

- Carboxymethyleel 1ulose
- Methylcellulose and Hydroxypropylmethylcellulose

Figure 3.--Commercially available gums.(506)

naturally or derived from food additives make up dietary fiber.

In order to facilitate research it would be desirable to fractionate plant-based foods into their various chemical constituents and accurately ascertain the quantity of each component. Current technology does not provide this approach, but a number of alternatives have been developed.

Historically, fiber analysis began in early ruminant nutrition studies.(507,508) These studies soon revealed that a significant portion of many forages were not digestable, and the amount of this fraction in a ration had a lowering effect on the availability of other components in the diet.

Crude fiber determination methods were developed in the early eighteenth century and were standardized by the Association of Official Analytical Chemists in 1887.(507) The method is still widely used even though its shortcomings are well documented.

New methods of analysis have been developed which have proven far more useful than crude fiber determinations. The increased interest in human nutrition and dietary fiber have produced a need for even better methods.

Crude fiber is defined as the resultant residue after treating a weighed food sample with solvents to extract lipids, then extracting with acid, dilute base and, finally weighing the sample.(299) This procedure is highly empirical, and strict adherence to procedural detail is required for reproductibility.

The resultant crude fiber is not of constant composition and does not accurately reflect hemicellulose and lignin amounts in the sample.(509-511) (see Appendix A)

The normal-Acid Fiber (NAF) method was developed as an alternative to the crude fiber method. An important difference is that the alkali stage was eliminated with a resultant minimization of variability encountered in the crude fiber method.

The results of this method are not greatly affected by variations in conditions, time of hydrolysis, sample size, and rate of heating (Appendix A). The crude fiber method is still more widely used than this method.

The Acid Detergent Fiber (ADF) work of Van Soest's is now regarded as classic in this area of research. His aim was to modify the NAF method and produce an acid fiber with a low nitrogen content.(509) The results of this work produced a method to measure a fraction that was closely correlated with the nutritive value of a forage. The ADF method produced a fraction composed mostly of cellulose and lignin.

The results of the ADF method correlate well with indigestible matter in ruminant nutrition and give accurate estimates of the cellulose and lignin content of forages. In regard to human nutrition problems arise in that recovery of one-two percent cellulose and lignin is difficult in small sample size and increasing the sample size results in problems with foaming and final filtration. Any samples with high lipid content must be

defatted. The major drawback to ADF is the inadequate measure of all dietary fiber in a sample (Appendix A).

The Neutral Detergent Fiber (NDF) method was also developed by Van Soest and is believed to yield accurate measurements of cell wall components in plant food stuffs. Apparently this method fractionates the dry matter of feeds into those components nutritionally available by normal digestive processes and those in which microbial fermentation is required.

In this method sodium lauryl sulfate, the detergent, solubilizes lipids and proteins, EDTA removes minerals, and heat gelatinizes and solubilizes starch (Appendix A).

The NDF method has proven useful for the estimation of total dietary fiber. Again problems have arisen when this method has been utilized for human foods. Precision is difficult due to small sample size and human foods are normally higher in starch and lipid contents thus requiring lipid and starch removal. Detergent soluble components may be lost in the process thus underestimating total dietary fiber in some samples. The sum of cellulose, lignin and hemicellulose are determined by the NDF procedure. A comparison of total dietary fiber and NDF fiber for selected foods is given in Appendix A,

The Unavailable Carbohydrate Method functions as a part of a more-or-less complete food carbohydrate analysis where unavailable carbohydrate is equated with total dietary fiber. The unavailable carbohydrate method is a quantitative index of

dietary fiber, but not a qualitative measurement of the dietary fiber components (Appendix A).

This method was elaborated by Southgate to give an index of total dietary fiber as the sum of its various components. Although this method does not isolate or characterize soluble polymers, it does yield values expressed in terms of sugar components. Problems arise with isolation of soluble proteins of foods high in sunflower or soy proteins. Amounts of pectins and gums are not quantitatively determined in this lengthy procedure.

