Analytical Schema for Fatty Acid Composition with Special Emphasis on trans Acids

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Abstract

Trans-fatty acids are available to us in our food supply from a few vegetables, ruminants and marsupials, animals fed feed that contain trans-fatty acids, and most commonly from partially hydrogenated vegetables oils. Partial hydrogenation of naturally occurring fatty acids straighten the fatty acid chain into a more crystalline structure changing liquid fats into a more solid fat with increased stability and flexibility for use by food manufacturers. Investigators have estimated our intake to be as high as 8% of total dietary fat intake. It has been shown that trans-fatty acids deposit into human tissues in the same configuration as hydrogenated oils. Animal studies, correlational and prospective studies have related trans-fatty acids to both cancer and heart disease. Consumers should be cautioned about trans-fatty acids in dietary recommendations which promote the use of foods containing trans-fatty acids. Food manufacturers should investigate means by which intake of trans-fatty acid intake could be decreased.

INTRODUCTION

THIS PRESENTATION WILL REVIEW THE SOURCES AND EXPOSURE LEVEL OF TRANS FATTY ACIDS IN OUR DIETS AND THE SUBSEQUENT INCORPORATION OF TRANS FATTY ACIDS INTO HUMAN TISSUES. THEORIES RELATING TRANS FATTY ACIDS TO CANCER AND HEART DISEASE WILL ALSO BE PRESENTED. TRANS-FATTY ACID VALUES DERIVED FROM A RECENT ANALYSIS OF SELECTED PROCESSED AND UNPROCESSED FOODS WILL BE REPORTED.

TRANS FATTY ACIDS ARE AVAILABLE TO US IN OUR FOOD SUPPLY MOST COMMONLY FROM PARTIALLY HYDROGENATED VEGETABLE OILS. RUMINANTS AND MARSUPIALS SYNTHESIZE TRANS BY MICROBIAL HYDROGENATION OF POLY-UNSATURATED FATTY ACIDS. YET, THE AMOUNTS OF TRANS FOUND IN ANIMALS ARE RELATIVELY SMALL. ANIMALS FED FOOD SOURCES CONTAINING TRANS SUCH AS POULTRY AND PORK ARE ANOTHER ANIMAL SOURCE. VEGETABLE PLANTS SUCH AS LEEK, PEAS, SPINACH, AND LETTUCE CONTAIN 3 TRANS-HEXADECANOIC ACID (16:1(3T) (1).

WHY PARTIALLY HYDROGENATE?

FATTY ACIDS ARE CARBON CHAINS WHICH CAN BE CHARACTERIZED AS SATURATED, MONOUNSATURATED AND POLYUNSATURATED FATTY ACIDS ACCORDING TO THEIR LENGTHS. THE SPECIFIC TYPES OF FATTY ACIDS ATTACHED TO THE GLYCEROL COMPOUND AS TRIGLYCERIDE DETERMINE ITS SHAPE. OILS CONSIST OF NATURALLY OCCURRING CIS DOUBLE BONDS WITH THE HYDROGENS ON THE

SAME SIDE OF THE DOUBLE BOND, WHICH CREATE BENDS IN THEIR GEOMETRY WHICH KEEP THEM LIQUID. SATURATED AND TRANS FATTY ACIDS ARE STRAIGHT CHAIN FATTY ACIDS WITH HYDROGEN BONDS ON OPPOSITE SIDES OF THE MOLECULE CAUSING THEM TO PACK TOGETHER INTO A CRYSTALLINE STRUCTURE THAT WILL FORM INTO A SOLID FAT. DUE TO THE RELATIONSHIP BETWEEN SATURATED FATS AND HEART DISEASE, THE FOOD INDUSTRY HAS MOVED AWAY FROM USING ANIMAL FATS IN MANUFACTURING PROCESSED FOODS. PARTIAL HYDROGENATION OF LIQUID OILS SUCH AS SOYBEAN, CORN, CANOLA, COTTONSEED AND PEANUT OILS SUPPLY FATS THAT HAVE A WIDER RANGE OF MELTING TEMPERATURES AND SUFFICIENT STABILITY TO ALLOW USE IN BAKING AND DEEP FAT FRYING. PARTIAL HYDROGENATION EXTENDS THE SHELF LIFE OF A PRODUCT. SOYBEAN OIL IS THE MOST COMMON OIL USED TODAY BECAUSE IT IS THE LEAST EXPENSIVE.

HYDROGENATION OF OILS PRODUCES A VARIETY OF TRANS ISOMERS WHICH DO NOT RETAIN THE BIOLOGICAL ACTIVITY OF THEIR NATURAL CIS FORMS. THEY ARE PREDOMINATELY 18:1 TRANS, 18:2 TRANS TRANS, 18:2 CIS TRANS OR TRANS CIS. ANIMALS PRODUCE MOSTLY 16:1 TRANS AND 18:1 TRANS OR VACCENIC ACID WITH THE TRANS ISOMER AT THE ELEVENTH POSITION. THESE ARE ADDED TO PRODUCE A SUM OF TOTAL TRANS FATTY ACID IN THE DIET. (SLIDE)

