How Important is Inadvertent Ingestion of Hazardous Substances at Work?

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Much is known about human exposure to workplace hazardous substances by inhalation and from skin contact, but there has been little systematic research into ingestion of hazardous substances used at work. This review attempts to identify whether inadvertent ingestion of hazardous substances is an important route of exposure in the workplace and examines possible methods that could be used to quantify ingestion exposure. A number of papers highlight jobs and substances where inadvertent ingestion may be important, typically through case reports or from a theoretical analysis. These scenarios involve exposure to some metals or metal compounds, pharmaceuticals, pesticides, some infectious agents, unsealed radioactive sources and some high molecular weight allergens. In total we estimate that about 4.5 million workers in the UK could have some regular non-trivial intake of hazardous substances by inadvertent ingestion. A conceptual analysis of inadvertent ingestion exposure highlights the role of hand-to-mouth and object-to-mouth events as the primary exposure processes. Two exposure ‘compartments’ are defined: the peri-oral area (i.e. the area of skin around the outside of the mouth) and the oral cavity. Several options are highlighted for exposure-related measurements, including peri-oral wipes, saliva samples, mouth-rinse samples, hand-wipes and under-nail scrapings. Further research is necessary to define which measurements may be most informative. Human behaviour has a key role in determining inadvertent ingestion exposure. For example, some people are habitual nail biters or repeatedly touch their mouth, both of which will increase the chance of ingesting contaminants on their hands. The frequency that people touch their face is dependent on the circumstances of their work and probably the degree of psychological stress they are under. A proper understanding of the importance of these factors will help in designing interventions to reduce the risks from ingesting hazardous substances at work. When making inhalation or dermal exposure measurements we recommend that details of personal behaviours should be recorded so that some estimate of ingestion risks can be inferred. It is possible that inadvertent ingestion of hazardous substances at work may become more important as employers put more emphasis on controlling inhalation and dermal exposures. Further research is necessary to ensure that risk reduction strategies for inadvertent ingestion of hazardous substances are appropriate and effective.

Keywords: chemical; conceptual model; ingestion; monitoring; review

INTRODUCTION

For hazardous substances to have a toxic effect on the body they must first pass across a functional barrier separating the environment from the internal organs.

The common routes of entry into the body are inhalation with the barrier being the lung surface, dermal absorption with the stratum corneum as the barrier and ingestion with the wall of the gastrointestinal tract as the barrier (Dinman and Dinman, 2000). In occupational settings inhalation exposure is most often singled out as the most important route in terms of potential toxicity, followed by dermal contact with chemicals and then ingestion.
The ingestion route of exposure has tended to be considered unimportant and rarely considered. This is probably owing to a number of reasons:

(i) the common belief that ingestion of hazardous substances can only occur by intentional means or acts of gross negligence, and hence can be avoided;

(ii) the recognition that many materials are only very poorly absorbed from the gut (i.e. they have low bioavailability) and as such are unlikely to produce toxic effects when swallowed in small quantities and because ingested materials may be metabolized in the liver and excreted before having the opportunity to exert any toxic effect;

(iii) the presumption that where a worker is exposed by inhalation, dermal contact and ingestion, the mass of material taken into the body by ingestion may be small in comparison with the other routes.

There are some obvious examples of all three assumptions being used in occupational hygiene. For example, people handling hazardous chemicals will not knowingly ingest the material unless there is some intent to self-harm. Exposure to some transition metal elements, such as zinc, nickel and chromium, while having toxic effects by inhalation, are poorly absorbed by the gut and are therefore not considered to be a serious risk by ingestion (IPCS, 1988, 1991, 2001). Indeed, there is evidence that ingestion of some compounds may have prophylactic properties. For example, there is some data from mice models that show ingestion of nickel can have a protective effect against nickel dermal sensitization (Artik et al., 2001) and similarly for methacrylate sensitization (Rustmyer et al., 2001).

Despite the pragmatic approaches to ingestion risks from chemicals at work there has been little systematic research on this topic and so there is no real understanding of the relative importance of this route of exposure. The technical guidance document on chemical risk assessment from the European Chemical Bureau (ECB) states, ‘There are no accepted methods for assessing exposure by ingestion. It is usually controlled by straightforward good hygiene practices such as segregating working and eating facilities and adequate washing prior to eating’ (ECB, 2003). However, as far as we are aware the effectiveness of this approach has never been fully investigated, although it seems reasonable to assume these approaches will provide an important contribution in controlling ingestion exposure.