The unavailable carbohydrate method was further modified by Englyst and Southgate.(513)

For studies of the polysaccharide composition of the plant cell wall Siege! developed a method that attempts to characterize components in specific fashion.(514) Polysaccharide degradation may occur in the delignification stage and alkali extraction. This method is not used frequently in human food analysis. A hypothetical complete analysis scheme proposed by Southgate is arduous and unrealistic for periodic genera! analysis.(512) (Appendix A)

Components of Dietary Fiber

The term fiber has caused much confusion and controversy. (10,45,518) Fiber illicits different responses from the botanist, cereal chemist, animal nutritionist and human nutritionist. There is yet no concise definition of fiber that conveys fully the

concept of fiber in human nutrition.(519) A major difficulty inherent in studies of human nutrition and food fiber has been a failure of agreement in what fiber actually is.(520) Until recently several terms have been used interchangeably indicating various fiber sources, thus producing experimental results often difficult to interpret and compare.(521)

Dietary fiber is a complex chemical substance of plant origin and the term generally refers to cell wall biopolymers. It is often defined as those components of foods that human enzymes do not break down in the digestive tract.

Terms often used to indicate fiber in human nutrition are:

CRUDE FIBER (CF)

DIETARY FIBER (DF)

PLANT FIBER (PF)

FIBER

NONPURIFIED PLANT FIBER (NPPF)

PURIFIED PLANT FIBER (PPF)

NONNUTRITIVE NATURAL FIBER

NONNUTRITIVE SYNTHETIC FIBER

UNDIGESTIBLE CARBOHYDRATE (UC)

UNAVAILABLE CARBOHYDRATE (UC)

PLANTIX (PX)

COMPLANTIX (CPX)

PARTIALLY DIGESTIBLE PLANT POLYMERS (PDPP)

PARTIALLY DIGESTIBLE BIOPOLYMERS (PDB).

The relationships of the components of dietary fiber and the proposed nomenclatures are shown in Figure 4.(76,515,517)

Industrial Applications of Food Fiber

Interestingly the role of dietary fiber in human nutrition has attracted the attention of the food industry. Breakfast cereal manufactures were the first to respond to the increased consumer awareness of dietary fiber.(522) Many commercially available products were already using bran as a component, thus little product development was required. Alterations in advertising emphasis have focused on the fiber component. Soon after breakfast cereal fiber emphasis got underway, the baking industry responded with "high fiber" products.(523) Promotional schemes emphasized the reduced caloric density and alluded to other possible benefits of fiber.(524)

Dietary fiber is now available in a variety of forms for manufacturers.(525)