70% OF ALL THE VEGETABLE OILS USED IN MANUFACTURING PROCESSED FOODS SUCH AS CRACKERS, COOKIES, SNACK AND FRIED FOODS, ETC. ARE PARTIALLY HYDROGENATED (2). SINCE PARTIAL HYDROGENATION CHANGES THESE NATURALLY OCCURRING CIS FATTY ACIDS TO TRANS ISOMERS, THERE MUST BE CONSIDERABLY LESS OF THE FATTY ACID FROM WHICH THEY WERE OBTAINED. WITHOUT ADEQUATE FOOD TABLES DESCRIBING THE ACTUALLY FATTY ACID CONTENT OF OUR FOODS, IT IS DIFFICULT TO ESTIMATE INTAKE OF NATURAL CIS AND MONO- AND POLYUNSATURATED FATS. YET, LARGE SCALE PROSPECTIVE AND RETROSPECTIVE DIETARY STUDIES REQUIRE THIS INFORMATION. SO THE QUESTION BECOMES HOW DO YOU REPORT THESE CHANGES TO THE PUBLIC AND INVESTIGATORS TO OBTAIN ACCURATE EXPOSURE LEVELS. IN 1988 CANADA BEGAN REPORTING TRANS FATTY ACIDS IN A SEPARATE CATEGORY FOR LABELING PURPOSES. THE U.S. DOES NOT ALLOW TRANS-CONTAINING DIENES (18:2 DOUBLE BONDS) TO BE RECORDED IN THE POLYUNSATURATED FATS REPORTED BUT THE FOOD SAFETY AND NUTRITION DIVISION OF FDA HAS MADE NO RECOMMENDATIONS CONCERNING THE TRANS-MONOENES (18:1 DOUBLE BOND) - THE PRIMARY SOURCE OF TRANS FROM VEGETABLE PRODUCTS (3). LET'S LOOK ON THE NEXT SLIDE TO SEE HOW THE AMOUNTS OF DIFFERENT FATTY ACIDS CHANGE WHEN YOU CORRECTLY REPORT THE TRANS FATTY ACID CONTENT ON THE LABEL.

HOW MUCH TRANS DO WE CONSUME?

INVESTIGATORS HAVE ATTEMPTED TO DOCUMENT THE AVAILABILITY OF TRANS FATTY ACIDS IN OUR FOOD SUPPLY. MARY ENIG HAS EXTENSIVELY INVESTIGATED THE TYPES AND AMOUNTS OF FATS AND OILS USED IN THE U.S. FOOD SUPPLY AND SHOWED THE AMOUNT OF TRANS INTAKE PER DAY, WITH ADJUSTMENTS FOR WASTAGE OF SHORTENINGS, SALAD AND COOKING OILS, AND DISCARDED WASTAGE OF BEEF, TO BE 12.8 GMS.(2). KUMMEROW SUGGESTS THAT THIS TOTAL OF 12.8 GMS MIGHT BE LOW SINCE CONFECTIONERY FAT WHICH CONTAIN 60-80% TRANS DUE TO THE USE OF COCOA BUTTER WAS NOT INCLUDED(4). HUNTER AND APPLEWHITE HAVE

SUGGEST LOWER VALUES OF 8 GRAMS PER DAY FROM THEIR ASSESSMENT OF TRANS IN THE U.S. DIET (5).

ENIG ALSO ANALYZED PROCESSED AND UNPROCESSED FOODS AND PUBLISHED TRANS 18:1 VALUES IN 1983 (6). THESE DATA HAVE BEEN USED BY OTHER INVESTIGATORS TO DETERMINE ACTUAL POPULATIONS INTAKES OF TRANS FATTY ACIDS. VAN DEN REEK IN 1986 FOUND NO SIGNIFICANT DIFFERENCE IN THE TRANS 18:1 CONTENT OF EIGHT ADOLESCENT GIRL'S DIETS CALCULATED USING THE ANALYSIS OF THE 220 ITEMS SUPPLIED BY ENIG'S PUBLICATION VERSUS ANALYZED VALUES PROVIDED BY DUPLICATE PORTIONS OF THE DIETS (7). ENIG HAS ESTIMATED THAT TRANS IS ABOUT 8% OF TOTAL DIETARY FAT IN THE AMERICAN DIET. 6.5%, A SLIGHTLY LOWER AMOUNT, WAS FOUND IN THESE ANALYZED DIETS. LONDON FOUND A 3.44 GRAM INTAKE PER DAY OR 5.83% OF FAT INTAKE IN A GROUP OF 115 WOMEN WHOSE INTAKES WERE ESTIMATED FROM AN EXPANDED VERSION OF THE VALIDATED HARVARD WILLETT FOOD FREQUENCY QUESTIONNAIRE WHICH UTILIZED AGAIN ENIG'S AND SLOVER'S DATA ON TRANS IN FOODS (8,9). HUNTER FOUND THAT 118 MEN CONSUMED 3.4 GRAMS PER DAY OF TRANS FATTY ACID OR 5.4% OF TOTAL FAT USING SACKS' UNPUBLISHED TRANS VALUES FOR PROCESSED AND UNPROCESSED FOODS (10). THE NEXT SLIDE REVIEWS THE PERCENT FATS ESTIMATED IN EACH OF THESE POPULATIONS.

DO TRANS FATTY ACIDS DEPOSIT IN HUMAN TISSUES?

YES, TRANS FATTY ACID DEPOSITS HAVE BEEN FOUND IN VARIOUS HUMAN TISSUES SUCH AS ADIPOSE, LIVER, HEART, PLACENTA, SEBUM, JEJUNUM, AS WELL AS, IN HUMAN MILK FAT (1). AUTOPSY SAMPLES FROM AMERICAN SUBJECTS HAD LEVELS OF TRANS RANGING FROM .4-5% (11). HUMAN TISSUES ARE REPORTED TO CONTAIN UP TO 14% TRANS (12). ADIPOSE AND LIVER TISSUES TEND TO HAVE HIGHER AMOUNTS. EMKEN COMPLETED A REVIEW OF THE LITERATURE AND PROVIDED TABLES ON THE TRANS FATTY ACIDS IN HUMAN TISSUES AND BLOOD LIPIDS IN A 1979 PUBLICATION (13).

