RESEARCH ARTICLE

Atherothrombotic disease risk factors in youth

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ABSTRACT

BACKGROUND: Atherosclerotic disease begins in childhood with the formation of the fatty streak. Atherosclerotic plaques form at the sites of the fatty streaks. There are no known risk factors to play a role in fatty streak formation. Since some people develop plaque at a young age and others do not develop plaque till an old age, it is clear that the key event in plaque formation must be what happens to the fatty streak. Risk factors for atherosclerotic disease are well known. The purpose of this paper is to demonstrate that the various atherosclerotic disease risk factors can be found in childhood.

MATERIALS AND METHODS: The author has reviewed his database of risk factors in those patients aged 19 years or less. The results are reported in this paper.

RESULTS: Lipid abnormalities occur earlier in life than do abnormalities of the other atherothrombotic disease (ATD, or atherosclerotic disease), with emphasis on the thrombosis that so often precipitates the acute cardiovascular event. Other ATD risk factors are mostly absent or minimally present in childhood and adolescence.

DISCUSSION: ATD begins in childhood. The ATD risk factors have been established over the years. ATD plaques have variable characteristic. There are plaques with central lipid cores covered by a fibrous cap.

CONCLUSION: The author has demonstrated that risk factors, mainly lipid risk factors, occur in childhood and adolescence. Given the high prevalence of ATD in adult life, the author advocates screening for ATD risk factors in persons aged 19 years or less.

Key Words: *Atherosclerotic disease; Atherosclerotic plaques; Childhood; Risk factors*

INTRODUCTION

It is common parlance that Atherothrombotic Disease (ATD, or atherosclerotic disease, with emphasis on the thrombosis that so often characterizes the acute event such as acute myocardial infarction, acute cerebral infarction, etc.) begins in youth with the formation of fatty streaks. ATD plaques then form at the sites of the fatty streaks. However, the fatty streaks form at Low-Density Lipoprotein Cholesterol (LDL-c) levels of 80 mg/dl-90 mg/dl (2.0 mmoles/L-2.25 mmoles/L) [1]. Additionally, some patients sustain their acute ATD events at younger ages, while others do not sustain their ATD events till much later in life. It is clear then that it is not necessarily the fatty streak of youth that is at the base of ATD, but rather what happens to that fatty streak. The factors that adversely affect the fatty streaks are termed causal ATD risk factors, to be distinguished from conditions that represent extant ATD, such as a history of an old AMI on EKG. In the author's professional experience patients with these causal ATD risk factors sustain their ATD events at an early age, whereas patients without these risk factors sustain ATD events at a later age. Additionally, there is no scenario in which someone who lives long enough and does not die of some other condition does not sustain an ATD event sometime prior to death [2,3]. The standard ATD risk factors have been defined and redefined over the years thanks to the pioneering work of the Framingham Heart Study and other investigators [4-9]. The aim of this report is to examine the prevalence of ATD risk factors in a large group of young Americans, aged 1-19 years, in the author's practice of family practice. The risk factors to be utilized are the Cholesterol Retention Fraction (CRF), Low-Density Lipoprotein Cholesterol (LDL-c), High-Density Lipoprotein Cholesterol (HDL-c), CT:HDL-c ratio (FF, or Framingham Fraction, where CT is total cholesterol), non-HDL cholesterol (non-HDL-c Chol), CT, Triglycerides (TG), Systolic Blood Pressure (SBP), 2 Hour Post-Prandial Blood Sugar (2 hr pp BSL), and Body Mass Index (BMI).

The Cholesterol Retention Fraction (CRF) is defined as (LDL-c minus HDL-c)/LDL-c and represents the author's best estimate of the cholesterol building up within the artery wall. This concept derived from a 1981 article (lost to the author and thus unattributal) which asks the question: "Is the LDL: HDL Ratio the Best Lipid Predictor?" Prior to this, the author had treated LDL-c and HDL-c as independent risk factors, but was unable to explain why some patients sustained an ATD event with relatively low LDL-c levels and some with relatively high HDL-c levels.