Work-related ingestion of hazardous substances may occur in one of four ways: (i) clearance of inhaled aerosols deposited within the ciliated airways of the lung, (ii) ingestion of contaminated food or beverages, (iii) transfer of contamination by hand-to-mouth or object-to-mouth contact and (iv) by direct deposition of contaminants around the mouth and into the oral cavity. In the first case, the amount of contamination available for ingestion can be estimated by sampling the airborne extra-thoracic size fraction, i.e. the coarsest part of the inhalable aerosol. In the second case the assessment of exposure is relatively straightforward because the consumption of food is purposeful and predictable, so exposure can be assessed by measuring the amount of chemical contamination in the food and the quantity of food consumed. As the guidance from the ECB explains, exposure by this route may be controlled by appropriate personal hygiene and segregation of eating areas. However, the mechanism identified in the third case describes behaviour that is peculiar to individuals and is therefore less obviously predictable and controllable. In most instances we expect that splashing or direct deposition of aerosols onto the face (the fourth mechanism) to be relatively unimportant. There are no suitable methods available to measure the potential for ingestion exposure where the underlying processes are unintentional.

The main aim of this article is to evaluate the probable importance of inadvertent ingestion exposure to chemicals for people at work and those who may be exposed as a consequence of work activities, e.g. bystanders or neighbours. The evaluation has been made by reviewing the available scientific literature on all aspects of human exposure and by considering the conceptual framework of this exposure route. The review does not consider the contribution to ingestion from inhaled contamination that may ultimately end up in the gut or the contribution from deliberate consumption. We have chosen to put some particular emphasis on carcinogenic substances because of the absence, in many cases, of health effect thresholds and the importance of any additional exposure in such cases.

**IDENTIFICATION OF SUBSTANCES AND TASKS WHERE INGESTION EXPOSURE MAY BE SIGNIFICANT**

Searches of the scientific literature using keyword combinations such as ‘ingestion and occupation’ or ‘ingestion and toxic’ revealed a variety of published material. These were filtered and the most relevant publications were studied. A great majority of the published material contained details of case study reports where accidental or inadvertent ingestion of toxic substances had caused some directly observable health effect. However, there were additional studies in which the ingestion route has been identified as a significant contributory factor based on information derived from biological monitoring. The exposure scenarios that were most widely published can be categorized in terms of substances,
i.e. metals, pesticides, pharmaceuticals, pathogens and radionuclides.

**Metals**

In occupational settings, metals are one of the few categories of materials where the ingestion route has received some attention. This is partly because toxic effects are well-understood and that there are well-defined exposure assessment methodologies available.

For example, removal of lead paint has the potential to cause significant ingestion exposure via hand-to-mouth contact and food contamination (Sen et al., 2002; Enander et al., 2004). The effect of transfer by hand-to-mouth contact while eating in the workplace is exemplified in a comparative study between Chinese and Malay workers in a lead battery production plant. The increased lead in blood levels in the Malay workers was attributed to their cultural tendency to eat food using the hands (Chia et al., 1991). Also in another study, urinary arsenic levels were increased during maintenance semiconductor manufacturing and this was judged to be mostly owing to ingestion of contamination on the hands (Hwang and Chen, 2000).

One Japanese study on lead refinery workers demonstrated that lead facial wipes and lead in fingernails produced high correlations with blood lead levels ($r = 0.73$ and 0.59, respectively). The study concluded that lead ingestion from the contaminated face and fingers contributed to elevations in the blood lead levels among workers (Karita et al., 1997). A similar study (Hwang and Chen, 2000), illustrated a high correlation between blood lead levels and the mass of lead detected on the lips of workers.

Various studies of electroplating workers have shown poor correlation between airborne levels and urinary nickel levels (Cattani et al., 2001; Kiilunen et al., 1997). It has been suggested that this might be due to dermal uptake, although personal hygienic behaviour might be a more important factor than overall cleanliness (Cattani et al., 2001; Makinen and Linnainmaa, 2004).