OHLROOGGE ET AL REPORTED ON THE AUTOPSY RESULTS OF 8 INDIVIDUALS WHOSE FAMILIES BELIEVED THE DECEASED HAD USED HYDROGENATED VEGETABLE OILS AS THEIR PRIMARY FAT SOURCES (11). THEIR WORK SHOWS THAT ALL THE TRANS ISOMERS PRODUCED DURING VEGETABLE OIL HYDROGENATION ARE INCORPORATED INTO HUMAN TISSUE IN A SIMILAR PATTERN AS FOUND IN THE HYDROGENATED OILS. SINCE SUBJECTS HAD CONSUMED HYDROGENATED PRODUCTS FOR 20-60 YEARS THE AUTHORS CONCLUDED THAT HUMANS DO NOT PREFERENTIALLY ACCUMULATE POSITIONAL ISOMERS IN OUR TISSUES. EMKEN REVIEWED THE ABSORPTION AND DISTRIBUTION OF POSITIONAL CIS AND TRANS ISOMERS IN RAT, EGG AND HUMAN TISSUE AND CONFIRMS FROM EXAMINATION OF HUMAN TISSUE THAT THRESHOLD LEVELS EXIST THOUGH THERE IS PREFERENTIAL INCORPORATION OF DIFFERENT CIS AND TRANS ISOMERS INTO BLOOD PLASMA (14). RESEARCH WILL HAVE TO ACCOUNT NOT ONLY FOR THE EFFECTS OF TOTAL TRANS FATTY ACIDS IN RELATION TO DISEASE BUT THE EFFECTS OF THE DIFFERENT ISOMERS IN RELATION TO HUMAN'S METABOLISM. UNFORTUNATELY, THERE ARE NO PUBLISHED NUTRIENT DATA THAT PROVIDE EPIDEMIOLOGISTS WITH THE CONTENT OF THESE TRANS OR POSITIONAL ISOMERS IN FOODS.

IN THE SPRING OF 1991 WE IN CONJUNCTION WITH FRANK SACKS AT THE CHANNING LABORATORY ANALYZED 21 MARGARINE, 10 OILS, 1 DIET MAYONNAISE, SHORTENING, BUTTER, CHICKEN, BEEF, PORK, AND LAMB FAT SAMPLES, AS WELL AS, SEVERAL PROCESSED FOOD SAMPLES SUCH AS POTATO CHIPS, MUFFINS, PIZZA, COOKIES, CRACKERS, DOUGHNUTS, PASTRY, PIES, AND CORN CHIPS. THESE DATA ARE BEING PROCESSED BUT THE NEXT SLIDE SHOWS TOTAL TRANS VALUES AND PERCENT OF TOTAL FAT FOR A VARIETY OF FOODS. THE NEXT SLIDE SHOWS THE DIFFERENT TRANS AND CIS ISOMERS THAT WERE FOUND IN SOYBEAN AND CANOLA OILS, SHORTENING, STICK MARGARINE, AND MCDONALD'S FRENCH FRIES.

CAN THE KNOWLEDGE THAT TRANS ARE DEPOSITED IN HUMAN TISSUES IN A SIMILAR PATTERN TO WHAT IS EATEN BE USEFUL?

CASE CONTROL STUDIES, THOSE THAT GATHER INFORMATION ABOUT PAST USE, CAN CREATE A BIAS DUE TO MEMORY. EPIDEMIOLOGISTS FEEL THAT BIOCHEMICAL MARKERS WOULD HELP IN DOCUMENTING LONG TERM INTAKE OF SUCH DIETARY COMPONENTS AS FAT SINCE THE HALF LIFE OF ADIPOSE TISSUE IS APPROXIMATELY 2 YEARS (15). TO INVESTIGATE THIS POSSIBILITY LONDON ET AL USED SUBCUTANEOUS FAT ASPIRATES OBTAINED FROM 115 POSTMENOPAUSAL WOMEN AND DIETARY INTAKES REPORTED BY THE HARVARD WILLETT FOOD FREQUENCY QUESTIONNAIRE (8). SPEARMAN CORRELATION COEFFICIENTS BETWEEN THE REPORTED DIETARY INTAKE AND THE ADIPOSE FAT ASPIRATES WERE SIGNIFICANTLY CORRELATED FOR TRANS FATTY ACIDS WITH A CORRELATION OF 0.51. (SLIDE) THESE CORRELATIONS ALSO SUPPORT THE UTILITY OF THE FOOD FREQUENCY QUESTIONNAIRE IN THE ASSESSMENT OF FAT INTAKE. WHEN THE COMPOUNDS ARE PRIMARILY SUPPLIED BY THE DIET AS IN TRANS FATTY ACIDS, ADIPOSE TISSUE DOES SEEM TO REFLECT ITS INTAKE.

35% OF CANCERS IN THE U.S. WITH A POSSIBLE RANGE OF 10-70% HAS BEEN THOUGHT TO LINK DIET TO CANCER (16). IF TRUE, THIS MAKES STUDYING DIETARY FACTORS IN RELATIONSHIP TO THIS DISEASE IMPORTANT. THE RELATIONSHIP OF TRANS FATTY ACID INTAKE TO CANCER HAS BEEN INVESTIGATED THROUGH SUCH MEANS AS ANIMAL STUDIES, CORRELATIONAL STUDIES BASED ON POPULATION GROUPS, AND VERY RECENTLY IN PROSPECTIVE DIET EPIDEMIOLOGIC STUDIES.