Inspection of the ATD database revealed that those ATD patients with relatively low LDL-c levels had very low HDL-c levels or were cigarette smokers (younger patients) or had hypertension with/without diabetes (older patients) whereas those patients who sustained an ATD event despite relatively high HDL-c levels usually had very high LDL-c levels or were cigarette smokers (younger patients) or had hypertension with/without diabetes (older patients). It thus became clear to the author that it was the ratio that was of paramount importance. Initially, the author utilized the LDL-c: HDL-c ratio, but the CRF predicted 5% more patients than did the simple ratio and so the author decided to use the CRF as his lipid predictor.

MATERIALS AND METHODS

The author set up his practice of family medicine on 4 November 1974 in Bowling Green, the county seat of Wood County, in northwest Ohio. As a family physician he cared for patients of all ages and both genders. The population of Wood County is mainly of European descent, the chief minority segment being of Latin American descent. Persons of African and Asian descent are present, though not in large numbers. The population of Wood County at last census was about 120,000. The county is mainly rural, Bowling Green being the largest city in Wood County. The city of Bowling Green has a population of about 28,000 persons, and is the home of Bowling Green State University, which contributes about half of the city's population. The University is the largest employer, though there a number of small industries in town. The rural area of Wood County is mainly agricultural.

When the author set up his practice in 1974, he wanted to be able to predict the population at risk of ATD. To do this, the author knew that he would need a database of the known ATD risk factors. Therefore he obtained blood pressure determinations and heights and weights (morphed into a body-mass index) on each and every patient virtually every time that patient presented for medical care. In 1983, when the overwhelming importance of cigarette smoking became apparent to him, the author requested tobacco use information on all new patients, beginning at age 15 years, and in 1991 when he took note of younger people smoking cigarettes, he lowered the age of tobacco use data questioning to age 10 years. (The author assumes that children aged 9 years or less do not use tobacco products, and in the few such patients for whom the author has data, this has held true.) At every appropriate instance, the author obtained a lipid profile, accompanied

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frequently by a two hour post-prandial blood sugar. The lipid profiles obtained prior to 1 January 1978 were limited to CT and TG. 2 hr pp BSL levels were determined on blood obtained exactly 2 hours after ingesting a standard 100 gram carbohydrate breakfast. On 1 January 1978, HDL-c measurements became available to the author, and with it the ability to calculate LDL-c according to the Friedewald formula. The method used to determine HDL-c levels was the world-wide gold standard precipitation method [10].

In 1999, the manufacturers of the auto-analyzers used to measure lipids changed the methodology of HLD-c measurement to the enzymatic method—without informing the medical community in general. The problem is that the two methodologies do not give the same results. The newer enzymatic method gives an HDL-c determination about 10 mg/dl (0.25 mmoles/L) higher than did the older precipitation method. Since LDL-c is not measured, but rather calculated by the Friedewald formula, the resultant calculated LDL-c will be on the order of 10 mg/dl (0.25 mmoles/L) lower for the enzymatic methodology than would have been calculated from the precipitation method. This difference is greatly magnified when the lipid predictor uses both LDL-c and HDL-c [11].

The author has in his personal possession the databases of eight published angiographic regression studies and has used those studies to determine the importance of the lipid and blood pressure risk factors [12-14]. This is of import since the author follows the advice of the late William E. Connor, MD, who stated that one treats putative risk factors, not to treat to a given level, but rather to prevent disease (in this case ATD) and the studies the author used all used the precipitation method of HDL-c measurement. Hence all lipid values noted in this paper use the values obtained using the precipitation method of HDL-c measurement, or the conversion of enzymatic determinations to their precipitation-method equivalents.

Finally, this study is not a randomized controlled clinical trial. All patients deemed at risk of ATD were offered treatment. Unfortunately, when the author set up his medical practice, his patient population was frequently not receptive to the ideas of preventive cardiology or interventional lipidology—and neither were the other medical professionals in the area. As a result, and because the ATD predictive tools were not very good and the medications used to treat cholesterol disorders were not very good either, a number of the author's patients sustained ATD events, and the author was able to separate out a separate ATD database. The characteristics of this latter database will be used to determine ATD risk for each of the standard risk factors.

