Review:
Interpreting Hair Mercury Levels in Individual Patients

Kern L. Nuttall
Consultant in Chemical Pathology, Bellingham, Washington

Abstract. Evaluation of mercury exposure in an individual patient ideally includes the presenting history, physical examination, consideration of the differential diagnosis, and mercury analysis of blood and urine specimens. Analysis of mercury in hair specimens may supply useful supplemental information about exposure to organic compounds such as methylmercury, particularly to help reconstruct the pattern of prior exposure. The most appropriate specimen is generally terminal-type hair from the occipital-neck junction, clamped to maintain strand alignment, and oriented to the scalp. Hair from the initial 0.5 cm adjacent to the scalp represents on average 1-3 wk before collection, and consideration of the time frame represented by the specimen is an important part of the evaluation. Literature reports describe hair mercury levels as high as 2400 µg/g. Hair mercury level is usually <1 µg/g in individuals who do not eat fish but may be >30 µg/g in those who frequently consume fish with high mercury content. Hair mercury level is often not correlated with blood mercury concentration or symptoms of mercury toxicity, and reports of hair contamination by exogenous mercury are not uncommon. Hair mercury level is notoriously prone to misinterpretation and should be used with an understanding of its limitations.

Keywords: hair analysis, mercury poisoning, methylmercury, organic mercury, urine porphyrins

Introduction

Using hair specimens to evaluate mercury exposure is a well-established method in group studies [1-3]. Hair in such studies is typically used to characterize the degree of mercury exposure for a study population, a goal that is relatively easy and straightforward. In an individual patient, however, the goal is often more demanding. The needs of the patient mean that an appropriate interpretation also include evaluation of the patient’s history, signs and symptoms, differential diagnosis, and similar issues. One reason to avoid hair analysis in these circumstances is that a spurious elevation has the potential for more significant consequences for a patient vs a study group. A consensus publication that gives detailed advice on specimen collection for trace element analysis in the clinical laboratory pointedly excludes hair collection with the comment: “of extremely dubious value” [4]. On the other hand, there are patient reports where hair mercury has provided important information, particularly for reconstructing past exposure (see Report 3 below). The present review discusses the limitations of using hair mercury analysis for individual patients, and is designed for pathologists and clinical chemists who are asked to interpret results generated in the clinical laboratory.

Whole blood and urine are the most reliable specimens for evaluation of mercury exposure in an individual patient [5]. However, there are also several reasons to consider hair specimens: (1) mercury has a longer half-life in hair, so it can be useful for evaluating exposures that occurred months earlier, (2) mercury remains stable for long periods in hair, making it easy to transport and
store, and (3) some mercury species, such as methylmercury, accumulate at higher concentrations in hair, making them relatively easy to measure [6]. A serious disadvantage is that it is impossible to distinguish between mercury incorporated during hair growth and that deposited from external sources [7]. Another disadvantage is that hair analysis is associated with quackery and poor quality analysis, associations that are well-documented [8]. Analysis of hair samples attributed to Napoleon Bonaparte produced reports claiming that he was deliberately poisoned with arsenic, despite the fact that an autopsy report at the time of death documented the cause as gastric carcinoma [9]. In brief, hair analysis is easy to perform but notoriously prone to misinterpretation; let those who use it beware.

Nomenclature

For the purposes here, the 3 oxidation states of mercury are labeled as mercury(0), mercury(I), and mercury(II) (pronounced “mercury zero,” “mercury one,” and “mercury two”). Mercury(0) is also known as elemental or metallic mercury. Mercury bound to a carbon atom is considered “organic,” examples of which include methyl- and ethylmercury ions. Organic mercury is always mercury(II). When not bound to carbon, mercury is considered “inorganic.”

*Methylmercury.* Methylmercury in the present context refers to the ion (H₃C-Hg⁺) and the adducts it forms primarily with sulfhydryl groups (R-SH → R-S-Hg-CH₃). Methylmercury in fish is present primarily as methylmercury cysteine, mostly in glutathione and proteins [10]. Methylmercury ion is not the same as methylmercury chloride (see Report 6 below), since the mercury-chloride bond is highly covalent and remains intact in dilute aqueous solution [10]. In some publications the term “methylmercury” may refer to dimethylmercury (H₃C-Hg-CH₃) [11], a compound that is insoluble in water and highly dangerous to handle in concentrated reagent form (see Report 3 below).

*Hair.* Hair is an appendage of the skin that grows from follicles, tens of thousands of which are embedded in the skin. Cells proliferate at the base of each follicle, move upward, and transform into the fibrous material known as hair. The hair shaft ranges from 15 to 120 µm in diameter, and consists of multiple layers of desiccated cells and ground substances. Much of the protein in hair is rich in the sulfur-containing amino acid cystine, which is largely responsible for the avid binding of mercury compounds. Aspects helpful to understanding hair as an analytic specimen are discussed below.

Additional information can be found in reviews [6,12-14] and dermatology texts [15].

*Hair types.* Hair can be divided into 4 basic types: terminal, intermediate, vellus, and lanugo [15]. Terminal hair has the largest diameter and length and is found in the scalp, beard, eyebrow, eyelash, armpit, and pubis. Intermediate hair is intermediate in diameter and length and is found on the arms and legs. Vellus hair has a small diameter and length and is found on the relatively “hairless” parts of the body, such as eyelids, forehead, and bald scalp. Lanugo is the very fine hair found on the fetal body. Terminal hair is the most appropriate for mercury analysis due to the nature of its growth cycle (see below). Implied in most discussions of hair mercury is the assumption that the specimens involve terminal-type hair.

