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**MEMORANDUM** **NOTE DE SERVICE**

TO / À: Director General
Program Management

ATTENTION: Dr. L. BLACK

FROM / DE: Regional Director
Northwest Territories Region

| SECURITY - CLASSIFICATION — DE SÉCURITÉ | |
|---|---|
| OUR FILE — N/RÉFÉRENCE | 151-1-5 (N3) |
| YOUR FILE — V/RÉFÉRENCE | |
| DATE | February 11, 1975 |

SUBJECT / OBJET: Arsenic - Yellowknife

The attached article has been brought to our attention by Dr. Ron Wallace, biologist with the Department of Environment in Yellowknife.

There is a great deal which is relevant to the present Arsenic situation in Yellowknife, and it is a useful reference in general terms.

Present situation is that 100 hair samples have been submitted to date for assay, mainly from mill workers at Giant Mine. No results as yet.

R.D.P. Eaton, M.B., Ch.B., D.P.H.
for Regional Director

| ACTION | PA date | SF date |
|---|---|---|
| ~~M 14~~ | 24/2/75 | |

INFORMATION

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Att.

/sa

M67 24 Feb 75
Duff, for info of your consultant, Dr. Patton. J'll forward further reports as received.
JH.

Thanks
Copied & routed
26/2/75. JH.

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INFORMATION

# ARSENIC IN THE MARINE AND AQUATIC ENVIRONMENTS: ANALYSIS, OCCURRENCE, AND SIGNIFICANCE

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## I. THE OLDEST POISON

"Arsenic" and "poison" are almost synonyms in the minds of most people. Though it is orders of magnitude less toxic than many modern agents, it has been available to dissatisfied spouses and the politically ambitious for thousands of years, a cheap and effective solution to many of the awkward situations that develop in human affairs.

Since the development of chemistry as an organized science, the poisonous properties of the element have been modified and tailored to specific uses. In 1910, the arsenical Salvarsan was introduced into the clinical treatment of syphilis by Paul Ehrlich. This was followed by a host of pharmaceuticals effective against amoeboid, trypanosomal, and other parasitic agents. Arsenic compounds have been used as insecticides, vermicides, fungicides, herbicides, and as the war gas lewisite, whose "virtue" was its ability to penetrate rubber gas masks. In their various toxic employments, except as herbicides, arsenicals have been superseded by more effective agents. There are, of course, numerous industrial uses of arsenic which are not related to its toxic properties, including the manufacture of alloys and semiconductors.

In nature, arsenic is widely but sparsely distributed. It can be detected at low levels in all living matter, although it has no known biological function. Schroeder and Balassa[1] have estimated that the average American intake of arsenic is 0.4 to 1.0 mg/day. They also observed that the highest levels of arsenic (2.7 to 8.9 ppm) were to be found in seafoods. These are often in excess of established health limits.[1-9]

The modern interest in environmental toxicology has resurrected some old problems, and the presence of high levels of arsenic in marine animals is of particular concern partly because of the connotations of the word "arsenic." Association of the word "arsenic" with a foodstuff is almost certain to affect its commerce, even though no harmful effect may be suspected or demonstrated. The legal limits for arsenic in foods were set during periods of public reaction to environmental poisoning incidents in which arsenic was suspected, but never proven, to be the agent.[9,10] In a review of this problem D. V. Frost[10] asserted that the British limit of one part per million in food

was based on an experiment with "treatment groups" consisting of single animals!

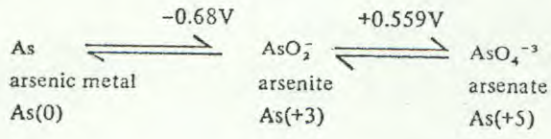
Arsenic is also traditionally suspected of carcinogenic properties, and this suspicion is supported by a trickle of epidemiological reports claiming, to take only one example, that 8,000 smelter workers have an increased incidence of respiratory cancer after long exposure to fumes containing, among other things, arsenic.[11] The historical association between the element and the disease is so strong that other causative agents were not considered in most of these reports. Controlled attempts to attribute carcinogenic properties to arsenicals have failed.[9,12,13]

The present review was prepared with the intent of making an objective judgment of the danger represented by arsenic in the aquatic and marine environments and its commercial products. The study of the literature has revealed much surprising information and also has raised a number of important questions which are now the focus of a research program in our laboratory.

## II. THE ANALYTICAL CHEMISTRY OF ARSENIC

### A. Chemical Properties of the Element

Due to its metalloid nature, the chemistry of arsenic is relatively complex.[14] It exists in three oxidation states: metallic, As(0); trivalent, As(+3); and pentavalent, As(+5)*:




The tri- and pentavalent states can be easily interconverted in solution without the use of catalysts; this permits several convenient separations to be performed, since the trivalent form is reactive with chelating and other reagents, especially those where sulfur is the donor atom(s).

Arsenic forms stable, covalent bonds with most nonmetals and with some metals.[15,16] Trivalent arsenic forms organic derivatives of arsine ($AsH_3$) containing one, two, or three alkyl or aryl groups. Remaining valency positions can be filled by hydrogen, halogens, some metals, or (for primary arsines) oxygen or sulfur. Pentavalent arsenic can form similar compounds, with restrictions; for example, $AsH_5$ and $AsCl_5$ do not exist, although $AsF_5$ does.

### B. Analytically Useful Reactions for the Determination of Arsenic

For an element with such a long history and for the sheer volume of effort that has been devoted to its chemistry and analysis, the analytical methods available for trace arsenic are generally somewhat less than satisfactory by today's standards. In the nanogram range, neutron activation and X-ray fluorescence methods offer adequate sensitivity, but these are very expensive for routine use and, except in unusual cases, the operations involved are overly complex. New adaptations of atomic absorption and emission now offer the potential of rapid, high sensitivity analysis.

In the microgram range, there are a number of simple, quantitative wet chemical methods that have been in use for many years. These have been refined into a large number of methods for arsenic analysis, all about equally precise and sensitive to 1 to 10 μg. An attempt has been made here to classify them.

**1. Arsine evolution and absorption** — Arsenite can be converted to gaseous arsine (b.p. −55°) by zinc and hydrochloric acid, by electrolysis,[17] or by sodium borohydride.[18] The first two reactions also produce quantities of hydrogen which can act as a convenient carrier for the minute traces of arsine.