RESULTS

The various ATD risk factors are listed in Table 1. The various risk factors are divided up into sextiles, with the exception that tobacco use and non-HDL Chol are divided into quintiles. The reasoning for dividing tobacco use into quintiles is obvious; that for non-HDL Chol is based on the National Lipid Association's guidelines [15]. Table 2 shows the risk categories devised by the author's work and his interpretation of the literature.

Cigarette smoking is the chief ATD risk factor [15]. Cigarette smoking is most commonly seen in younger ATD patients whereas ex-smokers are found in middle- to late-aged ATD patients and never smokers (including non-cigarette tobacco products) are generally found in late-aged patients. Obviously there are cross-overs between these three groups. Supporting research is available [16]. Table 3 reveals that cigarette smoking is uncommon prior to age 15 years, but is increasingly more common thereafter. At least in the author's data base, males and females have similar smoking rates. (The limitation of these tables is that children aged 9 years or younger were rarely asked about their cigarette smoking status, but when they were, their response was always in the negative).

CRF data is presented in Table 4 the CRF is the second most important ATD risk factor [17]. Only 57% of males and 59% of females have ideal (low risk) CRF values; 29% of males and 26% of females, intermediate-risk CRF values, and 14% of males and 15% of females, high-risk CRF values. This table also show that the CRF shifts to higher values with increasing age, perhaps slightly more so in females than in males. In males there is a decline in ideal CRF values after puberty, whereas in females, the percentage of ideal CRF values raise steadily, beginning with menarche.

CRF values are determined, by definition, by both LDL-c and HDL-c. Table 5 shows the prevalence of LDL-c values in the author's database. High-risk LDL-c values descend to the 125 mg/dl-149 mg/dl (3.1 mmoles/L-3.7 mmoles/L) sextile because the 125 mg/dl-149 mg/dl (3.1 mmoles/L-3.7 mmoles/L) sextile has the most patients in the author's ATD database. Only 49% of males and 42% of females in the child and adolescent database have ideal (low risk) LDL-c values. Another 29% of males and 34% of females have intermediate-risk LDL-c values and fully 22% of males and 34% of

TABLE 1

Lipid predictor sextiles

Lipid Predictor	I	II	III	IV	V	VI
CT	≤ 99 mg/dl	110-149 mg/dl	150-199 mg/dl	200-249 mg/dl	250-299 mg/dl	≥ 300 mg/dl
	≤ 2.56 mmoles/L	2.59-3.86 mmoles/L	3.89-5.16 mmoles/L	5.18-6.45 mmoles/L	6.48-7.75 mmoles/L	≥ 7.77 mmoles/L
LDL	≤ 99 mg/dl	100-124 mg/dl	125-149 mg/dl	150-174 mg/dl	175-199 mg/dl	≥ 200 mg/dl
	≤ 2.56 mmoles/L	2.59-3.21 mmoles/L	3.24-3.86 mmoles/L	3.89-4.51 mmoles/L	4.53-5.16 mmoles/L	≥ 5.18 mmoles/L
Non HDL Cholesterol	≤ 149 mg/dl	150-179 mg/dl	180-209 mg/dl	210-239 mg/dl	≥ 240 mg/dl	-
	≤ 3.59 mmoles/L	3.62-4.37 mmoles/L	4.40-5.1 mmoles/L	5.17-5.92 mmoles/L	≥ 5.95 mmoles/L	
TG	≤ 99 mg/dl	100-149 mg/dl	150-199 mg/dl	200-249 mg/dl	250-299 mg/dl	≥ 300 mg/dl
	≤ 1.13 mmoles/L	1.41-1.68 mmoles/L	1.70-2.25 mmoles/L	2.26-2.81 mmoles/L	2.82-3.38 mmoles/L	≥ 3.39 mmoles/L
FF	≤ 3.9	4.0-4.9	5.0-5.9	6.0-6.9	7.0-7.9	≥ 8.0
CRF	≤ 0.59	0.60-0.64	0.65-0.69	0.70-0.74	0.75-0.79	≥ 0.80

