POLYCHLORINATED BIPHENYLS, CHLORINATED PESTICIDES, AND SERUM LIPIDS IN RESIDENTS OF ANNISTON, ALABAMA

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Introduction

Organochlorines are lipophilic compounds and there have been early reports in laboratory animals that exposure to polychlorinated biphenyls (PCBs) or other organochlorines may result in elevated levels of lipids[1-2]. Different lipid components were usually affected. Hypercholesterolemia developed in rats fed with PCBs while elevated triglycerides and lowered total cholesterol, HDL and LDL cholesterol were reported in Aroclor 1254 fed monkeys[3-4]. Human studies also reported elevation in triglycerides, cholesterol, or both in different populations following different organochlorines exposures[5-7]. It was also argued that the elevation in PCB concentrations may instead be the result of hyperlipidemia[8]. Lipids, similar to organochlorines, tend to generally increase with age but the levels may then decrease in old age[9]. The complex relationships between serum concentrations of organochlorines, age, and serum concentrations of lipids are not well understood. We studied this relationship in the African American and Caucasian residents of Anniston, Alabama, participants of the Anniston Community Health Survey.

Materials and Methods

Anniston, Alabama, is a city of about 24,000 people where PCBs were manufactured from 1929 until 1971. To our knowledge no chlorinated pesticides were produced. With stratification by race and residential proximity to the plant, 1,110 randomly selected adults were interviewed. Of these, 765 had lipids and PCBs measured in samples collected in 2005-7. Serum levels of 35 PCB congeners with ortho-substituted chlorines (28, 44, 49, 52, 66, 74, 87, 99, 101, 105, 110, 118, 128, 146, 149, 151, 153, 156, 157, 138-158, 167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 195, 199, 196-203, 206, 209) and 9 organochlorine pesticides [hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCCH), γ-HCCH, oxychlordane, trans-nonachchlor, dichlorodiphenyltrichloroethanes (p,p'-DDE, p,p'-DDT, o,p'-DDT) and mirex] were measured by high resolution gas chromatography/isotope-dilution high resolution mass spectrometry at the Centers for Disease Control and Prevention's National Center for Environmental Health laboratory[10]. Serum total cholesterol, triglycerides, HDL, and LDL cholesterol were determined using automated enzymatic methods by the clinical chemistry laboratory at the Jacksonville Medical Center, Jacksonville, Alabama. Total serum lipids were calculated using the formula updated by Bernert et al.[11]

Data on demographics, lifestyle factors, and health status were collected using an interviewer administered questionnaire. Medications use was verified by a nurse during home or office visit. About a quarter of the study population were taking lipid lowering medication (n=187) including statins, other lipid lowering drugs, or a combination of lipid lowering drugs. After the exclusion of 3 participants with missing covariates, 575 subjects who were not on lipid lowering medication were included in the present analysis.

The sum of PCBs and the sum of organochlorine pesticides were used in the statistical analyses as the exposure variables. In this analysis, 8 PCB congeners (52, 49, 44, 101, 110, 151, 149, and 128) and γ-HCCH were excluded from the summation because of more than 60% of values below the detection limit. For the remaining PCB congeners and pesticides, values below detection limits were replaced by the detection level divided by the square root of 2. Organochlorine concentrations were skewed and they were natural log transformed. Lipid concentrations were normally distributed. Multiple linear regression modeling was used to evaluate relationships between 'outcomes' (total lipids, total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides) and exposure. All models were adjusted for age, sex, race/ethnicity, and body mass index (BMI) (weight in kilograms divided by squared height in meters). Smoking, alcohol consumption, family history of heart disease, or exercise did not alter model estimates and were not included in the final analyses.

Results and Discussion

Characteristics of Anniston study participants not on lipid lowering medication stratified by race are shown in Table 1. There were approximately equal numbers of Caucasians and African Americans and seventy percent were female. While the ages and BMI were similar, Caucasians had significantly higher total lipids and triglycerides than African-Americans but lower HDL. All mean serum lipid concentrations were within 'normal' range (total cholesterol 120-200 mg/dL; HDL 35-86 mg/dL, LDL 80-130 mg/dL, triglycerides <200 mg/dL)[12]. High mean BMIs indicate high level of obesity in this sample of Anniston population. African-Americans had on average about three times higher concentrations of the sum of PCBs and almost double the concentration of total pesticides. The range of exposures was wide with serum PCBs ranging from 0.1 to 170.4 ppb and pesticides concentrations ranging from 0.2 to 40.4 ppb whole weight.