OSTLUND-LINDQUIST FOUND THAT RATS FED DIETS CONTAINING 36.6% TRANS FATTY ACIDS HAD A SIGNIFICANTLY LOWER MUTAGENICITY IN THE LIVER THAN WITH DIETS FED NO TRANS (17). SELENSKAS FOUND THAT IN RATS FED A 38% TRANS FAT AT 5 AND 20% OF WEIGHT, TRANS FAT BEHAVES VERY MUCH LIKE A SATURATED FAT IN THE MODIFICATION OF MAMMARY TUMORIGENESIS AND DID NOT SHOW A DETECTABLE EFFECT IN MODIFYING TUMORIGENESIS (18).

CONTRARY TO THE ABOVE REPORTS AWAD CONCLUDES TRANS FATTY ACIDS DO PLAY A ROLE IN TUMOR GROWTH AND DEVELOPMENT IN MICE (19). DECREASED HOST SURVIVAL RATES WERE FOUND AND THE AUTHORS CONSIDER TRANS FATTY ACIDS AS A PROMOTER OF TUMOR DNA SYNTHESIS. THEY ALSO SUGGEST THAT THIS COULD OCCUR IF THE PLASMA MEMBRANE UPTAKE SYSTEM IS MODIFIED BY INCORPORATION OF THE ELAIDIC (18:1t) ACID INTO THE MEMBRANES. THIS STUDY WAS CRITICIZED BY HUNTER SINCE THE CONTROL DIET WAS OLIVE OIL THEREFORE COMPARISON WAS MADE BETWEEN A FREE FATTY ACID AND A TRIGLYCERIDE (20). HOGAN IN RESPONSE TO CRITICISM OF AWAD'S EXPERIMENTAL METHOD, CUSTOM

PREPARED EQUAL PROPORTIONS OF CIS AND TRANS FATTY ACIDS IN HER EXPERIMENT (21). RATS WERE FED A 25% ELAIDIC ACID OR OLEIC ACID DIET TO STUDY THE PROMOTIONAL EFFECT OF DIETARY TRANS-FATTY ACIDS ON LARGE INTESTINAL CARCINOGENESIS AND REPORTED THAT TRANS FATTY ACIDS ENHANCE LARGE INTESTINAL CARCINOGENESIS SINCE TWICE THE NUMBER OF TUMORS WERE FOUND IN THIS GROUP THOUGH THE NUMBER WAS NOT SIGNIFICANTLY DIFFERENT (P=.08). THE EXACT MECHANISM WAS UNCLEAR. THE AUTHORS PROPOSE THAT PERHAPS ALTERATIONS TO THE BACTERIAL FLORA AND BILE ACIDS OR MODIFICATION OF THE LIPID COMPONENT OF CELL MEMBRANES AFFECTING THE CELL GROWTH OR IMMUNOREGULATORY FUNCTION BY THE HOST MAY BE POSSIBLE MECHANISMS. THEY ALSO SUGGEST ALTERED MEMBRANE INTEGRITY MAY LEAVE THE CELLS MORE VULNERABLE TO CARCINOGENS.

IN REVIEW OF CORRELATIONAL DATA ENIG ET AL WERE THE FIRST TO SUGGEST THAT TRANS FATTY ACIDS MIGHT BE RELATED TO THE INCREASED INCIDENCE OF BREAST CANCER IN THE UNITED STATES (6). HER HYPOTHESIS WAS BASED ON THE OVERALL TREND OF SOURCES OF FAT IN THE AMERICAN DIET FROM 1909 TO 1972 FROM ANIMAL TO VEGETABLE FATS AND ON A SIGNIFICANT CONSISTENT ROLE FOR TRANS FATTY ACIDS IN THE POSITIVE CORRELATIONS FOR VEGETABLE FATS AND TOTAL CANCER DEATHS. DURING THIS TIME PERIOD ANIMAL FAT CONSUMPTION DECREASED 7 GRAMS PER CAPITA WHILE VEGETABLE FATS INCREASED 38 GRAMS PER CAPITA PER DAY. AT THE SAME TIME TOTAL FAT INCREASED FROM 31 GRAMS PER DAY. DATA FROM THE USDA BULLETIN, FATS AND OIL SITUATION, PUBLISHED IN 1975, SHOW THAT FROM 1965 TO 1972 50% OF THE TOTAL FAT INCREASE WAS DUE TO VEGETABLE OIL AND 40.9% TO VEGETABLE SHORTENING AND MARGARINE. SINCE 1986 OIL MANUFACTURES HAVE BEEN PROVIDING UNHYDROGENATED OR LIGHTLY HYDROGENATED LIQUID OILS TO THE CONSUMER. IN 1909 ENIG ESTIMATES THAT 4.4 GRAMS OF TRANS WAS CONSUMED PER DAY COMPARED TO 12.1 GRAMS IN 1972.