CT: Total Cholesterol; LDL: Low-Density Lipoprotein Cholesterol; Non HDL: Non High-Density-Lipoprotein Cholesterol; TG: Triglycerides; FF: Framingham Fraction or the ratio of total cholesterol to high-density-lipoprotein cholesterol (CT: HDL); CRF Cholesterol Retention Fraction or (LDL-HDL)/LDL

TABLE 2

Risk categories

Risk Factors	High	Intermediate	Low
CRF	≥ 0.70	0.60-0.69	≤ 0.59
LDL-C	≥ 125	100-124	≤ 99
HDL-C	≤ 29	30-39	≥ 40
FF	≥ 6.0	4.0-5.9	≤ 3.9
Non HDL-C Cholesterol	≥ 240	180-239	≤ 179
CT	≥ 200	150-199	≤ 149
Triglycerides	≥ 200	150-199	≤ 149
SBP-no Rx	≥ 140	120-138	≤ 118
2 hr pp BSL	≥ 200	125-199	≤ 124
BMI	≥ 30	20-29	≤ 19

CRF: Cholesterol Retention Fraction or (LDL-HDL)/LDL; LDL-C: Low-Density-Lipoprotein Cholesterol; HDL-C: High-Density-Lipoprotein Cholesterol; FF: Framingham Fraction or the ratio of total cholesterol to high-density-lipoprotein cholesterol (CT: HDL); Non HDL: Non High-Density-Lipoprotein Cholesterol; CT: Total Cholesterol; TG: Triglycerides; SBP-no Rx Untreated High Blood Pressure; 2 hr pp BSL: Blood Sugar Levels taken 2 hour post prandial; BMI: Body Mass Index

TABLE 3

Tobacco cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	+	Past	OT	NT	∑-	∑
			Male			
≤ 4	0 (0%)	0 (0%)	0 (0%)	350 (100%)	350 (0%)	350
≤ 9	0 (0%)	0 (0%)	0 (0%)	722 (100%)	722 (100%)	722
≤ 14	2 (~0%)	2 (~0%)	0 (0%)	859 (~100%)	859 (~100%)	863
≤ 19	135 (10%)	44 (3%)	6 (~0%)	1179 (86%)	1185 (87%)	1364
			Female			
≤ 4	0 (0%)	0 (0%)	0 (0%)	374 (100%)	374 (100%)	374
≤ 9	0 (0%)	0 (0%)	0 (0%)	691 (100%)	691 (100%)	691
≤ 14	4 (1%)	4 (1%)	0 (0%)	791 (99%)	791 (99%)	799
≤ 19	123 (9%)	36 (3%)	0 (0%)	1163 (88%)	1163 (88%)	1322

+ means current cigarette smoker; Past past cigarette smoker; OT use of other forms of tobacco; NT no history of cigarette smoking; ∑- means never used any form of tobacco

TABLE 4

CRF cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	CRF values						∑
	≤ 0.59	0.60-0.64	0.65-0.69	0.70-0.74	0.75-0.79	≥ 0.80	
			Male				
≤ 4	11 (55%)	4 (20%)	4 (20%)	1 (50%)		-	20
≤ 9	47 (61%)	13 (17%)	9 (12%)	7 (9%)	1 (1%)	-	77
≤ 14	90 (63%)	20 (14%)	18 (13%)	12 (8%)	4 (3%)	-	144
≤ 19	147 (57%)	40 (16%)	32 (13%)	21 (8%)	11 (4%)	5 (2%)	256
			Female	-			
≤ 4	11 (55%)	1 (5%)	6 (30%)		2 (10%)	-	20
≤ 9	34 (52%)	11 (17%)	11 (17%)	4 (6%)	6 (9%)	-	66
≤ 14	84 (56%)	21 (14%)	18 (13%)	12 (8%)	11 (7%)	3 (2%)	150
≤ 19	178 (59%)	36 (12%)	43 (14%)	21 (7%)	18 (6%)	8 (3%)	304