*Growth cycle.* The hair growth cycle has 3 phases: anagen, catagen, and telogen. Anagen is the metabolically active phase where the hair shaft lengthens, catagen is a brief transitional phase where metabolism slows, and telogen is the phase where growth has stopped and the hair is dead. The hair shaft is weakly retained for a variable period in telogen and ultimately shed before the growth cycle begins again. Telogen may last from weeks to years. Telogen in terminal-type hair is relatively short and is an important reason to prefer terminal hair for analysis. In contrast, intermediate-type body hair has a telogen phase lasting 2-6 yr [12].

*Trichogram.* The relative proportions of the 3 growth phases can be determined with a trichogram. A group of hairs is extracted, usually about 100, and the roots examined under magnification [6]. The bulb-shaped follicle tip of the hair root shows
morphologic features that are characteristic of the growth phase. Anagen is characterized by large follicles indicative of active growth, whereas telogen shows small, involuted follicles characteristic of the resting phase, and catagen has an intermediate size. Hair in the scalp is generally about 80-90% anagen, 10-20% telogen, and <1% catagen. The relative proportions can be altered by factors such as illnesses, drugs, and pregnancy [12]. Although trichograms and growth phases are not routinely determined for mercury analysis, they influence the results. When considering a single hair, only one in anagen will reflect recent exposure. When collecting a group of hair strands, the distribution of growth phases has the effect of producing an average result where the peaks tend to be lower and the valleys higher.

**Growth rate.** Hair grows between 0.6-3.36 cm/mo [12], although for convenience it is commonly assumed to grow 1 cm/mo. Scalp hair has a relatively short telogen phase lasting about 10 weeks and is generally the most rapidly growing, but scalp hair shows more variation across the scalp compared to other body regions. Specimens are ideally collected from a uniform site for this reason. The nape of the neck is recommended since this region is less susceptible to baldness and alopecia [6]. Pubic hair is slower growing than scalp hair, and the beard has the slowest growth rate for terminal-type hair.

**Mercury in hair.** Mercury content of hair comes from 2 primary sources, blood and exogenous contamination. Desquamated epidermis and secretions from sweat, apocrine, and sebaceous glands can possibly be sources of hair mercury [13], but in the present discussion these sources are assumed to be small. It is difficult to attribute the mercury content to only one source, particularly when the issue is examined closely. The mercury concentration in blood determines the amount incorporated into cells growing at the base of the hair follicle [16]. The amount taken up depends on the mercury species and remains stable once deposited [13]. For methylmercury, deposition is proportional to the simultaneous concentration in blood, but about 2 orders of magnitude higher [17]. It is about 1 order of magnitude higher for ethylmercury, whereas inorganic mercury is incorporated poorly if at all. The majority of mercury deposited during hair growth is generally methylmercury [18]; however, methylmercury does not necessarily represent the majority of mercury measured in hair because of the contamination problem. The inorganic mercury described below in Report 4, for example, came from surface contamination of hair and not by incorporation during growth.

**Cleaning hair.** Cleaning hair specimens to remove contamination prior to analysis often gives irreproducible results [6,13,19]. The hair surface is not uniform, but has numerous gaps and fissures, which makes the degree of penetration by exogenous mercury variable and difficult to predict. Also, some mercury species are bound relatively loosely, while other species are more tightly bound [20]. Cleansing that is vigorous enough to remove surface contamination has the potential to remove mercury deposited during growth. Evidence indicates that distinguishing between exogenous and endogenous mercury is impossible [7].

**Hair and blood.** Hair and blood collected at the same time represent different time frames, so their mercury levels are not necessarily correlated [6]. Blood reflects recent exposure, whereas hair adjacent to the scalp is indicative of exposure that occurred 1-3 wk earlier; thus, recent alterations in exposure patterns will not be reflected in hair. An example of a typical degree of correlation is seen below in Report 12. Hair and blood tend toward increased correlation when (1) mercury is present primarily as methylmercury, (2) blood mercury is stable over the relevant time period, and (3) no exogenous mercury contamination is present.

Hair can be used to estimate the earlier methylmercury concentrations in blood, although accurate reconstruction is complex [21]. The blood-to-hair ratio is 333 at equilibrium, that is, following a year or more of constant exposure [22]. Since exposure is seldom constant, using a single value for the ratio will provide only a rough estimate of the earlier concentration in blood. However, this approach is probably more accurate than methods based on dietary questionnaires [21]. Modeling studies
suggest that the timing of specimen collection plays a significant role in the determination of the hair-to-blood mercury ratio and is probably a major reason for different estimates of the ratio [22].

**Published Reports**

To put hair mercury levels into an appropriate clinical context, selected literature reports are summarized in Table 1 and described briefly below.

Reports describing individuals are listed first (roughly in order of decreasing hair mercury level), followed by group studies in adults; studies of children and of infants in utero are found at the ends of Reports 17 and 18. The descriptions emphasize details of hair analysis, although the published reports often do not. (Comments by the author follow in parentheses.) This literature review supports several conclusions: (1) hair mercury level is often not correlated with symptoms of toxicity, (2) hair mercury level is often not correlated with blood mercury concentrations, and (3) hair is generally most useful in evaluating exposure to organic mercury compounds (eg, methylmercury).

When comparing results generated by different laboratories, it is reasonable to compare relatively moderate concentrations to within 1 significant figure, that is, 15-24 µg/g is about 20 µg/g. Uncertainties tend to be greatest at low concentrations. Although several reports discussed below are from the older literature, their analytic methods appear sound. However, standardization of mercury analysis has received increased attention recently, suggesting that earlier studies are less comparable in regard to absolute concentrations [23].

**Report 1: fungicide-treated wheat in Iraq.**

Widespread mercury poisoning occurred in rural Iraq during the winter of 1971-72 following the distribution of fungicide-treated wheat for sowing [1]. Thousands of people were exposed and hundreds

Table 1. Published reports discussed in text.