**Pharmacologically active agents**

Pesticides and other pharmacologically active agents are widely used and most are absorbed through the gut to a greater or lesser extent. The dangers of accidental ingestion of pesticides is well known (Zavon, 1964), and steps to prevent accidental ingestion of large quantities of pesticides are well described in official precautionary advice (e.g. DEFRA, 2004).

Inadvertent ingestion of biocides or pesticides was identified by Garrod et al. (1999), who compared dermal and inhalation exposure to timber treatment biocides with biological monitoring data, and in a study of Australian pesticide workers using chlorpyrifos (Cattani et al., 2001). Both studies highlighted the role of eating and/or smoking in contaminated areas. Professional application of chlorpyrifos in the home may result in contamination of the hands of children in the house (Freeman et al., 2004), where the amount of pesticide on the hands was associated with surface contamination and the child’s hand-to-mouth behaviour. The children put their hand to their mouth 10 times per hour on average and placed possibly contaminated objects in their mouth ~4.5 times per hour. Shalat et al. (2003) investigated hand contamination and urinary pesticide metabolites in children and found a statistically significant correlation between these measures. They attributed the elevated urinary pesticide metabolite levels to inadvertent ingestion of pesticide from hand-to-mouth events.

Although we have not been able to identify any research that explicitly investigates inadvertent ingestion of pesticides by adults as a consequence of hand-to-mouth or object-to-mouth events, we believe that this is a probable route of exposure in adult workers or bystanders, but probably relatively less important than for young children. However, it is not possible to say how important this type of ingestion may be in relation to other routes of exposure.

Although there is some anecdotal evidence of ingestion exposure during manufacturing and administration of pharmaceutical products, little is published in the literature. However, there has recently been interest in workplace exposure to pharmaceutical agents used in chemotherapy. The ingestion route has been identified as potentially significant during the preparation of cytotoxic drugs by hospital pharmacists (Bauer and Fuortes, 1999; McDevitt et al., 1993).

**Infectious agents**

There are three main groups of workers who are at significantly increased risk of work-related disease from ingestion of micro-organisms: agricultural workers dealing with animals; health care workers and laboratory workers handling pathogenic agents. The main occupational infections amongst agricultural workers are zoonoses, where the causative agents may be viral, bacterial, fungal, protozoan or parasitic. There are ~20 relatively common infectious agents found in the UK where the transmission routes include ingestion.

Laboratory, health care and health-related workers are at risk of a number of infectious agents, including mycobacterium tuberculosis, human-immunodeficiency virus (HIV) and hepatitis B virus but most of these are not spread by ingestion. The main issue in the healthcare sector is infection control, i.e. transmission of infection from staff to patient or from patient to patient. Methicillin-resistant *Staphylococcus aureus* (MRSA) is of great topical
interest, together with the various forms of hepatitis. These are all transmittable infections, for which ingestion is a possible route, generally by the faecal–oral route. MRSA is likely to be transmitted by person-to-person contact, but the exact mechanisms of the infection remain unclear (Muto et al., 2003).

Ross et al. (1998) summarized data from occupationally acquired infections in the UK for 1 year from October 1996. They recorded 1037 new cases of disease, with the highest rates being found among workers in food production, catering, farming and those employed in care homes. The majority (89%) of reports were of diarrhoeal disease. For a subset of these reports the agents of interest were known: mainly campylobacter, salmonella or small round structured viruses, including Norwalk virus.

Radionuclides

There are very few occupational groups that are likely to be exposed to radionuclides, and even fewer where the potential for ingestion exposure exists. However, exposure to radionuclides is of special concern given their known carcinogenic potential. Data from the Central Index of Dose Information in the UK indicates that situations for which ingestion (and other) exposure is possible are those such as nuclear power, nuclear fuel fabrication and nuclear facility decommissioning. These represent a little over 50% of the persons exposed to radionuclides in the UK. In addition, many healthcare workers handle radionuclides used for tracers and radiotherapy treatments often in relatively uncontrolled settings.

Relevance of ingestion exposure to allergens

Exposure to allergens may occur via inhalation, dermal absorption or by ingestion, and has been widely reported in food processing industries (Cadot et al., 1996; Jeebhay et al., 2001). Some people may become sensitized and when re-exposed develop skin or respiratory symptoms, and very rarely, anaphylaxis.