Table 1. Characteristics of Anniston study participants not on lipid lowering medication stratified by race.

	Caucasian (n=289)		African American (n=286)	
	Mean	95% CI	Mean	95% CI
Age (years)	52.5	50.5-54.5	51.6	49.9-53.3
BMI (kg/m^2)	30.3	29.4-31.3	31.4	30.5-32.3
Σ PCBs (ppb whole weight)	3.3	2.8-3.9	9.3	7.3-11.2
Σ Pesticides (ppb whole weight)	3.2	2.6-3.8	5.8	5.1-6.6
Total lipids (mg/dL)	662	644-680	615	596-634
Total Cholesterol (mg/dL)	198	194-204	192	188-198
HDL cholesterol (mg/dL)	45.7	44.2-47.2	51.2	49.1-53.3
LDL cholesterol (mg/dL)	123	119-128	120	115-124
Triglycerides (mg/dL)	147	138-158	116	103-128

Results from multivariate linear regression models are shown in Table 2. Higher concentrations of PCBs and pesticides were associated with increasing total lipids, total cholesterol, and triglycerides. There was no significant association with HDL or LDL. Age was negatively correlated with levels of total lipids and total triglycerides. Total cholesterol and HDL were significantly higher in women than men, while triglycerides were significantly lower. BMI was positively correlated with total lipids and triglycerides, but negatively correlated with HDL. Serum concentration of total lipids, total cholesterol, and triglycerides were substantially and significantly lower in the African American than Caucasian subjects, while HDL was significantly higher.

Table 2. Results of multivariate regression models in those not on lipid lowering medications.

	Total lipids	Total Cholesterol	HDL	LDL	Triglycerides
	β (p-value)	β (p-value)	β (p-value)	β (p-value)	β (p-value)
Σ PCB	25.4 (<.001)	5.23 (0.04)	0.52 (0.57)	3.51 (0.12)	14.7 (0.006)
Σ Pesticides	37.9 (<.001)	5.94 (0.03)	-0.39 (0.70)	2.30 (0.35)	21.4 (<0.001)
Age	-1.55 (0.01)	0.03 (0.86)	0.05 (0.45)	0.16 (0.34)	-1.56 (<0.001)
Sex (Female)	-9.09 (0.51)	5.36 (0.17)	6.10 (<0.001)	2.21 (0.53)	-21.8 (0.009)
BMI	1.60 (0.02)	-0.03 (0.88)	-0.55 (<0.001)	0.16 (0.41)	1.74 (0.0002)
Race (African American)	-93.9 (<0.001)	-13.6 (<0.001)	6.21 (<0.001)	-8.50 (0.02)	-62.3 (<0.001)

While some of the estimates of associations among lipids and PCBs and pesticides are strong and statistically significant, these models explain only a small portion of variation in lipid concentrations (R^2) ranging from 6% to 13%. Positive correlation between age and total lipids (r = 0.66) turns to negative correlation when PCBs and pesticides are added to the model (r = -0.52; data not shown). Because of the instability of estimates (for age) and low predictive value of the models overall, residual confounding or collinearity could be present. Furthermore, African Americans that on average have almost three times higher PCBs and two times higher concentrations of pesticides showed substantially lower total lipids and triglycerides and higher levels of HDL than Caucasians in these adjusted models (Table 2), similar in direction and even more pronounced in magnitude to the unadjusted data (Table 1). The possibility that the observed associations among lipid components and PCBs/pesticides are spurious cannot be excluded.

Possible explanation of differences in lipid levels include higher activity of lipoprotein lipase in African Americans, which lowers levels of triglycerides, while higher activity of hepatic lipase in Caucasian decreases HDL cholesterol[13-14]. Higher serum HDL and lower LDL and triglycerides among African Americans were reported in a weight loss study of obese African American and Caucasian adolescents, and in African and Caucasian populations in South Africa at (presumably) background levels of exposure[15-16].

The study strengths include relatively large size and individual measurements of lipid and organochlorines concentrations. We were limited in not having detailed dietary information, measures of genetic variability, or information on other confounders of lipid metabolism. We were also not able to measure any 'actual' change in concentration of lipid parameters or organochlorines over time. Whether serum PCBs and pesticides may have any causal effects on serum lipids in humans, as suggested by some authors, cannot be determined from this or other cross-sectional data[17].

Because lipid concentrations are important risk factors for heart disease and diabetes, follow up studies are warranted to properly address the associations among aging, organochlorines levels, and lipid metabolism in the context of the growing obesity epidemic affecting the industrial societies.

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