If arsine is absorbed into a pyridine solution of silver diethyldithiocarbamate, a stable, intense red color develops.[19] Separation and analysis are accomplished in one operation, the sensitivity (0.2 μg) is superior to other similar procedures, and the precision is good.[20] The method has been adopted by the American Public Health Association[21] and the Association of Official Analytical Chemists.[22]

Alternately, arsine can be absorbed into a suitable trapping agent such as alkaline iodine. In this case separation and determination are independent operations, but the development of the blue arsenomolybdate color is the most common determination step.[1,17,23,24] The sensitivity is somewhat less than the silver diethyldithiocarbamate method.[20]

*Throughout this review, "arsenic" will refer to the element regardless of oxidation state; "arsenite" will refer to the +3 oxidation state; and "arsenate" to the +5 state. "Elemental arsenic" will refer to the free element.

Predating both these methods is the venerable Gutzeit procedure where the arsine-bearing gases are passed over a paper or string impregnated with mercuric chloride (reviewed in Sandell[24]). The size and intensity of the resulting black stain are compared with standards. Aside from the subjective component of the determination introduced by visual comparison, it is necessary to keep experimental conditions meticulously constant. It is still the most sensitive wet chemical procedure for detecting arsenic; Satterlee and Blodgett[25] developed a modification that permitted detection of 40 ng of the element.

Arsine evolution procedures as normally constituted do not distinguish chemical forms of arsenic; most statutory limits on arsenic refer only to total arsenic. Gorgy et al.[26] distinguished arsenite and arsenate in seawater by measuring the arsine evolved in samples with and without prior reduction by iodide of arsenate to arsenite. They claimed that zinc and hydrochloric acid was an inefficient reductant for the arsenate-arsenite conversion, but Clement and Faust[27] were able to demonstrate that partial reduction of arsenate by zinc and hydrochloric acid does in fact occur, and have proposed a method employing dimethylformamide to effectively inhibit this reduction. Less than 1% of arsenate present is detected with their procedure.

Recently, Braman and Foreback[28] have used a combination of pH and reductants (boron hydrides) to distinguish arsenite, arsenate, methylarsonic acid, and dimethylarsinic acid (the latter two are evolved as methylarsines).

The relative freedom from interferences has been responsible for much of the popularity of arsine-evolution methods. However, if the appropriate elements are present, hydrogen sulfide, phosphine ($PH_3$), stibine ($SbH_3$), and germane ($GeH_4$) will be generated.[29] Some arsenic compounds such as dimethylarsinic (cacodylic) acid are converted to corresponding arsines which can potentially interfere in subsequent determination.[30]

Some workers report incomplete recovery of arsenic by this method.[17,31] As long ago as 1933, Gross established that some nitrogen heterocycles interfered seriously with the evolution of arsine; this is especially important since this class of compounds notoriously resists oxidative decomposition.[32]

2. Molybdate methods – Molybdic acid forms complexes with phosphate, arsenate, silicate, and germanate. These complexes can be reduced by a number of agents to produce a characteristic blue color.[24] For arsenate the method can be refined to a sensitivity of 1 $\mu$g,[20] and with suitable preliminary separations arsenic can be determined on a relatively routine basis.[17, 24,29,33-37] Some of these authors have also made use of these complexes for the solvent extraction of arsenic.[38]

3. Coprecipitation – Traces of inorganic arsenite and arsenate can be coprecipitated with ferric hydroxide.[24,33] We have found this method to be effective in improving reproducibility when determining arsenic in natural waters. Undoubtedly, the presence of much iron overwhelms the variable effects of other ions; some interfering ions may be left behind in the coprecipitation. Less than a microgram of arsenic can be recovered from a liter of water or seawater.

4. Solvent extraction – From strong hydrochloric acid solutions, arsenite can be quantitatively extracted into benzene, from which it can be completely recovered by extraction with water.[39] The amount extracted into benzene varies from 0 to 100% as acidity is increased from 2 to 8 N. Other acids and solvents may not substitute, since a specific complex is formed. Carbon tetrachloride, for example, extracts incompletely.[24] Most metals are left behind, except germanium.

Arsenite will form complexes with many sulfur compounds such as potassium xanthate,[33] diethylammonium diethyldithiocarbamate,[24] ammonium pyrrolidine-dithiocarbamate,[40] 2,3-dimercaptopropanol, zinc dibenzyldithiocarbamate (our observation), and toluene-3,4-dithiol. These last two reagents are stable in strong acid where many interfering metals do not form complexes.

These complexes are useless for colorimetry but are helpful in separation, since arsenic can be recovered by oxidation to the pentavalent form which is released from the complex. Extraction of a sample prior to reduction will yield arsenic present in the trivalent form; after reduction, an amount of arsenic is recovered equivalent to the pentavalent arsenic present in the original sample.[41]

5. Distillation – Arsenic in the +3 state can be distilled from hydrochloric or hydrobromic acid solution.[24] This technique has been employed for the concentration of arsenic from

water samples.[42] Lunde[43] has successfully employed distillation for the resolution of total arsenic into inorganic and organic forms; only inorganic arsenic would be expected to be found in the distillate. However, Satterlee and Blodgett[25] reported the existence of an arsenic-containing component of tissue samples which was volatile at 56 to 80°, and until the existence and nature of this component can be established, distillation should not be accepted as an absolute method of separating organic and inorganic arsenic.

### C. Instrumental Methods

Success in developing instrumental techniques for arsenic has been limited. Of the methods outlined below, few would seem to be practical for large numbers of routine analyses on the basis of cost or time. Some offer increased sensitivity and may be useful on those occasions when preconcentration is not practical and others when the element is combined in an extremely refractory form (as described in Section II.D).

1. X-ray fluorescence – This is fundamentally a multi-element technique and no references specific to arsenic are available. The method is insensitive to the chemical form of elements and has been used by Conacher (personal communication) for the analysis of the arsenic-containing compound isolated from fish. Because of the low energy of the emitted X-rays, however, the attenuation due to the sample matrix must be corrected. With samples such as liquids, this task is quite straightforward, but with more complex matrices such as tissue or rock, it is necessary to prepare standards in similar matrices or to reduce samples to a simpler matrix. Marcie[40] accomplished the latter with biological materials by extracting metals with diethyldithiocarbamate in chloroform and drying the extract onto a filter.

The sensitivity of X-ray fluorescence analysis is limited in principle only by counting time, and by manipulation of parameters very great sensitivity can be achieved in some cases.

2. Neutron activation – Like the previous method, this approach depends on the availability of an expensive facility, in this case a neutron generator or reactor. The detection limit is about one nanogram of arsenic, but for maximum sensitivity in natural samples, separation of the generated arsenic-76 is generally necessary. It is therefore somewhat awkward for routine use. Commercial facilities exist that do this analysis, but they are expensive. Both activation and counting are essentially independent of sample matrix, but if a separation is necessary, the problems involved in sample decomposition (Section II.D) are rendered more serious by the handling of highly radioactive materials.