Exposure to allergens may affect the aetiology of allergy in two ways; it is an important risk factor for sensitization and subsequent re-exposure may influence the expression of symptoms of allergy (such as respiratory, skin and gastric symptoms). Studies of bakery and animal research workers found that new symptoms and sensitization were related to exposure intensity, although there is very little information about the significance of the ingestion route.

The prevalence of self-reported food-allergy is relatively common in the general population, where inhalation exposure is less likely than in work situations. However, IgE-mediated sensitization to foods in adults is low—estimated at 1–2% (Kagan, 2003). The agents causing food allergy in adults are peanuts, tree nuts, fish and shellfish. Reports of food allergy, attributable to food agents encountered at work, include seafood and spices but there are no reports of occupational nut allergy. The prevalence of sensitization is likely to be higher in food industry workers where the exposure to food allergens is greatest. However, it is not completely clear whether sensitization occurs due to occupational ingestion or inhalation. The study of the occupational allergy is unique as exposure can be well characterized, but it is difficult to assess the influence of the route of allergen exposure on disease aetiology. For adults there is limited data on the epidemiology of food allergy, and less about the relationship between exposure to food allergens and indicators of disease.

ESTIMATED PREVALENCE OF INGESTION EXPOSURE IN GREAT BRITAIN

Four experienced occupational hygienists examined the UK’s official Standard Occupational Classification (SOC) list (Office for National Statistics, 2000). This list categorizes all occupations into four different tiers—major groups, sub major groups, minor groups and unit groups. Each hygienist was required to state for which unit groups there was a likelihood of significant exposure by ingestion for six broad groups of substances: pesticides (including non-agricultural pesticides, which are now classified as biocides), metals, pharmaceuticals, radionuclides, pathogens and high molecular weight compounds. Significant exposure was not defined since hazardous materials differ in their toxic potential—ingestion of any amount of a carcinogenic substance is significant. Hence, it was left up to the expert to decide what should be considered as significant exposure for each substance. Where it was judged likely there was significant potential for ingestion exposure the hygienist provided a score to indicate the proportion of that group that were assessed to be exposed. The ratings of all four persons were then combined and used to estimate the numbers of workers with significant ingestion exposure in each group. The number of people employed in each group was obtained from the UK Office of National Statistics; hence, the proportion of the entire working population for which ingestion exposure might be an important entry route of hazardous substances in the workplace was estimated.

The number of persons exposed within the nine major SOC groups and 353 unit groups was estimated. Among the major groups, ‘skilled trades’ were judged to contain the greatest number of persons exposed to all groups of contaminants (49% of total persons exposed). This was followed by ‘associate professional and technical occupations’ (24%).

Totally 127 (36%) of the unit groups on the SOC list were rated as jobs where ingestion exposure could
play a role. Owing to missing employment numbers for 15 standard occupational codes, the number of persons exposed within each unit group was estimated for 112 of the 127 jobs rated as being exposed. Approximately 4.5 million workers in the UK were judged as possibly being exposed by inadvertent ingestion (15.6% of the UK’s working population). Metals (1.5 million workers exposed) followed by pathogens (~1 million) were the substance groups for which exposure by ingestion was considered most prevalent, followed by high molecular weight substances (0.75 million) and pharmaceuticals (0.89 million). Some 32 000 workers were likely to be exposed to radionuclides via ingestion (Table 1).

Further details of this aspect of our research are given in Supplementary Data in the online edition of this issue (Supplementary data are available at Annals of Occupational Hygiene online).

HOW PEOPLE MIGHT BE EXPOSED BY INADVERTENT INGESTION?

Scope and terminology

The processes leading to inadvertent ingestion of hazardous substances must involve transfer of the substance from the environment into the mouth. For this to be a realistic proposition the contaminant substance or the mixture that it is contained in must be a relatively non-volatile solid or liquid, so that it may remain available during the transfer processes. The processes of transfer must include movement of contaminated hands or objects into the mouth, or contact of contaminated hands or objects with the skin around the mouth (the peri-oral area) followed by migration of this contamination into the mouth. Splashing into the mouth or onto the face are also relevant mechanisms, although probably much less important.