<table>
<thead>
<tr>
<th>Report</th>
<th>Patient &amp; gender</th>
<th>Hair mercury (µg/g)</th>
<th>Blood mercury (µg/L)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-55 M/F</td>
<td>400-1600</td>
<td>200-800</td>
<td>range of severe symptoms [24]</td>
</tr>
<tr>
<td></td>
<td>- 60 F</td>
<td>1065</td>
<td></td>
<td>contamination without symptoms</td>
</tr>
<tr>
<td>2</td>
<td>20 F</td>
<td>2436.0</td>
<td></td>
<td>severe symptoms with some recovery [26]</td>
</tr>
<tr>
<td></td>
<td>8 F</td>
<td>1397.6</td>
<td></td>
<td>severe symptoms</td>
</tr>
<tr>
<td></td>
<td>16 F</td>
<td>328.6</td>
<td></td>
<td>no apparent symptoms</td>
</tr>
<tr>
<td>3</td>
<td>48 F</td>
<td>1100</td>
<td>4000</td>
<td>fatal dimethylmercury exposure [27]</td>
</tr>
<tr>
<td>4</td>
<td>46 F</td>
<td>474</td>
<td></td>
<td>contamination from soap [29]</td>
</tr>
<tr>
<td>5</td>
<td>13 F</td>
<td>339</td>
<td></td>
<td>fish diet without symptoms [31]</td>
</tr>
<tr>
<td>6</td>
<td>37 M</td>
<td>64.5</td>
<td></td>
<td>mild Minamata disease [32]</td>
</tr>
<tr>
<td>7</td>
<td>38 F</td>
<td>22.5</td>
<td>19</td>
<td>cosmetic cream without symptoms [34]</td>
</tr>
<tr>
<td>8</td>
<td>40 M</td>
<td>12</td>
<td>58</td>
<td>fish diet and difficulty concentrating [35]</td>
</tr>
<tr>
<td>9</td>
<td>48 M</td>
<td>6.0</td>
<td></td>
<td>calomel causing excessive salivation [37]</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>2.4</td>
<td>335</td>
<td>mercury(0) injection without symptoms [38]</td>
</tr>
<tr>
<td>11</td>
<td>F adults</td>
<td>6.5-32.6</td>
<td></td>
<td>fish diet without symptoms [39]</td>
</tr>
<tr>
<td>12</td>
<td>adults</td>
<td>0.03-37.76</td>
<td>0.25-107.6</td>
<td>symptoms from mercury(0) [19]</td>
</tr>
<tr>
<td>13</td>
<td>adults</td>
<td>0.56-13.6</td>
<td></td>
<td>fish diet with subtle symptoms [40]</td>
</tr>
<tr>
<td>14</td>
<td>M adults</td>
<td>0-15.7</td>
<td></td>
<td>fish diet and increased heart disease [3]</td>
</tr>
<tr>
<td>15</td>
<td>adults</td>
<td>0.10-5.67</td>
<td></td>
<td>mercury(0) in dentists [43]</td>
</tr>
<tr>
<td>16</td>
<td>adults</td>
<td>0.04-0.32</td>
<td>0.11-1.4</td>
<td>low fish diet [18]</td>
</tr>
<tr>
<td>17</td>
<td>children</td>
<td>0.58-17.14</td>
<td></td>
<td>fish diet without symptoms [44]</td>
</tr>
<tr>
<td>18</td>
<td>prenatal</td>
<td>0.5-26.7</td>
<td></td>
<td>maternal fish diet in the Seychelles [2]</td>
</tr>
</tbody>
</table>

*a* range; *b* range in maternal hair
died when some of the treated seed was ground into flour and consumed as bread. One study of this incident compared hair mercury levels vs clinical symptoms in 184 exposed individuals [24]. “Head” hair was collected from the first 3 cm adjacent to the scalp and cut into 1 cm segments for sequential analysis by neutron activation. The following categories were described: (1) severe symptoms associated with hair mercury in the range of 400-1600 µg/g, (2) moderate symptoms at 200-800 µg/g, (3) mild symptoms at 120-600 µg/g, and (4) no symptoms at <300 µg/g. Severe symptoms were defined as coma, paralysis, or loss of vision, hearing, or speech; moderate symptoms as partial paralysis, tunnel vision, difficulty hearing, or disarticulation; and mild symptoms as slight tremor, mild ataxia, or blurred vision. Infants <1-yr-old usually showed more severe symptoms. Individuals did not always fit the general pattern; one adult (~60-yr-old) did not have any symptoms despite a hair mercury level of 1065 µg/g. (This report characterizes the degree of variability between hair mercury levels and the development of symptoms. Since hair was collected from survivors after peak exposure, the study was not indicative of fatal cases. The markedly elevated hair mercury levels unassociated with symptoms were presumably due to external contamination from an activity such as sowing treated grain or visiting a mill where the contaminated wheat was ground [25]. Note that a mercury concentration of 500 µg/g in an individual patient could be associated with severe, moderate, mild, or even no symptoms. To stress this point, toxicity is assessed by signs and symptoms in the patient, not by laboratory data.)

Report 2: fungicide-tainted meat in USA. In 1969 in Alamogordo, New Mexico, an 8-yr-old girl developed progressive ataxia, confusion, agitation, and visual impairment [26]. When other family members developed similar symptoms, it was discovered the family was eating meat contaminated with methylmercury-containing fungicide. Discarded seed-grain had been collected by the father and fed to the family hogs, which were subsequently butchered and eaten. Hair from several family members was analyzed by neutron activation. Hair mercury level in the 8-yr-old presenting patient was 1398 µg/g. More than a year latter she remained blind, unable to sit without being propped in a chair, and appeared only slightly aware of her surroundings. A 20-yr-old sister (hair mercury 2436 µg/g) was also severely affected, although she later showed improvement. A 16-yr-old sister (329 µg/g) remained asymptomatic as did the father (186 µg/g). The mother was asymptomatic but subsequently delivered a severely affected infant. (This report documents the devastating effects of organic mercury exposure but suggests that obvious neurologic symptoms are not likely when hair mercury level is <300 µg/g. Asymptomatic patients were not evaluated for more subtle deficits. Mercury was also measured in serum but these data are difficult to interpret because methylmercury accumulates in red blood cells; whole blood is preferred to serum for that reason [5].)