Lunde[5] described the activation analysis of arsenic, bromine, and iodine in marine oils and has published much work based on this method since.[6-8,43-46] Activation analysis has been employed by Ruch et al.,[47] Heydorn,[48] Uthe and Bligh,[49] and Seydel[50] in the analysis of environmental samples. The work of Ruch and co-workers illustrates how complex the postirradiation work-up can be: after irradiation carrier arsenic was added; the sample was digested with hydrogen peroxide, perchloric acid, and hydrofluoric acid; the arsenic was distilled as the pentabromide, and finally reduced to the metal and counted.

3. Atomic absorption – This method is generally unsatisfactory with regard to sensitivity, the limit being in the 1 to 3 ppm range. The hollow-cathode lamp is noisy due to the volatility of the element. The Perkin-Elmer Corporation claims increased sensitivity in a system where arsine is generated and collected in a balloon whence it is blown through an argon-hydrogen flame in a single pulse.[51] More recently the same manufacturer has introduced microwave-excited lamps which take advantage of the volatility of arsenic, and two- to fivefold greater sensitivity is claimed; the very recent introduction of the graphite tube furnace by Perkin-Elmer has enabled the detection of as little as .01 ng arsenic when combined with the microwave-excited lamp and a smoke corrector. Samples may be processed at rates up to 20 or 30/hr (Woolson, personal communication). These extreme sensitivities are compromised somewhat by the small sample volumes allowed (up to 100 μl), making preconcentration necessary to achieve the higher sensitivities.

4. Atomic emission – Arsine gas has been passed through an electric discharge and the resulting line at 229 nm detected.[18] A sensitivity of one nanogram is claimed, but the equipment is not yet commercially available. The method has been recently extended to permit analysis of As(+3), As(+5), and methylated arsenic compounds in a single sample.[28]

5. Polarography – Arsenite ion can be detected with good sensitivity. Using single-sweep polarography, Whitnak and Brophy[52] claimed a sensitivity of 5 ppb in natural waters. Offner and Witucki[53] proposed the use of polarography for the emergency detection of high levels of toxic metals in suspect water supplies; arsenic could be detected below its acutely toxic concentration. More recently, the introduction of differential pulse polarography has pushed the sensitivity limits to 0.3 ppb in defined samples.[54] The same laboratory has used the method on natural samples successfully, but without reporting the sensitivity limit.[55]

6. Coulometry – In alkaline media, arsenite can be titrated with electrogenerated iodine. The excess iodine appearing at the end point can be detected polarographically or photometrically. The sensitivity of the method rivals that of arsine-based methods, but rather more extensive sample preparation is necessary to eliminate the many possible interferences.[56-58]

D. Decomposition of Biological Samples

Comparison of published analytical procedures gives no consensus on a suitable means for decomposing samples of biological materials for arsenic analysis. Much of the older work refers to ordinary digestion with nitric and sulfuric acids. Chapman[3] used this technique in the analysis of marine materials; he obtained a level of 67 ppm in lobster tissue digested with these acids as opposed to 8 ppm in undigested tissue. Rogers and Heron,[17] Sugawara et al.,[33] Sandell,[24] Gorsuch,[59] and Winkler,[60] among others, have used acid digestion with apparent success. Down and Gorsuch[61] reported complete recovery of added radioactive arsenic, but Portmann and Riley,[35] doing similar analyses, reported high losses of arsenic. They decided on the use of nitric acid alone, claiming that the high temperatures necessary to fume sulfuric acid caused volatilization of arsenic. Sachs et al.[30] maintained that a long period of fuming was necessary to completely destroy carbon-arsenic bonds; furthermore, they lost no arsenic using this procedure.

Evans and Bandemer[23] developed the old technique of ashing in the presence of magnesium nitrate.[62] With numerous modifications it has been used for the assay of arsenic in potatoes,[34] poultry,[111] and marine fish.[63] We have found it satisfactory, but it is considered inadequate by Portmann and Riley[35] and Carey.[64]

Why has arsenic recovery proved to be so consistently difficult? A detailed study of the literature brings forward the following considerations:

1. In principle, arsenic can be lost from digestion mixtures that are very hot and/or possess the appropriate composition. Arsenious (As(+3)) oxide is volatile;[14] one would expect oxidizing conditions to prevent this loss. The presence of fluoride, chloride, or bromide would be expected to result in losses of the volatile arsenic trihalides. Local reducing conditions, such as the hot carbon of charred organic matter, could conceivably result in unwanted evolution of arsine; this caution has been stated,[24] but to my knowledge has never been tested.

2. The classic work of Chapman[3] and Coulson et al.,[4] that of Lunde,[43,44] and our own observations indicate that essentially all the arsenic present in animals is in a form other than ionic arsenite or arsenate. It is probably in organic form.

3. Organoarsenic compounds differ in their stability to oxidation.[65] Methylarsonic acid and dimethylarsinic (cacodylic) acid are both very refractory to wet digestion procedures;[30,62] we have only achieved satisfactory recovery of arsenic from these using a modified dry-ashing procedure. Newberry[62] employed persulfate oxidation to decompose cacodylic acid; others have been successful employing perchloric acid, a potentially hazardous expedient.[66]

4. The efficiencies of oxidation procedures have been monitored with radioactive arsenic and conditions have been established assuring full recovery of radioarsenic.[35,59,61] In these experiments, the added arsenic was in the inorganic form; there is no assurance that all of the arsenic in organic form was fully released, or if released, was not lost by volatilization.

Hamilton et al.[67] appreciated the difference between "incorporated" arsenic, where radioarsenic was allowed to be incorporated into a live animal, and "spiked" arsenic, where the element was added directly to a dead tissue sample. By ashing at 450° *without* magnesium nitrate, they observed losses of 86% and 29%, respectively: that is, arsenic which has been incorporated into animal tissues is much more volatile than the added

inorganic arsenic. It is unfortunate that these experiments were not done with the ashing aid.

The syntheses that can be made from these points are:

1. Since the recovery of arsenic from biological samples has never been measured against an absolute method like neutron activation analysis, to our knowledge, it is conceivable that most published surveys of total arsenic levels may be low or at least inconsistent.