As we indicated at the outset, our review does not consider the contribution to ingestion from inhaled contamination that may deposit in the nose or upper airways and ultimately end up in the gut, or the contribution from deliberate consumption of contaminated food or drink. In many cases the contribution of inhaled aerosol to ingestion of chemicals will not be insignificant, but we believe that it is easily predicted from the knowledge of the aerosol concentration and size distribution. In addition, we consider that this process is a part of understanding the toxicokinetics of substances taken into the body rather than part of the exposure assessment process, i.e. it is translocation within the body.

The International Programme for Chemical Safety (IPCS) has prepared a glossary of terms used in exposure assessment (WHO, 2002). At the heart of their approach is the idea that exposure is ‘contact between an agent and a target’, where the contact takes place at some exposure surface over some defined time period. In this scheme the exposure surface is not seen as some definite or even real surface but is an adaptable concept. For our purposes we have defined the exposure surface for ingestion as a hypothetical surface covering the mouth, including the lips. We have chosen this definition because we believe it is appropriate to focus on the peri-oral area given that we hypothesize that material deposited there may easily be transported into the mouth for ingestion.

Two further terms are important for us to construct a clear conceptual picture of ingestion exposure: intake and uptake. In the IPCS glossary the term ‘intake’ is defined as the ‘process by which an agent crosses an outer exposure surface of a target without passing an absorption barrier’, such as the gastrointestinal wall. The term ‘uptake’ refers to the ‘process by which an agent crosses an absorption barrier’. We have attempted to follow this scheme throughout this paper.

Development of a conceptual model of inadvertent ingestion exposure

It is possible to construct a simple conceptual model of exposure processes leading to ingestion uptake. From our analysis we believe this should comprise two main routes: the direct pathway where the contamination is introduced into the mouth by either the subject’s hand or an object and the indirect pathway where contamination is transferred to the peri-oral area and then into the mouth. Transfer will be determined by the subject’s personal behaviour (e.g. hand-to-mouth contact, licking lips, etc.) or flow of sweat. In all cases we believe that the

<table>
<thead>
<tr>
<th>Contaminant group</th>
<th>Total number of exposed workers (×1000)</th>
<th>Proportion of total exposed (%)</th>
<th>Proportion of total UK working population (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pesticides</td>
<td>320</td>
<td>7.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Metals</td>
<td>1500</td>
<td>33</td>
<td>5.2</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>890</td>
<td>20</td>
<td>3.1</td>
</tr>
<tr>
<td>Radionuclides</td>
<td>32</td>
<td>0.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Pathogens</td>
<td>980</td>
<td>22</td>
<td>3.4</td>
</tr>
<tr>
<td>High molecular weight</td>
<td>750</td>
<td>17</td>
<td>2.6</td>
</tr>
<tr>
<td>Total</td>
<td>4500</td>
<td>100</td>
<td>15.6</td>
</tr>
</tbody>
</table>
hands play a central role in the exposure process. The conceptual model is shown graphically in Figure 1.

The model comprises four compartments (surfaces, hands, peri-oral and oral cavity) that may contain a mass of contamination that can be exchanged with other compartments. It is clear that for some of the compartments there may be a two-way exchange of contamination while for others there is only flux of material in one direction. Contamination can enter the system from the air or directly from sources onto surfaces. We exclude material being inhaled and then depositing in the upper airways and being swallowed, although we do allow for the possibility of contamination being transferred directly from a source to the peri-oral or oral compartments, e.g. by splashing. We assume that once in the mouth the contamination can only be swallowed or spat out.

We have deliberately chosen to consider the oral compartment as part of the exposure process, but it is shown below the dotted line in the figure indicating that it is an internal compartment (the dotted line represents the boundary for ‘intake’). The peri-oral area is shown above the intake boundary since we consider it as an external exposure compartment, although within the ‘uptake’ boundary.

Transfer between compartments is from episodic events, i.e. as mass transfer per event. Transfer events are not all identical and even for a single transfer pathway. The mass exchanged will be a function of many variables: some related to the substances involved (e.g. physical state, solubility volatility, stickiness of the material), some to the process (e.g. method of handling the object, the pressure of contact) and perhaps also to the duration of the transfer process. We have no a priori view about whether the transfer process will result in a fixed proportion of the contaminant in the compartment moving (which corresponds to the use of a ‘transfer efficiency’) or some other relationship.