Powdered cellulose

Microcrystalline cellulose

Wheat bran

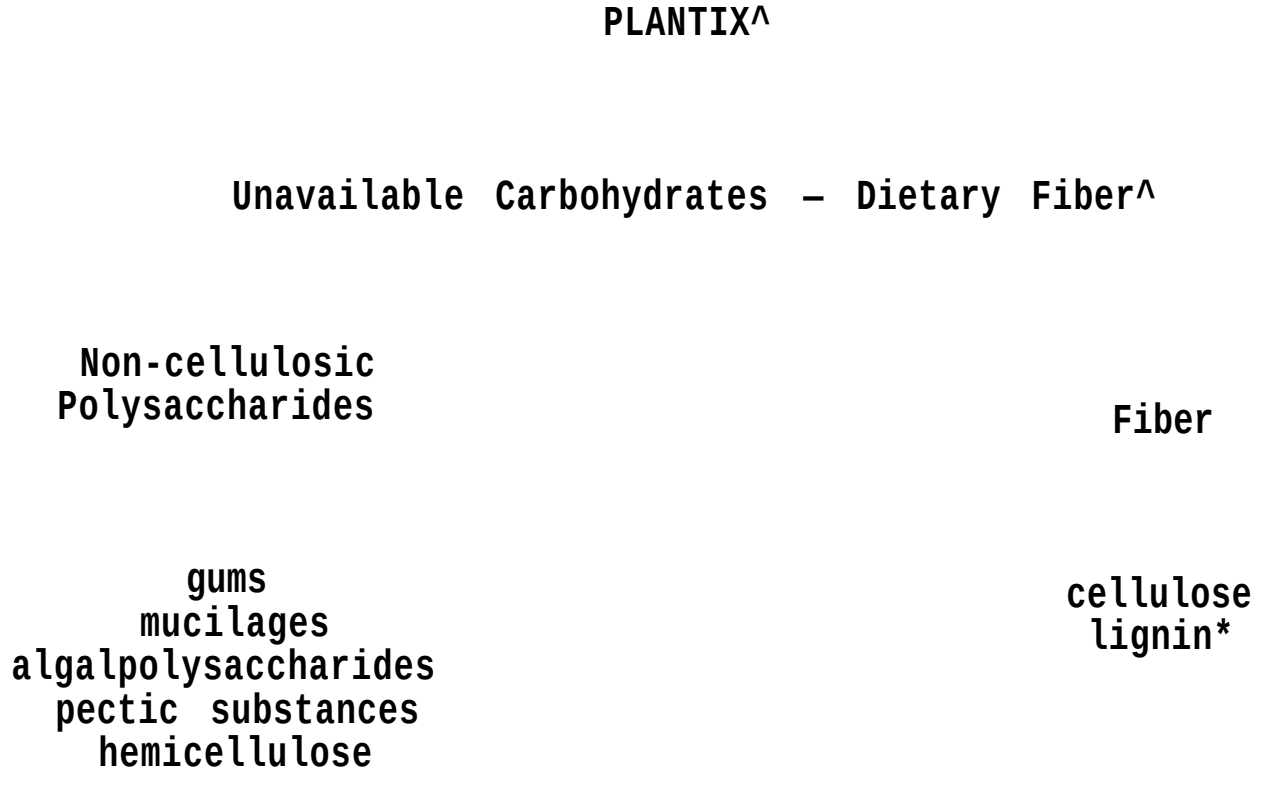
Corn bran

Soy bran

Oat hulls

Linseed meal (from cotton)

Rice bran



A. After Spiller and Shipley (517)

B. After Southgate (515)

* An aromatic polymer, not a carbohydrate,

Figure 4.--Classification and nomenclature of dietary fiber,

Corn germ meal

Wheat germ flower

Brewers spent grains

Wheat shorts

Wheat middlings

Nuts (fibrous skins)

Soybean hulls

Peanut hulls

Coconut kernal residue

Citrus pectin.

The first two materials are essentially purified cellulose products. The remaining products are normal by-products from various processing methods.

Powdered cellulose (alpha-cellulose) is usually derived from maple, birch and beech wood pulp. Bark is removed from the wood which is chipped, "cooked" in pressure digesters with appropriate solvents to dissolve lignin. The softened pulp is washed, bleached, then ground to appropriate size and texture.

Microcrystalline cellulose differs from powdered cellulose. Cellulose pulp is treated in a manner that hydrolyzes the fiber, breaking down the bundle-like structure of cellulose producing crystals. Drying processes cause the recombination of these crystals into an aggregate. Microcrystalline cellulose is commercially available in sizes ranging from two to two hundred microns.(299)

Purified cellulose is used in many foods because it achieves a lowered calorie objective and has specific functional properties including binding, consistency control, and absorption.(526) It is presently being used in flour based products, snack products, processed meats, sauces, salad dressings, sausage casings, and breedings for meat and fish.(299)

Wheat bran is probably the most widely used of any of the many by-products of commodity processing that are available as commercial sources of dietary fiber. Extensive studies of wheat fractions have produced considerable information in regard to particle size, density, hydration capacity, and ion exchange capacity.(522,527)

The development and introduction of high fiber breads by the baking industry has been a considerable undertaking. Many dietary fiber materials were discovered to be nonacceptable in bread formulas due to raw ingredient supply levels, color, flavor, and texture.(522,528,529) The most widely used fiber components are wheat bran and powdered cellulose followed to a lesser extent by corn and soy brans. Cellulose has been the most successful in producing a high fiber "white type bread." Citrus products have had problems with producing a bitter taste.(299)

Critics of the purified cellulose type breads claim that they are made with "sawdust." Such criticism reveals a lack of understanding to the wide spread nature of cellulose in foods consumed by humans. The use of this purified cellulose has permitted

the production of a bread with characteristics more similar to conventional white bread but with a much higher fiber content than even whole grain breads. An additional claim can be made for decreased caloric density.