A PROSPECTIVE STUDY ALLOWS INVESTIGATORS TO OBTAIN INFORMATION ABOUT SUBJECTS AND THEN WAIT YEARS TO LOOK AT DISEASE RISK. IN 1986 A LARGE COHORT OF 47,800 MEN COMPLETED A MODIFIED VERSION OF THE HARVARD WILLETT FOOD FREQUENCY QUESTIONNAIRE. ANALYSIS OF THE QUESTIONNAIRE PROVIDED INFORMATION ON THE TOTAL TRANS FATTY ACID INTAKE FROM DIET. THERE WERE 271 CASES OF PROSTATE CANCER OF ALL STAGES AND 125 CASES OF STAGE C AND D PROSTATE CANCER. STAGE C AND D ARE THE AGGRESSIVE TYPES OF FATAL PROSTATE CANCER. UNPUBLISHED DATA PROVIDING THE RELATIVE RISKS FOR THE PROSTATE CANCER CASES FOR TRANS FATTY ACID INTAKES DIVIDED INTO 5 QUINTILES FOR ALL STAGES AND FOR THE MORE FATAL STAGES SHOWED INCREASED RELATIVE RISKS AND POSITIVE TRENDS. STRONGER TRENDS WERE SEEN FOR STAGES C AND D. IT IS HYPOTHESIZED THAT PERHAPS TRANS FATTY ACIDS ARE INVOLVED IN THE LATE PROMOTION OF THE DISEASE TO THE MORE FATAL STAGES. IN ANOTHER STUDY, ALSO UNPUBLISHED, THERE WERE 120 CASES OF PROSTATE CANCER AND AGAIN THERE WAS EVIDENCE THAT TRANS FATTY ACIDS MAY BE INVOLVED IN PROSTATE CANCER. THESE ARE THE FIRST PROSPECTIVE STUDIES CONNECTING DIETARY TRANS FATTY ACID TO CANCER. FURTHER INVESTIGATION INTO THE ROLE OF TRANS FATTY ACIDS AND CANCER IS NECESSARY.

HOW DO TRANS FATTY ACIDS AFFECT HEART DISEASE?

THE HEART DISEASE ISSUE IN RELATIONSHIP TO TRANS FATTY ACIDS CENTERS AROUND TWO HYPOTHESIS. FIRST, TRANS FATTY ACIDS ARE THOUGHT TO DECREASE PROSTAGLANDIN PRODUCTION AND THEREBY INCREASE THE ESSENTIAL FATTY ACID (EFA) REQUIREMENT OF LINOLEIC ACID (22). IF TRANS TRANS OR CIS TRANS 18:2 ISOMERS ARE THE SOLE DIETARY SOURCES THE REQUIREMENT FOR EFA MAY CHANGE BECAUSE CIS TRANS AND TRANS TRANS GEOMETRIC ISOMERS DO NOT HAVE EFA CAPABILITIES (23). 18:2 CIS IS A PRECURSOR OF ARACHIDONIC ACID, THE PRINCIPAL PRECURSOR OF PROSTAGLANDINS. IF AS EVIDENCE INDICATES THAT CERTAIN TRANS FATTY ACIDS ARE ELONGATED AND DESATURATED, THEY MAY DECREASE THE AVAILABILITY OF CIS 18:2 AND AFFECT PG SYNTHESIS BY DISPLACING THEM WITH VARIOUS PHOSPHOLIPID FRACTIONS. HIGH LEVELS OF DIETARY TRANS TRANS IS KNOWN TO IMPAIR DELTA 6 DESATURASE ACTIVITY AND DECREASE PROSTAGLANDIN SYNTHESIS.

IN THE RATS TRANS FATTY ACIDS ARE COMPLETELY ABSORBED (24), OXIDIZED (25), AND CHOLESTEROL ESTERS ARE BOTH SYNTHESIZED (26) AND HYDROLYZED (27) YET ALL OCCURS AT A SLOWER RATE THAN THEIR CIS COUNTERPARTS. DECREASED PROSTAGLANDIN SYNTHESIS HAS BEEN FOUND IN RATS (28). YET, OTHERS HAVE FOUND THAT WHEN ADEQUATE LINOLEIC ACID IS SUPPLIED IN THE DIET THE "ILL EFFECTS" OF TRANS FATTY ACIDS ARE NEGATED (27). O'KEEFE IN 1990 WAS ABLE TO INVESTIGATE THE EFFECT OF TRANS ISOMERS OF MARINE OILS, EPA AND DHA, ON HUMAN PLATELETS (30). HE FOUND THAT TRANS EPA AND DHA EXHIBIT DIFFERENT INHIBITORY EFFECTS ON ARACHIDONIC ACID METABOLISM IN HUMAN PLATELETS COMPARED TO THE RESPECTIVE CIS FATTY ACIDS.

LET'S ADVANCE TO THE SECOND HYPOTHESIS RELATING TRANS FATTY ACIDS TO HEART DISEASE. TRANS FATTY ACIDS ARE ALSO THOUGHT TO ACT SIMILAR TO SATURATED FATTY ACIDS AND RAISE LDL LEVELS AND LOWER HDL LEVELS. SEVERAL AUTHORS FOUND IN BOTH RABBITS AND SWINE THAT TRANS FATTY ACIDS WERE HYPERCHOLESTEROLEMIC BUT NOT ATHEROGENIC (31,32). VERGROESEN FOUND IN 1972 THAT TRANS ISOMERS OF OLEIC ACID RAISED CHOLESTEROL LEVELS (33). MENSINK ET AL IN 1990 SUPPORTED AN EFFECT OF TRANS ISOMERS ON CHOLESTEROL LEVELS AND FURTHER DELINEATED THAT TRANS FATTY ACIDS ADVERSELY AFFECT THE CHOLESTEROL FRACTIONS (34). HE STUDIED HEALTHY MEN (25) AND WOMEN (34) AND FED THEM 3 MIXED NATURAL DIETS FOR 3 WEEKS THAT VARIED ONLY BY RANDOMLY ADJUSTING 10% OF THE CALORIES FROM CIS 18:1 TO TRANS 18:1 TO SATURATED FAT. THE RESULTS OF THEIR THREE DIETS ARE PRESENTED IN THE NEXT SLIDE. LDL CHOLESTEROL LEVELS WERE HIGHER THAN THE OLEIC DIET AND HDL LEVELS WERE LOWER THAN OLEIC OR SATURATED FAT DIETS. THE EFFECT IS LESS STRONG THAN SATURATED FAT BUT IT CHANGES THE MORE FAVORABLE HDL LIPID PROFILE BY INCREASING LDL AND LOWERING HDL. THE TRIGLYCERIDE VALUES INCREASED AS THEY DID FOR THE SATURATED FAT DIET. CAUTION IS SUGGESTED FOR THOSE PATIENTS AT INCREASED RISK OF ATHEROSCLEROSIS TO AVOID A HIGH INTAKE OF TRANS FATTY ACID.

