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Age-Related Decreases in Chromium Levels in 51,665 Hair, Sweat, and Serum Samples From 40,872 Patients—Implications for the Prevention of Cardiovascular Disease and Type II Diabetes Mellitus

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This report shows, for the first time using modern analytical techniques, highly significant age-related decreases in chromium levels in 51,665 hair, sweat, and serum samples obtained from 40,872 patients referred by their physicians to an independent medical research clinic and laboratory ($r = -.598$ to $-.762$, $P < .0001$ for all correlations). Males were found to have significantly lower mean chromium levels than females ($P < .05$ to $.0001$). There was good correlation between chromium levels in hair, sweat, and serum ($r = .536$ to $.729$, $P < .0001$ for all correlations), indicating that hair and sweat chromium levels are valid additions to the serum levels in assessing chromium status. Chromium measurements in sweat, hair, and serum were performed using graphite furnace atomic absorption spectrophotometry. The influences that age-related decreases in chromium levels might have on increasing the risk to develop age-related impaired glucose metabolism, disordered lipid metabolism, coronary heart disease, arteriosclerosis, and type II diabetes mellitus are outlined, and the role that refined carbohydrates play in the development of compromised chromium status is presented.

CHROMIUM has been recognized to be essential for humans since the 1960s.[1] Chromium acts primarily by regulating insulin action[2]; in the presence of chromium in a physiological form, much lower amounts of insulin are required, since chromium acts by increasing insulin efficiency.[2] Aging is associated with elevated blood glucose and circulating insulin, decreased insulin efficiency, elevated cholesterol and triglycerides, decreased high-density lipoprotein cholesterol, decreased nerve conduction, and decreased lean body mass; all of these changes also occur in chromium deficiency.[2] Patients with type II diabetes mellitus have lower serum chromium levels than nondiabetics,[3] and chromium supplementation in diabetics has been shown to improve glucose tolerance, decrease blood cholesterol and triglycerides, and increase high-density lipoprotein cholesterol.[4-8]

Serum chromium levels in patients with angiographically proven atherosclerosis have been shown to be lower than in angiogram-negative controls.[9,10] The aorta in patients dying of coronary artery disease has been shown to contain significantly less chromium than in accident victims.[11] Chromium has also been shown to reverse atherosclerotic plaque buildup in rabbits.[12,13]

More than 30 years ago, Schroeder et al[14] reported that the chromium concentration of all tissues tested, except the lungs, decreased with age; it was presumed that the increased chromium content of lungs was due to inhalation of chromium-containing air pollutants.

More recent studies also showed increased lung chromium levels in people not known to have received excessive exposure to chromium.[15] The increased chromium in the lungs associated with aging has been confirmed using more reliable modern analytical procedures, but the decline in tissue chromium associated with aging has not been confirmed using modern analytical methods and procedures.[2]

We report here the results of a retrospective computer analysis of chromium levels in 51,665 samples of hair, sweat, and/or serum from 40,872 patients, according to age and sex. This is the first report in a series on an ongoing study of trace and toxic element levels in hair, blood, and sweat in a large patient population; the second report details age-related increases in aluminium, arsenic, cadmium, lead, and mercury in more than 37,000 patients.[16]

PATIENTS AND METHODS

Patients

The study population of 40,872 patients is derived from an ongoing study of ambulatory outpatients who were referred for laboratory tests

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by their physicians to a private medical referral research clinic and laboratory between January 1985 and April 1996. As part of the assessment, chromium levels were measured in hair, serum, and/or sweat. The distribution of tests and patients is outlined in Table 1. The large majority of these ambulatory, nonhospitalized individuals included in this report had some form of ill health for which they were seeking medical care; a small minority were seeking preventive medical advice without evident health problems. No discrimination was made between these two groups or between patients as regards ethnic origin, place of residence, occupation, clinical symptoms, signs, diagnoses, medication, nutritional supplementation, or dietary or life-style habits.

The following were excluded from the analysis: (1) results of any subsequent repeat analyses on the same person; (2) subjects whose sex was not recorded; and (3) those whose age was recorded as zero, since, unfortunately, the computer system was originally set up in 1984 in such a way that all patients aged less than 1 year and all those whose age was not reported were both automatically recorded by the computer as age zero. The number of males and females in each age group for each of the three tissues sampled is shown in Table 1.