CRF: Cholesterol Retention Fraction or (LDL-HDL)/LDL

TABLE 5

LDL-C cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	CRF value						∑
	≤ 99	100-124	125-149	150-174	175-199	≥ 200	
≤ 4	9 (45%)	9 (45%)	1 (5%)	1 (5%)	-	-	20
≤ 9	27 (35%)	33 (43%)	11 (14%)	6 (8%)	-	-	77
≤ 14	64 (44%)	49 (34%)	22 (15%)	8 (6%)	-	1 (1%)	144
≤ 19	125 (49%)	74 (29%)	40 (16%)	15 (6%)	1 (~0%)	1 (~0%)	256
≤ 4	4 (20%)	10 (50%)	5 (25%)	1 (5%)	-	-	20
≤ 9	19 (29%)	22 (33%)	22 (33%)	2 (3%)	-	1 (2%)	66
≤ 14	55 (37%)	51 (34%)	37 (25%)	6 (4%)	-	1 (1%)	150
≤ 19	129 (42%)	102 (34%)	54 (18%)	14 (5%)	3 (1%)	2 (1%)	304

LDL-C: Low-Density-Lipoprotein Cholesterol

TABLE 6

HDL-C cumulative distribution in ∑ male and female general population: ∑∑ cigarettes (Low end)

Age	CRF value						∑
	≤ 19	20-24	25-29	30-34	35-39	≥ 40	
				Male			
≤ 4	-	-	-	3 (15%)	3 (15%)	14(70%)	20
≤ 9	-	1 (1%)	1 (1%)	6 (8%)	8 (10%)	61	77
≤ 14	-	1 (1%)	4 (3%)	11 (8%)	15 (10%)	113 (78%)	144
≤ 19	-	2 (1%)	15 (6%)	26 (10%)	38 (15%)	176 (68%)	257
				Female			
≤ 4	13 (65%)	7 (35%)	-	-	-	-	20
≤ 9	53 (69%)	19 (25%)	3 (4%)	2 (3%)	-	-	77
≤ 14	95 (66%)	37 (26%)	8 (6%)	4 (3%)	-	-	144
≤ 19	155 (60%)	69 (27%)	17 (7%)	9 (3%)	5 (2%)	2 (1%)	2 57

females have high-risk LDL-c values. While the percentage of high-risk LDL-c levels rises initially in males, it stabilizes at 22% thereafter. In females, the percentage of high-risk LDL-c levels rise in childhood, but then falls progressively with menarche.

Table 6 show the findings for HDL-c. Only 68% of males and 75% of females have ideal HDL-c levels. 25% of males and 20% of females have intermediate-risk HDL-c levels. Interestingly, while the percentage of high-risk HDL-c levels rise in males with increasing age, this rise is not seen in

females.

The FF (CT: HDL-c) is an alternate way of using a lipid ratio to examine ATD risk [18, 19]. It differs from the CRF in that cholesterol attributable to TG is included in the ratio. Table 7 show the data for FF. 60% of both males and females have ideal (low-risk) FF values and another 34% of both males and females have intermediate-risk FF levels. Again, however, the FF rises with increasing age, though not to the same extent as does the CRF.

Non-HDL-c has been touted as a lipid predictor [15]. It is measured by subtracting HDL-c from CT. Non-HDL-c levels are shown in Table 8. 82% of males and 81% of females have ideal Non-HDL-c levels. High-risk Non-HDL-c rises with increasing age, but to nowhere near the CRF or FF.

CT levels contain all of the cholesterol in the blood and were the standard means of measuring ATD risk prior to the advancement of HDL-c as a lipid predictor in 1975 [18]. Table 9 give the levels for CT. 37% of males and 29% of females have ideal CT levels while 51% of males and 56% of females have intermediate-risk levels.

TG levels are shown in Table 10. Ideal TG levels are seen in 89% of both males and females. 2hr pp BSL levels are shown in Table 11. Ideal 2 hr pp BSL levels are seen in 98% of males and 99% of females. SBP (untreated) levels are shown in Table 12. Ideal SBP levels are found in 75% of males and 82% of females.