The frequency and duration of contacts plus the type of contacts will be determined by the personal characteristics of the subject and the constraints of the process. For example, certain people will be more likely to bite their nails, some people may be more likely to touch their face. In some situations where people are more anxious they may engage in nervous habits such as face touching or in situations where they are busy with a task then they may touch their face or mouth less frequently. Human behaviour as determined by personality traits is likely to be particularly important in determining who is at risk from inadvertent ingestion.

The role of hands and objects in transferring contamination to the mouth

There is a considerable body of work on children and infants frequency of mouthing their fingers and objects (e.g. Reed et al., 1999; Juberg et al., 2001; Steenbekkers, 2001; Tulve et al., 2002; Kranz et al., 2004). Most studies show a clear trend in decreasing mouthing with age, although there is substantial unexplained variation in mouthing between children. For example, Tulve et al. (2002) found that children less than 24 months had on average 81 events per hour whereas children older than 24 months had on average 42 events per hour. However, because of the differences in methodology used by the different research studies and the divergence between metrics (e.g. number of events per hour and total mouthing time) it is difficult to generalize the findings from these studies further.

The frequency that adults touch their face or place objects in their mouth is almost certainly less than young children. A study amongst 44 university students evaluated the proportion of 10 s time intervals that they touched their face or mouthed an object (Woods and Miltenberger, 1996). When
the experimental conditions were ‘neutral’ the subjects touched their face on average 3.9 times per hour ($SD = 6\%$) and mouthed objects 1.6 times per hour ($SD = 5.8\%$). Making the subjects anxious increased the proportion of time they engaged in these behaviours (9.5 per hour for face touching and 2 per hour for mouthing), with the difference in face self-touch being statistically significant. Interestingly the standard deviation for both habits also increased in the anxious state suggesting that some subjects may be more affected than others by the increased anxiety.

Data on hand-to-face contacts for adults in three situations: laboratory and pesticide workers, manufacturing and engineering workers, and office workers were obtained by Zainudin (2004). The average number of contacts differed significantly for the three groups, with the office workers showing the greatest number of contacts (6 per hour on average) and the laboratory and pesticide workers showing the lowest (almost none). The author hypothesized that the differences between the three groups was due to the tasks that they had to undertake. The laboratory personnel and pesticide workers were almost constantly using their hands to complete their work tasks, whereas the office workers had only occasional need to use their hands to control their work tasks. The manufacturing and engineering workers were intermediate.

Some people have a greater tendency to exhibit repetitive habits such as finger sucking or nail biting that would increase the likelihood of inadvertent ingestion. Woods and Miltenberger (1998) found that 10% of students reported that they bit their nails and Long and Miltenberger (1998) report that between 23 and 40% of the general population bite their nails, with the peak ages for nail biting being between 10 and 19 with a gradual reduction in the prevalence after the age of 40. The results of a questionnaire study of about 2500 Italian high school students showed that 55% of pupils reported some nail biting or hand-to-mouth contact with their nails, with the peak ages for nail biting being between 23 and 40% of the general population. Making the subjects anxious increased the proportion of time they engaged in these behaviours (9.5 per hour for face touching and 2 per hour for mouthing), with the difference in face self-touch being statistically significant. Interestingly the standard deviation for both habits also increased in the anxious state suggesting that some subjects may be more affected than others by the increased anxiety.

How important is inadvertent ingestion of hazardous substances at work in comparison to other exposure routes?

Where airborne concentrations are high and the material is easily absorbed into the systemic circulation through the lung, or where dermal contamination is high and the rate of uptake through the skin is rapid, in these scenarios, any contribution from ingestion is likely to be small. There is also likely to be a ‘self-limiting’ psychological element to ingestion exposure in that workers involved in particularly contaminated or highly hazardous environments will be more careful in terms of hand-to-mouth activity, which may explain some of the results from Zainudin (2004). In addition, it is more likely that there will be measures in place to prevent workplace eating, smoking and drinking at such worksites. Where respiratory protective equipment is worn the ability to touch hands, fingers or objects to the peri-oral area will be restricted and hence the opportunity for inadvertent ingestion exposure will also be reduced. However, the effectiveness of cleaning of respirators becomes important in limiting direct transport onto the peri-oral compartment.