Report 3: fatal dimethylmercury in USA. In 1997, a 48-yr-old chemistry professor at Dartmouth College was hospitalized after 5 days of progressive deterioration in balance, gait, and speech [27]. While working in a hood 5 months previously, the patient had accidentally spilled several drops of a concentrated dimethylmercury reagent from the tip of a pipet onto the back of her latex-gloved hand. Blood mercury level was 4000 µg/L and urine mercury level was 234 µg/L on admission 5 mo later. A long strand of scalp hair, analyzed sequentially in 2 mm segments, showed that mercury appeared 17.4 days post-incident and peaked at 21.8 days at 1100 µg/g. Hair growth was 1.38 cm per mo. The patient’s neurologic deterioration continued despite treatment and she died 298 days post-exposure. The long interval between exposure and the onset of symptoms is characteristic of this type of poisoning, although the reason for the latent period is unclear. Dimethylmercury is a particularly dangerous form of organic mercury, which penetrates latex gloves readily. (This report illustrates the reconstruction of exposure history using sequential hair analysis; additional details are available elsewhere [28]. The long latency period makes hair particularly useful in this circumstance. In contrast, methylmercury found in fish is less toxic than dimethylmercury and is roughly a million times more dilute.)
Report 4: contamination from soap in Tanzania. Mercury exposure from gold mining was studied near Lake Victoria [29]. Scalp hair was collected from gold miners, fishermen, and residents of Mwanza City. Although hair mercury levels among 15 city residents averaged 3.44 µg/g, an elevated hair mercury level of 474 µg/g was found in a 46-yr-old asymptomatic hotel manager. Several other outliers were also discovered, mostly from individuals using soap labeled as germicidal and containing 2% mercury iodide (oxidation state not specified). (This report describes a well-documented case of external contamination; such cases illustrate a significant reason why an isolated hair mercury concentration is best interpreted with caution in an individual. A separate report describes the common use in Tanzania of soaps and skin-lightening products containing inorganic mercury, many manufactured in Europe [30].)

Report 5: fish and gold mining in Brazil. Hair mercury level was examined in a family of 10 living next to a mercury-contaminated lake in a remote region of the Amazon [31]. Gold mining activities are common in this region, many fish species are high in mercury, and fish consumption is frequent. Hair was cut from the occipital area of the scalp and analyzed sequentially in 3 cm segments. The range of hair mercury in the family was 8-339 µg/g, had no obvious pattern in terms of age or gender, and showed considerable individual variation over time. The maximum level occurred in a 13-yr-old female; speciation showed 54% was due to methylmercury. The study concluded that fish was the main route of the mercury exposure, but other significant sources were also present. Some members of the family were engaged in gold mining activities, which may have included burning amalgam to recover gold. After the results of mercury testing were known, the family members were interviewed to look for stigmata of methylmercury poisoning, specifically, numb fingers, narrowing of visual fields, and impaired gait, speech, and hearing. No such signs or symptoms were found. (This report gives an example of a significantly elevated hair mercury unassociated with symptoms, although the clinical evaluation was very limited. Speciation indicated that only 54% was methylmercury from fish, illustrating the usefulness of this procedure. Most of the remainder was probably due to external contamination from gold mining activities.)

Report 6: Minamata disease in Japan. Methylmercury chloride, produced as a by-product in a factory that manufactured acetaldehyde was discharged into Minamata Bay of Japan, where it accumulated in local fish and shellfish [32]. Discharge of methylmercury in this region began in the early 1950s and ended in 1968. As many as 200,000 people may have been exposed, although 2265 carry the official diagnosis that authorizes government compensation. Minamata disease is regarded as a subtype of methylmercury poisoning in Japan. Characteristics of Minamata disease in adults include blurred vision, hearing loss, peripheral neuropathy, ataxic gait, and dysarthria. Fetal exposure is characterized by an extensive spongiosis of the cerebral cortex. Patients with long-standing Minamata disease were examined to investigate the pattern of paresthesias [32]. One case involved a 77-yr-old male who showed 64.5 µg/g mercury in hair in 1960 when he was 37 yr-old (specimen details not reported). Even decades after exposure, his touch thresholds remained increased compared to controls. (This report illustrates Minamata disease associated with relatively moderate hair mercury, although the concentration measured in 1960 may not represent the peak of exposure. Methylmercury chloride is not the same as the form of methylmercury commonly associated with fish, since the mercury-chloride bond is highly covalent and remains intact in dilute aqueous solution [10]. Methylmercury chloride may be more toxic and have a different pattern of accumulation in marine organisms. For example, whereas shellfish accumulated methylmercury chloride discharged in the Minamata incident [32], shellfish are typically low in mercury content [33].)

Report 7: antifreckle cream in Hong Kong. Hair analysis was requested in a 38-yr-old housewife in Hong Kong because she had previously worked in an electroplating factory and had recently developed low back pain [34]. She was otherwise asymptomatic. Arsenic, cadmium, lead, and thallium concentrations were within normal limits, but the hair
mercury level was elevated at 22.5 µg/g (specimen details not reported). Additional testing showed that the mercury concentration was 19 µg/L in blood and 69 µg/day in urine. The source was found to be an antifreckle cosmetic cream containing 6.5% inorganic mercury (compound not identified). Blood mercury levels declined within 2 weeks after the product was withdrawn, consistent with systemic absorption of inorganic mercury from the product. (Inorganic mercury in the blood is not efficiently incorporated into hair, which suggests the hair content described here is due to external contamination, all or in part, when hands covered with traces of cream touched the hair. Inadvertent oral ingestion might have occurred from events such as preparing food or eating prior to washing the hands. Absorption through the skin is a possibility, although it seems likely that blood and urine mercury concentrations would be higher in that circumstance.)