LAINE IN 1982 LOOKED AT THE EFFECTS OF LIGHTLY HYDROGENATED OIL ON HEALTHY COLLEGE MEN AND WOMEN BY OFFERING THREE TYPES OF DIETS-CORN, UNHYDROGENATED SOY OIL AND HYDROGENATED SOY OIL (35). THE HYDROGENATED OIL DIET DID NOT MAINTAIN THE SAME LEVEL OF POLYUNSATURATED FAT AS A

PERCENTAGE OF TOTAL ENERGY. HDL LEVELS WERE NOT LOWERED BUT MENSINK FEELS THAT HER FINDINGS DO NOT CONTRADICT HIS DUE TO THE CHANGES IN FATTY ACID INTAKE. ANDERSON SUPPORTED THIS HYPOTHESIS IN 1961 (36). HE EXCHANGED HYDROGENATED CORN OIL FOR CORN OIL IN 27 MEN. THERE WAS NOT ONLY A DEFINITE INCREASE IN SERUM CHOLESTEROL BUT TRIGLYCERIDES ALSO INCREASED. MATTSON IN 1985 DID NOT FIND A HYPERCHOLESTEROLEMIC EFFECT OR INCREASE IN TRIGLYCERIDE LEVELS WHEN COMPARING TRANS VERSUS CIS 18:1 OLEIC ACID (37).

WILLETT ET AL IN A PROSPECTIVE DIET HEART DISEASE STUDY OF 85,095 WOMEN FOUND 356 CASES OF CHD. THE RELATIVE RISK OF CHD IN RELATION TO ENERGY ADJUSTED TRANS FATTY ACID INTAKE AMONG WOMEN WITHOUT CHANGE IN MARGARINE CONSUMPTION OVER THE TEN YEARS BEFORE REPORTING THEIR DIETARY INTAKE ON A 60 ITEM FOOD FREQUENCY QUESTIONNAIRE SIGNIFICANTLY INCREASED FROM THE FIRST TO THE FIFTH QUINTILE. THE FOOD PREDICTORS OF TRANS FATTY ACID INTAKE IN STEP-WISE REGRESSION ANALYSIS SHOWS THAT MARGARINE IS THE MOST IMPORTANT DETERMINANT FOLLOWED BY BEEF, COOKIES, AND WHITE BREAD. RELATIVE RISKS OF CHD FOR SPECIFIC FOODS SHOWS THAT THE RISK OF TRANS FATTY ACID INTAKE IS COMING FROM HYDROGENATED VEGETABLE OIL VERSUS BEEF.

THOMAS ET AL IN 1983 ALSO LOOKED AT THE RISK OF ISCHEMIC HEART DISEASE IN RELATIONSHIP TO TRANS LEVELS FOUND IN ADIPOSE TISSUE OF 136 MEN WHO DIED OF HEART DISEASE VERSUS THE FAT OF 95 CONTROLS WHO DIED OF OTHER CAUSES (38). THEY FOUND THAT THE CASES HAD A HIGHER TOTAL TRANS AND 16:1 AND 18:1 TRANS CONTENT IN THEIR ADIPOSE TISSUE AND THAT A RATIO OF THE TRANS FATTY ACIDS TO ANIMAL FATTY ACIDS WAS HIGHER IN THE CASES SUGGESTING THAT THE CASES CONSUMED MORE TRANS FATTY ACIDS THAN THE CONTROLS.

VERSCHUREN AND ZEVENBERGEN HAVE RECENTLY REVIEWED THE SAFETY OF HYDROGENATED OILS IN RESPECT TO BOTH CANCER AND HEART DISEASE (39). THEY REPORT THAT THE AD HOC PANEL OF THE AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY 1985) PROPOSES THAT TRANS FATTY ACIDS DO NOT POSE AN ADVERSE HEALTH EFFECT TO HUMANS. THEY FEEL THAT INCRIMINATION OF TRANS HAS RESULTED FROM USING INAPPROPRIATELY HIGH LEVELS OF TRANS IN EXPERIMENTS THAT ARE NOT AVAILABLE TO HUMANS AND THAT THE BODY IS REACTING TO THAT LEVEL IN A WAY THAT WOULD NOT NORMALLY OCCUR. THEY ALSO FEEL THAT STUDIES HAVE NOT ADEQUATELY CONTROLLED FOR COMPARISONS BETWEEN HYDROGENATED AND UNHYDROGENATED OILS OR FOR APPROPRIATE FATTY ACID COMBINATIONS.