One obstacle facing the food industry is that health claims in relation to dietary fiber have not all been substantiated. Thus in marketing techniques one is faced with limited ability to make health related claims. At present most labeling claims are related to "fewer calories," "increased dietary fiber," "less carbohydrate," and "get the roughage you know you need."

Current research by food processors is placing a degree of emphasis upon the consumers' heightened interest in dietary fiber and realize the existence of a market for high fiber products. The awareness of such a market has led to valuable basic research into fiber characteristics. Practical applications of this knowledge has led to many high fiber food products currently on the market.(530) Current research is also being aimed at more efficient use of fiber obtained from processing by-products.(299)

If the nutritionist accepts the idea of need for more fiber in American diets, the food technologist must be ready to answer some formidable questions in regard to fiber evaluation and what foods are the best vehicles. Work is now being carried on in order to produce standardization of methods in the evaluation of various fiber sources,(530)

If fiber is found to be a disease preventive measure in human

health, the vehicle selection becomes a complex situation. The material must be introduced into food products in such a way as to do the greatest good for the greatest number of individuals without detrimental effects to any sub-population.

CHAPTER XI

SUMMARY

The fiber hypothesis has brought forth much controversy. Although epidemiological evidence outweighs experimental data, we are seeing an emergence of facts about dietary fiber.

In regard to fiber's effect upon diverticulosis we see that colonic motor activity is affected. The exaggerated colonic intraluminal pressures of diverticulosis correlate with its pathology, i.e. hypertrophy of muscle. A hypertrophy believed to result from the propulsion of hard, small, low-volume stools. Lowered colonic pressure changes have been seen in diverticular disease patients given bran.(363) Bran supplementation has also been seen to improve patients symptomatica!ly.(296) The therapeutic value of bran in prevention of the disorder is not proven. Post-operative studies however indicate a possible prophylactic effect in those suffering from diverticular disease. (531)

Relationships between cancer and dietary fiber have been demonstrated by epidemiological data and studies with laboratory animals. Colonic cancer being the most often indicated in fiber-depleted diets. Research is being carried out as to whether these associations are causative and to determine possible meahanisms of action. Fecal bacteria determinations have often shown differences among populations with high and low rates of large

bowel cancer. These populations showed differences in fiber consumption but no great differences were seen in fat consumption or fecal steroids. The fiber hypothesis of colonic-rectal cancer is supported by such findings but does not refute the fat hypothesis. Fiber may exert its protective effects through binding to ingested carcinogens, diluting their concentration or decreasing their incubation time.

In regard to fiber's effect on fecal weight there seems to be agreement. The precise mechanism by which fiber increases fecal weight has not been determined but several theories are proposed.

CD

Transit time alterations by dietary fiber is a complex picture. Generally, investigators agree that transit time decreases as stool weight increases, but there are accounts of nonsignificant changes with increased fecal weight. It has also been reported that in those individuals with fast transit times prior to fiber supplementation there has been a slowing down of transit time. Heaton has suggested that the fiber has "normalized" colonic activity.(498) The concept of transit time is often over simplified, and should be considered in light of the mixing and streaming of the gastrointestinal contents. The passing of a single marker or a dye may not be indicative of actual processes. The data being gathered do suggest a significant influence of dietary fiber on food residue's passage through the gastro intestinal tract.

Fiber's relationship to coronary heart disease may be indirect A diet high in fiber is probably a diet already low in cholesterol. Caloric density is also generally lower in the higher fiber foods. If one accepts the idea of decreased transit time with increased dietary fiber, it is suggested that if food travels through the gastrointestinal tract more rapidly there is less opportunity for food to be broken down and absorbed. It has already been proposed that fiber in some way binds bile salts and alters both its metabolism and reabsorption. This decreased efficiency of reabsorption has been seen as a means of lowering body cholesterol pools via bile synthesis. Those that place reliance on this hypothesis indicate that this would yield a slowing of hardening of the arteries, as well as decreased incidence of gallstones.

