THE EFFECT OF EVAPORATED MILK AND WHOLE CORNMEAL ON INTESTINAL TRANSIT TIME AND HYDROGEN RESPONSE IN LACTOSE MALABSORBER NIGERIANS

By

Bernice Olu Adeleye

Bachelor of Science in Home Economics

Oklahoma State University

Stillwater, Oklahoma

1980

Submitted to the Faculty of the Graduate College
of the Oklahoma State University
in partial fulfillment of the requirements
for the Degree of
MASTER OF SCIENCE
July, 1981

THE EFFECT OF EVAPORATED MILK AND WHOLE CORNMEAL ON INTESTINAL TRANSIT TIME AND HYDROGEN RESPONSE IN LACTOSE MALABSORBER NIGERIANS

Thesis Approved:

Esther Winterfeldt
Thesis Adviser

Mary Alice Kenney

P. Larry Claypool

Norman N Durham
Dean of the Graduate College

ACKNOWLEDGMENT

The opportunity to work on this project was afforded me by Dr. Donna Payne-Bose. Although circumstances beyond control prevented her full contribution to this work, she made a noteworthy contribution.

My appreciation goes to Dr. Esther Winterfeldt, my adviser, for her assistance and guidance in the course of my study and in completion of this thesis. The encouragement and help she offered me was immeasurable.

My special acknowledgment and profound gratitude to Dr. Robert D. Morrison, a member of my committee and statistician who did the statistical design and analysis of this study. His willingness, readiness to help and unflinching support made the completion of this thesis possible. The tremendous help he offered me will forever remain in my memory.

I wish to express my gratitude to other members of my committee, Dr. Mary Kenny and Dr. P. L. Claypool for their support in the final preparation of this thesis.

I am indebted to Dr. Asegash Tsegaye with whose help the data used for this study was collected. I appreciate her self sacrifice and invaluable contribution.

Finally, my greatest appreciation goes to the members of my family - my husband, Niyi, and our children, Seun and Banke, with whose endurance, cooperation and love my academic achievements were made possible. They

are the major architects of my success. It is to them I dedicate this thesis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Figure Page

CHAPTER I

INTRODUCTION

Milk is the most acceptable food for infants, either from human or animal sources, but after infancy many humans cannot absorb the carbohydrate in milk. The disaccharide, lactose, is one of the solid components in milk; other nutrients are fats and protein. This disaccharide is unique because milk is the major source of the sugar. Lactose is hydrolyzed to the monosaccharides glucose and galactose by lactase, a specific intestinal betagalactosidase that acts only on lactose, primarily in the jejunum (1). Congenital, secondary, and primary forms of lactase deficiency have been described in man (2). The exact onset of this deficiency is as yet inconclusive.

Lactase presence in the intestine of infants enables them to absorb the lactose in breast-milk without any intolerance. As Kretchmer (1) states:

> Lactase is not present in the intestine of embryo or the fetus until the middle of the last stage of gestation and its activity attains a maximum immediately after birth. Therefore, it decreases, reaching a low level, for example, immediately after weaning in rats, and after one and a half to three years in most children (p. 72).

For many years it has been thought that all humans had the ability to absorb lactose. This erroneous belief might have been perpetuated by the initial research conducted in the United States and Europe which stated that "in normal humans, everywhere, lactase production remains

at a high level through life, which permits milk consumption without adverse effects regardless of age" (3, p. 823).

The implication of indiscriminate milk ingestion was revealed when the research conducted at the John Hopkins University School of Medicine demonstrated that lactose intolerance not only exists, but that there is a difference between races. Furthermore, the study shows that milk consumption might induce illness in some people (4). Other studies conducted in different parts of the world confirm lactose malabsorption and intolerance among Sub-sahara Africans and their overseas descendants, Native Americans, Near Eastern people, Italians and Greeks, Spaniards and Northern Europeans, Indians, Southern Asians, and Far Easterners (5). These reports indicate that "more groups all over the world are intolerant to lactose than are tolerant" (1, p. 73). As Kretchmer (1) reports,

> . . . real adult tolerance to lactose has so far been observed only in Northern Europeans, approximately ninety percent of whom tolerate lactose, and in a number of two nomadic pastoral tribes in Africa, of whom about eighty percent were tolerant. Although many other generally tolerant groups will be found, they will belong to a minority of human species (p. 73).

The high incidence of lactose intolerance and lactose malabsorption reported by many researchers indicated that lactose malabsorption is "worldwide and not uncommon" (6, p. 394). Lactose tolerance studies conducted in Nigeria confirm high incidence of lactose malabsorption among the Nigerian population except the nomadic Fulani ethnic group of the North (6, 7, 8, 9).

The four major tribes of Nigeria are the Hausa, Fulani, Ibo, and Yoruba. The Yoruba and the Ibo ethnic groups settled in the southern states of the country. These ethnic groups are non-milk producing and non-milk drinkers. The occurrence of tsetse flies (a deadly insect to

cattle) is a serious deterrent to cattle raising in this part of the country. In contrast, the Hausa and Fulani of the Northern States are exposed to dairy milk, and they do drink either fresh or fermented milk.

The Fulanis are traditionally herdmen and are one of the early people to have practiced dairying, probably as early as 4000 B.C. (10). This group drinks the milk collected from their cows fresh and sell the unconsumed milk to the town and village people in a fermented form called nono, a yogurt-like product almost devoid of lactose. At times nono is thickened with millet or other cereals to produce another different product. The typical Fulani is found to possess a remarkable tolerance to lactose (9). Their offspring (Hausa-Fulanis), as a result of intermarriage with the Hausa, have an entirely different life pattern compared with their ancestors; they have different patterns of milk ingestion and response to lactose.

Milk consumption was not introduced to the southern ethnic groups until the late nineteenth century when Britain colonized this part of the country. Many Yoruba and Ibo youngsters migrated to Europe to acquire an education. In the process, they were exposed to European diets, which usually included milk and milk products, and adopted this eating pattern. Although few in number, these Nigerian youngsters made an impact on milk consumption among the non-milk consuming ethnic groups of the southern states of Nigeria. The milk consumed by these non-milk producing areas are imported from abroad in powdered and canned evaporated form.

Although milk consumption is not new to the majority of the southern ethnic groups of Nigeria, many elderly and some young adults still resent milk drinking. Milk consumption, however, is gaining more

popularity among the elites most especially as in tea, coffee, cocoa, and corn pap (a gruel made from whole corn, and a popular breakfast meal of many Nigerians). The awareness of the nutritive value of milk might be a factor in the increased milk consumption among young educated Nigerians.

In response to this increased milk demand and consumption in the Nigerian population, both the public and private sectors of the economy are seeking modern animal husbandry techniques to eliminate the deterrent associated with cattle raising in the southern states and increase the existing milk production establishments in the northern states in order to meet the demand and reduce importation of milk to the barest minimum. The success of this effort would mean an increased milk availability to the Nigerian population at reasonable cost.

Significance of the Study

Milk consumption, as a beverage, is not a common practice among many Nigerians. The major forms of milk consumption are in tea, coffee, cocoa, and considerable amounts of milk is consumed with corn pap. With the current wave of milk demand and consumption in Nigeria and the commitment of both private and public concerns to boost milk production, milk is likely to assume a significant role in supplementing high carbohydrate foods commonly consumed in the population. Thus, more milk would be used in meal preparation and directly added to foods and not much as a beverage. Information available in the literature on lactose malabsorption when milk is consumed with other foodstuffs are very scanty. There is no available information on the effect of milk-whole corn products on the intestine transit time or hydrogen response of

lactose malabsorbers.

Previous studies reported lactose malabsorption in an average of 81 percent of the Nigerian population (8). Corn pap, a whole corn product, is one of the common breakfast meals of many Nigerians to which milk is added. It would, therefore, be appropriate to assess the effect of evaporated milk and evaporated milk with whole corn product on intestinal transit time and hydrogen response of lactose malabsorber Nigerians.

Purpose and Objectives

"Excessively rapid small bowel transit is commonly considered to be a cause of malabsorption and diarrhea" (11, p. 546). Bond and Levitt (12) reported decreased intestinal transit time when some quantity of dietary fiber was added to the diet. Most investigations on lactose malabsorption have focused on determining the occurrence of this condition in the population. Most of these studies failed to relate to the true pattern of milk consumption in the population studied. This research was designed to assess the effect of evaporated milk with whole cornmeal test meal on the intestinal transit time and to compare the breath hydrogen response of this test meal to undiluted evaporated milk test meal in a group of lactose malabsorber Nigerians.

The two major objectives of this study were: (1) to determine if there was any difference in the intestine transit time when evaporated milk (EM) was consumed as compared with the consumption of evaporated milk with whole cornmeal test meal (EMWC), (2) to compare the breath hydrogen responses of EM meal with an EMWC meal, and (3) to make recommendations for further studies based on the findings of this study.

Hypotheses

The hypotheses postulated for this study were as follows: (H_1) there will be no significant difference in the intestine transit time when EM test meal is consumed compared with EMWC test meal. (H_2) there will be no significant difference in the hydrogen response when EM test meal is consumed compared with EMWC test meal.

Assumptions and Limitations

The data in this study were obtained using the gas chromatographic procedure, an analysis based on gas produced as a result of colonic bacteria fermentation of unabsorbed lactose. It is assumed that hydrogen production occurs almost entirely in the colon, and small bowel production of hydrogen would be negligible (11). It was the researcher's assumption that the amount of expired breath hydrogen would reflect the degree of lactose malabsorption and could be quantified by gas chromatograph. The extent to which human subjects could be controlled in an experimental situation was recognized as a limitation of this study.

Definitions

The following terms are defined for the purpose of this study:

Breath hydrogen analysis (BHA): A technique for investigating lactose malabsorption. The fermentation of unabsorbed lactose exposed to intestinal bacterial results in intraintestinal production of hydrogen gas (13) which is expired through the lungs. The expired breath hydrogen is collected in a breath hydrogen collection apparatus and analyzed by gas chromatography.

Lactose malabsorption: Expired breath hydrogen above 20 ppm (14)

after the ingestion of 240 ml. of undiluted evaporated milk containing 24 gm. lactose.

Transit time: The time recorded for the first of three successive breath hydrogen values greater than the fasting hydrogen concentration that occurred sixty minutes after ingesting of the test meal. This time is taken to represent the small intestine transit time of the lactose as it passes through the gut.

Evaporated milk: Kotschevar (15, p. 255) described evaporated milk as: "milk meeting high standards, with 7.9 percent milkfat and 18.0 percent non-fat milk solids; homogenized and fortified with vitamin D to yield twenty-five United States Produced (USP) units per fluid ounce."

Lactose: A reducing disaccharide, that yields D-galactose and D-glucose on hydrolysis (16).

Malabsorber: Abnormal absorption of nutrients (17). This could be due to reduction in the number of functioning villi, a lack of specific enzymes (such as lactase in lactose malabsorption) or other variety of intestinal malfunctions.

CHAPTER II

REVIEW OF LITERATURE

In early encounters, milk intolerance was often attributed to the allergic reaction to the protein fraction of milk or an intestinal disturbance. Although as early as the 1920's the right concept to this problem was being sought, it was not until the late 1960's that it became clear that intolerance to milk, a symptomatic effect of lactose malabsorption, was not an intestinal disturbance but a condition associated with low intestinal lactase. Various studies had reported high incidence of lactase deficiency in different races and many ethnic groups around the world (3, 8, 18, 19). Simoons (5) described lactase deficiency as a "condition characterizing the vast majority of the world's people and was the early and normal state of mankind" (p. 595).

Many studies had been conducted to understand the incidence of lactose malabsorption and to devise an easy diagnostic method to measure the occurrence of lactase deficiency and lactose malabsorption in man. In this review, lactose and lactase deficiency, lactose malabsorption, the prevalance of lactose malabsorption in the world population and detection methods for lactose malabsorption as well as intestinal transit time of unabsorbable carbohydrates will be discussed.

Lactose and Lactase Deficiency

Lactose is a β 1$\rightarrow$4 glycosidic linkage disaccharide, synthesized

only by cells of lactating mammary glands (1). Lactose, a reducing disaccharide is found only in milk, otherwise it does not occur in nature (16). Lactose in cow's milk was estimated at 5 percent and 7 percent in human milk (20). When lactose is hydrolyzed by mineral acids or by the action of the enzyme lactase, equimolar quantities of D-glucose and D-galactose are produced.

Lactase, the enzyme that hydrolyses lactose is a β-galactosidase. Three β-galactosidases have been identified: a specific β-galactosidase with maximum activity at pH 6.0, located in the brush border; β-galactosidase with similar pH optimum located in the cytoplasm but inactive against lactose; and lysosomal β-galactosidase with pH optimum of 4.5 (10). The specific brush border β-galactosidase located in the jejunum has been described as the only β-galactosidase with the property of digesting lactose (1).

There has been considerable agreement about the pattern of intestinal lactase activity in the majority of the world's population and in the ability to digest lactose. In man, as in many other species, it has been observed that lactase activity culminates with birth, followed by gradual decline in lactase activity, reaching a low level immediately after weaning in rats and one and a half to three years in most children (1). The disaccharidase regression continues as one grows, reaching its lowest level in adulthood. Disintegration of intestinal lactase activity had been observed in almost all races investigated except the Caucasians, the Fulani and Tussi, the majority of whom tolerate considerable amounts of lactose in adulthood (10).