IN CONCLUSION TRANS FATTY ACIDS ARE PRIMARILY SUPPLIED TO HUMANS THROUGH THEIR CONSUMPTION OF HYDROGENATED VEGETABLE OILS. THEY ARE READILY DEPOSITED INTO OUR TISSUES BUT ARE NOT ACCUMULATED OVER TIME. THERE HAS BEEN TREMENDOUS CONTROVERSY ON THE SIGNIFICANCE OF TRANS FATTY ACIDS IN OUR DIETS BUT THERE IS NOW EVIDENCE FROM PROSPECTIVE STUDIES THAT THEY INFLUENCE INCIDENCE OF PROSTATE CANCER IN MEN AND HEART DISEASE IN WOMEN. THE PUBLIC NEEDS TO BE INFORMED AS TO THE EXTENT BY WHICH TRANS ARE AVAILABLE IN THEIR FOODS AND THE IMPORTANCE OF ADEQUATE EFA INTAKE IN THEIR DIET SINCE TRANS FATTY ACIDS INCREASE THE NEED FOR EFA. PEOPLE SHOULD BE INFORMED OF CONCERNS AND THOSE WITH

SPECIAL RISKS SHOULD BE COUNSELLED TO INCORPORATE INFORMATION CONCERNING TRANS INTO THEIR DIETARY CHOICES. FOOD MANUFACTURERS SHOULD INVESTIGATE MEANS BY WHICH INTAKE OF TRANS FATTY ACID INTAKE COULD BE DECREASED. FURTHER INVESTIGATION INTO THE EFFECTS OF TRANS FATTY ACIDS ON BOTH DISEASES IS NECESSARY.

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Analytical Schema for Fatty Acid Composition with Special Emphasis on trans Acids

1) COMMON TRANS ISOMERS

16:1 TRANS

18:1 TRANS

18:2 TRANS TRANS

18:2 CIS TRANS

18:2 TRANS CIS

SUM TO EQUAL TOTAL TRANS

2) COMPOSITION OF VARIOUS FOODS

MARGARINE STICK - 1 TEASPOON

	ACCORDING TO USDA (GRAMS)		*ACCORDING TO CAPILLARY GAS CHROMATOGRAPHY (GRAMS)
	SATURATED	0.65	.67
CIS,	MONOUNSATURATED	1.88	.75
CIS,	POLYUNSATURATED	1.31	1.76
	TRANS		.65

* UNPUBLISHED VALUES SUPPLIED BY DR. FRANK SACK'S

3) COMPOSITION OF VARIOUS FOODS

SHORTENING - 1 TEASPOON	ACCORDING TO USDA (GRAMS)	*ACCORDING TO CAPILLARY GAS CHROMATOGRAPHY (GRAMS)
	SATURATED	1.07	1.03
CIS,	MONOUNSATURATED	1.90	1.18
CIS,	POLYUNSATURATED	1.11	1.14
	TRANS		0.63

* UNPUBLISHED VALUES SUPPLIED BY DR. FRANK SACK'S

4) TRANS FATTY ACIDS AVAILABLE IN U.S. FOOD SUPPLY

	TRANS (g/person/day)
VEGETABLE FATS	
SHORTENING	6.70
SALAD AND COOKING OILS	2.67
MARGARINE	2.35
TOTAL VEGETABLE FATS.....	11.72
ANIMAL AND DAIRY FATS	
BUTTER	0.15
BEEF FAT	0.26
EDIBLE TALLOW	0.07
DAIRY	0.62
LARD	0.01
TOTAL ANIMAL FATS.....	1.11
TOTAL TRANS.....	12.83

ENIG, 1990

5) TRANS FATTY ACID AVAILABILITY

CATEGORY	1984 g/person/day	1989
Household salad and cooking oils	0.31	0
Household shortenings	0.55	0.31
Margarines and spreads	2.85	2.53
Mayonnaise and pourable salad dressings -		0.10
Food-service fats and oils	1.54	1.63
Industrial fats and oils	1.00(est)	
Salted snacks	-	0.50
Cookies	-	0.36
Crackers	-	0.34
Bread,cake,and related products	-	0.72
Panfried French fries	-	0.28
Meat and dairy products	1.38	1.34
TOTAL.....	7.63	8.11

Hunter, 1991

6) TRANS FATTY ACID ESTIMATES

POPULATION	CALCULATED (g/day)	ANALYZED (g/day)	% OF TOTAL FAT
ADOLESCENT GIRLS (VAN DEN REEK,1986)	2.8	2.6	5.3 (18:1 T)
WOMEN (LONDON,1991)	3.4		5.8 (TOTAL T)
MEN (HUNTER,1992)	3.4		5.4 (TOTAL T)

7) TRANS FATTY ACID CONTENT

	GRAMS	PERCENT OF TOTAL FAT
ANIMAL SOURCES		
BUTTER	0.12	2.9%
BEEF	0.90	3.2%
CHICKEN	0.15	1.0%
VEGETABLE SOURCES		
SOYBEAN OIL	0.02	.4%
SHORTENING	0.63	14.7%
MARGARINE STICK	0.65	16.3%
MARGARINE TUB	0.28	7.0%
MARGARINE DIET	0.13	6.8%
PROCESSED FOODS		
POTATO CHIPS (SOY)	0.11	1.1%
POTATO CHIPS (CANOLA)	0.43	4.3%
PIZZA	0.27	2.2%
CORN CHIPS (SOY)	1.37	15.0%
CORN CHIPS (CANOLA)	1.78	19.6%
FRENCH FRIES (MCD)	3.43	35.0%
FRENCH FRIES (BK)	2.41	24.6%

8)

TRANS AND CIS ISOMERS OF VARIOUS FOODS

FATTY ACIDS (100 GMS FOOD)	SOYBEAN OIL	CANOLA OIL	SHORTENING	MARGARINE	FRIES
16:1w7 t	0	0.05	0	0.02	0
18:1w9 c	20.3	47.3	24.9	9.8	21.0
18:1w7 c	1.7	4.0	2.4	8.9	2.9
18:1w12 t	0	0	2.7	2.2	6.4
18:1w9 t	0	0	3.7	2.8	9.1
18:1w7 t	0	0	4.0	2.9	8.0
18:1 t *	0	0.2	5.1	11.3	11.0
18:2w6 cc	54.1	26.3	24.1	37.7	8.1
18:2w6 tt	0	0	1.2	.3	1.2
18:2 ct *	.6	0	3.2	.5	.5