2. The nature of the organic forms of arsenic in organisms must be understood, and the chemical properties examined before measurements of arsenic can be relied upon. Subsequent toxicological investigations of the arsenic compounds will then permit interpretation of these measurements in terms of the hazards they may represent. An analogous situation is found in the recent emphasis on distinguishing inorganic and organic mercury in order to make a realistic assessment of "total hazard."[68,69]

## III. THE TOXIC PROPERTIES OF ARSENIC

### A. Effect of Chemical Form

In view of the variety of arsenic compounds as well as the extreme stability of some of them, an assumption that all arsenic compounds have the same toxicity is wrong and dangerous. The toxicities of arsine gas and cacodylic acid differ by over 400 times, while an experimental pharmaceutical compound, arsenocholine, is nontoxic when fed as 1% of an animal's diet.[9] The Merck Index (8th ed.) and most regulatory agencies treat all arsenicals alike; Frost[10] claims that some useful drugs remain unused because of a web of misconceptions surrounding the element.

The toxicities of groups of arsenic compounds decrease in the following approximate order (assembled from Moeschlin,[70] Frost,[9] Schroeder and Balassa,[1] Vallee,[12] and Webb[71]):

1. arsines (trivalent inorganic or organic),
2. arsenite (inorganic),
3. arsenoxides (trivalent with two bonds joined to oxygen),
4. arsenate (inorganic),
5. pentavalent arsenicals such as arsonic acids,
6. arsonium compounds (four organic groups, with a positive charge on arsenic), and
7. metallic arsenic.

Arsine gas is primarily a hemolytic agent; erythrocyte catalase is inhibited, leading to accumulation of hydrogen peroxide and destruction of the membrane.[70] Substituted arsines have toxicities resembling arsine gas. There is no effective antidote.

Inorganic arsenite or its anhydride arsenious oxide are the most common commercial forms of arsenic. The latter is the "white arsenic" of agricultural interest and the form which was most often used for antisocial purposes. Its acute toxic effects are dramatic: a latent period is followed by rapid collapse, then shock and death. Specific antidotes are available, typically British Anti-Lewisite (2,3-dimercaptopropanol), which are often successful in treating acute and chronic poisoning.

Chronic poisoning by arsenite leads to a host of serious and progressive symptoms: disturbances of peripheral circulation, polyneuritis (numbness and loss of reflexes), mental disturbances, liver cirrhosis, hyperkeratosis and pigmentation of the skin, kidney damage, and changes in heart rhythm.[70] Diagnosis is complicated by the observation that individuals tend to manifest symptoms differently.

Peoples[72] demonstrated that arsenic does not appear in the milk of cows fed arsenious acid, nor does it reach significantly high levels in the tissues (0.2 ppm in muscle at a feed level of 1.25 ppm). Rat, guinea pigs, rabbits, and hamsters show a wide variability in accumulation of arsenic. Organs show great variability as well, muscle and brain generally containing the lowest levels, while (depending on the species) liver, heart, spleen, skin, and blood contain the highest.

Schroeder et al.[73] maintained 83 rats from weaning until natural death on drinking water containing 5 ppm arsenite. Most tissues accumulated 27 to 47 ppm arsenic except aorta and red blood cells, which reached 315 and 282 ppm, respectively. Otherwise, no symptoms developed and the rats survived a normal 3½-year life span. The significance of this experiment is to cast doubt on the significance of experiments involving arsenic and rats. Water levels of less than 2.5 ppm have been responsible for severe human illness in Taiwan. The experiments of Peoples[72] indicated

little correspondence in accumulation patterns even within the rodent family.

Arsenoxides and pentavalent arsenicals vary considerably in toxicity. These groups include the early chemotherapeutic agents devised by Ehrlich and others to combat syphilis and parasites. A specific symptomatology is associated with occasional reaction to long-term treatment with these drugs, but these are deemed to be allergic in nature.[70] Like all effective drugs, however, these are toxic in sufficiently high doses.

Arsanilic acid, a pentavalent compound, has been in use for years as an additive in animal feeds.[74] It improves "health, appearance, production efficiency, and survival in poultry and swine";[76] it must by law be removed from the animals' diet some time before slaughter and has been demonstrated to clear rapidly from the animals.

Investigating arsanilic acid, Overby and Frost[75,76] fed swine with the arsenical until their tissues contained 3.9 to 8.4 ppm arsenic. The dried, acetone-powdered liver tissue was fed to rats and chickens. The rats promptly eliminated the arsenic in feces and urine. Considerable arsenic (49%) was retained from a control liver diet containing arsenious oxide. Chickens, surprisingly, accumulated *neither* form of arsenic. These experiments would have been more convincing if whole muscle and liver tissue had been fed instead of highly processed liver powder.

Arsonium compounds are quite stable and probably nontoxic. Metallic arsenic, which occurs naturally in central Europe, has been eaten for centuries by mountain people who claimed general beneficial effects on the health.[1]

B. Public Health Problems Due to Arsenic

There are many reported incidents of widespread or isolated poisoning by arsenic in many forms, but to my knowledge, there are *no instances of poisoning by arsenic accumulated naturally by food organisms.*

Throughout the 19th Century and even after, numerous cases of an unusual illness were reported in Europe. The illness, which was frequently fatal, was eventually associated with the presence of wallpaper containing arsenical pigments. The means of transport of the arsenic from the wallpaper remained a mystery until Gosio established that the action of molds on the damp wallpaper was liberating a gaseous form of arsenic. This was eventually identified as trimethylarsine. The literature of "Gosio gas" has been reviewed by Challenger.[77]

In 1900, thousands of British beer drinkers were afflicted by an intoxication which was attributed to arsenic in one of the ingredients. Frost[10] has disputed these conclusions, assembling a rather convincing argument that the responsible contaminant was selenium. However good or bad the evidence, the incident resulted in the establishment in Britain of legal tolerances for arsenic that remain for the most part in effect today.

Most other cases of nondeliberate, nonoccupational poisoning by arsenic have involved drinking water. Arsenic occurs in several minerals and in some cases can enter the ground water in solution or suspension. Chronic arsenic poisoning from wells in the southwest region of Taiwan is the apparent cause of a condition known as "black-foot disease."[78] Victims suffer increasing impairment of peripheral circulation culminating in loss of extremities or death from edema. Water levels of inorganic arsenic up to 2.5 ppm correlate geographically with the incidence of black-foot disease. Arsenic levels in the blood of Taiwanese victims are the same as those in unaffected family members, but significantly higher than in Danish control subjects.[48]

In Madoc, Ontario, in 1935, a well was incriminated in a long history of illness in a family. A young farmer had died of kidney failure, and three of four children had died shortly after birth. The health of family and livestock was poor and a relative who came to manage the farm after the owner's death also became ill. Investigation showed that the well had been drilled through a stratum of arsenopyrite whose insoluble particles were carried in suspension in the water. Water samples contained up to 10 ppm arsenic.[79]

Many employees of a firm in Perham, Minnesota, were found to be afflicted with subacute arsenic poisoning. This was traced to well water levels of 21 and 11.8 ppm arsenic; the source was eventually attributed to the former storage and/or burial of arsenical pesticides on the site.[80]

Chronic arsenicism from water has been observed in Antofagasta, Chile,[81] Cordoba Province, Argentina,[82] and other places, but the literature on these is obscure and difficult to track down.