In an individual with "normal" intestinal lactase activity, lactose upon ingestion combines with lactase at the brush border and is broken

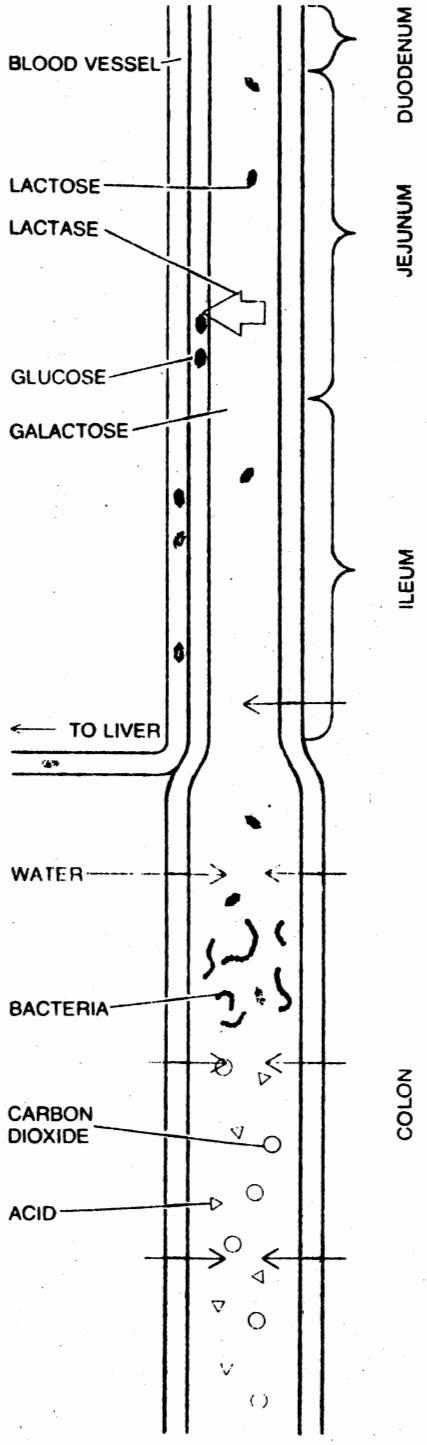
down into its simple sugars (glucose and galactose). The products of the hydrolysis of lactose could be utilized by local cells and the excess sugar passively diffuses across the mucosa into the bloodstream. This is followed by uptake into the appropriate cells. With the fall in the intestinal lactase activity, lactose ingestion in higher proportion to the intestinal lactase constitutes a problem (see Figure 1). Some of the intact lactose passes into the bloodstream while most of it goes to the ileum and colon. The unhydrolyzed lactose increases the intestinal content by acting osmotically, drawing water from the tissues into the intestine.

In the colon, lactose is fermented by colonic bacteria, resulting in production of carbon dioxide, hydrogen and other organic acids. Symptomatic effects of colonic lactose fermentation may be those of any fermentative diarrhea, including a bloating feeling, flatulence, bleaching, cramps, and watery explosive diarrhea (1). The symptoms associated with lactose malabsorption was illustrated in a step by step manner by Kretchmer, Ransome-Kuti, Hurwitz, Dungy, and Alakija (6). Reflecting on their own experience with this condition, they noted that

> The first clinical signs of lactose intolerance developed within 1-2 hours of ingestion of 2 g. per kg. of this disaccharide, and took the form of a vague feeling of hunger rapidly followed by bloating, eructation, and flatulence. Diarrhea ensued rapidly as a watery, fermentative explosion with bouts occurring every 15 to 30 minutes for 2-5 hours, associated with transitory wave-like cramps and a loss of appetite (p. 393).

When these or similar symptoms were experienced by lactose malabsorbers as a result of milk ingestion, they would either eliminate milk from their diet or limit milk intake to the amount that could be tolerated.

The incidence of lactase deficiency resulting in lactose malabsorption or milk intolerance had been well studied; the cause and prevalence



Source: Kretchmer, M., Lactose and lactase, Sci. Am. 227:75, (1972)

Figure 1. Digestion of Lactose.

had been documented.

Lactose Malabsorption

The incidence of lactase deficiency and the resulting lactose malabsorption were recognized decades ago. Jacob (21), an American Pediatrician, recognized that diarrhea observed in babies after the ingestion of milk could be associated with carbohydrate ingestion. As early as 1921, Howland (22) suggested that deficiency in the hydrolysis or enzymatic breakdown of lactose might be a major factor in some (patients') abnormal response to carbohydrates. Holzel, Schwarz and Sutchiffee (23) in 1959 reported severe diarrhea, malnutrition and even death in infants who reacted to milk ingestion due to their inability to digest lactose. These reported incidences and many others sparked studies of lactase deficiency. The high incidence of lactase deficiency observed in various studies nullified the early report which indicated that lactase production remains at a high level in normal humans everywhere throughout life and opened a new chapter to the study of the cause and prevalence of lactase deficiency.

Several possible causes of lactase deficiency have been examined. These causes have been broadly grouped into three major categories: congenital, secondary, and primary (24). Congenital lactase deficiency is an intestinal lactase deficiency often seen in premature infants and young children. Occurrence of this condition in infants could be associated with fleeting intestinal injury or delayed acquisition of lactase (25). It is relatively rare. Some children with this syndrome at birth eventually develop normal lactase activity within several months to a year or two after the development of the deficiency (25).

Secondary or acquired lactase deficiency could result from gastroenteritis, tropical sprue, mucoviscoidosis, infectious hepatitis, regional enteritis and protein calorie malnutrition (24). Primary lactase deficiency occurs in adults who, in infancy and childhood, consumed reasonable amounts of milk without any discomfort but in adulthood, could not digest lactose. This form of lactase deficiency is the most frequent (3) and has been the major focus of lactose studies.

Four major hypotheses have been postulated for the etiology of lactase deficiency in man (3). These include: (1) common occurrence of diseases that damage the intestinal mucosa and inhibit lactase production in some ethnic groups, (2) drugs or other diet components that inhibit lactase production, (3) adaptation to lactase production with milk consumption, and (4) inherent lactase deficiency. The proponents of these hypotheses have carefully presented their case. While one or more or a combination of these hypotheses might be true, the genetic etiology of lactase deficiency had been strongly favored (3, 9, 26, 27).

The genetic etiology of lactose malabsorption was strengthened by genetic study of lactose digestion in Nigerian families. Ransome-Kuti, Kretchmer, Johnson and Gribble (9) found that if both parents were lactose malabsorbers all the progeny would malabsorb lactose, but in families where one parent was a lactose malabsorber, the offspring contained some or all individuals who were capable of absorbing lactose. From this family pedigree data, the researchers concluded that the "ability to digest lactose is transmitted as an autosmal dominant and represents the mutated gene or a polymorphism" (9, p. 431).

Prevalence of Lactose Malabsorption in the World Population

Lactose malabsorption is a common phenomenon in the majority of the adult population and not a rare disorder as formerly thought. Except the Caucasian and a few of other tribes, lactose malabsorption and lactose intolerance have been reported at a high level in many adults and older children all over the world (4, 8, 19, 28, 29, 30). To those minority groups of the world's population who retained ability to tolerate large amounts of lactose in their diet at adulthood, Kretchmer (10, p. 812) suggested that "we are dealing with a mutation so that transcription of information necessary for the synthesis of this enzyme (lactase) do not become quiescent but remain active." He therefore postulated that there was a deficiency in repression of the genetic complex in these small groups of people.

Stephenson and Letham (31) criticized the derogatory use of the terms "lactase deficiency" and "lactose malabsorption" as disease conditions and abnormalities, respectively. In their view, lactase deficiency is a "normal state in most of the adult population of the world" (p. 296).

Prevalence of adult lactase deficiency has been reported in Indians. Reddy and Pershad (29) investigated lactase deficiency in eleven adult Indians, using peroral biopsy technique. All the adult subjects had a low level of intestinal lactase and 50 percent experienced symptoms of intolerance. In the same study, out of 15 children aged 7 months to 7 years, all nine children under the age of 3 years showed normal intestinal lactase; intolerance symptoms were reported in 20 of 54 children

on which lactose tolerance tests were performed.

Investigation of lactose intolerance in 30 healthy Canadian West Coast Indians and 16 non-Indians of Northern European extraction showed lactose intolerance in 63.3 percent of the Indians, while 68.4 percent of them experienced intolerance symptoms. Only one (6.3 percent) non-Indian was lactose intolerant and none reported abdominal discomfort (32). Lactose malabsorption and intolerance had been reported in other Indian groups (33, 34, 35, 36). Caskey, Payne-Bose, Welcher, Gearhard, Nance, and Morrison (36) studied lactose malabsorption in 60 Oklahoma Native American Indians. The subjects were grouped into six different age groups with ten subjects in each group. The result showed lactose malabsorption in 90 percent of the 45 to 64 years age group, 70 percent in the 13 to 19 years age group, while only 20 percent of ages 3 to 5 malabsorbed the lactose load. Lactose malabsorption was approximated to 82 percent in age 13 or older.

Lactose malabsorption among African ethnic groups and their overseas descendants has been extensively investigated. Cautrecase, Lockwood, and Caldwell (18) studied 60 hospital patients (41 negroes and 19 whites). Lactose tolerance test was performed after ingestion of 2 gm. per kg. of body weight. The result indicated that only 3 of the 19 whites were lactose malabsorbers, as against 27 of the 41 negroes. A similar study conducted on 40 healthy subjects (20 blacks and 20 whites), volunteers from Maryland State House of Correction reported intestinal lactase deficiency in 18 (70 percent) of the adult blacks in contrast to only 1 (5 percent) of the whites (4).

Apart from the adult black population, lactose malabsorption has been reported at a significantly high level in pre-school black children

(37). Paige, Bayless, Ferry, and Graham (38) in a different study, observed that a significant number of black children in an organized school feeding program rejected milk, compared with their white counterparts; milk rejection was associated with lactose-induced symptoms and lactose malabsorption.

The high incidence of lactose malabsorption among black Americans triggered investigation of lactose malabsorption in many parts of the world. Various studies were conducted among different African ethnic groups. Olatunbosun and Adadevoh (8) reported an overall lactase deficiency of 81 percent in 83 randomly selected patients attending the general out-patient department of the University College Hospital in Ibadan, Nigeria. When the analysis was considered based on the ethnic origin of the subjects, 84 percent of 48 Yorubas, 60 percent of 15 Hausa/Fulani, 82 percent of 11 Ibos, and all 9 Nigerians belonging to other ethnic groups were found to be lactose malabsorbers. Lactose tolerance test performed on 102 subjects (41 Yoruba, 33 Fulani, 17 Hausa, and 11 Caucasian) in Nigeria indicated that 99 percent of the Yoruba, after the age of three, malabsorbed lactose. Lactose malabsorption was reported in 64 percent of the Hausa and Fulani, and in only 20 percent of the Nomadic Fulani who are migratory cattlemen (6).

In other African groups, Jersky and Kinsley (39) reported 90 percent lactose intolerance in 38 healthy Southern African Bantus. Although the Masai tribe of East Africa are traditionally nomadic cattle-raising and regular milk drinking people, lactose tolerance test revealed lactose malabsorption in 62 percent of 21 Masai children examined (40). Incidence of lactose malabsorption among 72 Kenyan boarding school children was reported at 73 percent (24).

Results obtained from lactose studies from other ethnic groups of the world paralleled those reported earlier. Chung and McGill (41) reported 100 percent lactase deficiency in eleven healthy oriental subjects. Investigation of lactase deficiency in 140 Thai adults utilizing jejunal biopsies indicated that virtually all the Thai subjects examined had abnormal lactase levels and 85 percent had diarrhea or abdominal cramps or both (42).

Gilat, Kuhun, Gelman, and Mizrahy (19) estimated jejunal lactase in Jewish Communities in Israel. Lactose tolerance test was performed in 217 subjects in addition to 41 peroral and 22 surgical biopsies. Lactase deficiency was found in 60 percent of biopsied subjects. Lactose tolerance test revealed intolerance in approximately 71 percent of the population sampled. Leichter (43) investigated the possible effect of environment on lactase deficiency by performing lactose tolerance test on 32 healthy North American Jewish adults in Western Canada. The data collected in this study was compared with the study of Jewish Communities in Israel. Mean blood glucose rise of 4.1 mg. per 100 ml. of blood was reported in 22 (68.8 percent) of the subjects, a result similar to the compared data. Further study of Mediterranean groups using 67 adult Arab villagers reported 80.6 percent incidence of lactose malabsorption in the Arab group (44). Bolin, Davis, Seah, Chua, Yong, Kho, Siak, and Jacob (45) concluded from the data obtained on 90 indigenous Asian subjects in Singapore that lactose intolerance was a common phenomenon among the indigenous Asian population.

Kretchmer (10), in reviewing the information gathered from a number of ethnic groups, found that "many of the people in the world lack lactase in adult life and if given sufficient milk will show a degree of

intolerance, ranging from milk discomfort to fermentative diarrhea and vomiting" (p. 809).