Methods

Samples of the three tissues were obtained without reference to time of day or timing of the last meal. Hair collection was from the occipitonuchal region, measuring no more than 4 cm in length, cut as close to the scalp as possible, and prepared for analysis in a way previously described.[17,18] Blood was taken from the antecubital vein and collected in a Vacutainer trace element–free tube (Becton-Dickinson, Cowley, Oxford, UK) with or without a tourniquet, and the serum was separated. Sweat collection was by means of passive sweating as described previously.[18]

Chromium analyses were performed on a Pye Unicam PU9000 atomic absorption spectrophotometer or a Hitachi Z-8200 Polarised Zeeman atomic absorption spectrophotometer, using standard electrothermal graphite furnace techniques according to the manufacturers' protocols (Phillips Scientific, Cambridge, UK; and Hitachi Scientific Instruments, Berks, UK). Calibration of all methodologies was made on a daily basis using weighed-in commercial primary standards (Spectrosol mineral standard solutions; Merck Chemicals, Leics, UK). The intrabatch and interbatch coefficient of variation was consistently less than 5%. For serum assays, precision and accuracy were monitored using Seronorm quality control sera (Nycomed UK, Birmingham, UK). Since there is no published certified value for chromium in the Seronorm material, we measured the chromium concentration in the material against the weighed-in primary standards. The material is assayed on a daily basis as an internal quality control. In the case of hair and sweat analyses, there are no commercially available quality-control materials; internal quality-control solutions were therefore prepared from the commercially available primary standards; in the case of the hair standard, this has been validated against the NIES reference material (National Institute for Environmental Studies, Ibaraki, Japan) and the European Community Bureau of Reference Material 397 (Brussels, Belgium).

Table 1. Chromium Measurements in Hair, Sweat, and Serum

	Male	Female	Total
Sample (n)			
Hair	8,491	13,522	22,013
Sweat	6,130	11,807	17,937
Serum	3,808	7,907	11,715
Total	18,429	33,236	51,665
Patients with only 1 tissue sampled (n)			
Hair	6,481	10,606	17,087
Sweat	3,368	6,761	10,129
Serum	1,691	3,902	5,593
Total	11,540	21,269	32,809
Patients with 2 tissues sampled on same day (n)			
Hair and sweat	740	1,201	1,941
Hair and serum	95	160	255
Sweat and serum	847	1,744	2,591
Total	1,682	3,105	4,787
Patients with 3 tissues sampled on same day (n)			
Hair, sweat, and serum	1,175	2,101	3,276
Patient total (n)	14,397	26,475	40,872

Statistics

Student's t test was applied to the relationship between chromium levels in hair, sweat, and serum for each of 16 age groups for males and females ranging in age from 1 year to 75 years plus. Pearson's rank correlation was applied to all chromium measurements with respect to age (Table 2) and to correlations between chromium hair and sweat, hair and serum, and sweat and serum levels (Table 3). Calculations were made using Excel Version 7 for Windows '95 (Microsoft, Berks, UK).

RESULTS

Figure 1 and Table 2 show a statistically significant age-related decrease in chromium levels in hair, sweat, and serum for both males and females. Chromium levels decreased by up to 49% in hair, 47% in sweat, and 42% in serum over a 75-year-plus age range ($r = -.598$ to $-.762$, $P < .0001$ for all correlations).

Males have statistically significantly lower chromium levels than females in each of the tissues sampled in several age groups: in hair, 25 to 49 years; in sweat, 20 to 59 years, and in serum, 35 to 54 years ($P < .05$ to $<.0001$; Table 2).

There were statistically significant correlations between chromium levels in hair and sweat, hair and serum, and sweat and serum for both males and females ($r = .536$ to $.729$, $P < .0001$ for all groups; Table 3).

DISCUSSION

This is the first time that age-related decreases in chromium levels in humans have been demonstrated using modern analytical techniques since Schroeder demonstrated the decreases in humans in various tissues; it is also the first time, as far as we know, that a difference in mean chromium levels between males and females in the relevant age groups has been demonstrated (discussion follows).

In the United Kingdom, the estimated safe and adequate level for chromium intake is greater than 25 μg/d,[19] and in the United States, the estimated safe and adequate daily dietary intake (ESADDI) of chromium for adults is 50 to 200 μg/d.[20] No adequate study of the chromium content of the average UK diet has been published, but in the United States, the mean chromium content per 1,000 kcal for 216 meals of 22 female and 10 male subjects collected for 7 consecutive day, was approximately 15 μg.[21] The content of 22 daily diets designed by nutritionists to be well-balanced was similar, ranging from 8.4 to 23.7 μg/1,000 kcal, with a mean chromium content of 13.4 ± 1.1 μg/1,000 kcal[22]; thus, individuals would need to