Lastly, BMI levels are shown in Table 13. 50% of males and 63% of females have BMI values of 19 or less. 45% of males and 33% of females have BMI levels of 20-29, which are not non-ideal for adults, but are clearly abnormal for children and adolescents. The main BMI portion in this latter group is the 20-24 range. As the tables show, all ATD risk factors worsen with age.

DISCUSSION

ATD begins in childhood. The ATD risk factors have been established over the years, thanks to the pioneering work by the Framingham Heart Study as noted previously. ATD plaques have variable characteristic. There are plaques with central lipid cores (cholesterol—not TG) covered by a fibrous cap [19]. There are ATD plaques which are mainly defined by smooth muscle cell hypertrophy. And there are fibrous plaques. These are the main types, but certainly there are plaques that combine these characteristics. It is tempting to suppose that the first type of plaque is related to dyslipidemia;

TABLE 7

FF cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	CRF value						∑
	≤ 3.9	4.0-4.9	5.0-5.9	6.0-6.9	7.0-7.9	≥ 8.0	
				Male			
≤ 4	13 (65%)	7 (35%)	-	-	-	-	20
≤ 9	53 (69%)	19 (25%)	3 (4%)	2 (3%)	-	-	77
≤ 14	95 (66%)	37 (26%)	8 (6%)	4 (3%)	-	-	144
≤ 19	155 (60%)	69 (27%)	17 (7%)	9 (3%)	5 (2%)	2 (1%)	257
				Female			
≤ 4	12 (60%)	6 (30%)	1 (5%)	1 (5%)	-	-	20
≤ 9	40 (60%)	18 (27%)	7 (10%)	1 (1%)	1 (1%)	-	67
≤ 14	90 (60%)	36 (24%)	18 (12%)	4 (3%)	2 (1%)	1 (1%)	151
< 19 _	183 (60%)	79 (26%)	26 (8%)	6 (2%)	6 (2%)	6 (2%)	306

FF: Framingham Fraction or the ratio of total cholesterol to high-density-lipoprotein cholesterol (CT: HDL)

TABLE 8

Non HDL cholesterol cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	CRF value					∑
	≤ 149	150-179	180-209	210-239	≥ 240	
			Male			
≤ 4	19 (95%)	1 (5%)	-	-	-	20
≤ 9	67 (87%)	6 (8%)	4 (5%)	-	-	77
≤ 14	122 (85%)	17 (12%)	4 (3%)	-	1 (1%)	144
≤ 19	211 (82%)	34 (13%)	11 (4%)	-	1 (~0%)	257
			Female			
≤ 4	18 (90%)	2 (10%)	-	-	-	20
≤ 9	54 (81%)	11 (16%)	1 (1%)	1 (1%)	-	67
≤ 14	120 (79%)	25 (17%)	5 (3%)	1 (1%)	-	151
≤ 19	249 (81%)	44 (14%)	9 (3%)	-	4 (1%)	306

Non HDL: Non High-Density-Lipoprotein Cholesterol

TABLE 9

CT cumulative distribution in ∑ male and female general population: ∑∑ cigarettes (including newborns)

Age	CRF value						∑
	≤ 99	100-149	150-199	200-249	250-299	≥ 300	
				Male			
≤ 4	40 (50%)	18 (23%)	19 (24%)	3 (4%)	-	-	80
≤ 9	40 (25%)	28 (18%)	75 (47%)	15 (9%)	-	-	158
≤ 14	41 (15%)	61 (22%)	151 (54%)	27 (10%)	2 (1%)	-	282
≤ 19	42 (9%)	124 (28%)	228 (51%)	54 (12%)	2 (~0%)	-	450
				Female			
≤ 4	39 (57%)	7 (10%)	17 (25%)	4 (6%)	1 (1%)	-	68
≤ 9	39 (28%)	14 (10%)	69 (49%)	16 (11%)	3 (2%)	-	141
≤ 14	39 (15%)	41 (16%)	137 (53%)	39 (15%)	3 (1%)	-	259
< 19	40 (9%)	95 (20%)	258 (56%)	68 (15%)	6 (1%)	1 (~0%)	468