Detection Methods

Most of the early studies on lactose malabsorption and lactose intolerance were conducted using the lactose tolerance test (LTT) (18, 46, 47, 48). This test is an oral lactose tolerance test, usually performed in the morning with the subject in a fasting state. The dose of lactose used is 2 gm. per kg. of body weight with a maximum dose of 50 gm. of lactose dissolved in water. Blood samples are taken at the blood capillary or the venous at 30 or 15 minute intervals for 120 minutes after the ingestion of lactose. The samples are then analyzed for glucose. Unless otherwise stated, a standard rise in blood glucose less than 20 mg. per 100 ml. of blood with occurrence of symptoms, including nausea, bloating, cramps, or diarrhea would be indicative of lactose malabsorption.

The lactose tolerance test reflects the level of technology available to detect the absence or presence of lactose malabsorption at that time. The large dose of lactose used in LTT was necessary to obtain a measurable and reproducible increment in blood glucose (49).

The accuracy of LTT depends on the sampling procedure. The venous blood sample may give false lactose tolerance results compared with the capillary blood sample (50). Recent critics of LTT have capitalized on the "megadose" of lactose used in the test (30, 49). The lactose dose used in detecting lactose malabsorption in this test has been described as "unphysiological". The use of purified lactose has been criticized

as unrealistic since lactose in its natural form occurs with protein and fat which retards gastric emptying. Lactose tolerance tests failed to provide reliable information on how an individual's intestine would react to small quantities of lactose as in an 8-oz. glass of milk.

Actual diagnosis of lactase deficiency requires collection of a biopsy speciman from the intestine by use of peroral biopsy technique. The instrument for obtaining intraluminal biopsies of the intestinal mucosa was described by Crosby and Kugler (51) as:

> consisting of a capsule containing a rotating knife which is spring-activated and triggered by suction. The suction first draws a bit of mucosa into the capsule before the knife is sprung. The capsule is held captive by a polyethylene tube 2 mm. in diameter, which also serves to transmit suction and to retrieve the capsule (p. 241).

When the tissue from the capsule is examined for lactase, the results are expressed in units of disaccharidase per two units per gram of the mucosa. Lactase levels less than two units per gram of wet weight would show a clinical symptom of lactose malabsorption (52).

While peroral biopsy provides a definitive diagnosis of lactase deficiency, its administration requires expert knowledge. Utilization in children might be virtually impossible. In adults, a lot of persuasive work must be done to get enough volunteers to participate in this type of study.

Other methods which have been used in lactose malabsorption studies include radiological tests and modified lactose tolerance tests. A biochemical test based on the changes in the breath concentration of either carbon-14 or hydrogen derived from bacterial fermentation of unabsorbed lactose could also be used to determine lactose malabsorption. Other than the breath hydrogen test, the other techniques mentioned above had found less use in lactose malabsorption studies.

Breath hydrogen analysis or test (BHA or BHT) has found its widest application since its introduction in determination of lactose malabsorption. This method is a quantitative analysis of expired breath hydrogen with gas chromatography. The test is administered after 8-12 hour overnight fast. The ingestion of unabsorbed sugar causes an intestinal production of gas (hydrogen) as a result of colonic bacteria fermentation (53). The hydrogen is diffused from the colon to the blood and expired through the lungs. The expired breath hydrogen is collected in a bag constructed for collection of the breath hydrogen sample. During sampling, the subject inhales through the nose and exhales through the mouth into the bag. The sampling intervals might vary from 10 to 30 minutes, covering a period ranging from 210 minutes (54) to 360 minutes (49). The collected sample is analyzed by gas chromatography. A breath hydrogen response greater than 20 ppm. is an indication of lactose malabsorption.

Breath hydrogen analysis had been shown to be more specific and sensitive (55, 56) than the lactose tolerance test. A realistic dose as small as 12.5 gm. of lactose could be used to determine lactose malabsorption (57). Other specific advantages of this technique are easy operation of the analytic equipment, detection of a very low level of hydrogen and a very simple sampling apparatus that could be used in field or clinical situations (11, 57). In addition to these, the technique is suitable for application in children without the discomfort associated with venous and capillary blood sampling or the inconveniences in peroral biopsy test. The amount of lactose that could be tolerated without any ill effect could be determined (58); intestinal transit time of unabsorbed carbohydrates could also be measured by this technique

(11, 12).

Intestinal Transit Time of Unabsorbable Carbohydrates

It had been observed that gastric emptying starts almost immediately after ingestion of a meal (59). Transit time is required for complete absorption of a given ingested substance (11). In some conditions it had been observed that minimal value for transit was needed for "normal" absorption; and a very rapidly transmitted fraction of ingested meal could be malabsorbed (11).

The early studies on transit time utilized barium in determining the small bowel transit time of a given substance (60, 61), but the shortcomings of the barium technique include the inconsistency of result and problem in reproducibility of the data (11).

Bond and Levitt (11), in developing a simple technique which reliably reflects the transit time of ingested foodstuff in the small bowel, utilized pulmonary hydrogen measurement in 42 subjects. Small bowel transit time in this study was described as the "time interval between ingestion of a nonabsorbable fermentable carbohydrate (lactulose) and the resulting rise in the rate of pulmonary hydrogen excretion" (p. 547). Comparing bowel transit time obtained by this method with polyethylene glycol (PEG) and lactulose incubated with a mercury-weighted polyethylene tube passed to the ileum of the subject, an average difference of eight minutes was observed between the two methods. The researchers realized that breath hydrogen measurement slightly overestimated the small bowel transit time. Nevertheless, breath hydrogen measurement appears to provide relatively accurate measure of the time required for

the head of the lactulose column to traverse the small bowel.

In lactase deficiency individuals as discussed earlier, decreased absorption of lactose would result in concentration of the unabsorbed lactose in the small intestine. Rapid transition of the unabsorbed lactose might result in its malabsorption.

Transit time varies with the form and quantity of ingested substance. Some investigators reported decreased intestinal transit time when dietary fiber was added to food (12, 62, 63) and this effect depends on the particle size and type of dietary fiber (64). Bond and Levitt (12) reported decreased small bowel transit time with bran when compared with lactulose. In a different study, the same authors reported decreased transit time with increased quantities of ingested lactulose (11). Another factor determining the rate of intestinal transit time is the rate of gastric emptying of a substance whose transit time is being measured.

CHAPTER III

RESEARCH DESIGN

This study was designed to assess the effect of evaporated milk (EM) and evaporated milk with whole cornmeal (EMWC) test meals on the intestinal transit time and to compare the hydrogen response of the two test meals in a selected group of lactose malabsorber Nigerians.

Description of Subjects

The list of Nigerian students at Oklahoma State University (OSU) was obtained from the Nigerian Student Union President. Fifteen volunteers were obtained by contacting every fifth person on the list. Of these persons contacted, twelve agreed to participate in the study. These twelve subjects received a test meal of 240 ml. of undiluted evaporated milk, an equivalent of 480 ml. of fresh whole milk, containing 24 gm. of lactose. Ten out of the twelve subjects proved to be lactose malabsorbers based on expired breath hydrogen greater than 20 ppm. Four of the lactose malabsorbing subjects further received, in addition to the initial evaporated milk test meal, a whole cornmeal with equivalent amount of milk test (240 ml.). The test was administered to each subject after at least twelve hours overnight fast with two days interval between tests. All ten subjects would have received the EMWC test meal but the testing period was concluded due to uncontrollable factors after four subjects had been completed. The samples collected from the ten

subjects for the milk test were analyzed and reported but the complete data are available for those subjects who received both test procedures. The four subjects who received both test meals included one female and two males from the southern part of Nigeria, and one male from the northern part of Nigeria. Their age ranged from twenty-four to thirty years with a mean age of twenty-five years.

None of the four subjects was diabetic or had diarrhea within recent months. During the study period, none of the subjects was on any type of drug. No subject reported having gastrointestinal disturbance or other intestinal-related diseases prior to the study. All subjects reported having consumed a minimum amount of canned or powdered milk, as in tea, coffee, cocoa, and corn-pap while in Nigeria, except the Hausa/Fulani who claimed to have consumed large amounts of fermented milk (nono) from infancy until adulthood. Each subject signed a statement of informed consent to participate in this study (Appendix A). The detailed description of four subjects who received the two test meals is illustrated in Table I.

Experimental Procedure

The study covered a three-week period with at least two days between treatments. A week before the test period, the subjects were instructed to restrict milk and milk products in their diet. Subjects were also instructed to abstain from gas-forming foods such as vegetables from the cabbage family, legumes, and fast food hamburgers a day previous to the test. These food guidelines were necessary because in many instances enormous hydrogen concentration had been detected in the basal samples of subjects who claimed to have consumed one or more of

these food products in their last meal after more than a twelve-hour fast. A twelve-hour fast, from eight o'clock at night to eight-thirty the following morning without drink, except water, was required prior to the test. The purpose of the fast was to keep the basal hydrogen concentration to the minimum.

TABLE I

DESCRIPTION OF SUBJECTS

Subject	Nigerian tribe	Sex	Age	Ht. (cm)	Wt. (kg)
1	Yoruba	Female	30	159	56
2	Ibo	Male	24	155	60
3	Yoruba	Male	28	149	61
4	Hausa/Fulani	Male	29	173	72

On the subject's arrival in the laboratory, the basal breath hydrogen was taken. Basal breath hydrogen of less than 20 ppm. was necessary for the test to continue. A basal hydrogen of 20 ppm. or above was indicative of lactose malabsorption. Subjects with such high basal hydrogen were asked to return and repeat the test in another two days. Immediately after ingestion of the test meal another sample was taken representing the zero breath hydrogen sample. Subsequent samples were taken at ten-minute intervals. The standard testing period was

established at 210 minutes, except when the transit time occurred after 210 minutes. The subject took the EM test meal first, then returned in another three days for the EMWC test meal. The sampling procedures for both test meals are discussed under sample collection and analysis.

To observe if there was any difference in the hydrogen response after the standard testing period of 210 minutes, one subject out of the four subjects volunteered to continue the test for 720 minutes. The subject repeated each test twice to determine the reproducibility of each trial. The sample collection followed the same pattern except that sampling time was extended to 720 minutes. Samples were collected at ten-minute intervals for the first 360 minutes; afterwards, samples were taken every thirty minutes through 720 minutes.

Test Meal Preparation

Two test meals were compared in this study, that is, the undiluted evaporated milk and evaporated milk with whole cornmeal test meals. Whole yellow cornmeal and evaporated milk (Carnation brand) were used in the preparation of the test meals. The nutrition information on the label of the yellow whole cornmeal and evaporated milk are included in Appendix A. The whole cornmeal had no preservatives or additives. Both the milk and the whole cornmeal were obtained from the Consumer's I.G.A. store in Stillwater.

The whole cornmeal was reground into powdered form with a Thomas-Wiley laboratory Mill model 4 using a 1 mm. screen. After thorough mixing of the ground cornmeal, it was weighed in 60 gm., individualized portions into a 6½ X 1½ X 9 ml. clear polyethylene ziplock storage bag kept in the freezer until they were ready for use.

Two hundred and forty milliliters of undiluted evaporated milk was measured in a graduated cylinder, poured in a paper cup and consumed by the subject within one to two minutes after the basal breath sample. The evaporated milk whole cornmeal meal was prepared by adding 60 ml. of water to 60 gm. of preweighed cornmeal in a four quart saucepan and thoroughly mixed. Another sixty milliliters of boiled water was added to the mixture and then boiled for five minutes with continuous stirring. An equal amount of milk as used for the milk test (240 ml.) was added to the boiled mixture and boiled for another five minutes; then refrigerated in the saucepan for three minutes and consumed by the subject within three to five minutes after the basal hydrogen sample was taken.

Breath Hydrogen Collection and Analysis

The samples were collected in bags constructed of double layers of a three-mil multilaminar material of polyester, aluminum, and polyethylene. A teflon tubing connector was attached to each of the heat-sealed bags. The subjects were instructed to inhale through the nose and exhale through the mouth into the bag. The expired breath samples passed through a column of $Ba(OH)_2$ and anhydrous $CaSO_4$ which served as a moisture absorber. A total of twenty-two samples were collected from each subject for each test, making a total of forty-four samples per subject for each test meal. The samples collected from one subject who continued the test beyond 210 minutes totalled 184 samples with forty-six samples collected for each of the two repeated test meals.

The breath hydrogen concentration in each sample was measured using the method developed by Payne-Bose, Gearhart, and Morrison (57). The method utilized a helium carrier Hewlett-Packard 5830A gas chromatograph

equipped with a thermal conductivity detector (TCD) and an 0.5 ml. sample loop. The bags were randomly picked and the hydrogen concentration in the collected samples were measured by gas chromatography. The peak areas of the detected hydrogen concentration were automatically measured by the equipment, thereby eliminating errors of manual computation.

The hydrogen concentration in each breath sample was reported in parts per million (ppm). Information obtained from the analyses was recorded on the breath hydrogen test data sheet (Appendix A) which also contains information about the test meal consumed and the sampling time. The subjects were instructed to report any discomfort such as gas, flatulence, abdominal cramping, diarrhea, etc., they felt after the ingestion of the test meals as the sampling progressed. The symptoms as reported by the subjects were recorded on the data sheet.