If dietary fiber has a relationship to coronary disease its most important role may be in combating obesity. High fiber diets not only are normally lower in calories, but have been shown to generally produce satiety more rapidly than highly refined foods.

A correlation exists between obesity and diabetes.(532) High-fiber, high-carbohydrate diets have been shown to have beneficial effects on glucose tolerance and the insulin dependency of many diabetics. More and more consideration is being given to fiber's effects upon hypoglycemic rebound.

Another protective influence of fiber is its suggested role in lowering or alleviating certain toxic effects of various drugs, chemicals and food additives.(533) It should be noted that

indications are that different plant fibers vary significantly in their ability to counteract toxic effects.

The widespread interest in dietary fiber is shared by those working in nutrition and medicine as well as by the lay person. The latter often seeing it as a "health" food which will cause phenomenal changes in his well being. This perception of dietary fiber's role in nutrition is a logical offshoot to the trends in the "back to nature" movement of late. It may just be this movement that has spurred much of the fiber research being done by the food industry. An obvious market is ready and waiting to consume high fiber "health foods,"

These popular concepts about food fiber need to be tempered with some of its possible harmful side effects. One of the advantages of white flour is that the major source of phytates is removed, Phytate's effect on calcium absorption may have been overstated, but with the recognition of the importance of the trace minerals, one must consider fiber's effect on them. If the intake of such divalent metal ions as zinc, chromium, magnesium, and copper is marginal at best in some populations a deficiency state is a recognized possibility in high phytate content diets.

Anatomically over consumption of fiber may produce pathological states involving the gastrointestinal tract.

In those cases where caloric adequacy is a problem, one would be wise to attempt to reduce fiber amounts thus increasing caloric density. It has also been reported that certain food fiber

may contain trypsin and chymotrypsin inhibitors, thus adding to the problems of those already existing on a marginal diet.

CHAPTER XII

CONCLUSIONS AND RECOMMENDATIONS

Any dietary component when considered alone produces debatable information. Dietary fiber is no exception especially in light of all that has been attributed to it. Fiber may not have all these "health" promoting characteristics, but the controversy over fiber has greatly stimulated its research. That research has already proven beneficial in several health problems and may provide more.

Dietary fiber's correlation with leading diseases is currently a favorite basis for many hypotheses. Despite the controversy surrounding dietary fiber there appears to be potential for fiber in preventative medicine through good nutrition that uses food as the mode of conveyence.

In general it is recommended that people increase the overall consumption of dietary fiber in light of its relationship to intraluminal pressures. Increased dietary fiber has a high correlation with larger and softer stools. Resultant reduced intraluminal pressures in the lower gastrointestinal tract relieves symptoms of diverticular disease and related gastrointestinal disorders. Reduction in such pressures may play a role in the prevention of muscle hypertrophy and lessen the danger of high pressure damage to weakened areas in the bowel wall.

These same alterations brought about by fecal matter density and volume may act as a preventative measure in constipation thus

aiding in reducing defecation straining and lessening the intraabdominal pressures that may lead to retrograde pressures in the venous system therefore reducing the likelihood of vericose veins and hemorrhoids.

Another important aspect of increased fiber consumption is its relation to caloric density and energy consumption. Higher fiber foods tend to be lower in calories per unit than fiber depleted or low fiber foods. Overnutrition is a major health problem in developed countries of the world. It is therefore recommended that we encourage increased consumption of high fiber foods in order to take advantage of lowered caloric density, and satiety factors related to less refined foods.

There is increasing evidence that coronary heart disease is essentially the result of habitual overnutrition. Epidemiological studies indicate that prevalence of the coronary heart disease in various countries correlates with the per capita caloric consumption. This correlation appears to exist in all four primary coronary risk factors: (1) systolic blood pressure, (2) serum cholesterol, (3) fasting blood sugar levels and (4) serum uric acid levels. The major emphasis in any discussion of dietary fiber and heart disease should center not on the "curative" effects of a single food component, fiber, but on the effects of reduction of fiber in the diet in total. The factor which most strongly relates fiber depleted diets with increased incidence of heart disease is not simply fiber but the increased caloric density and