Report 8: high-mercury fish in the USA. A 40-yr-old male with complaints of sleep disturbances and difficulty concentrating was found to have 12 µg/g hair mercury [35]; specimen details were not described. Further testing revealed a blood mercury level of 58 µg/L. An investigation by the Wisconsin Division of Public Health determined the mercury was derived from frequent dietary ingestion of fish and that the primary source was imported sea bass. Salmon and other fish consumed by the patient were much lower in mercury content. Sea bass was removed from the diet, although other fish was not. Follow-up 200 days later showed that the blood mercury level had fallen to 5 µg/L. (Difficulty in mental concentration has many causes and attributing such complaints to mercury exposure may or may not be accurate. However, switching from a diet of high-mercury fish clearly reduces exposure and this is a reasonable approach when confronted by subtle symptoms in a patient with modestly elevated mercury levels. Moderate levels of mercury exposure do not justify chelation therapy, which presents its own problems [36]. While avoiding high-mercury fish may be suitable for middle-class residents of Wisconsin, Report 11 suggests it may be counterproductive for those living in different circumstances.)

Report 9: iatrogenic calomel in USA. Recent mercury analysis of hair collected in 1815 from President Andrew Jackson (1767-1845) showed 6.0 µg/g [37]. Several months prior to collection of the hair specimen, Jackson was known to have ingested mercury(1) chloride (Hg₂Cl₂, calomel) to the point of developing excessive salivation. Calomel was a common laxative and physicians of the era were acquainted with salivation as a cardinal sign of excessive use. The authors suggest that Jackson received significant mercury exposure from medical sources, a fact supported by historical accounts, but that his death was probably unrelated to heavy metal poisoning. (This report provides an interesting historical perspective, and medicinal use is one reason mercury exposure may have been higher in the past than at present. Some of the conclusions reached by the authors were disputed by others [38], which supports the contention that hair analysis is often easier than the interpretation that follows; see Report 10 below.)

Report 10: self-injection of mercury(0). A person of unreported age and gender came to medical attention after self-injecting mercury(0); subsequent concentrations of mercury were 335 µg/L in blood, 1320 µg/L in urine, and 2.4 µg/g in hair [38]. Data were published in a brief letter to emphasize the fact that inorganic mercury in blood is not incorporated efficiently into hair. The letter was submitted to dispute an assumption made in Report 9, specifically, that hair is an adequate specimen to monitor exposure to inorganic mercury. (When injected, liquid mercury(0) becomes trapped in locations like the capillary bed of the lung where the droplets remain lodged for years [5]. The patients often remain asymptomatic, although the subsequent blood and urine concentrations can be dramatically elevated. Such cases emphasize the variable nature of mercury toxicity and the fact that symptoms are often poorly correlated with concentrations in hair, blood, and urine [5].)

Report 11: fish diet in Brazil. The range of hair mercury levels was 6.5-32.6 µg/g (median 18.3) in 31 women 15 to 45 yr-old living in remote locations in the Brazilian Amazon [39]; “hair was cut from
the occipital area close to the scalp.” Fish was usually consumed several times a day and was typically the best source of essential nutrients. Clinical examination of the women revealed no tremor, paraparesis, or sensory disturbances indicative of methylmercury poisoning. The health status of the group included high maternal and infant mortality, common gastrointestinal parasites, endemic malaria, and periodic dengue and yellow fevers. The benefits of eating fish in this region were hypothesized to outweigh the risks of methylmercury exposure. (This report suggests that clinical examination is unlikely to detect neurologic deficits due to methylmercury exposure when hair mercury is relatively low; the lack of clinically apparent signs is consistent with Reports 1 and 2. Testing for more subtle deficits was not done.)

**Report 12: gold mining and fish in the Philippines.** A region in the Philippines was evaluated for mercury(0) exposure from long-term gold mining, although the exposure pattern included methylmercury from frequent fish consumption [19]. More than 300 inhabitants and miners were examined for neurologic symptoms and tested for functions such as tremor, short-term memory, and mental concentration. The range of hair mercury levels (n = 316) was 0.03-37.76 µg/g (median 2.72, mean 4.14); “hair was selected from the part nearest the scalp.” The range of blood mercury levels (n = 323) was 0.25-107.6 µg/L (median 8.2, mean 11.48); Spearman (nonlinear) correlation was r = 0.61 (n = 316) between blood and hair mercury levels. Hair mercury was not correlated with any symptoms of mercury intoxication. (This report illustrates the lack of correlation between hair mercury and toxicity, particularly when the exposure pattern is complex. The study collected a large amount of quality data, but the subsequent interpretation proved difficult and the authors used considerable data massaging. The predicament is understandable, since mercury is clearly toxic and the authors would presumably like their data to be more conclusive. When one is willing to ignore preconceptions, however, interpretation of mercury results is often inconclusive at the relatively modest concentrations discussed in this report.)