Statistical Analysis

A split plot design was used in this study. In this design, the subject was considered as a block and served as his or her own control. The test meal represented the treatment and was considered as the main plot. The ten minute sampling intervals were the subplots. This design method was specifically appropriate for this study because the effects due to subject were removed. The study of variation due to time lag and individual differences are also facilitated.

Analysis of variance (ANOVA) was employed to obtain the differences in transit time, hydrogen response to EM and EMWC test meals for 210 minutes and beyond the standard test period of 210 minutes. Correction of basal hydrogen (subtraction of basal hydrogen response from the abso-

absolute value) was used as a baseline in plotting the graphs instead of absolute value.

CHAPTER IV

RESULT AND DISCUSSION

Twelve subjects received the first test meal consisting of 240 ml. of undiluted evaporated milk. Ten of these twelve subjects were determined to be lactose malabsorbers. Four of the ten lactose malabsorbers received, in addition to the initial milk test, evaporated milk with whole cornmeal to compare the intestinal transit time and hydrogen response of undiluted evaporated milk (EM) to evaporated milk with whole cornmeal (EMWC) test meals. The data collected from the milk test in the four subjects were combined with the results obtained from the EMWC meal test to study the difference between the two test meals. Test period lasted for 210 minutes except when the transit time occurred later. The pattern of hydrogen response was observed beyond 210 minutes in one of the four subjects. This subject repeated each test twice and the expired breath hydrogen measurement continued for 720 minutes (12 hours). The expired breath hydrogen was quantified with a Hewlett-Packard 5830A gas chromatograph.

Transit Time

Transit time was determined by analyzing each sample and recording the hydrogen as detected by the analytic equipment. The assumption for the breath hydrogen determination in this study was based on the theory that the hydrogen was solely produced in the colon as a result of

bacterial fermentation of the unabsorbed lactose (11). The hydrogen produced diffused through the intestinal wall to the blood stream and eventually expired through the lungs. The expired breath hydrogen values were recorded every ten minutes following the ingestion of the test meal. Transit time was defined as the time required for the first of three successive breath hydrogen values greater than the fasting breath hydrogen concentration that occurred sixty minutes after ingestion of the test meal.

The intestinal transit time of the ten subjects for the evaporated milk test is shown in Figure 2. Figures 6 and 7 in Appendix B show the hydrogen response of the ten subjects plotted over time. The observed transit time points for all ten subjects are shown, however no statistical analysis was performed on the data collected for the milk test for the ten subjects.

In Figure 3 the comparison of intestinal transit time for the four subjects who received both test procedures - evaporated milk and evaporated milk with whole cornmeal test meals is shown. The mean intestinal transit time for the four subjects on the EM meal was 102.50 minutes, ranging from 80 to 120 minutes, compared with 197.50 minutes for the EMWC meal, ranging from 150 to 250 minutes. An average difference of ninety-five minutes was observed between the mean of transit time of the two test meals. This showed a significantly ($P = 0.016$) slower passage of EMWC meal through the intestine compared with EM meal. The statistical analysis is shown in Table II. The F-value of 1.82, ($P = 0.317$) indicates no significant difference in the intestine transit time among subjects. Coefficient of variation (=CV) of 47.43 percent was obtained in the experiment.

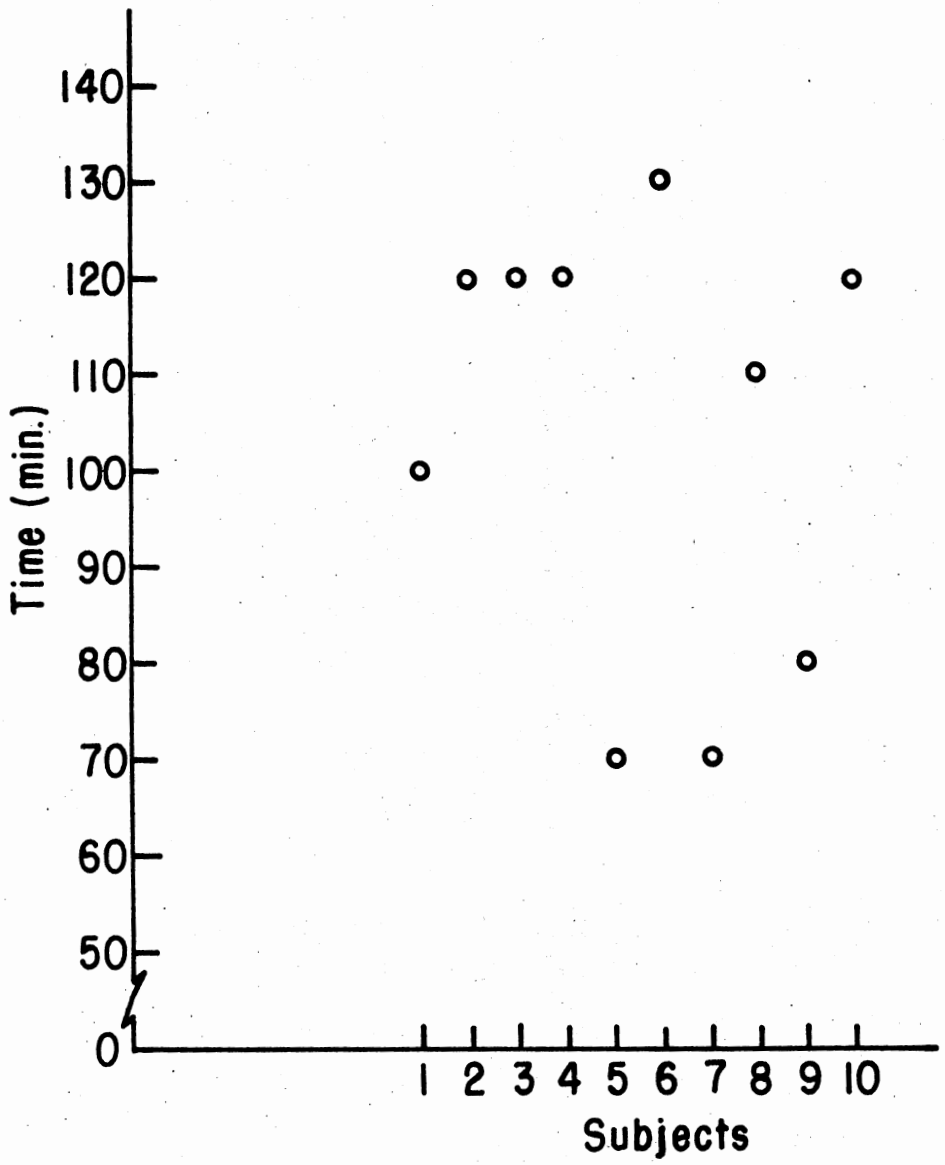


Figure 2. Intestinal Transit Time of Ten Subjects After Ingestion of 240 ml. of Undiluted Evaporated Milk During a 20 Minute Breath Hydrogen Analysis Test. Each Point on the Graph Represents the Observed Transit Time for Each Subject.

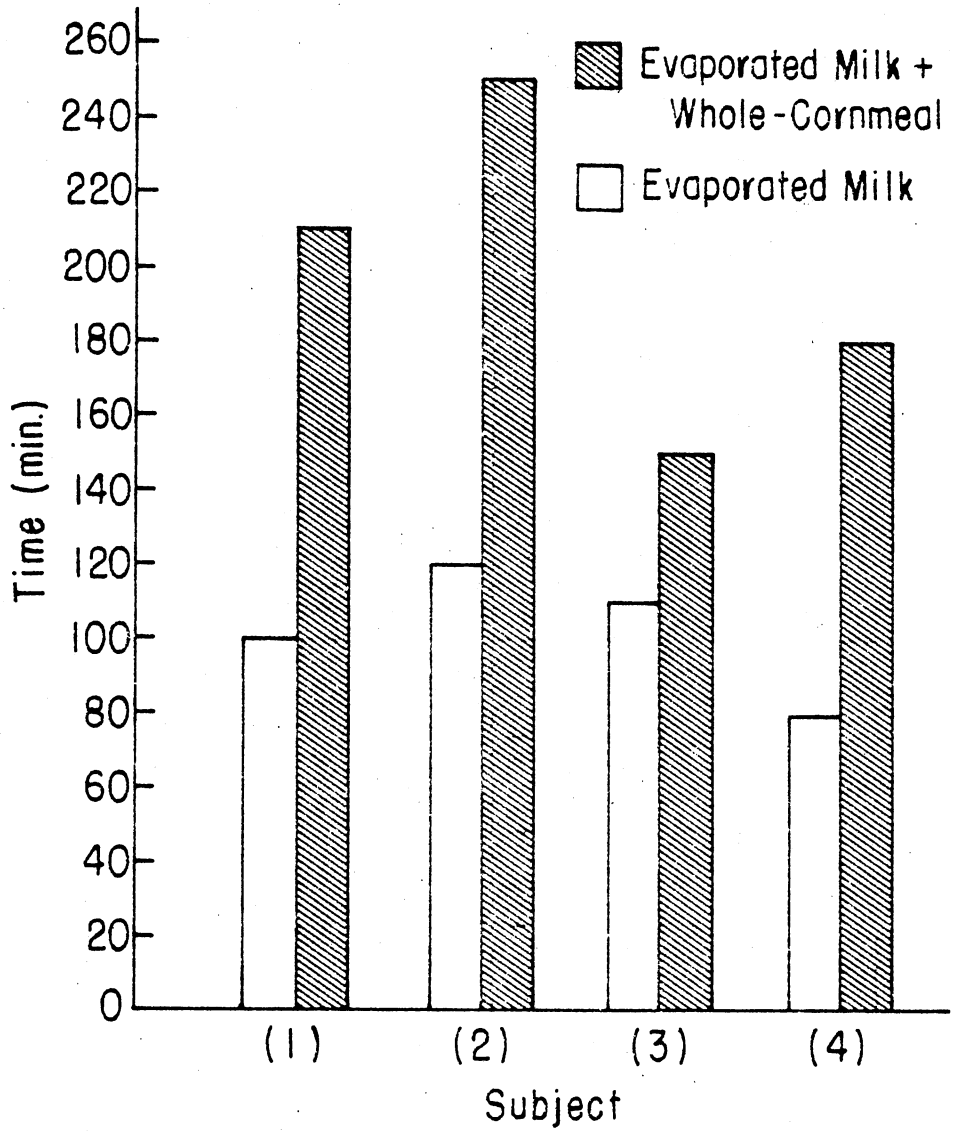


Figure 3. Comparison of Intestinal Transit Time of Four Subjects After Ingestion of EM and EMWC Meals (Each Meal Consisted of 240 ml. of Undiluted Evaporated Milk, Which Contained 24 gm. of Lactose).

TABLE II

ANALYSIS OF VARIANCE FOR THE TRANSIT TIME OF EVAPORATED MILK AND EVAPORATED MILK WITH WHOLE CORNMEAL TEST MEALS

Source	df	Ms	F	PR>F
Subjects (S)	3	1367	1.82	0.317
Meal (M)	1	18050	24.07	0.016
S*M (error)	3	775	---	---

Effect of Whole Cornmeal on Hydrogen Production

A split plot design was used. Figures 8 to 11 in Appendix B show the responses of the four subjects who received both test meals using basal hydrogen correction as the baseline. Mean values for the subjects on both test meals are shown in Figure 4. The hydrogen response for EM meal rose sharply after ninety minutes, reaching its peak at 210 minutes. The rise of the hydrogen production observed for the EMWC meal started at 140 minutes; the rise was gradual, unlike the EM meal. No peak value was obtained until the test was stopped because the subject could not continue without food any longer.