Table 2. Chromium Levels in Hair, Sweat, and Serum by Age and Sex

Group	Age (yr)	Male Cr Level (mean ± SD)	Male No. of Patients	Female Cr Level (mean ± SD)	Female No. of Patients	P*	Male and Female Cr Level (mean ± SD)	Male and Female No. of Patients
Hair (mg/kg)								
1	1-4	0.98 ± 0.14	388	0.98 ± 0.14	165	NS	0.98 ± 0.14	553
2	5-9	0.93 ± 0.13	715	0.92 ± 0.12	309	NS	0.93 ± 0.13	1,024
3	10-14	0.87 ± 0.12	454	0.87 ± 0.11	281	NS	0.87 ± 0.12	735
4	15-19	0.81 ± 0.10	282	0.80 ± 0.10	406	NS	0.81 ± 0.10	688
5	20-24	0.75 ± 0.09	367	0.75 ± 0.10	625	NS	0.75 ± 0.10	992
6	25-29	0.74 ± 0.08	627	0.74 ± 0.09	1,309	<.001	0.74 ± 0.09	1,936
7	30-34	0.70 ± 0.10	1,175	0.72 ± 0.08	2,340	<.001	0.72 ± 0.08	3,515
8	35-39	0.68 ± 0.10	1,242	0.70 ± 0.08	2,292	<.001	0.69 ± 0.09	3,534
9	40-44	0.66 ± 0.10	1,034	0.67 ± 0.09	1,704	<.0001	0.67 ± 0.09	2,738
10	45-49	0.63 ± 0.11	598	0.64 ± 0.09	1,154	<.0001	0.64 ± 0.10	1,752
11	50-54	0.59 ± 0.10	470	0.59 ± 0.10	902	NS	0.59 ± 0.10	1,372
12	55-59	0.56 ± 0.10	372	0.57 ± 0.10	703	NS	0.57 ± 0.10	1,075
13	60-64	0.52 ± 0.10	318	0.53 ± 0.10	527	NS	0.52 ± 0.10	845
14	65-69	0.52 ± 0.11	229	0.52 ± 0.10	390	NS	0.52 ± 0.10	619
15	70-74	0.50 ± 0.10	122	0.50 ± 0.10	221	NS	0.50 ± 0.10	343
16	75 plus	0.50 ± 0.12	98	0.50 ± 0.10	194	NS	0.50 ± 0.10	292
Total			8,491		13,522			22,013
r (Cr/age)†		−.741		−.732			−.736	
Sweat (µg/kg)								
1	1-4	3.87 ± 0.59	278	3.86 ± 0.54	146	NS	3.86 ± 0.58	424
2	5-9	3.81 ± 0.50	577	3.78 ± 0.52	293	NS	3.80 ± 0.51	870
3	10-14	3.68 ± 0.49	430	3.68 ± 0.48	336	NS	3.68 ± 0.48	766
4	15-19	3.32 ± 0.51	291	3.33 ± 0.47	437	NS	3.32 ± 0.49	728
5	20-24	3.07 ± 0.51	298	3.08 ± 0.47	718	<.05	3.08 ± 0.48	1,016
6	25-29	2.93 ± 0.46	405	3.00 ± 0.47	1,157	<.001	2.98 ± 0.47	1,562
7	30-34	2.81 ± 0.50	635	2.92 ± 0.44	1,520	<.001	2.89 ± 0.46	2,155
8	35-39	2.68 ± 0.51	689	2.81 ± 0.47	1,673	<.001	2.77 ± 0.48	2,362
9	40-44	2.60 ± 0.55	624	2.73 ± 0.48	1,500	<.001	2.69 ± 0.50	2,124
10	45-49	2.52 ± 0.52	478	2.63 ± 0.48	1,192	<.001	2.60 ± 0.50	1,670
11	50-54	2.39 ± 0.55	398	2.48 ± 0.53	890	<.001	2.45 ± 0.54	1,288
12	55-59	2.27 ± 0.56	321	2.39 ± 0.55	730	<.05	2.35 ± 0.56	1,051
13	60-64	2.13 ± 0.53	279	2.21 ± 0.54	488	NS	2.18 ± 0.54	767
14	65-69	2.13 ± 0.52	219	2.17 ± 0.53	366	NS	2.15 ± 0.53	585
15	70-74	2.08 ± 0.57	110	2.10 ± 0.53	203	NS	2.09 ± 0.54	313
16	75 plus	2.04 ± 0.57	98	2.04 ± 0.50	158	NS	2.04 ± 0.52	256
Total			6,130		11,807			17,937
r (Cr/age)†		−.762		−.615			−.657	
Serum (µg/L)								
1	1-4	0.50 ± 0.10	33	0.51 ± 0.10	16	NS	0.51 ± 0.10	49
2	5-9	0.51 ± 0.11	156	0.51 ± 0.10	72	NS	0.51 ± 0.10	228
3	10-14	0.48 ± 0.10	190	0.50 ± 0.10	148	NS	0.49 ± 0.10	338
4	15-19	0.46 ± 0.09	150	0.46 ± 0.08	262	NS	0.46 ± 0.09	412
5	20-24	0.44 ± 0.07	197	0.44 ± 0.07	460	NS	0.44 ± 0.07	657
6	25-29	0.43 ± 0.07	254	0.42 ± 0.07	701	NS	0.42 ± 0.07	955
7	30-34	0.40 ± 0.07	382	0.41 ± 0.06	963	NS	0.41 ± 0.06	1,345
8	35-39	0.38 ± 0.07	461	0.40 ± 0.06	1,133	<.0001	0.40 ± 0.06	1,594
9	40-44	0.38 ± 0.07	446	0.39 ± 0.06	1,081	<.01	0.38 ± 0.06	1,527
10	45-49	0.36 ± 0.07	370	0.38 ± 0.06	900	<.0001	0.37 ± 0.06	1,270
11	50-54	0.34 ± 0.07	302	0.35 ± 0.06	631	<.01	0.35 ± 0.06	933
12	55-59	0.33 ± 0.07	255	0.34 ± 0.07	511	NS	0.33 ± 0.07	766
13	60-64	0.32 ± 0.07	243	0.32 ± 0.08	387	NS	0.32 ± 0.08	630
14	65-69	0.31 ± 0.06	164	0.31 ± 0.06	283	NS	0.31 ± 0.06	447
15	70-74	0.30 ± 0.07	110	0.30 ± 0.06	165	NS	0.30 ± 0.07	275
16	75 plus	0.29 ± 0.07	95	0.29 ± 0.06	194	NS	0.29 ± 0.06	289
Total			3,808		7,907			11,715
r (Cr/age)†		−.620		−.598			−.609	