**Report 13: fish diet in Brazil.** The relationship of methylmercury exposure and subtle symptoms was examined in a remote river-dwelling population on the Amazon River of Brazil [40]. Fish is a major source of food in this region and gold mining activities are frequent. Hair mercury in 129 adults showed a range of 0.56-13.6 µg/g (median 3.7, mean 4.2, SD ±2.4); about 2 cm of hair “was taken near the root just above the neck.” Neurobehavioral testing was administered by formally trained psychologists using methods such as bead threading to evaluate manual dexterity in a standardized fashion. Assessment included measures of learning, memory, and mood. Hair mercury level was correlated with a statistically significant reduction in fine motor speed (r = -0.27, Pearson correlation); dexterity, concentration, and some aspects of verbal learning and memory demonstrated lesser degrees of correlation. Although important in terms of the population, the decreases in function were “too small to detect or to evaluate as to clinical significance for one individual …” (This report describes a low but measurable degree of correlation between methylmercury exposure and subtle symptoms of poisoning. The type of neurobehavioral testing described would not be useful to evaluate mercury exposure in an individual, at least at this level of exposure. Furthermore, the deficits were identifiable only in comparison to a specific control group, the selection of which could influence the conclusions reached. These data were used to calculate a reference limit for Table 2.)

**Report 14: fish diet in Finland.** The relationship of methylmercury exposure and cardiovascular disease was investigated prospectively in a population of 1871 Finish men 42-60 yr-old [3]. The range of hair mercury levels was 0-15.7 µg/g (mean 1.9, SD ±1.9); hair was collected from “the scalp” [41]. After an average of 13.9 yr of monitoring, men in the highest third of hair mercury (≥2.03 µg/g) had a 1.6-fold increased risk of an acute coronary event. The authors concluded that high mercury level in hair may be a risk factor for acute coronary events and that mercury exposure may attenuate the protective effects of fish on cardiovascular health. (This report is a good example of the power of a prospective study. Since selenium probably provides...
some protection from oxidative damage associated with mercury, the risk in this population may be accentuated by the relatively low levels of selenium in Finland [41]. To put the risk of oxidative stress into some perspective, an earlier study noted that Finnish men with high stored iron levels had a 2.2-fold increase in the risk of acute myocardial infarction [42]. Mercury is probably less important in terms of coronary heart disease than the traditional risk factors of age, cholesterol, hypertension, diabetes, and smoking.

**Report 15: mercury(0) in dentists in Scotland.** To evaluate the effects of mercury(0) exposure from working with dental amalgams, some Scottish dentists were given a battery of computerized tests to examine functions such as reaction time, spatial memory, word recognition, and word recall [43]. In 161 dentists, the range of hair mercury levels was 0.10-5.67 µg/g (median 0.80, mean 1.00, SD ±0.77); “head hair” was collected by the individual involved. Specimens also included pubic hair, urine, and finger and toe nails. Among 161 controls, the range of mercury in scalp hair was 0.04-3.86 µg/g (median 0.47, mean 0.57, SD ±0.48), and in pubic hair was 0.03-2.54 µg/g (median 0.37, mean 0.46, SD ±0.36). Differences between dentists and controls were found in 2 of 8 tests given, with the control group performing worse on one of these. The study concluded that mercury at the concentration studied did not have a detrimental effect on the functions tested. Selection of an appropriate control group proved difficult and may have influenced the conclusions reached. (This report emphasizes the difficulty in selecting controls and interpreting subtle test measures. The report includes data on pubic hair, which was used to calculate reference limits in Table 2 for scalp and pubic hair from the control group. Since the study was more concerned with mercury in urine, there was no comment on aspects like fish consumption. However, the relatively low hair mercury values indicate that fish consumption was not frequent in the study population.)

**Report 16: low fish diet in Sweden.** Among 27 Swedish adults who had consumed no fish for ≥2 yr, the range of hair mercury was 0.04-0.32 µg/g (median 0.06) [18]; hair was “cut as close to the scalp as possible.” The range of blood mercury levels was 0.11-1.4 µg/L (median 0.28); blood mercury was also analyzed for methylmercury and inorganic fractions. Inorganic mercury in blood was strongly associated with the number of amalgam fillings but was not correlated with mercury in hair. The study concluded that: (1) inorganic mercury in blood does not contribute to mercury in hair, (2) mercury in hair reflects mostly methylmercury exposure, (3) the methylmercury comes mostly from eating fish, and (4) when animals are raised on fish-containing feeds, other foods—such as chicken and pork derived from these animals—can be minor sources of methylmercury. (This report provides evidence that hair mercury reflects mostly methylmercury exposure, at least when external contamination and other forms of organic mercury are not involved. Note that hair mercury concentrations were greater than zero even under conditions of minimal exposure.)

**Report 17: fish diet in children in Brazil.** The effect of mercury was examined in children 3 to 7 yr-old living in riverside communities in the Brazilian Amazon [44]. Functions such as balance, trunk-limb coordination, and sensory perception were evaluated with tests designed for field conditions. For example, static balance was evaluated by standing on tiptoe for a specified period. Among 72 children who frequently consumed fish, the range of hair mercury levels was 0.58-17.14 µg/g (median 4.70); “scalp hair” was collected. In a control group of 114 children with lower fish consumption and similar socioeconomic background, the range of hair mercury levels was 0.385-7.57 µg/g (median 1.85). Both groups showed a high proportion of “non-normal” performance when tested, suggesting that test results were related more to socioeconomic factors than to mercury. The authors concluded that using better educated urban children as a control group would probably have made it appear that mercury was associated with developmental problems in the children. (This report provides a good example of the fact that selection of the control group is often a major determinant of the outcome. Attributing poor performance on subtle test measures to mercury...
exposure is difficult even in children, a group generally more sensitive to mercury than adults. Mercury exposure was relatively high even in the control group; in other words, this study is a comparison of relatively high exposure to higher exposure.)

Report 18: prenatal exposure in the Seychelles. As part of the ongoing Seychelles Child Development Study, 711 children were evaluated at 66 mo of age for prenatal exposure to methylmercury [2]. The Seychelles are an island chain in the Indian Ocean where methylmercury exposure is typical of populations that depend on fish as a major dietary source. Prenatal exposure was assessed from “a segment of maternal hair representing growth during pregnancy”; the range of hair mercury was 0.5–26.7 µg/g (mean 6.8, SD ±4.5). No adverse association was found between mercury exposure and tests of language, letter and word recognition, visual-spatial ability, and social behavior.