The mean hydrogen response obtained for the four subjects for the standard test period of 210 minutes was 3.44 ppm. for the EMWC meal compared with 19.61 ppm. for the EM meal. Analysis of variance on hydrogen production is shown in Table III. The table shows a highly significant interaction between test meal and time. This is seen in Figure 4

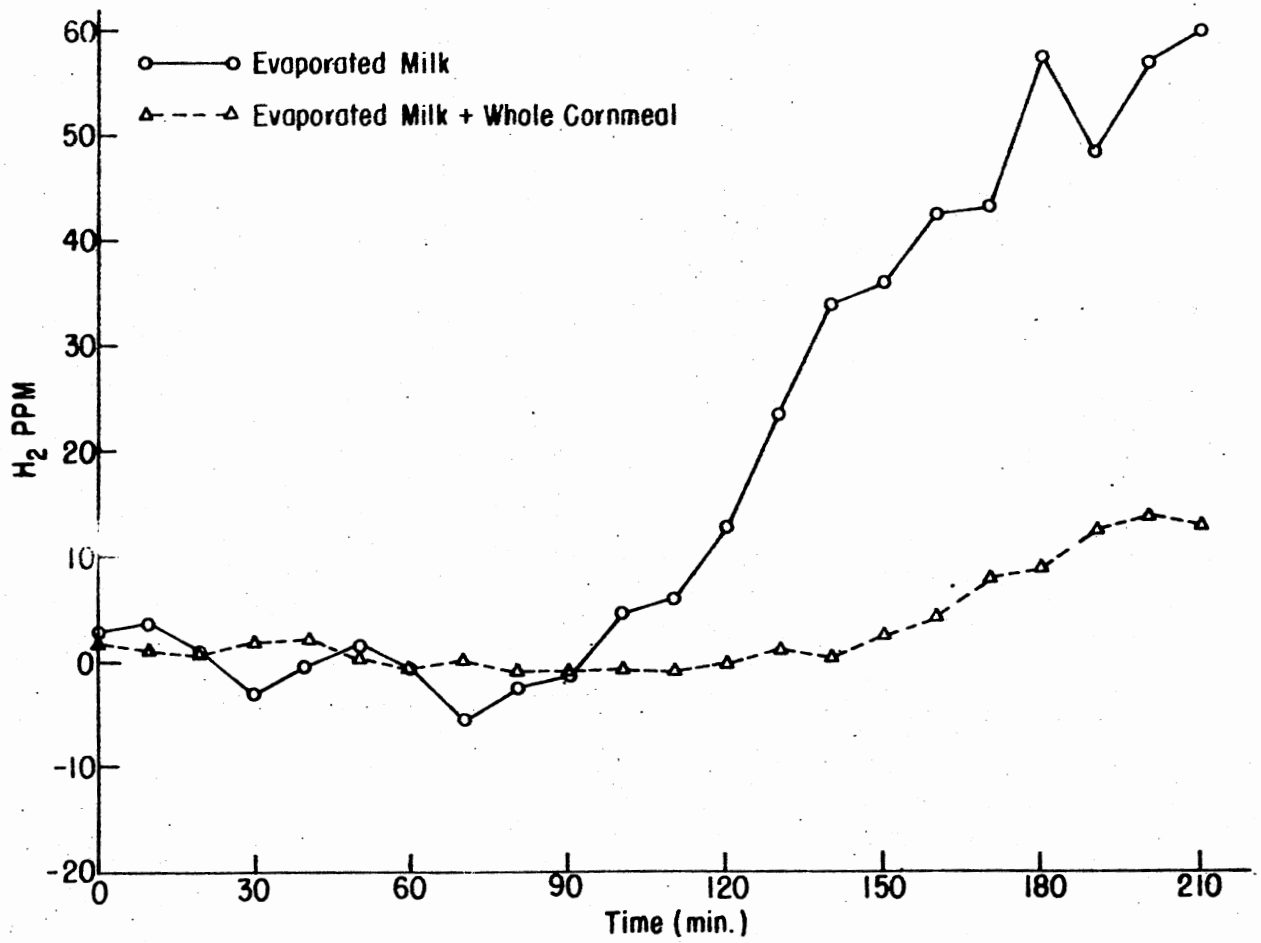


Figure 4. Comparison of Mean Values of Breath Hydrogen Responses of Four Subjects Following Ingestion of Evaporated Milk and Evaporated Milk with Whole Cornmeal (Each Meal Consisted of 240 ml. of Evaporated Milk Which Contained 24 gm. of Lactose).

of the responses plotted over time for the two test meals in that the two lines are not parallel. The F-value was significant at P = 0.0001. No significant difference was observed due to subjects (P = 0.18). Total hydrogen production in response to different test meals was statistically significant at P = 0.025 with an F-value of 17.39. Hydrogen production over time period showed a very strong significance with an F-value of 7.16 (P = .0001).

The common lactose intolerance symptoms reported during the tests were a bloated feeling and flatulence. None of the subjects reported diarrhea or abdominal cramping. The symptoms were reported between 80 to 160 minutes after the ingestion of the test meals by all subjects. No symptom was reported after 180 minutes. The subjects reported no difference in the symptoms when EM or EMWC test meal was consumed.

TABLE III

ANALYSIS OF VARIANCE FOR THE HYDROGEN RESPONSE OF EVAPORATED MILK AND EVAPORATED MILK WITH WHOLE CORNMEAL TEST MEALS

Source	Df	Ms	F-value	PR>F
Subjects (S)	3	2164.98	3.27	0.18
Meal (M)	1	11505.28	17.39	0.025
S*M (error a)	3	661.60	---	---
Time (T)	21	1622.74	7.16	0.0001
S*T (error b)	63	226.55	---	---
M*T	21	768.3	7.06	0.0001
S*M*T (error c)	63	108.86	---	---

Comparison of the Breath Hydrogen Responses of the Two Test Meals Beyond the Standard Test Period of 210 Minutes

The initial objective of this part of the study was to compare the elimination time of both test meals by means of comparison of the time it takes for the hydrogen response values to equal the fasting hydrogen response value after the fermentation of the unabsorbed lactose. Only one subject volunteered to continue the test much beyond 210 minutes because of hunger. Thus the data collected from this one subject were inadequate for any conclusion for the elimination time of the unabsorbed lactose in EM and EMWC meals. It was decided, therefore, to compare the response values of the two test meals for 720 minutes in that one subject. The subject repeated each test meal twice in which measurements continued for 720 minutes.

The hydrogen responses for the two repeated test meals were plotted in Figure 5 using the basal hydrogen correction value as a baseline. These curves represent the shape of breath hydrogen analysis on a lactose malabsorber. The two dotted curves were the two replicates of the EMWC test meal. The two curves varied somewhat, but the total area under the curves was similar. The two solid curves represent the replicates of EM meal. The curves of the first EM meal (test 1) differs substantially from the second EM meal (test 2). The difference between the two replicates might be attributed to extensive fasting during the testing periods. Usually, at least a two-day interval between one test to another would be allowed. However, due to a change of technician and anticipated change in analytical equipment, this was not possible. This

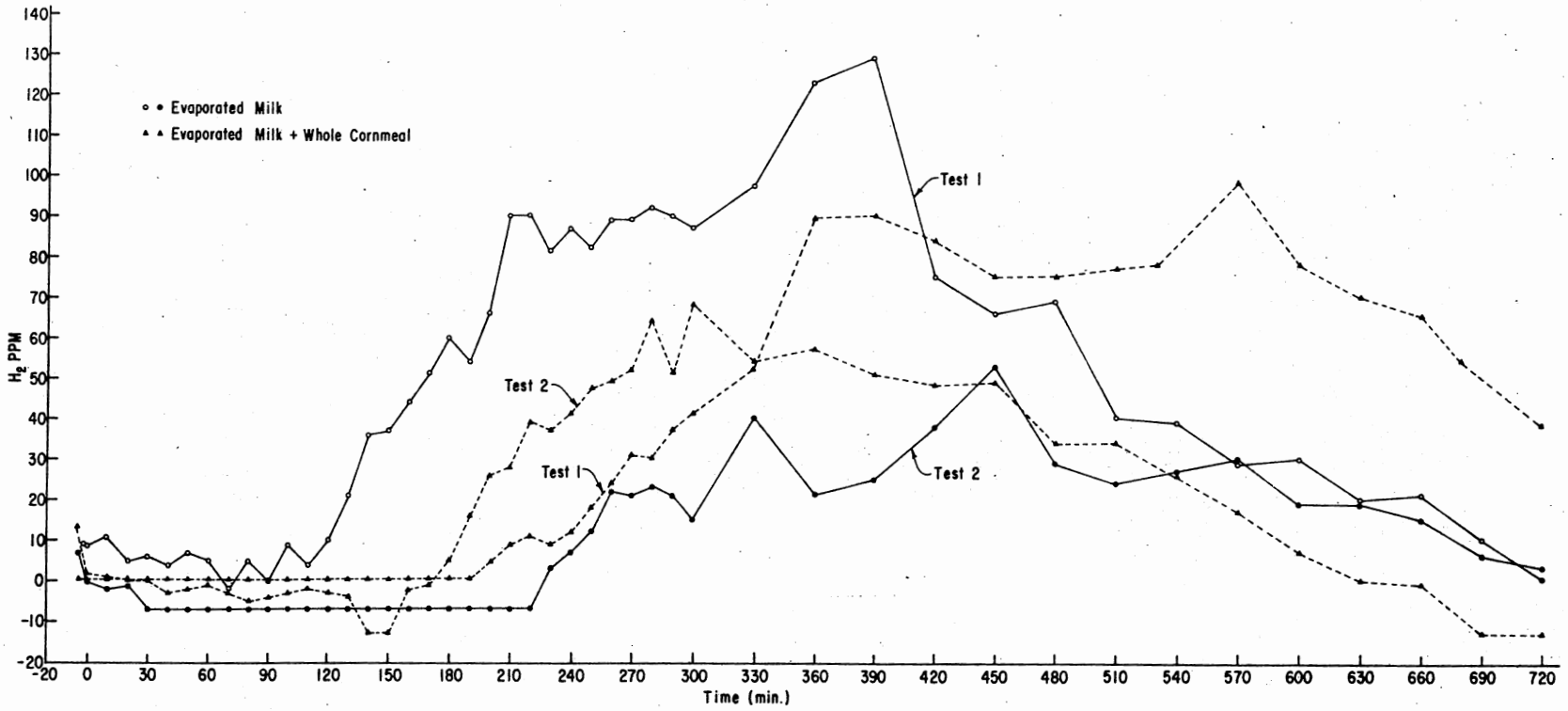


Figure 5. Breath Hydrogen Response Versus Time of the Repeated Test of Evaporated Milk and Evaporated Milk with Whole Cornmeal Measured for 720 Minutes (Each Test Consisted of 240 ml. of Evaporated Milk Which Contained 24 gm. of Lactose).

test was, therefore, done one day following the EMWC meal (test 2). That is, in addition to twelve-hour fast before the EMWC meal test 2, and twelve-hour fast during this test, the subject did not receive a substantial meal except one brief meal consisting of one boiled egg, one fresh apple and a glass of apple juice and unrestricted amount of water before the second EM test meal was taken the following day. From this observation, it could be hypothesized that extensive fasting prior to lactose product intakes by a lactose malabsorber reduces the amount of unabsorbed lactose that reaches the colon for colonic bacterial fermentation; thus less total amount of hydrogen would be produced. This difference, though not intentional, is of research interest as it highlights how a lactose malabsorber might respond to lactose product intakes after a prolonged fasting period.

The mean hydrogen production for the repeated EM meal was 28.36 ppm. compared with 24.59 ppm. for the EMWC meal. Analysis of variance for the replicate of each test meal showed an F-value of 0.03, and $P = 0.87$, showing no significant difference in the total hydrogen production between the replicates of the test meals. F-value of 4.96 ($P = 0.0001$), is statistically significant due to sampling time. Despite the variability in the hydrogen response curves, when the total area under the curves for each pair of test meal hydrogen responses was examined, no significant difference was observed.

CHAPTER V

SUMMARY AND CONCLUSION

The major objectives of this study were to assess the effect of evaporated milk and whole cornmeal cooked with evaporated milk on intestinal transit time and to compare the pattern of breath hydrogen response of the two test meals in selected groups of subjects. For this purpose, twelve healthy Nigerian nationals volunteered to participate. Ten were found to be lactose malabsorbers having a breath hydrogen greater than 20 ppm. Four out of these ten subjects received a further second test meal of evaporated milk with whole cornmeal (EMWC).

A split plot design was used, in which each subject served as his or her own control. The data was statistically analyzed using analysis of variance.

The average duration of gastro-intestinal passage of the EMWC meal was longer (197.5 minutes) compared with the EM meal (102.5 minutes). The range of intestine transit time of 80 - 120 minutes observed for the EM meal in this study agreed with what had been reported in the literature (65).

The hydrogen response for the EM meal occurred earlier and rose sharply compared with EMWC meal (90 vs 140 minutes). There was a significant difference in the mean hydrogen response when the test period was limited to 210 minutes. The mean hydrogen response obtained for EM meal was 19.61 ppm. compared with 3.44 ppm. for EMWC meal. But when the

test period was extended to 720 minutes in one subject, no statistically significant difference was obtained between the two test meals. A mean hydrogen response of 28.36 ppm. was obtained for the repeated EM meal compared with 24.59 ppm. for the EMWC meal. The total area under the curves when the hydrogen responses were plotted over time for the two test meals were much alike.

Lack of a statistically significant diffence when the hydrogen measurement continued for 720 minutes indicated that delayed gastric emptying of the EMWC meal could be a major factor in the lower hydrogen response observed when the test period was limited to 210 minutes and probably the prolonged transit time observed for the EMWC meal. The slow delivery of the EMWC meal and its prolonged exposure to the intestinal tract did not increase lactose absorption, since no significant difference was observed in the hydrogen response of the two test meals when the hydrogen measurement was extended to 720 minutes. This result should be expected if there was no lactase present in the intestine to hydrolyze lactose, regardless of the form in which milk is offered. The observed slower passage and prolonged exposure of lactose in EMWC meal to the intestine could only be beneficial to lactase deficient individuals if the prolonged exposure of lactose to the intestine enhanced the absorption of other nutrients in milk and that of other foods consumed with it.

In all the four subjects who participated in this study, two common symptoms reported were bloating and flatulence. There was no difference in the symptoms reported when EM and EMWC meal was consumed.

Referring to the two hypotheses postulated for this study, the first hypothesis that there will be no significant difference in the

intestine transit time when EM meal is consumed compared with EMWC meal was not supported. A significant difference at P = 0.016 was obtained between the two test meals. The acceptance or rejection of the second hypothesis that there will be no significant difference in hydrogen response when EM meal was consumed compared with EMWC meal is premature because when the breath hydrogen response measurement was limited to a standard testing period of 210 minutes, the difference was significant at P = 0.0001. When the test period was extended to 720 minutes for one of the test subjects, this difference was lost. Therefore, further studies in larger population would provide a more conclusive evidence supporting or not supporting the hypothesis.