CT: Total Cholesterol

TABLE 10

TG cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	CRF value						∑
	≤ 99	100-149	150-199	200-249	250-299	≥ 300	
				Male			
≤ 4	22 (85%)	3 (12%)	1 (4%)	-	-	-	26
≤ 9	79 (84%)	10 (11%)	3 (3%)	-	1 (1%)	1 (1%)	94
≤ 14	150 (80%)	24 (13%)	7 (4%)	3 (2%)	2 (1%)	1 (1%)	187
≤ 19	235 (73%)	53 (16%)	22 (7%)	6 (2%)	4 (1%)	3 (1%)	323
				Female			
≤ 4	16 (76%)	5 (24%)	-	-	-	-	21
≤ 9	77 (75%)	23 (23%)	1 (1%)	-	1 (1%)	-	102
≤ 14	137 (63%)	57 (26%)	13 (6%)	3 (1%)	5 (2%)	1 (~0%)	216
≤ 19	262 (64%)	102 (25%)	31 (8%)	6 (1%)	10 (2%)	1 (~0%)	412

TG: Triglycerides

TABLE 11

2 hr pp BSL cumulative distribution in ∑ male and female general population: ∑∑ cigarettes

Age	CRF value						∑
	≤ 99	100-124	125-149	150-174	175-199	≥ 200	
				Male			
≤ 4	9 (100%)	-	-	-	-	-	9
≤ 9	30 (75%)	10 (25%)	-	-	-	-	40
≤ 14	81 (74%)	26 (24%)	1 (1%)	1 (1%)	-	-	109
≤ 19	158 (78%)	40 (20%)	3 (1%)	1 (~0%)	-	-	202
				Female			
≤ 4	2 (50%)	2 (50%)	-	-	-	-	4
≤ 9	28 (78%)	8 (22%)	-	-	-	-	36
≤ 14	80 (74%)	27 (25%)	1 (1%)	1 (1%)	-	-	108
≤ 19	196 (80%)	46 (19%)	4 (2%)	1 (~0%)	-	-	246

2 hr pp BSL Blood Sugar Levels taken 2 hour post prandial

TABLE 12

SBP-no RX cumulative distribution in ∑ male and female general population: ∑∑ cigarettes (High end)

Age	CRF value						∑
	≤ 118	120-128	130-138	140-158	160-178	≥ 180	
				Male			
≤ 4	161 (100%)	-	-	-	-	-	161
≤ 9	530 (99%)	5 (1%)	1 (0%)	-	-	-	536
≤ 14	967 (92%)	64 (6%)	15 (1%)	5 (~0%)	1 (~0%)	-	1052
≤ 19	1373 (75%)	299 (16%)	105 (6%)	57 (3%)	5 (~0%)	1 (~0%)	1840
				Female			
≤ 4	178 (99%)	1 (1%)	-	-	-	-	179
≤ 9	433 (98%)	10 (2%)	-	-	-	-	443
≤ 14	844 (92%)	50 (6%)	13 (1%)	1 (~0%)	-	-	908
≤ 19	1432 (82%)	225 (13%)	71 (4%)	16 (1%)	1 (~0%)	1 (~0%)	1746

SBP-no Rx untreated high blood pressure

TABLE 13

BMI cumulative distribution in ∑ male and female general population: ∑∑ cigarettes (High end)

Age	CRF value						∑
	≤ 19	20-24	25-29	30-34	35-39	≥ 40	
				Male			
≤ 4	323 (92%)	25 (7%)	1 (~0%)	1 (~0%)	-	-	350
≤ 9	634 (88%)	74 (10%)	9 (1%)	5 (1%)	-	-	722
≤ 14	898 (73%)	259 (21%)	57 (5%)	17 (1%)	4 (~0%)	-	1235
≤ 19	1000 (50%)	678 (34%)	231 (11%)	73 (4%)	20 (1%)	8 (~0%)	2010
				Female			
≤ 4	351 (94%)	20 (5%)	2 (1%)	-	1 (~0%)	-	374
≤ 9	627 (91%)	58 (8%)	4 (1%)	1 (~0%)	1 (~0%)	-	691
≤ 14	838 (73%)	224 (19%)	64 (6%)	16 (1%)	6 (1%)	2 (~0%)	1150
≤ 19	869 (63%)	349 (25%)	112 (8%)	35 (3%)	14 (1%)	6 (~0%)	1385

BMI: Body Mass Index

the second, to hypertension; and the third, to cigarette smoking and perhaps diabetes. Plaque composition would then depend upon the risk factor mix. Treatment of prevent each type of plaque would of course depend upon the risk factors involved.