Similar long-term studies are ongoing in the Faroe Islands in the North Atlantic, where prenatal methylmercury exposure occurs primarily from maternal consumption of pilot-whale meat. Although neurologic examinations in this cohort generally detect no abnormalities [45], more subtle defects are found. To give one example, auditory evoked potentials were decreased when tested 14 yr after birth [46]. Evoked potentials are determined through electromyographic response to an auditory signal and are thought to reflect electric activity from structures such as the auditory nerve. Prenatal exposure was reflected by mercury levels in cord blood and maternal hair collected at parturition 14 yr earlier. The geometric average was 4.22 µg/g in hair (n = 855) and 22.6 µg/L in cord blood (n = 835). (Since the fetal period is the most sensitive to mercury, these reports were included for perspective on prenatal exposure.)

Evaluating Hair Mercury

Interpretation of mercury exposure in an individual patient is ideally based on a combination of patient history, signs and symptoms, consideration of the differential diagnosis, and analysis of mercury in whole blood and urine specimens [5]. Analysis of hair specimens may provide useful supplemental information in some circumstances, although attempts to interpret mercury exposure in an individual based only on hair analysis are usually of dubious value [6]. Steps to consider in the evaluation of hair specimens are discussed below. A similar approach to blood and urine specimens has been described previously [5].

Specimen collection. The ideal hair specimen is terminal-type hair collected from a standardized site such as the scalp at the occipital-neck junction and labeled to maintain orientation to the skin. It is unnecessary to include hair roots unless the growth phase of a strand(s) is to be determined. Instruments such as plastic clips or hemostats can be used to maintain strand alignment. For transport and storage, the main concern is protection from dust; unused plastic urine cups or plastic bags are usually adequate. Weighing errors tend to be minimized when sample sizes are >10 mg; this represents a minimum of about 150 segments of hair 1 cm in length [6]. A bundle about the thickness of a pencil eraser usually represents about 50 mg [47]. Useful information may be gleaned from hair analysis when specimen collection is not ideal. However, the quality of the specimen plays a major role in the reliability of the interpretation.

Environmental influences. Hair closest to the scalp is generally the least likely to be contaminated. Individuals in a mercury-contaminated environment have increased likelihood of hair contamination; specimen collection while in a contaminated environment has the potential to increase the degree of contamination. Mercury(0) in particular is easily absorbed from the environment [20]. Showering before hair collection is unlikely to remove species such as adsorbed mercury(0) but may dislodge mercury-containing particulate matter. The mercury content of hair can be altered by exposure to cosmetics such as soaps, creams, shampoos, hair sprays, lotions, dyes, bleaches, and waving solutions. Any product that touches the hand has the potential to be transferred to hair in minute but analytically significant amounts (see Report 7 above). While most concern is for potential contamination, significant mercury loss from hair
can also occur from products such as “cold waving” solutions that contain thioglycolate [13].

**Analytical issues.** Adequate analysis of mercury concentrations in hair requires mass spectrometry, atomic absorption, neutron activation, or a similar instrumental method. Acceptable analytical results are most likely to come from laboratories that participate in proficiency testing. Proficiency testing for mercury in blood and urine specimens is available through organizations such as the Centre de Toxicologie du Québec (http://www.ctq.qc.ca). A proficiency program for hair mercury has been described [23]. In 2000, 19 laboratories participating in this interlaboratory comparison program showed a range of 13.6-17.8 µg/g for a target mean of 15.9 µg/g. This probably represents the best level of performance that can be expected among different laboratories, although it applies only to specimens that have been carefully powdered and homogenized. A specimen of hair may not be homogeneous, particularly in terms of the time frame, even when taken from the same patient at the same time.

**Time frame.** Scalp hair 1 cm in length corresponds roughly to 1 mo and the segment in the first 0.50 cm adjacent to the scalp represents on average 7-21 days before collection [6]. A 3 cm length cut into uniform pieces before sampling will give an average concentration over approximately 3 mo. Sampling from the proximal end represents an earlier time period, whereas the distal end corresponds to a later period. The time frame represented by hair can be estimated when the following information is available: (1) length collected, (2) distance from the scalp, and (3) orientation to the scalp. Sampling shorter segments of hair has the potential to give higher peak mercury concentrations, since a peak will be averaged over a shorter time period. Segment lengths often vary as much as 0.2-3 cm (see Reports 3 and 5 above).

**Hair-to-blood ratio.** Although hair and blood specimens collected at the same time may not be correlated [47], hair mercury level can be used to estimate the earlier methylmercury concentration in blood (see hair and blood above). Adopting 300 as the approximate hair-to-blood ratio (limited to one significant figure), 1 µg/g hair mercury is suggestive of an earlier 3 µg/L methylmercury in blood. More accurate estimates require more complex calculations [21]. Obviously, contaminated specimens will give spurious estimates.

**Urine.** In most circumstances, urine mercury level reflects exposure to inorganic mercury or to highly soluble organic species such as merbromin. Less than 10% of methylmercury is usually excreted in urine, although the percentage tends to rise with increasing exposure [17]. When assessing chronic methylmercury exposure, a relatively low level of urine mercury suggests that inorganic species are not involved.

**Reference limits.** Selected reference limits for mercury concentration in hair are listed in Table 2. A reference interval is a measure of the mercury distribution in the population studied and is unrelated to the point at which toxicity develops. Therefore, a reference interval is useful primarily to define where an individual stands relative to the population in question. The single most important determinant for hair mercury is the amount of fish in the diet [47]. Reference limits for the US population are available for scalp hair (first cm adjacent to scalp at the occipital-neck junction) [47]. Specimens were collected from children 1-5 yr-old and women 16-49 yr-old, but are generally applicable to children and adults of both genders. However, the limits may not be representative of specific geographic regions such as King County.