Recommendation

The subject of lactose malabsorption has generated much research interest in the last few decades. Most of the research had been concerned with determining the occurrence of lactose malabsorption in many parts of the world using "unphysiological" dose of lactose (2 gm. per kg. of body weight) in aqueous solution. Studies are needed reflecting the true pattern of milk consumption in different cultures. Further studies similar to the one conducted but using a larger population would yield important information. Other studies showing hydrogen response with each variable (evaporated milk and whole cornmeal) measured separately as well as combined would yield vital information as to the usual intestinal response of the lactose malabsorber. The effect of dietary fiber consumption with milk (as in milk added to fiber containing breakfast cereals) or other lactose products on the intestinal transit time and hydrogen response in lactose malabsorbers is an important area

yet to be explored.

Further studies examining the effect of prolonged transit time observed when products that retard gastric emptying, such as EMWC meal on the absorption of other nutrients in milk would be of interest. Intestinal transit time has been measured and defined in many different ways by different authors; studies are needed to develop a reliable means of measuring intestinal transit time and establishing a universal definition for the term.

SELECTED BIBLIOGRAPHY

1. Kretchmer, N.: Lactose and lactase. Sci. Am. 227(4): 71, 1972.

2. Bayless, T. M. and Huang, S.,: Inadequate intestinal digestion of lactose. Am. J. Clin. Nutr. 22:250, 1969.

3. Simoons, F. J.: Primary adult lactose intolerance and the milking habit: a problem in biological and cultural interrelations. Am. J. Dig. Dis. 14:819, 1969.

4. Bayless, T. M. and Rosenweig, N. S.: Racial differences in incidence of lactase deficiency. J. A. M. A. 197:968, 1966.

5. Simoons, F. J.: New light on ethnic differences in adult lactose intolerance. Am. J. Dig. Dis. 18:595, 1973.

6. Kretchmer, N., Ransome-Kuti, O., Hurwitz, R., Dungy, C., and Alakija, W.: Intestinal absorption of lactose in Nigeria ethnic groups. Lancet., 2:392, 1971.

7. Olatunbosun, D. A. and Adadevoh, B. K.: Lactose intolerance in Nigerian children. Acta Paediatr. Scand. 61:715, 1972.

8. Olatunbosun, D. A. and Adadevoh, B. K.: Lactase deficiency in Nigerians. Am. J. Dig. Dis. 16:709, 1971.

9. Ransome-Kuti, O., Kretchmer, N., Johnson, J. D., and Gribble, J. T.: A genetic study of lactose digestion in Nigerian families. Gastroent. 68:431, 1975.

10. Kretchmer, N.: Memoria lecture: lactose and lactase a historical perspective. Gastroent. 61:805, 1971.

11. Bond, J. H. and Levitt, M. D.: Investigation of small bowel transit time in man utilizing pulmonary hydrogen (H_2) measurement. J. Lab. Clin. Med. 85:546, 1975.

12. Bond, J. H. and Levitt, M. D.: Effect of dietary fiber on intestinal gas, production and small bowel transit time in man. Am. J. Clin. Nutr. 31:S169, 1978.

13. Solomons, N. W., Viteri, F. E., and Hamilton, L. H.: Application of a simple gas chromatographic technique for measuring breath hydrogen. J. Lab. Clin. Med. 90:856, 1977.

14. Solomon, N. W., Viteri, F. E., and Rosenberg, I. H.: Development of an interval sampling hydrogen (H_2) breath test for carbohydrate (CHO) malabsorption in children. Evidence for a circadian pattern of H_2 concentration. Pediat. Res. 12:816, 1978.

15. Kotschevar, L. D.: Quantity Food Purchasing. 2nd ed. New York: John Wiley and Sons, 1975.

16. Lehninger, A. L.: Biochemistry. 2nd ed. New York: Worth Pub. Inc., 1978.

17. Robinson, C. H. and Lawler, M. R.: Normal and Therapeutic Nutrition. 15th ed. New York: The Macmillan Pub. Co., Inc., 1977.

18. Cuatrecasas, P., Lockwood, D. H., and Caldwell, J. R.: Lactase deficiency in the adult: a common occurrence. Lancet. 1:14, 1965.

19. Gilat, T., Kuhun, R., Gelman, E., and Mizrahy, O.: Lactase deficiency in Jewish Communities in Israel. Am. J. Dig. Dis., 15:895, 1970.

20. Linstromberg, W. W. and Baumgarten, H. E.: Organic Chemistry. 5th ed. Massachusetts: The D. C. Heath and Comp., 1978.

21. Jacob, A.: Milk-sugar in infant feeding. Trans. Am. Pediat. Soc. 13:150, 1901.

22. Howland, J.: Prolonged intolerance to carbohydrates. Trans. Am. Pediat. Soc. 33:11, 1921.

23. Holzel, A., Schwarz, V., Sutcliffee, K. W.: Defective lactose absorption causing malnutrition in infancy. Lancet. 1:1126, 1959.

24. Pieters, J. J. L. and Rens, V. R.: Lactose malabsorption and milk tolerance in Kenyan school age children. Trop. Geog. Med. 25:365, 1973.

25. Gray, M. G.: Intestinal disaccharide deficiency and glucose-galactose malabsorption. In Stanbury, J. B., Wyngaarden, J. B., and Fredrickson, D. S. eds: The metabolic of inherited disease. 3rd ed. New York: McGraw-Hill Co., 1972.

26. Lisker, R. B., Gonzalez, B., and Daltabult, M.: Recessive inheritance of adult type of intestinal lactase deficiency. Am. J. Human. Genet. 27:662, 1975.

27. Launiala, K. and Pyorala, K.: Recessive inheritance of the adult type of lactase deficiency. Lancet. 2:823, 1973.

28. Figueroa, R. B., Melgar, E., Jo, M., and Garcia, O. L.: Intestinal lactase deficiency in an apparently normal Peruvian population. Am. J. Dig. Dis. 16:881, 1971.

29. Reddy, V., and Pershad, J.: Lactase deficiency in Indians. Am. J. Clin. Nutr. 25:114, 1972.

30. Bolin, T. D., Crane, G. G., and Davis, A. E.: Lactose intolerance in various ethnic groups in Southeast Asia. Aust. Ann. Med. 17:300, 1968.

31. Stephenson, L. S. and Latham, M. C.: Lactose intolerance and milk consumption: the relation of tolerance to symptom. Am. J. Clin. Nutr. 27:296, 1974.

32. Leichter, J. and Lee, M.: Lactose intolerance in Canadian West Coast Indians. Am. J. Dig. Dis. 16:809, 1971.

33. Alzate, H. and Gonzalez, J.: Lactose intolerance in South American Indian. Am. J. Clin. Nutr. 22:122, 1969.

34. Duccan, I. W. and Scott, E. M.: Lactose intolerance in Alaskan Indians and Eskimos. Am. J. Clin. Nutr. 25:867, 1972.

35. Bose, D. P. and Welsh, J. D.: Lactose malabsorption in Oklahoma Indians. Am. J. Clin. Nutr. 26:1320, 1973.

36. Caskey, D. A., Payne-Bose, D., Welsh, J. D., Gearhart, H. L., Nance, M. K. and Morrison, R. D.: Effect of age on lactose malabsorption in Oklahoma Native Americans as determined by breath hydrogen analysis. Am. J. Dig. Dis. 22:113, 1977.

37. Bayless, M. B., Ferry, G. D. and Graham, G. G.: Lactose malabsorption in preschool black children. Am. J. Clin. Nutr. 30:1018, 1977.

38. Paige, D. M., Bayless, T. M., Ferry, G. D. and Graham, G. G.: Lactose malabsorption and milk rejection in Negro children. John Hopkins Med. J. 129:163, 1971.

39. Jersky, J. and Kinsley, R. H.: Lactase deficiency in South African Bantu. S. Afr. Med. J. 41:1194, 1967.

40. Jackson, R. T. and Latham, M. C.: Lactose malabsorption among Masai children of East Africa. Am. J. Clin. Nutr 32:779, 1979.

41. Chung, M. H. and McGill, D. B.: Lactase deficiency in Orientals. Gastroent. 54:225, 1968.

42. Keusch, G. T., Troncale, F. J., Thavaramara, B., Prinyanont, P., Anderson, P. R., and Bhamarapravathi, N.: Lactase deficiency in Thailand effect of prolonged lactose feeding. Am. J. Clin. Nutr. 22:638, 1969.

43. Leichter, J.: Lactose tolerance in a Jewish population. Am. J. Dig. Dis. 16:1123, 1971.

44. Gilat, T., Malachi, E. G. and Shocket, S. B.: Lactose tolerance in an Arab population. Am. J. Dig. Dis. 16:203, 1971.

45. Bolin, T. D., Davis, A. E., Seah, C. S., Chua, K. L., Yong, V., Kho, K. M., Saik, C. L. and Jacob, E.: Lactose intolerance in Singapore. Gastroent. 59:76, 1970.

46. Cook, G. C. and Kajubi, S. K. Tribal incidence of lactase deficiency in Uganda. Lancet. 2:725, 1966.

47. Peternel, W. W.: Lactose tolerance in relation to intestinal lactase activity. Gastroent. 48:299, 1965.

48. Dunphy, J. V., Littman, A., Hammond, J. B., Forstner, G., Dahlquist, A., and Crane, R. K.: Intestinal lactase deficit in adults. Gastroent. 49:12, 1965.

49. Solomon, M. W., Garcia-Ibanez, R., Viteri, F. E.: Reduced rate of breath hydrogen excretion with lactose tolerance tests in young children using whole milk. Am. J. Clin. Nutr. 32:783, 1979.

50. McGill, D. B., and Newcomer, A. D.: Comparison of venous and capillary blood samples in lactose tolerance testing. Gastroent. 53:371, 1967.

51. Crosby, W. H. and Kugler, H. W.: Intraluminal biopsy of the small intestine. Am. J. Dig. Dis. 2:236, 1957.

52. Littman, A., Cady, A. B. and Rhodes, J.: Lactase and other disaccharidase deficiencies in a hospital population. Israel J. Med. 4:110, 1968.

53. Levitt, M. D.: Intestinal gas production. J. Am. Dietet. A. 60: 488, 1972.

54. Payne-Bose, D., Welsh, J. D., Gearhart, H. L. and Morrison, R. D.: Milk and lactose-hydrolyzed milk. Am. J. Clin. Nutr. 30:695, 1977.

55. Newcomer, A. D., McGill, D. B., Thomas, P. J. and Hofmann, A. F.: Prospective comparison of indirect method for detecting lactase deficiency. New Engl. J. Med. 293:1232, 1975.

56. Bond, J. H. and Levitt, M. D.: Quantitative measurement of lactose absorption. Gastroent. 70:1058, 1976.

57. Gearhart, H. L., Bose, D. P., Smith, C. A., Morrison, R. D., Welsh, J. D., and Smalley, T. K.: Determination of lactose malabsorption by breath analysis with gas chromatography. Analytical Chem. 48:393, 1976.

58. Levitt, M. D. and Donaldson, R. M.: Use of respiratory H_2 excretion to detect carbohydrate malabsorption. J. Lab. Clin. Med. 75:937, 1970.

59. Hunt, J. N. and Knox, M. T. Regulation of gastric emptying. In: CF ed.: Handbook of physiology. Washington D. C., 1968.

60. Lonnerblad, L.: Transit time through small intestine: Roetgenologic study on normal variability. Acta Radiol. Suppl. 88, 1951.

61. Kim, S. K.: Transit time in the normal bowel study. Am. J. Roetgenol. 104:522, 1968.

62. Srivasta, G. S., Smith, A. N. and Painter, M. S.: Sterculia Bulk-forming agent with smooth-muscle relaxant versus bran in diverticular disease. Urit. Med. J. 1:315, 1976.

63. Cummings, J. H., Hill, M. J., Jenkins, O. J., Pearson, J. R. and Wiggins, H. S.: Changes in fecal composition and colonic function due to cereal fiber. Am. J. Clin. Nutr. 29:1468, 1976.

64. Connell, A. M.: The effects of dietary fiber on gastrointestinal motor function. Am. J. Clin. Nutr. 31:S154, 1978.

65. Calloway, D. H., Murphy, E. L. and Bauer, D.: Determination of lactose intolerance by breath hydrogen. Am. J. Dig. Dis. 14:811, 1969.

APPENDICES

APPENDIX A

STATEMENT OF INFORMED CONSENT, BREATH HYDROGEN DATA COLLECTION SHEET AND EVAPORATED MILK AND WHOLE CORNMEAL INFORMATION

STATEMENT OF INFORMED CONSENT

Procedure:

The subject will arrive in the Food and Nutrition Laboratory, Home Economic West in the morning after having a relaxed and peaceful night. No food or drink (except water) must be consumed for 12 hours before arriving for the test. The subject is free to ask any questions and should feel comfortable with the laboratory environment.

The study involves collection of breath samples from each individual subject. This is done by exhaling through a plastic tube which is connected to the breath bag. The subject will drink evaporated condensed milk or evaporated milk with a cooked cereal. Unless otherwise required and agreed to by the subject , breath samples will be taken every ten minutes for the next 210 minutes.

The subject will remain in the laboratory during the testing period.