A massive wildlife kill has been attributed to the careless use of an arsenical herbicide.[83]

C. Arsenic and Cancer

Arsenic and cancer, especially skin cancer, have been associated for over 100 years,[9,10] but the objective validity of the association has not been established.[12,89] The weight of epidemiological evidence supports a relationship, but opportunities to attribute increased incidences of cancer unequivocally to arsenic have been few. Typical is the report[11] mentioned in the introduction to this review, where the carcinogenic properties of the element are accepted *a priori*. Much harder to dismiss, however, is the report of Tseng et al.[84] which establishes a strong geographical correlation between arsenic levels in water in the "black-foot disease" area of Taiwan and the skin cancer rate (which reaches as high as 1%). This also established a statistically indisputable association between skin cancer and hyperpigmentation, hyperkeratosis, and the black-foot syndrome. A breakdown of the data by age indicated that at least 20 years' exposure was necessary for the initiation of skin cancer: there were no cases in subjects under 20 years of age, but the prevalence rate in those over 59 was 10%.

Attempts to induce cancer with arsenic under controlled conditions have been uniformly negative.[9] Baroni et al.,[13] for example, working with large numbers of animals, and using promoters and initiators of tumors, were unable to attribute carcinogenic properties to arsenic. They nevertheless advanced their conclusions cautiously; possibly they were conscious of the weight of medical tradition. Rats and dogs fed sodium arsenate for two years at chronically toxic levels failed to develop cancers.[85]

There are many possible reasons for the dichotomy between epidemiological and experimental data. Epidemiological measurements might be considered more sensitive because they involve large numbers over long periods (for example, Tseng et al.,[84] cited above) and can involve unknown synergistic factors in cancer initiation; they are, however, burdened with the uncertainty that is inescapable in field measurements.

Mutagenesis and chromosome damage are associated with carcinogenesis, and provide more sensitive biological tests for cell damage. Petres[86] noted aneuploidy and other chromosomal defects in the lymphocytes of patients chronically exposed to arsenic. Later, Petres and Berger[87] detected impairment of cell division and DNA synthesis in cultured human lymphocytes by quite low concentrations of arsenic. Increased frequencies of genetic recombination have been noted in fruit flies exposed to arsenate.[88]

The relationship between arsenic and cancer, however, must be considered unsolved.

## IV. ARSENIC IN THE MARINE AND AQUATIC ENVIRONMENTS

A. In Seawater

Measurements of arsenic in seawater rarely depart from the range of 1 to 8 ppb. A variety of methods which are more or less selective for different forms of the element have been used to determine it.

Sugawara et al.[33] swept arsenic from seawater by ferric hydroxide coprecipitation, digested the precipitate with nitric and sulfuric acids, separated the arsenic with xanthate, and determined it by the molybdenum blue reaction. They assumed that particulate matter as well as dissolved inorganic arsenite and arsenate would be caught in the precipitate. They would not have detected those soluble organoarsenic compounds which do not absorb to ferric hydroxide, and their digestion procedure might not have decomposed organic arsenic that was collected by the procedure (see Section II.C). In a seawater sample from Sugashima Island they found 1.7 ppb arsenic.

Portmann and Riley[35] concentrated inorganic arsenic from seawater by cocrystallization with thionalide, followed by nitric acid digestion of the precipitate. They developed the arsenomolybdate color directly in the digest; as a blank, they used seawater from which arsenic had presumably been removed by ferric hydroxide. Interference from dissolved phosphate, which occurs at similar levels in seawater, was eliminated by the thionalide step; however, particulate phosphate may possibly have been carried down with the thionalide crystals and freed by digestion to reactive orthophosphate. Seawater near Liverpool contained 2.0 ± .02 (sic) ppb arsenic.

Arsenic as arsenate was measured by Johnson[37] using an elaboration of the determination of dissolved phosphate. Phosphate and arsenate both react with molybdate, but the arsenate can be selectively reduced to arsenite which does not react. Using this differential method, he estimated ranges in the Caribbean at 2.3 to 8.3 ppb (as As), in the Gulf of Mexico at 0.8 to 4.5 ppb, and in the

western Atlantic at 1.5 to 3.8 ppb, with rather large errors.

Activation analysis of seawater has revealed levels of 1.6 to 5.0 ppb in the English Channel.[90]

Other determinations of arsenic in seawater have been done in the early part of the century using crude methods that gave very high results. These are reviewed by Portmann and Riley.[35]

Inorganic arsenic in the sea seems to exist mainly in the form of arsenite. Atkins and Wilson's report[91] merely compared data taken from the literature, and Gorgy et al.[26] did the measurements under controlled conditions. About two thirds of inorganic arsenic is in the form of arsenite (determined by not reducing the sample with iodide prior to arsine evolution; there are analytical difficulties involved here which are discussed in Section II.B).

Simple thermodynamic calculations predict that under normal conditions of pH and oxygen, arsenic should exist at equilibrium entirely as arsenate.[35] Recently, however, Johnson[92] demonstrated that marine bacteria can reduce added arsenate to arsenite so that the observed ratio may represent a dynamic balance between spontaneous oxidation and biological reduction.

Schroeder and Balassa[1] regard the level of arsenic in the sea as biologically significant. Arsenate is accumulated by the phosphate transport systems of many organisms,[93,94] and seafoods contain generally higher levels of arsenic than terrestrial foods.[1]

B. In Fresh Water

One would expect the arsenic content of fresh water to vary with its source. Geochemical processes, as well as the less significant contributions by arsenical herbicides[10,83] and contaminated phosphate detergents,[95] vary geographically in both quality and quantity. Levels of 0.4 to 10,000 ppb have been reported (Table 1).

Clement and Faust[27] measured arsenate/arsenite ratios in natural waters and found, as might be expected, that in aerated streams most arsenic was present as arsenate and in anaerobic reservoirs most was present as arsenite, while ground water showed intermediate levels.