Abbreviation: NS, Not statistically significant ($P > .05$).

*Male/female difference in Cr level, Student's t test.

†$P < .0001$ for all values.

Table 3. Chromium Measurements in Hair, Sweat, and Serum: Correlations Between Different Samples

Sample	Male	Female	Both
Hair and sweat			
No. of subjects	2,487	4,234	6,721
Hair Cr (mean ± SD)	0.69 ± 0.16	0.68 ± 0.13	0.68 ± 0.14
Sweat Cr (mean ± SD)	2.79 ± 0.74	2.76 ± 0.62	2.77 ± 0.66
r (hair Cr/sweat Cr)	.684	.573	.625
Hair and serum			
No. of subjects	1,269	2,262	3,531
Hair Cr (mean ± SD)	0.66 ± 0.15	0.67 ± 0.12	0.67 ± 0.13
Serum Cr (mean ± SD)	0.38 ± 0.09	0.39 ± 0.08	0.39 ± 0.08
r (hair Cr/serum Cr)	.574	.536	.553
Sweat and serum			
No. of subjects	2,021	3,845	5,866
Sweat Cr (mean ± SD)	2.71 ± 0.73	2.76 ± 0.62	2.74 ± 0.66
Serum Cr (mean ± SD)	0.38 ± 0.09	0.39 ± 0.08	0.39 ± 0.08
r (sweat Cr/serum Cr)	.729	.683	.702

NOTE. Hair chromium results are expressed in mg/kg, sweat chromium in μg/kg, and serum chromium in μg/L.
$P < .0001$ for all correlations (Student's *t* test).

consume greater than 3,000 kcal to ingest the ESADDI minimum of 50 μg. In fact, Anderson[2] considers that chromium intake appears to be marginal throughout life. In 1980, it was first suggested by one of us (J.M.H.) that the high chromium content of wine may account for the lower coronary artery disease mortality observed in France,[23] and evidence that there is a cardioprotective effect of drinking red wine has recently been published.[24-26]

The lower mean chromium levels in males in the 30- to 59-year age groups occur at the time of life when there are maximal differences in the male/female prevalence of coronary artery morbidity and mortality. In one UK dietary survey,[27] it was found that men had a higher refined-carbohydrate intake than women in these age groups, which could account for the lower chromium levels in males observed in this study. It may also be that female hormones may contribute to the observed higher chromium levels in these tissues.