As noted earlier, fatty streaks are common in childhood and form in the absence of the standard ATD risk factors. The commonest abnormality in childhood and adolescence is a non-ideal BMI (20-29), but the main rise in BMI, in both males and females, occurs in the second decade of life and is in the 20-24 BMI range. Significant BMI abnormalities are rarely seen in the first decade of life, becoming more common in the second decade. There is a clear progression from BMI values from 19 or less to 20-24 and 25-29 in the second decade of life.

CRF abnormalities are the earliest occur in childhood, being present in the first decade of life. HDL-c abnormalities are more common in males, whereas LDL-c abnormalities are more common in females. Both contribute to a non-ideal CRF. (Such findings also occur in the ATD population database) [2, 3]. The CRF was originally evolved to estimate the amount of cholesterol accumulating within the artery wall. This can be due to excess cholesterol entering the artery wall (LDL-c) or to inadequate removal from the artery wall by reverse cholesterol transport (HDL-c). CRF abnormalities appear to predate the BMI abnormalities. Interestingly, low-risk levels of LDL-c appear to rise with age in the teenage years, more so in females than in males, and the author believes that, in females, this is due to the beneficial effect of estrogen upon LDL-c. The author has observed amelioration of dyslipidemia in female children who have passed through menarche. (Feeman, unpublished data)

All of the ATD risk factors show the same worsening with time, but only the cholesterol lipid predictors occur throughout childhood. Thus children and adolescents should be screened for lipid risk factors—especially if there is a family history of ATD or dyslipidemia. It costs nothing to inquire about cigarette smoking status, and this should begin in the second decade of life. SBP determinations should be routine as well—as they cost nothing to perform. BMI determinations are likewise free to determine. A 2 hr pp BSL is more challenging, but since glucose intolerance is uncommon within the first two decades of life, one could simply determine a fasting blood sugar level and then do a 2 hr pp BSL should the fasting blood sugar level be elevated.

Here it should be noted that when LDL-c is excessively high (170 mg/dl [4.1 mmoles/L] or higher), the HDL-c is unable to compensate and ATD events will occur eventually, though the lower the CRF, the older the patient is when the ATD event occurs [2, 3]. This has led to the concept of the Cholesterol Threshold (C Thr), which is present whenever the CRF is 0.70 or higher and/or LDL-c is 170 mg/dl (4.1 mmoles/L) or higher. Dyslipidemia therapy is warranted whenever the C Thr is present. Conversely if HDL-c is excessively low, the CRF will always be high, and so the LDL-c guidelines are followed. Even with these considerations, the author recommends the use of the CRF as the main screening tool for dyslipidemia since the CRF predicts better than the other lipid predictors.

The importance of early detection of the ATD risk factors is that the amount of plaque present depends upon the severity of the risk factor and the length of time that that particular risk factor has been operational. In his own practice of family medicine, the author has seen countless middle-aged patients with lipid abnormalities and no prior lipid testing, in which cases the author has no idea of how long the dyslipidemia has been operative and hence how much plaque is present. In such cases, the author must offer treatment immediately in an attempt to ward off future clinical events. When previous lipids are known, the author is better able to quantify ATD risk (based on the degree and duration of the lipid abnormality) and hence better able to know the appropriate time to initiate therapy.

CONCLUSION

The standard ATD risk factors can be found in childhood and adolescence. These standard risk factors act upon pre-existing fatty streaks and early plaques, leading to clinical ATD events later in life—and the longer these risk factors go undetected and hence untreated, the earlier will those ATD events occur in adulthood. The author strongly urges the screening of children and adolescents for ATD risk factors.

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