C. In Sediments

Sediments play a variable part in the aquatic chemistry of various elements. It is now established that mercury can be rendered soluble from sediments by bacterial action.[68] Very little is known of the importance of sediments to the circulation of arsenic.

Portmann and Riley[35] found 6.6 ppm in a red clay sediment from a point in the western Atlantic. Carpenter (in Reference 98) observed levels of 3 to 15 ppm in Puget Sound and deep sea locations, and 290 to 980 ppm on the sea bottom near a smelter. We have measured levels of 1.9 to 1.8 ppm in Trinity Bay, Newfoundland (Penrose and Hayward, unpublished data).

Measurements on cores from Lake Michigan by Ruch et al.[47] revealed levels of 2 to 43 ppm, with most between 4 and 9 ppm. Most significantly they observed a positive correlation between arsenic (and other trace elements) and organic carbon. The arsenic present here may be derived from dead organic matter that had accumulated arsenic during life, or the complexing properties of the decomposing organic matter may have simply

TABLE I

Some Published Arsenic Levels in Fresh Water*

| Location | Arsenic concentrations (ppb) | Reference |
|---|---|---|
| Waikato River, New Zealand | 30–70 | 96 |
| Kansas River, U.S. | 3–8 | 95 |
| Mojave Desert, 24 wells | 6–40 | 31, 52 |
| Nagoya University, Japan | 0.4 | 33 |
| Madoc, Ontario; a well implicated in human poisoning | 10,000 | 79 |
| Southwest Taiwan; many wells implicated in human poisoning | 0–2,500 | 78 |

*The U.S. Public Health Service recommends a maximum level of 10 ppb As in drinking water and a mandatory maximum to 50 ppb.[97]

resulted in the nonbiological accumulation of trace metals from the water. Since the arsenic was generally concentrated only in the upper few centimeters of sediment, the authors attributed the high levels to human activity. There was no apparent geographical correlation with industrial activity, however, the highest levels being in the middle and central eastern part of the Lake. The lowest levels, in fact, were found near the Chicago-Waukegan area, so it might be assumed that the arsenic is simply an indicator of organic matter.

### D. In Food Webs

The generally high levels of arsenic in marine products were discovered early.[2,3] Chapman's samples were taken from the Thames Estuary where he found levels of 140 to 1,000 ppb As in the seawater, so it is not surprising that the levels found in his animal samples were so high (Table 2). Many authors have since reported high levels of arsenic in marine foods.[4-8,43,44,46,98-100]

In 1966, Schroeder and Balassa reported arsenic levels in commercially available seafoods of 1.5 to 8.9 ppm (Table 2); foods of terrestrial origin rarely exceeded 1.5 ppm and most were much less.[1] This observation has sparked some concern over the safety of seafoods in general with respect to arsenic; among the questions being pursued is whether arsenic, like many contaminants, is concentrated in the higher levels of food chains. Few deliberate attempts have been made to resolve this question, but it is possible to interpret information available in the literature to yield some enlightenment.

Fernandez del Riego[99] surveyed a variety of marine organisms and plankton samples, and obtained a range of 4.5 to 55.5 ppm (dry weight). However, if one classifies the organisms according to their position in the food web (Table 3), it is clear that arsenic concentrations are not magnified in food chains. This is not to say, however, that they do not obtain the arsenic from their food; Fernandez del Riego observed that the arsenic contents of samples of organisms changed between the time of capture and after a month in an aquarium. Scallops declined in arsenic content, while *Mytilus edulis* increased slightly.

Seydel[50] measured arsenic concentrations in sediments, benthos, phytoplankton, zooplankton, and water from a number of stations in Lake Michigan. No species compositions or statistical treatments were reported. There appears to be no concentration of arsenic from sediments, phytoplankton, or zooplankton into benthos (Table 3).

TABLE 2

Some Published Arsenic Levels in Marine Animals

| Location | Observation (Levels converted to elemental arsenic per wet weight where necessary) | | Reference |
|---|---|---|---|
| Thames Estuary | Oysters | 4.5 ppm | 3 |
| | Scallops | 33 | |
| | Mussels | 60 | |
| | Cockles | 19 | |
| | Whelks | 18 | |
| | Lobsters | 28 | |
| | Prawns | 55 | |
| | Shrimps | 18 | |
| | Crabs | 35 | |
| | Plaice | 7.5 | |
| | Soles | 5.3 | |
| U.S. Commercial Market | Haddock | 2.2 ppm | 1 |
| | Kingfish | 8.9 | |
| | Oysters | 2.9, 2.7 | |
| | Scallops | 1.7 | |
| | Shrimp | 1.5 | |
| | Clams | 2.5 | |
| | Conch | 3.1, 5.6 | |

[1] Partially taken from Schroeder, H. A. and Balassa, J. J., Abnormal trace metals in man, *J. Chronic Dis.*, Pergamon Press Ltd., 19, 85, 1966. With permission.

TABLE 3

Surveys of Arsenic in Food Webs

| Author | Component of Ecosystem | Arsenic (average ppm) |
|---|---|---|
| Fernandez del Riego[99] | Plankton | 21.3 (5)* |
| | Filterfeeders on phytoplankton | 20.2 (13) |
| | Filterfeeders on zooplankton | 8.5 (2) |
| | Predators on benthic organisms | 26.0 (7) |
| | Predators on fish | 24.8 (6) |
| Seydel[50] | Sediments | 15.2 (14) |
| | Benthos | 6.7 (19) |
| | Phytoplankton | 5.8 (20) |
| | Zooplankton | 6.2 (9) |
| | Water | 1.6 (ppb)(10) |
| Lunde[6] | Filterfeeders on phytoplankton | 9.1 (3) |
| | Feeders on zooplankton | 3.4 (5) |
| | Predators on benthic organisms | 5.0 (3) |
| | Predators on fish | 2.2 (1) |

*Numbers in parentheses are numbers of samples and/or species.

since her data were listed by station, it is possible to calculate correlation coefficients among all pairs of components, and in fact, no significant correlation is found.

Although his work has concentrated on fish oils, Lunde[6] recorded some arsenic levels in whole dried fish tissue (Table 3). Here the concentrations decrease as one ascends the trophic levels.

In a two-component autotroph-grazer system, Boothe and Knauer[101] demonstrated that arsenic was concentrated in the feces of the grazer (kelp crab). Oddly, this was interpreted as an instance of biological amplification of arsenic, whereas it demonstrates that the element is excluded by the herbivore. We have evidence (Black and Penrose, unpublished) that the arsenic of macroalgae consumed by sea urchins is not accumulated, but excreted in a soluble organic form.