In genetic terms, we are hunters-gatherers who have been placed in modern industrialized western society.[28,29] It is possible that there has been a lack of evolutionary necessity for an efficient long-duration chromium conservation system, since throughout evolution dietary carbohydrate was not refined and therefore probably contained sufficient chromium for dietary carbohydrate to be metabolized. Only recently have refined carbohydrates been extensively consumed. Refining removes greater than 90% of the naturally occurring chromium, thereby producing a relative chromium deficiency, with insufficient chromium available for optimal carbohydrate metabolism.[30]

Today's increased longevity is much greater than the average estimated life expectancy of 25 to 30 years in primitive humans.[31,32] Our modern diets have an excess of refined carbohydrates that have been stripped of chromium content,[30] and refined carbohydrates also cause increased urinary chromium losses.[2,33] This increase in chromium-depleted refined-carbohydrate consumption, along with the absence of an efficient long-term chromium conservation mechanism, would account for the highly statistically significant age-related decreases in chromium levels observed in this study, with levels decreasing by up to 49% in hair, 47% in sweat, and 42% in serum over a 75-year-plus time span.

The data presented in this report are derived from a broad, ambulatory, nonhospitalized population, and on the basis of the referral patterns to this unit, it is extremely unlikely that a significant proportion of the subjects were moribund or malnourished, which could have influenced the levels in light of the knowledge that serious coronary disease is associated with reduced serum chromium.[9-11] However, we do recognize that it would have been valuable to have comprehensive demographic data on each individual patient in the study, but such an undertaking is beyond the resources of this unit.

The highly statistically significant correlations between chromium levels in hair and sweat, hair and serum, and sweat and serum for both males and females ($r = .536$ to $.729$, $P < .0001$

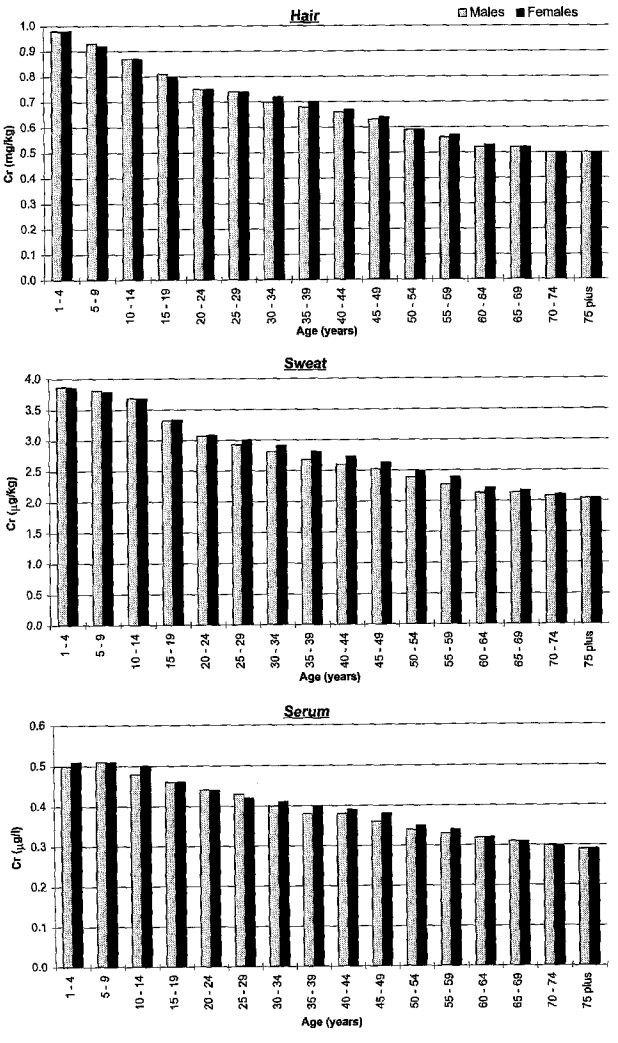

Fig 1. Chromium levels in hair, sweat, and serum by age and sex. (▨) Males; (■) females.

for all groups) indicate that sweat and hair chromium levels are relevant adjuncts to the serum chromium level in the assessment of chromium status in humans.

These observed decreases in chromium concentrations with age may have profound health consequences in terms of diabetic and cardiovascular disease morbidity and mortality. The role of improved chromium nutrition requires further investigation, including monitoring the responses of cardiovascular risk factors such as glucose tolerance, lipid parameters, and insulin function, all of which have been shown to improve with chromium supplementation.[2]

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