Discomforts:

Few if any discomforts should be experienced. If the subject is a lactose malabsorber, he/she may experience mild stomach cramps, intestinal gas or diarrhea. (These discomforts, if experienced, should last only a short time.)

I have had the chance to ask and receive answers to any questions concerning procedures of this test. I have been told that I can withdraw my consent and to discontinue my participation at any time. On the basis of information I have received, I agree that there has been no attempt either written or oral, to make me to waive any of my legal rights. I also agree to receive the total payment due to me when I complete the entire study. I thereby give my informed consent to participate in the research study.

Signature _____

Date _____

Name _____ Date _____

Race _____ Age _____ Sex _____ Phone _____

Food _____ Weight _____ Height _____

Bag #	Time	Minutes	Area Count	ppm	Symptoms & Comments

INFORMATION ON A CAN OF CARNATION EVAPORATED MILK

Carnation Evaporated Milk (Vitamin D Added)
Carnation Company, Los Angeles, CA 90036, U.S.A.
Reg. S. S. A. No. 1158 "A"
Ingredients: Milk, Disodium Phosphate, Carrageenan, and Vitamin D_3.

Homogenized: by adding one part of water to one part of the contents of this can, a resulting milk product will be obtained which will not be below the legal standard for whole milk. It is unsweetened. "from Contented Cows"

Nutrition Information

Per Portion
Portion Size: 1/2 cup
Portions per Container: 3¼

Calories	170
Protein	8 grams
Carbohydrate	12 grams
Fat	10 grams

Percentage of U.S. Recommended Daily Allowances (U.S. RDA.):

Protein	20	Niacin	*
Vitamin A	4	Calcium	30
Vitamin C	*	Iron	*
Thiamine	2	Vitamin D	25
Riboflavin	20	Phosphorus	25

*Contains less than 2% of the U.S. RDA of these nutrients.

INFORMATION ON A FIVE POUND BAG OF YELLOW WHOLE CORNMEAL

Hodgson Stone Buhr Ground Yellow Whole Grain Unsifted Cornmeal
Hodgson Mill Enterprises. Inc. Ozark County Grainesville. No. 65655.

Important

For added flavor and nutritional value, Hodgson Mill products contain all the original oils, vitamins, and minerals of Whole Grain.

Contains Natural Fiber. No Preservatives, Artificial Coloring, Flavoring BHA or BHT.

APPENDIX B

FIGURES

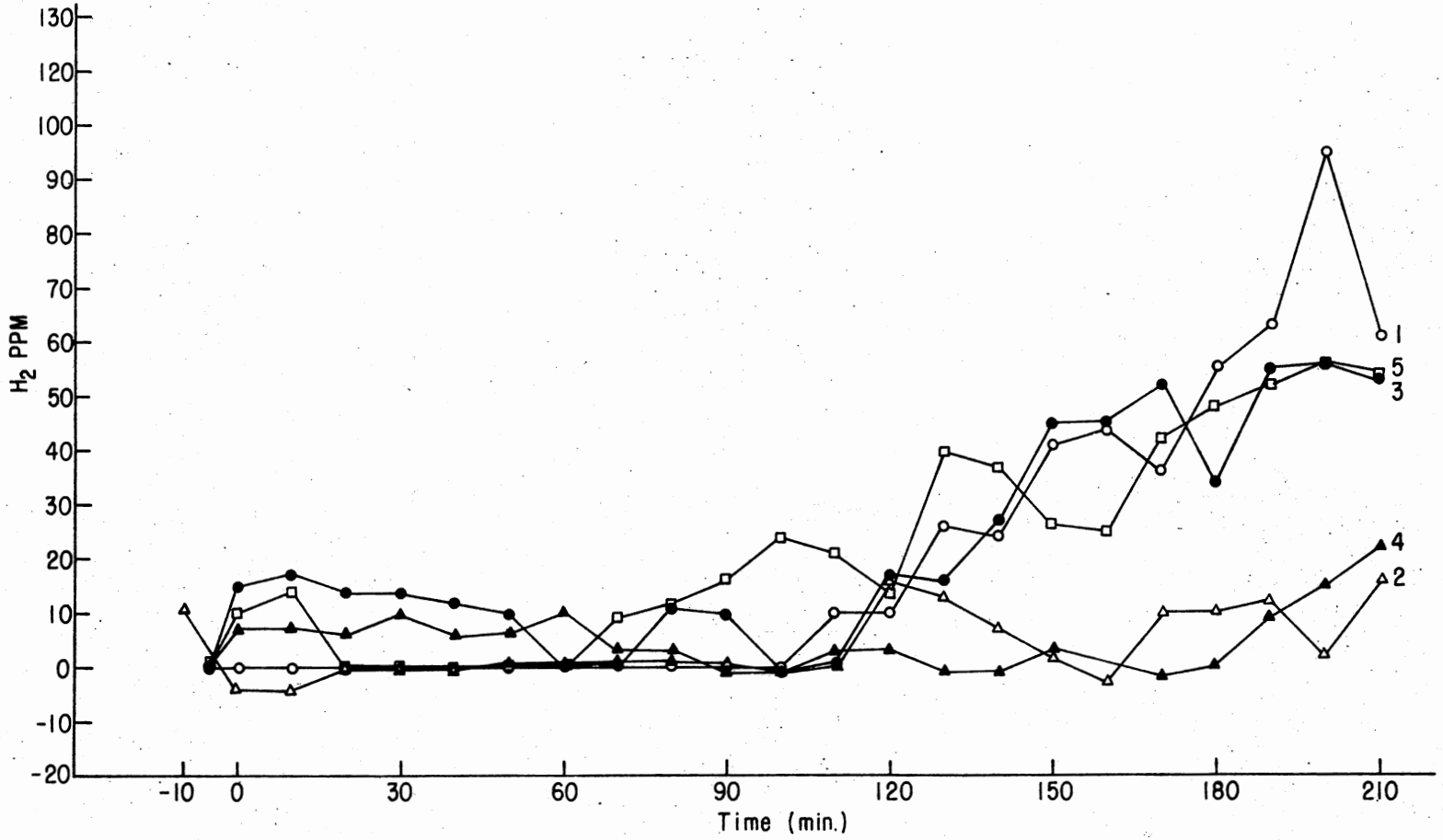


Figure 6. Breath Hydrogen Response Versus Time for Subjects 1, 2, 3, 4, and 5 After Ingestion of 240 ml. of Undiluted Evaporated Milk (Each Curve Represents Individual Subject's Expired Breath Hydrogen).

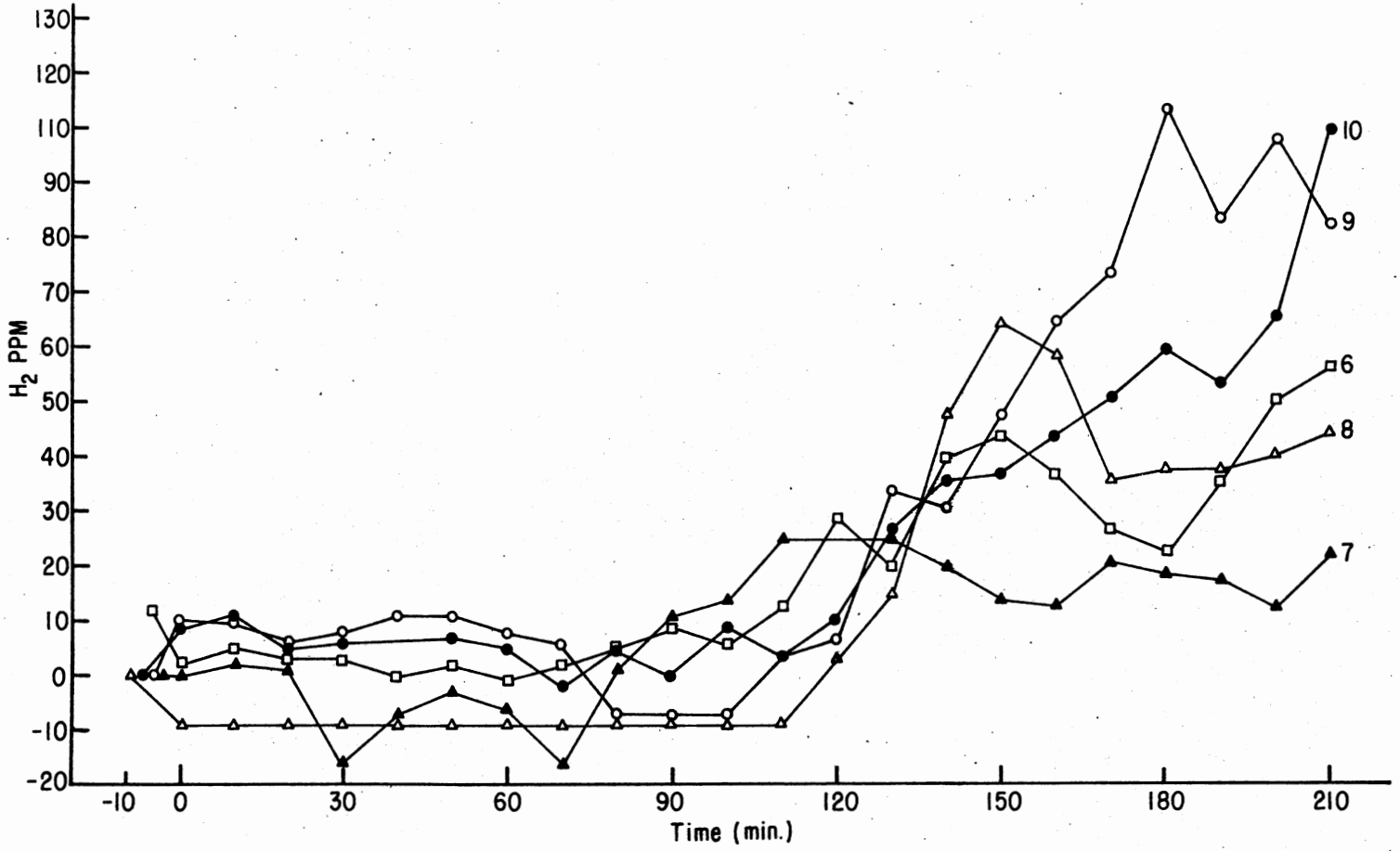


Figure 7. Breath Hydrogen Response Versus Time for Subjects 6, 7, 8, 9 and 10 After Ingestion of 240 ml. of Undiluted Evaporated Milk (Each Curve Represents Individual Subject's Response).

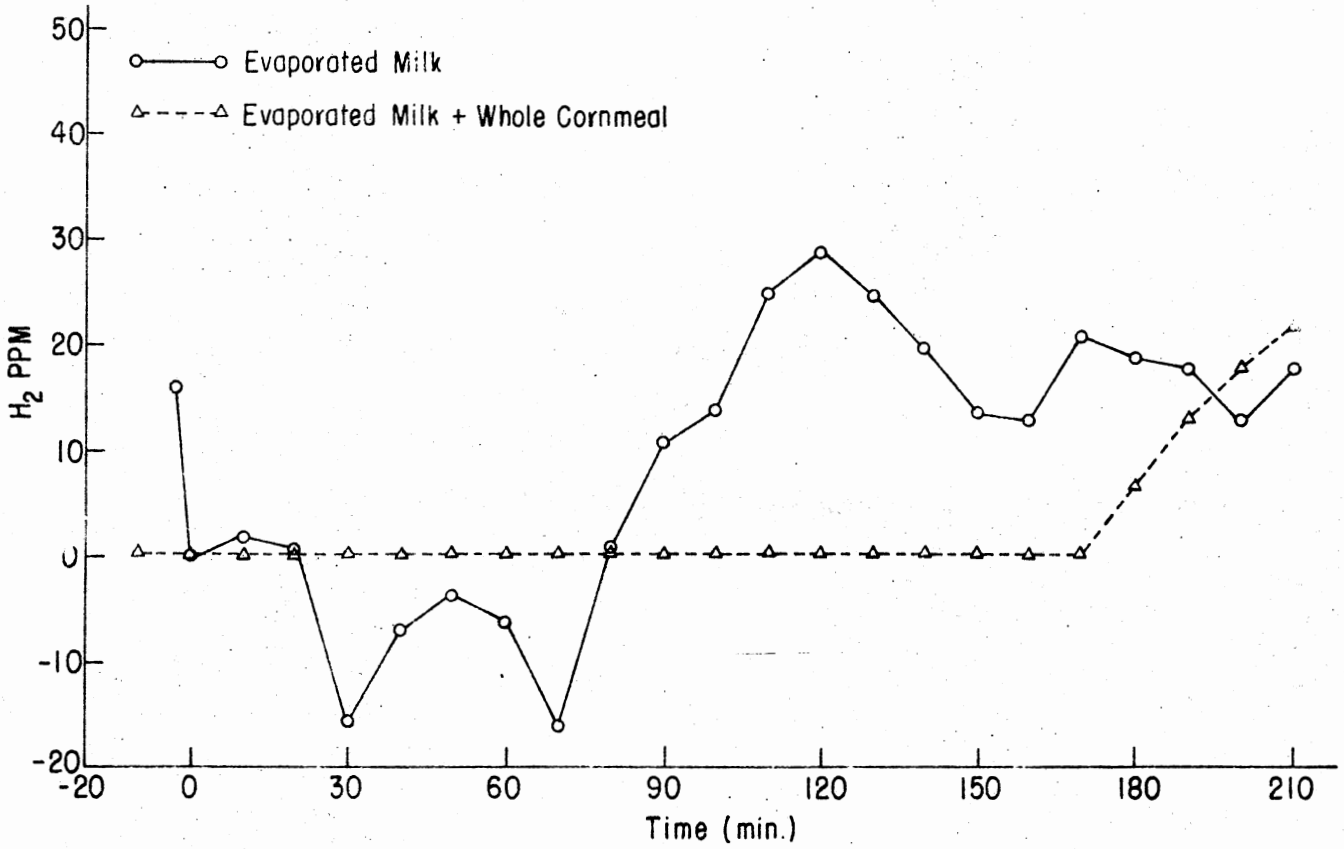


Figure 8. Subject 1 - Breath Hydrogen Response Versus Time After Ingestion of Evaporated Milk and Evaporated Milk with Whole Cornmeal Test Meals (Each Meal Consisted of 240 ml. of Evaporated Milk Which Contained 24 gm. of Lactose).