If man is added to the top of the marine food web, the classic works of Chapman[3] and of Coulson et al.[4] become relevant:

In Chapman's experiment, a volunteer ate a pound of lobster containing 33 mg of naturally occurring arsenic. Some 24.3 mg were recovered from the urine over the next 48 hr. A second volunteer responded similarly. Chapman found the arsenic in the urine to be in the same stable (chemically refractory) form as before ingestion.

A more thorough investigation of this observation was conducted by Coulson et al.[4] Two subjects ate shrimp containing totals of 1.18 and 0.98 mg arsenic; in both cases arsenic recovery in the urine was over 100%. Small amounts of arsenic appeared in the feces. The same subjects later ingested a 1 mg dose of arsenious oxide; this substance was about 60% excreted over a week (mainly in the urine) and the remainder apparently incorporated (Table 4).

The same report described detailed experiments done on rats fed diets of 1. "low-arsenic" shrimp and 2. "high-arsenic" shrimp, 3. "low-arsenic" shrimp plus arsenious oxide, 4. stock feed, and 5. stock feed plus arsenious oxide. After a year of feeding, the rats retained essentially none of the natural shrimp arsenic, but about one twentieth of the inorganic arsenious oxide (Table 5). All animals, including those that accumulated much arsenic, appeared normally vigorous and healthy. Weight gain was the same for all groups, and histological examination revealed no injury to spleen, liver, and kidney.

E. The Environmental Chemistry of Arsenic

It is now well established that the danger represented by environmental mercury cannot be expressed as a simple function of total mercury concentration.[68,69,102] Mercury undergoes interconversions in nature among the free metal, ionic

TABLE 4

Excretion by Humans of Arsenic in Shrimp and as Arsenious Oxide

| Time (days) | Subject A Feces (μg) | Subject A Urine (μg) | Subject A Total (%) | Subject B Feces (μg) | Subject B Urine (μg) | Subject B Total (%) |
|---|---|---|---|---|---|---|
| Pre-experiment | 7 | 26 | | 15 | 29 | |
| 1 (shrimp fed) | | (1,180 μg) | | | (980 μg) | |
| 1 | 23 | 1,014 | 84.9 | 18 | 780 | 77 |
| 2 | 9 | 221 | 16.6 | 16 | 198 | 17.4 |
| 3 | 6 | 149 | 10.3 | 11 | 90 | 5.9 |
| 4 | 9 | 50 | 2.2 | – | 104 | 7.7 |
| 5 | – | – | – | – | 78 | 5.0 |
| 6 | – | – | – | – | 44 | 1.5 |
| 13 ($As_2O_3$ fed) | | (1,000 μg) | | | (1,000 μg) | |
| 13 | 19 | 308 | 29.4 | 31 | 340 | 32.8 |
| 14 | – | 200 | 17.4 | – | 258 | 22.9 |
| 15 | – | 108 | 8.2 | – | 140 | 11.1 |
| 16 | – | 102 | 7.6 | – | 150 | 12.1 |
| 17 | – | 79 | 5.3 | – | 122 | 9.3 |
| 18 | – | 69 | 4.3 | – | 98 | 6.9 |
| 19 | – | 41 | 1.5 | – | 108 | 7.9 |

(Abridged from Coulson, E. J., Remington, R. E., and Lynch, K. M., Metabolism in the rat of the naturally occurring arsenic of shrimp as compared with arsenic trioxide, *J. Nutr.*, 10, 255, 1935. With permission.)

TABLE 5

Retention by Rats of Arsenic in Shrimp and as Arsenious Oxide*

| Diet | Total As intake (mg) | Retained As (mg) | | As in liver (ppm) |
|---|---|---|---|---|
| Stock diet (0.20 ppm) | 0.95 | 0.178 | (18.7%) | 0.92 |
| Stock diet plus arsenious oxide (17.9 ppm) | 76.1 | 3.99 | (5.2%) | 49.10 |
| Shrimp, low As (1.20 ppm) | 5.42 | 0.23 | (4.6%) | 2.21 |
| Shrimp, low As plus arsenious oxide (17.9 ppm) | 75.98 | 4.46 | (5.9%) | 56.60 |
| Shrimp, high As (17.7 ppm) | 75.53 | 0.16 | (0.4%) | 2.82 |

*Only 52-week data reproduced here. Each diet at 52-week point is represented by four rats.

(From Coulson, E. J., Remington, R. E., and Lynch, K. M., Metabolism in the rat of the naturally occurring arsenic of shrimp as compared with arsenic trioxide, *J. Nutr.*, 10, 255, 1935. With permission.)

compounds by organisms has been initiated by Lunde,[114] who grew species of marine and fresh water microalgae in the presence of radioactive arsenite and arsenate. Arsenic was found to be incorporated into several lipids and a water-soluble organic compound; acid hydrolysis converted the lipid arsenic to the water-soluble form.

## V. HOW DANGEROUS IS ENVIRONMENTAL ARSENIC?

### A. Arsenic in Marine Products

Arsenic concentrations have been surveyed in commercial marine species in Britain, Spain, the U.S., Norway, the U.S.S.R., Canada (Spencer, personal communication), and probably other countries. There is little doubt that high levels of arsenic are a widespread phenomenon in the oceans. It is equally unlikely that this has been brought about by man's activities; in only localized instances have unusually high arsenic levels in water, sediments, or living matter been correlated with man-made sources of arsenic.[3,98] The element is ubiquitous in nature[112] and it is not surprising that marine organisms seem to have evolved means for dealing with it.

In relatively short-term experiments the arsenic contained in crustaceans[3,4] and flatfish (Charbonneau, personal communication) has been shown to clear rapidly from the systems of mammals. The long-term effects of exposure will be much more difficult to determine: is some small fraction of ingested arsenic retained, perhaps through conversion by intestinal flora to inorganic or some other form? In any event, short residence time in the organism is not synonymous with lack of toxicity. Arsenic levels in seafoods should continue to be monitored until benignity can be demonstrated. Current knowledge permits the separate determination of organic and inorganic arsenic[43] so that the constituent of known toxicity (inorganic arsenic) can be independently observed.

Present regulatory levels of arsenic in foods are 1 ppm in Great Britain and 2.6 ppm in the U.S.[1] The experiments which established these tolerances were based on the assumption that the arsenic was in inorganic form. Frost[9,10] has documented the effect of public hysteria demonstrated during the British beer poisoning episode of 1900 on the setting of the very low limit; virtually all seafoods sold in that country must exceed it. It is clear that new tolerances must be established.