concurrent overnutrition (malnutrition) that attends the "westernization of the diet." The modern diet makes the ingestion of excess calories, i.e. physiological excesses of nutrients, an easy possibility. Thus a derangement of diet exists, so easily obtainable, rather than a disorder of the individual. Many of our familiar carbohydrate foods (sugars, flours, and breakfast cereals) are processed in such a way as to remove a high portion of the dietary fiber materials with resultant foods not only more easily ingested but more calorically dense than their less processed counterparts. One of the more dramatic examples is the use of refined sugars in the increasingly popular sweetened beverages. The shortened ingestion time coupled with lessened bulk produced a secondary lessening of satiety level thus enhancing the likelihood of over consum.ption especially in regard to calories (and secondly a lack of other nutrients that accompany the calories in less processed or refined foods).

If this view is correct, the prevention of the disease may be closely correlated with the maintenance of a thin physiological physique. The content and type of fat in the diet may become of little or no importance if the total diet makeup and energy intake is correct for body size, age, sex and metabolic state.

Dietary fiber's relationship to cancer is less clear, but it is believed that the fiber depleted diet promotes fecal stasis. The resultant increase in transit time allows for increased bacterial proliferation, increased time for conversion of potential

carcinogens and contact with intestinal mucosa. I suggest that the increased consumption of dietary fiber may provide protection via one of the following effects attributed to dietary fiber: (1) decreased transit time, thus reduced exposure to carcinogens or potentially toxic materials, (2) increased peristalsis as a result of increased water-binding properties of various fiber components, (3) increased volatile fatty acid production with a cathartic effect, (4) bile acid metabolism alterations, (5) dilution of intestinal contents and (6) binding capacities which may reduce the absorbability and reactivity of other intestinal contents.

Development of a recommended intake of dietary fiber should be considered as a distinct possibility. At present there is no consensus of what constitutes a suitable level, hence parameters need to be established to assess recommended levels in average adult humans. The following criteria might be used as a starting point: (1) establish fiber intake which produce 140-150 g/day of feces (a level which normally decreases transit time but does not interfere with predicted motility), (2) adjust fiber intake to levels which produce transit times of 24-48 hours, and (3) use of fecal weight and transit time correlations to arrive at dietary needs of fiber which produce the desired fecal weight.

Consideration must be given in regard to body weight, age, sex and the various sources or types of fiber ingested. The level will probably approximate .3-.5 g bran or equivalent per kg body weight as a minimum.

In regard to diabetes there is no one "diabetic diet" appropriate for all cases. Individual variations, disease severity, the type and extent of insulin therapy administered and the level of physical activity will alter the dietary needs. Caloric content of the diet must be established in regard to the patient's desirable weight as compared to actual weight. The overweight diabetic requires a dietary regimen aimed at achieving a "diabetic" ideal weight of about ten percent lower than the statistically desirable weight. Once this level is reached the diet must be altered to maintain this reduced weight. Insulin treatment without a carefully coordinated dietary regimen risks the possibility of insulin-induced hypoglycemic shock and the dire consequences of poorly controlled metabolism.

The single most important objective in adult onset diabetes should be weight reduction. Responsiveness of cells to insulin largely depends upon their size.

In light of the relationship of weight to diabetes and the experimental evidence indicating lessened plasma glucose, more normalized insulin and glucagon responses after ingestion of high fiber meals, we need to stress this relationship and encourage continued investigations into these responses.

Implementation of increased awareness and use of high fiber foods has already begun in that the public has been exposed to "natural" and/or return to "nature" concepts (perhaps not always supported with sound reasoning or evidence) as well as an ever

widening selection of commercially available "high fiber" foods. Perhaps the better vehicle for such increased usage of dietary fiber will be through encouragement of the use of a varied diet with emphasis on increased use of vegetables, fruits, and legumes. In this manner one would remain within the scope of traditional nutritional education without the incorporation of new "high fiber" food products. The advantages of such encouragement include using an existing system, thus lessening learning time, and expense, using readily available food vehicles and perhaps incorporate what is referred to as "food specific satiety."