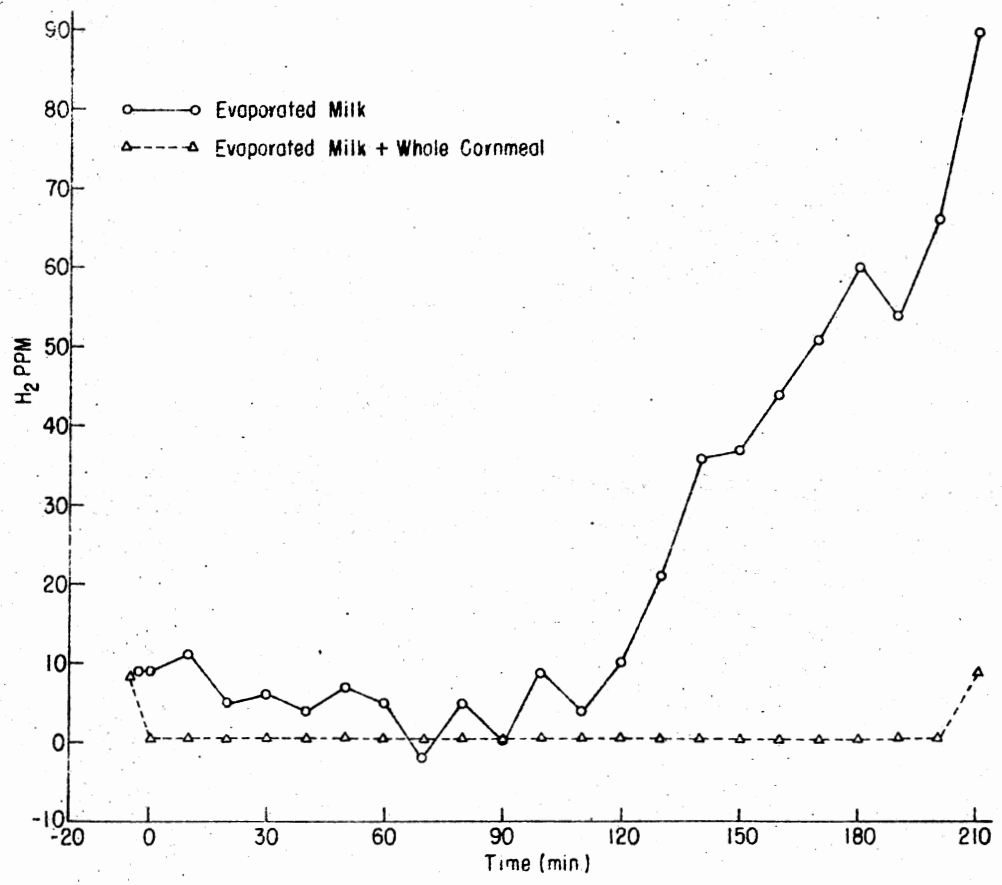


Figure 9. Subject 2 - Breath Hydrogen Response Versus Time After Ingestion of Evaporated Milk and Evaporated Milk with Whole Cornmeal Test Meals (Each Meal Consisted of 240 ml. of Evaporated Milk Which Contained 24 gm. of Lactose).

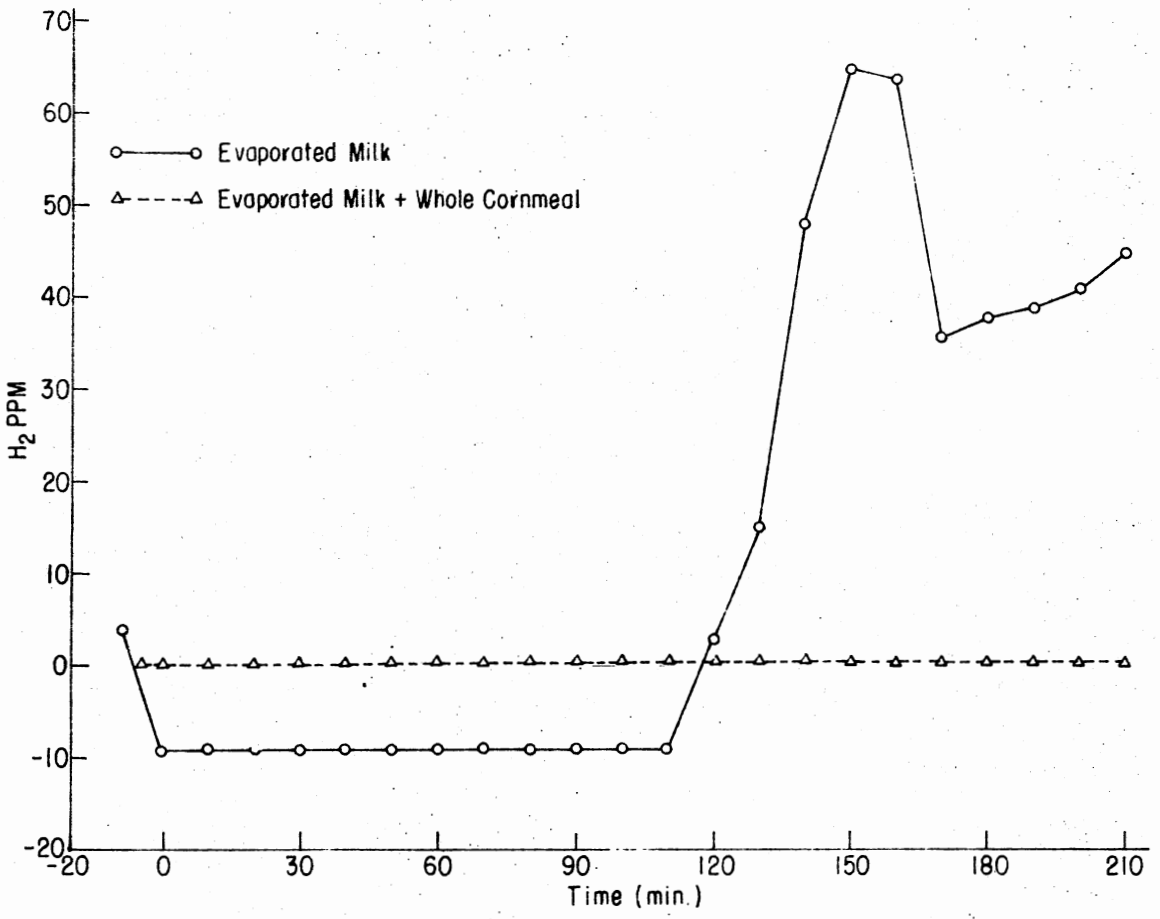


Figure 10. Subject 3 - Breath Hydrogen Response Versus Time After Ingestion of Evaporated Milk and Evaporated Milk with Whole Cornmeal Test Meals (Each Meal Consisted of 240 ml. of Evaporated Milk Which Contained 24 gm. of Lactose).

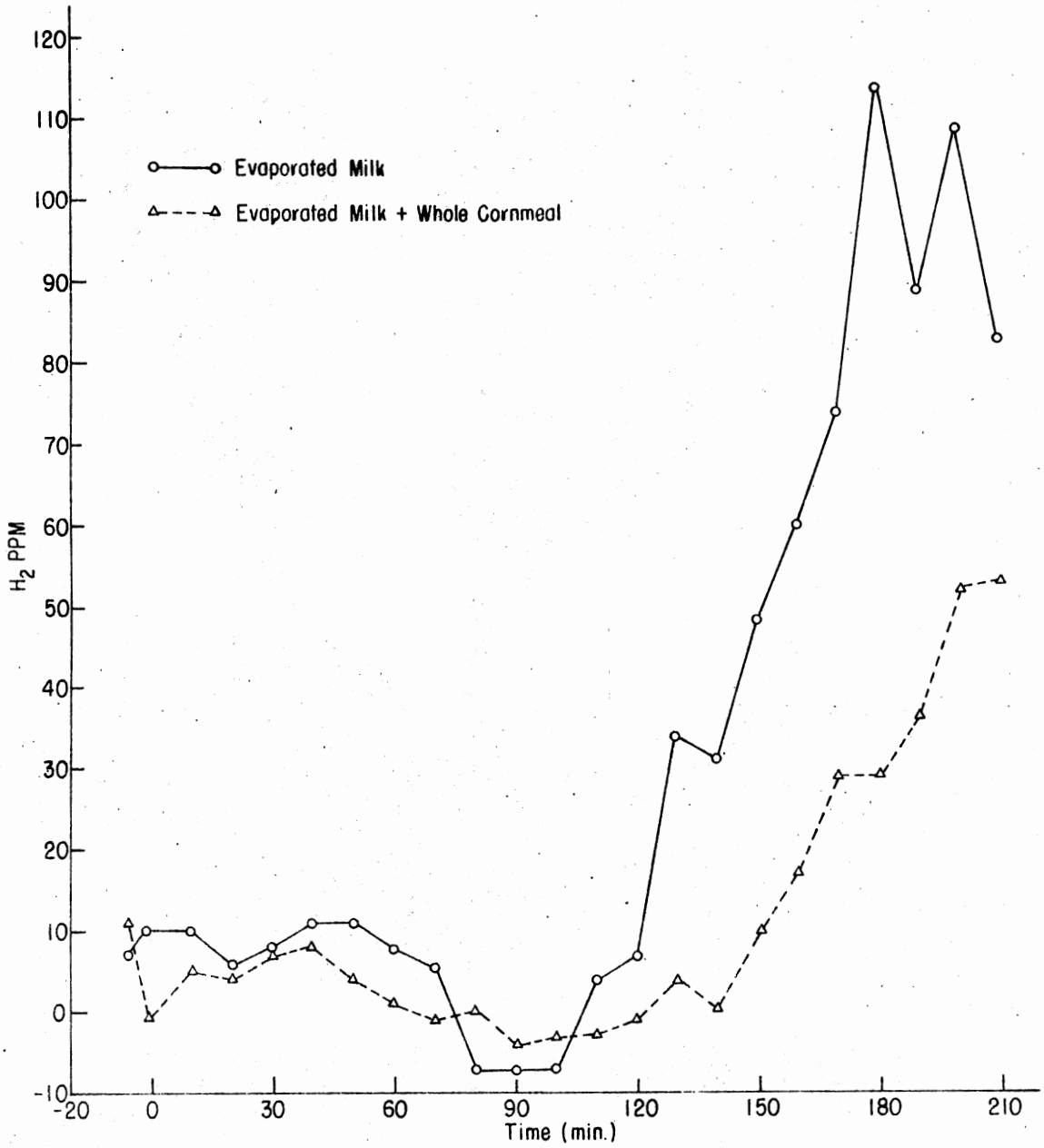


Figure 11. Subject 4 - Breath Hydrogen Response Versus Time After Ingestion of Evaporated Milk and Evaporated Milk with Whole Cornmeal Test Meals (Each Meal Consisted of 240 ml. of Evaporated Milk Which Contained 24 gm. of Lactose).

VITA[1]

Bernice Olu Adeleye

Candidate for the Degree of

Master of Science

Thesis: THE EFFECT OF EVAPORATED MILK AND WHOLE CORNMEAL ON INTESTINAL TRANSIT TIME AND HYDROGEN RESPONSE IN LACTOSE MALABSORBER NIGERIANS

Major Field: Food, Nutrition and Institution Administration

Biographical:

Personal Data: Born in Esa-Odo, Oyo State, Nigeria, June 9, 1949, the daughter of Chief and Mrs. James Balogun.

Education: Graduated from Christ Apostolic Church Secondary School, Ilesa, Oyo State, Nigeria in December, 1969; obtained the Bachelor of Science in Home Economics with a major in Food, Nutrition and Institution Administration from Oklahoma State University in July, 1980; completed the requirements for the Master of Science with a major in Food, Nutrition and Institution Administration at Oklahoma State University, Stillwater, Oklahoma, in July, 1981.

Experience: Clerical Typist, Esa-Oke Grammar School, Esa-Oke, Oyo State, Nigeria, 1970 to 1972; Clerical Officer, University of Ibadan, Oyo State, Nigeria, 1973 to 1977.

Organizations: Nigerian Student Union Organization and African Students Fellowship.