### B. The Public Image of Arsenic

It is one thing to establish that there are situations in which arsenic is not harmful. It is a very different problem to convince people of it. The homicidal ladies in Kesselring's play *Arsenic and Old Lace* did not employ arsenic at all. They used strychnine, but the name "arsenic" was chosen because of its much greater dramatic impact. Centuries of tradition, folklore, and literature surround the element and will not simply evaporate in the face of objective scientific discourse.

A parallel example of psychological resistance is the ongoing, and still uphill, battle to fluoridate community water supplies. Fluoride has been blamed for everything from cancer to left-handedness,[113] and the objective atmosphere necessary for scientific judgment of the issue has been lost. Whenever taken before the public, fluoridation is almost always voted down.[10]

The public image of arsenic is clearly much worse than that of the (publicly) almost unknown element fluorine. The power of publicity, ill-informed or not, is very real. Research undertaken on arsenic in food involves a responsibility to maintain a "low profile" when expressing results through channels other than scientific journals.

### C. Research Needs

The foregoing review of the importance of arsenic to the marine products industry has revealed several areas where further research is warranted.

1. A general survey of arsenic levels in economically important species, according to species, age, weight, and location should be conducted. Certain species, especially invertebrates, accumulate very high levels of arsenic. Marine plants, which in some areas accumulate much arsenic, are sources of additives used in many food products. Is the arsenic lost or concentrated by processing into additives?

2. The biochemistry of arsenic in marine animals must be studied. The end product of arsenic metabolism in witch flounder, at least, appears to be a single compound (Penrose, to be published). It should be isolated, structurally analyzed, and synthesized in order that toxicologi-

mercury (+1 and +2 states, in soluble and insoluble salts). and mono- and dimethylmercury. Each compound has its unique toxic properties, from the relatively benign calomel (mercury (+1) chloride) to the extremely neurotoxic methylated forms.

The accumulated evidence leaves no doubt that arsenic exists in more than the inorganic form in the environment. In the last section (and Tables 4 and 5), the data of Coulson[4] clearly illustrated a distinction between inorganic arsenic and the form of arsenic found in shrimp. Chapman[3] had already reported distinct biological and chemical properties in the arsenic found in lobster, and Sadolin[103] had made an unsuccessful attempt to chemically define the arsenic compound in cod. More recently, Lunde[44] has demonstrated that essentially all of the arsenic in several samples of fish extract exhibited ion-exchange behavior different from inorganic arsenite or arsenate, and he has recently developed a technique for the separation and analysis of inorganic and organic arsenic.[43]

Like mercury, arsenic is susceptible to methylation by microorganisms. The liberation of arsenic in volatile form from fungal cultures was studied by Gosio in the 19th Century and the gas was identified as trimethylarsine by Challenger et al.[104] McBride and Wolfe[105] have demonstrated the anaerobic methylation of arsenic by a *Methanobacterium* species and extracts; they identified the product as dimethylarsine by means of the ratios of specific activities of $^{14}C$ and $^{74}As$ in products and substrates.

Methylarsines are strong reducing agents and could not be expected to persist for long in the free state. Methyl- and dimethylarsines may oxidize to methylarsonic and dimethylarsinic acids;[16] Braman and Foreback[28] claim to have detected these acids in natural waters and human urine. Another possible fate for methylarsines is suggested by the fact that they form coordination compounds with many metals, some of which are extremely stable.[16]

Microorganisms are also capable of demethylating arsenic: von Endt et al.[106] demonstrated that $^{14}C$ was released from $^{14}C$-methanearsonic acid in soil. Woolson and Kearney[107] demonstrated both reductive and oxidative pathways for cacodylic acid.

The route of entry of arsenic into marine animals is unknown. Ullman et al.[108] measured arsenic in calico bass immediately before and one month after the contamination of lakes with arsenite; no increase was detected. Lunde[45] found that rainbow trout would not incorporate into organic form inorganic arsenic dissolved in their water; they did incorporate inorganic arsenic from their food. This introduces the possibility that the conversion into organic form may be mediated by the animal's intestinal flora. In the same report he compared arsenic contents of fish kept for up to five months on "marine" feed (cod liver and coalfish; 1 ppm As) or on "terrestrial" feed (minced meat; $< 0.3$ ppm As). Arsenic concentrations in the "marine" group approximately doubled from the initial value, while those in the "terrestrial" group gradually declined to less than one half. Part, if not most, of the arsenic in these fish may be derived from lower stages of the food web, probably over very long periods.

The distribution of two methylated arsenic compounds in an aquarium ecosystem was studied by Isensee et al.[109] The compounds chosen were cacodylic acid, because of its agricultural importance, and dimethylarsine, because it is known to be produced by at least one microorganism[105] and also because it is easily generated from cacodylic acid by reduction. The radioactivity from the arsenicals was accumulated by algae and *Daphnia* to a much greater extent than by snails and fish. The compounds were labeled in the methyl carbons rather than in the arsenic atom, and the radioactivity was recovered from the snails as a series of compounds. Therefore, it is not certain whether the radiocarbon measured was still attached to arsenic, particularly in view of work by the same group demonstrating demethylation of cacodylic acids in soils.[107] The experiments are now being elaborated using radioactive arsenic (Woolson, personal communication).

A recent review of the arsenic cycle in natural waters by Ferguson and Gavis[110] lists many of the known and the possible transformations of arsenic that can occur under natural conditions. They have assumed, however, that trimethylarsine is the form in which arsenic occurs in marine organisms; this is most unlikely since trimethylarsine is a very volatile compound (b.p. 50.2°) which would not be found in heat-dried materials[63,111] and could easily be distilled from samples, which it is not.[43] Although trimethylarsine is almost certainly generated in nature,[77] it has not been shown to exist as such in organisms.

Study of the biosynthesis of arsenoorganic

cal, biochemical, and nutritional studies may be performed.

3. "Arsenic" should be recognized as a range of compounds of limited interconvertibility. Analytical standards should be established for each arsenical compound that is found in commercial species. The current practice of assessing "total hazard" in terms of "total arsenic" no longer makes sense in view of current knowledge. The same holds true for many other elements regarded as hazardous, especially mercury and possibly selenium, tin, antimony, and lead.

4. The source of the arsenic in marine animals should be investigated along with the possible existence of an "arsenic cycle." Seydel's[50] data do not support a correlation between sediments, water, and living material in a lake environment, and yet it is a fact that animals in some areas accumulate much higher levels of arsenic than in others. Does it come from the water or from particulate matter? Or does it actually ascend the food chain and accumulate in animals over a period of time longer than that involved in most experiments?

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