The increased utilization of dietary fiber will probably do no harm, except in a few specific instances. Current evidence indicates that a general increase in use along with proper intake of other nutrients will prove beneficial to man.

When considering the effects of dietary fiber one must remember all the variables involved, i.e. components of the fiber, stage of plant development upon extraction and the extraction process itself. These variables as well as the physiological and hereditary aspects of the test animal are crucial in determining fiber's influence. All test animal results cannot necessarily be applied to humans. I do encourage the use of the appropriate test animals and increased utilization of human subjects.

This author would like to caution against relying upon indiscriminate associations with various fibers and their effects. One must remember that the "type" of fiber varies with the maturity

of the plant as well as the extraction process utilized for obtaining "pure" fiber. It is most likely that the influences of individual fiber components may greatly vary as compared to the "whole" plant with its mixture of fibers and other nutrients. A natural matrix effect of these fibers and nutrients may produce a completely different effect than a similar amount of purified component.

A current trend in the consumer awareness of "health foods" is the use of individual nutrients sometimes in pharmacological rather than physiological levels. This practice could have dire consequences in some individuals, especially those in marginal nutritional status in regard to those nutrients most affected by dietary fiber (i.e. fats, fat soluble compounds, and minerals). I would like to reiterate that the best way to increase intake of dietary fiber is through a good mixed diet. Such a diet enhances our ability to gain the essential nutrients as well.

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APPENDIX A

FIBER ANALYSIS METHODOLOGY

APPENDIX A: FIBER ANALYSIS METHODOLOGY

Standard (AOAC) Crude Fiber Analysis

Air-dry sample

Extract with diethyl ether or petroleum spirit

Heat 30 min in boiling 0.255 N H_2SO_4

Filter and wash residue with hot water

Heat 30 min in boiling 0.344 N NaOH

Filter, wash with hot acid, hot water and finally alcohol

Dry and weigh

Ignite at 600^0

Reweigh

$$\text{Crude fiber} = \frac{\text{loss in weight}}{}$$

Summary of crude-fiber method (512)

Air-dry sample
(finely ground, 0.3 -v 1 mm sieve)

Extract with ethanol:benzene
8 h

Boil under reflux in IN H0SO4
(1 g/200 ml acid)
60 min

Filter, wash with hot water
alcohol and diethyl ether

Dry and weigh

On a replicate

Measure total nitrogen

Ash at 500^0

$$\text{Normal-acid fiber} = \frac{\text{loss in weight - (total N x 6.25)}}{}$$

Summary of normal-acid-fiber method (512)

Air-dry or fresh sample

Boil under reflux in IN H_2SO_4 containing
20 g CTAB/liter
0 g/100 ml acid)
60 min

Filter, wash with hot water and
acetone

Dry and weigh

Acid-detergent fiber ~ gain in weight

Summary of acid-detergent fiber method (512)

Air-dry or fresh sample

Boil under reflux with buffered
SLS (30 g/liter) solution
containing borate, phosphate, EDTA,
and 2-ethoxy ethanol
(0.5 '^^ 1 g/lQO ml

Filter, wash with hot water and acetone

Dry and weigh

Ignite

Reweigh

$$\text{Neutral-detergent fiber} = \frac{\text{loss in weight}}{}$$

Summary of neutral-detergent fiber method (512)

Food Sample

Extract with 90% v/v ethanol

Residue dried and weighed

Starch measured in residue

Total nitrogen measured

$$\text{Unavailable carbohydrate} = \frac{\text{residue insoluble in alcohol - (starch + total N X 6.25)}}{}$$

Total unavailable carbohydrate (512)

Food Sample

Extraction of Starches
lipids, pigments, etc.

Extraction of water-soluble
components

Fractionation

Acidic Components

Pectin
Alginates

Neutral Components

Starch
-glucans
Arabino-xylans
Arabino-galactans
Galacto monnans
Cellulose ethers,
etc.