* UNKNOWN POSITIONAL ISOMERS

FRANK SACKS, UNPUBLISHED ANALYSIS (1991)

9)

	TRANS FATTY ACID
FFQ (MEAN)	5.83 +/- 1.68
ADIPOSE (MEAN)	4.35 +/- 1.13
CORRELATION	0.51

* SPEARMAN CORRELATION COEFFICIENTS LONDON ET AL., 1991

10)

RELATIVE RISK OF PROSTATE CANCER

CASES	STAGES	Q1	Q2	Q3	Q4	Q5	TREND
271	A,B,C,D	1.0	1.0	1.08	1.04	1.46	1.81
125	C,D	1.0	0.95	1.03	1.34	1.96	2.84

* CALORIE ADJUSTED

GIOVANNUCCI ET AL., (1992)

11)

FOOD PREDICTORS OF TRANS-FATTY INTAKE IN STEP-WISE REGRESSION ANALYSIS

FOOD	CUMULATIVE R2
MARGARINE	0.39
BEEF, MAIN DISH	0.68
COOKIES	0.77
WHITE BREAD	0.82

12)

TRANS FATTY ACIDS IN HUMAN TISSUE

TISSUE	TRANS CONTENT (%)	METHOD
ADIPOSE	2.4-12.2	IR
LIVER	4 -14.4	
HEART	4.6- 9.3	
AORTA	2.3- 8.8	
MATERNAL DEPOT FAT	1.5- 6.8	IR
PLACENTA	0 - 0.5	
FETAL LIVER	0 - 0.5	
HEART	1.0 - 8.2	IR
AORTA	2.0 - 8.0	
MYOCARDIUM	0.27-1.53	GLC
JEJUNUM	0.38-1.21	
AORTA	0.67-1.53	
SCALP LIPIDS	1% OF 16:1T	GLC
SEBUM	1.7% OF 18:1T	
HUMAN MILK FAT	2-4% 18:1T	GLC

DATA TAKEN FROM EMKEN, 1979

13)

TRANS FATTY ACIDS IN BLOOD LIPIDS

	% 18:1 T	%18:2 TT + CT
SERUM LIPIDS	1.9	0.8
ERYTHROCYTE LIPIDS	2.4	0.7

DATA TAKEN FROM EMKEN, 1979

14)

ESTIMATED DAILY CONSUMPTION OF SPECIFIC POSITIONAL OCTADECENOIC ACID ISOMERS

	POSITIONAL OCTADECENOIC ACID ISOMER (G) BASED ON SOYBEAN OIL								
	6	7	8	9	10	11	12	13	14
c 18:1	0.01	0.14	0.24	6.41	0.37	0.54	0.68	0.14	0.03
t 18:1	0.01	0.27	0.65	1.56	1.53	1.26	0.82	0.48	0.29

DATA TAKEN FROM EMKEN, 1981

15)

LIPID/ LIPOPROTEIN	OLEIC DIET	TRANS-FATTY ACID DIET	SATURATED FAT DIET
		MMOL PER LITER	
TOTAL CHOLESTEROL*	4.46 +/-0.66	4.72 +/-0.72	5.00 +/-0.71
LDL*	2.67 +/-0.54	3.04 +/-0.61	3.14 +/-0.57
HDL*	1.42 +/-0.32	1.25 +/-0.29	1.42 +/-0.32
TRIGLYCERIDES*	.81 +/-0.35	.94 +/-0.40	.94 +/-0.47
CHOLESTEROL/HDL RATIO	3.14	3.78	3.52

* AVERAGE VALUES OF MEN AND WOMEN (59) MENSINK ET AL., (1990)

16)

RELATIVE RISK OF CHD IN RELATION TO ENERGY-ADJUSTED TRANS-FATTY ACID INTAKE AMONG WOMEN WITHOUT CHANGE IN MARGARINE CONSUMPTION 1970-1980 (N=356 CASES)*

	QUINTILE					
	1	2	3	4	5	CHI (P,TREND)
RR	1.0	1.23	1.11	1.36	1.67	3.17
CI		(0.50-1.79	(0.79-1.68)	(0.89-2.09)	(1.05-2.66)	(.002)

*ADJUSTED FOR AGE, BMI, HYPERTENSION, ALCOHOL INTAKE, SMOKING, MENOPAUSAL STATUS, PMH USE, ENERGY,DIETARY LIPIDS, FAMILY HISTORY OF MI BEFORE AGE 60, AND MULTIPLE VITAMIN USE.

Relative Risks of CHD for specific foods.*

	<1/m	1-3/m	1/wk	2-4/wk	5-6/wk	1/d	2-3/d	4+/d	p, trend
Margarine (1 tsp)	1.0	0.83		1.03	1.07		1.03	1.66 (1.10-2.49)	(0.02)
Beef, Pork, Lamb (Main dish)	1.0	1.21	1.14	0.95	1.22 (0.61-2.43)				(0.86)
Cookies (1)	1.0	1.05		1.02	1.49		1.55 (1.02-2.34)		(0.007)
White bread (1 slice)	1.0	0.85		1.07	1.26		(1.43) (1.08-1.90)		(0.003)

* From separate proportional hazards models, controlling for age, time period, BMI, alcohol intake, smoking, menopausal status, postmenopausal hormone use, family history of MI before age 60, history of hypertension, multiple vitamin use.