### Table 2. Selected reference limits for hair mercury.

<table>
<thead>
<tr>
<th>Hair mercury ≤ (µg/g)</th>
<th>n</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.73&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1726</td>
<td>scalp hair in US adults [47]</td>
</tr>
<tr>
<td>0.55&lt;sup&gt;a&lt;/sup&gt;</td>
<td>639</td>
<td>US adults on low fish diet</td>
</tr>
<tr>
<td>2.75&lt;sup&gt;b&lt;/sup&gt;</td>
<td>447</td>
<td>US adults eating fish ≥3 times/mo</td>
</tr>
<tr>
<td>0.64&lt;sup&gt;a&lt;/sup&gt;</td>
<td>838</td>
<td>US children</td>
</tr>
<tr>
<td>2.00&lt;sup&gt;a&lt;/sup&gt;</td>
<td>208</td>
<td>US children eating fish ≥3 times/mo</td>
</tr>
<tr>
<td>1.18&lt;sup&gt;b&lt;/sup&gt;</td>
<td>168</td>
<td>pubic hair in Scottish adults [43]</td>
</tr>
<tr>
<td>1.68&lt;sup&gt;b&lt;/sup&gt;</td>
<td>163</td>
<td>scalp hair in Scottish adults</td>
</tr>
<tr>
<td>3.16&lt;sup&gt;b&lt;/sup&gt;</td>
<td>137</td>
<td>scalp hair in Chinese children eating fish ~ 3 times/wk [48]</td>
</tr>
<tr>
<td>9.0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>129</td>
<td>scalp hair in Report 13 [40]</td>
</tr>
</tbody>
</table>

<sup>a</sup> 95th percentile; <sup>b</sup> mean + 2 SD
Washington, or for specific subgroups such as sport and subsistence fishers. Data from the control group in Report 15 were used to calculate reference limits for mercury levels in scalp and pubic hair. This group of Scottish adults is probably representative of most groups who do not regularly consume fish. This is in contrast to Chinese children 4-11 yr-old who regularly consumed fish an average of 3 times/wk (SD ±1.9) [48]. For comparison purposes, the adults described in Report 13 were included in Table 2.

**Toxicity.** Toxicity is evaluated by examining the patient for appropriate signs and symptoms. Clinical examination for suspected methylmercury poisoning typically emphasizes neurologic findings such as paraparesis, tremor, and numbness of the limbs [39]. More subtle abnormalities of mercury poisoning can be detected in group studies through testing methods such as described in Reports 12, 13, 15, 17, and 18. Most of these tests lack specificity when applied to individuals. Laboratory measurement of a biological marker, such as urine porphyrin excretion, is often easier than other testing methods [49,50]. When no abnormality can be identified, it is reasonable to assume that an individual is not experiencing significant toxicity due to mercury exposure [5].

**Speciation.** In the clinical laboratory, mercury is determined as total mercury without regard to the chemical forms present. At a minimum, speciation divides total mercury into inorganic and organic fractions. Further characterization depends on the specific assay. Although speciation is seldom performed in clinical laboratories, it is available in some research settings. Inorganic mercury is incorporated less efficiently into growing hair than methylmercury [17], it may be possible to attribute an elevated inorganic fraction to exogenous contamination (see Report 5 above). Organic mercury in hair is less likely to be caused by contamination, although exceptions can be found (see Report 1 above).

**Sequential analysis.** Step-wise analysis over several centimeters of hair has the potential to provide useful information (see Report 3 above). Sequential analysis of a single hair strand obviously requires considerable effort and excellent analytic sensitivity. Sequential analysis of hair bundles does not require as much sensitivity but depends on proper strand alignment. Sequential analysis may be complicated by the fact that strands in telogen reflect different time periods relative to those in anagen.

**Conclusions**

The goal of interpretation is to understand the relationship of laboratory results to the specific circumstances of the patient. This is often obvious when massive mercury poisoning produces acute symptoms, but it becomes increasingly difficult when lower exposure levels are involved and symptoms shift to more chronic patterns [36]. Confidence in an interpretation increases when laboratory results present a coherent pattern consistent with patient findings.

An adequate evaluation for mercury exposure includes patient history, physical examination, and consideration of alternative diagnoses for the signs and symptoms present. While whole blood and urine are usually the most important specimens for mercury analysis, hair may supply useful supplemental information in some situations. Hair is most useful for exposure to organic compounds such as methylmercury and less useful for inorganic mercury. Hair may be particularly helpful in reconstructing a pattern of earlier exposure. An adequate specimen generally requires >10 mg of terminal-type hair, clamped to maintain strand alignment, and collected at a known distance and orientation to the skin. The most common location for collection is the occipital region adjacent to the scalp. Consideration of the time frame represented by a specimen is an important part of an evaluation, and hair from the initial 0.5 cm next to the scalp represents on average 1-3 wk before the collection date. The manner in which the hair specimen is sampled for analysis also affects the time frame.

The literature reports that are summarized above describe hair mercury levels as high as 2400 µg/g. Hair mercury concentration is usually <1 µg/g in individuals who do not eat fish but may be >30 µg/g in those who frequently consume fish with high mercury content. Hair mercury is often not
correlated with signs of toxicity and reports of contamination by exogenous mercury are not uncommon.

Toxicity is evaluated by signs and symptoms in the patient, and not by laboratory results or reference intervals. Clinically obvious neurologic signs may be present when hair mercury is >300 µg/g; at lower concentrations, more subtle symptoms may be present but are often difficult to differentiate from other causes. While there are excellent reasons to limit mercury exposure, attributing subtle symptoms to relatively modest levels of mercury exposure remains unconvincing in many patients. Hair analysis for mercury is best used with an appreciation of its limitations since there is considerable potential for misinterpretation.

References