Fractionation of
water-insoluble
components

Non-cellulose Cellulose Lignin

Complete fractionation of all polysaccharides (512)

Food^	NDF	Total Dietary Fiber
Bread, white	4.2	4.6
Flour, white	2.9	3.5
Flour, whole meal	10.3	11.0
All bran	27.9	29.7
Cornflakes	5,9	11.7
Bran^	53.9	48.0
Applet	14.7	9.2
Orange	10.5	13.7
Lettuce	25.4	37.2
Carrot	10.8	38.6
Pea	51.0	47.6
Potato	14.1	18.8

(g per 100 g dry matter)

A. Analysis carried out in different samples therefore comparison not exact.

B. Endosperm levels vary in brans.

C Different varieties analyzed - refers to apple, fresh.

Comparison of total NDF and total dietary fiber in selected foods (513)

A comparison of crude fiber and dietary fiber in foods commonly considered good sources of fiber.

Food	Crude Fiber* g/100 g	Dietary Fiber"^ g/100 g
Breads and cereals		
All bran cereal	7.8	26.70
Puffed wheat	2.0	15.41
Cornflakes	0.7	11.00
Whole wheat bread	1.6	8.50
Puffed wheat, sugar :oated	0.9	6.08
Vegetables		
Peas, canned	2.3	6.28
Sweetcorn, cooked	0,7	4,74
Broccoli tops, boiled	1.5	4,10
Carrots, boiled	1,0	3.70
Lettuce, raw	0,6	1.53
Fruits		
Peaches, with skin	0.6	2.28
Strawberries, raw	1.3	2.12
Apples, without skin	0.6	1.42
Nuts		
Peanuts	1.9	9.30
Brazil	3.1	7.73
Peanut butter	1.9	7.55

* Crude fiber data from U.S.D.A, Handbook 8, Composition of Foods,
•• Southgate et al, (513)

APPENDIX B

DIETARY FIBER IN SELECTED FOODS

APPENDIX B: DIETARY FIBER IN SELECTED FOODS

Comparison of selected foods fiber content as determined by various methods (517)

g/lQO g dry matter

	Crude Fiber	Plantix (NDF + P)	1 ctin	Neutral Detergent Fiber
Apples (peeled)	4	29	17	12
Carrots	6	28	19	9
Lettuce	12	21	4	17
Cabbage	8	19	5	14
Squash	6	18	3	15
Oranges	3	16	12	4
Potatoes (peeled)	1	12	7	5

Pectin = soluble + insoluble pectins.

NDF = cellulose + hemicellulose + lignin.

Dietary Fiber in Various Foods (513)

	Total Dietary Fiber	Noncellulosic Polysaccharides	Cellulose	Lignin
Flours		g/100 g		
White	3J5	252	0.60	0.03
ulT .	7-87	5,70	1.42	0.75
Whole meal	9.51	5,25	2.46	0.80
Bran	44,00	32.70	8.05	3.23
Breads				
White	2.72	2.01	0.71	Trace
Brown	5.11	3,53	1.33	0.15
Whole meal	8,50	5!95	1.31	].24
Leafy vegetables				
Broccoli tips (boiled)	4,10	2,92	1.15	0.03
Brussel sprouts (boiled)	2,86	1.99	0.80	0.07
Cabbage (boiled)	2.83	1.76	0.69	0.38
Cauliflower (boiled)	1.80	0.67	1.13	Trace
Lettuce (raw)	1.53	0,47	1.06	Trace
Onions (raw)	2,oO	1,55	0.55	Trace
Legumes				
Beans, baked (canned)	7,27	5,67	1.41	0.19
Peas, frozen (raw)	7.75	5.48	2.09	0.18
Root vegetables				
		2.22	1.48	Trace
Carrots, young (boiled)	3.70	3.77	1.13	Trace
Parsnips (raw)	4.90	1.50	0.70	Trace
Turnips (raw)	2.20			
Potato				
Main crop (raw)	3.51	2.49	1.02	Trace
Canned (drained)	2.51	2.23	0.28	Trace
Other				
Tomato (fresh)	1.40	0,65	0.45	0.30
Tomato (canned, drained)	0.85	0.45	0.37	0.03
Sweetcorn (cooked)	4.74	4.31	0.31	0.12
Sweetcorn (canned)	5.69	4.97	0.64	0.08

After Southgate et al. (513)