The proportion of material likely to be absorbed via ingestion will increase for substances that are easily transferred to the hand and are either not visible, such as pathogens, small masses of radionuclides or pesticides, or are not viewed by the worker as being hazardous as may be the case with metal dust contamination among mechanics or engineers.

The relative contribution to body burden from inhalation, dermal and ingestion routes will be a complex function of the exposure in each of these three compartments, the time course of each exposure and the bio-availability of the material. Pharmacokinetic issues such as first-pass and local metabolism of the chemical as it transits the barrier organs (lung, skin and gut) will also impact on the relative contributions to body burden from each route. The time-course of exposure to each compartment will be particularly important; inhalation uptake will tend to end when the worker finishes the task or goes home from work whereas dermal uptake may continue through skin for significant periods after because of contaminated or unwashed clothes. Similarly ingestion uptake may continue for hours or days after work as a result of nail biting or hand-to-mouth contact with unwashed skin.

In terms of the potential importance of the ingestion exposure route we examine two hypothetical workplace scenarios. First, let us assume that a worker is involved in the demolition of lead-painted steelwork using flame-cutting gear. Assuming an average airborne lead exposure for the job of 1000 $\mu g \, m^{-3}$ and a dermal lead exposure of 100 $\mu g \, cm^{-2}$, which is comparable with the maximum we have measured in a lead refinery (Hughson, 2005), it is possible to estimate the respective uptake from each route of exposure (see Table 2). In making this estimate it is assumed that the workplace is poorly controlled. For example, it is assumed that the worker would remove their gloves and respirator frequently over the day to eat, drink and smoke cigarettes or to...
Table 2. Calculated overall uptake for contaminants in two workplace scenarios

<table>
<thead>
<tr>
<th>Route</th>
<th>Lead worker (inorganic lead)</th>
<th>Pesticide worker (chlorpyrifos)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhalation exposure route</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air concentration (µg m⁻³)</td>
<td>1000</td>
<td>5</td>
</tr>
<tr>
<td>Respirator protection factor</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Inhaled concentration (µg m⁻³)</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>Inhaled air volume (m³)</td>
<td>10</td>
<td>1.2</td>
</tr>
<tr>
<td>Inhalation intake (µg)</td>
<td>1000</td>
<td>6</td>
</tr>
<tr>
<td>Absorption (%)</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>Inhaled uptake (µg)</td>
<td>700</td>
<td>6</td>
</tr>
<tr>
<td><strong>Ingestion exposure route</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surface loading (µg/cm²)</td>
<td>100</td>
<td>13</td>
</tr>
<tr>
<td>Contact area (cm²)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Contact frequency (events per hour)</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Mass on peri-oral area (µg)</td>
<td>40,000</td>
<td>1300</td>
</tr>
<tr>
<td>Transfer efficiency into mouth (%)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Ingestion intake (µg)</td>
<td>4000</td>
<td>130</td>
</tr>
<tr>
<td>Absorption (%)</td>
<td>15</td>
<td>93</td>
</tr>
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<td>Ingestion uptake (µg)</td>
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<td>120</td>
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<tr>
<td><strong>Dermal exposure route</strong></td>
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</tr>
<tr>
<td>Surface loading (µg cm⁻²)</td>
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<td>13</td>
</tr>
<tr>
<td>Mass loading rate (µg cm⁻² h⁻¹)</td>
<td>NA</td>
<td>13</td>
</tr>
<tr>
<td>Exposed skin area -hands (cm²)</td>
<td>960</td>
<td></td>
</tr>
<tr>
<td>Flux (µg cm⁻² h⁻¹)</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Dermal uptake (µg)</td>
<td>480</td>
<td></td>
</tr>
<tr>
<td><strong>Aggregate exposure</strong></td>
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<td></td>
</tr>
<tr>
<td>Total uptake (µg)</td>
<td>1300</td>
<td>606</td>
</tr>
<tr>
<td>% ingested uptake</td>
<td>46</td>
<td>20</td>
</tr>
<tr>
<td>% inhaled uptake</td>
<td>54</td>
<td>1</td>
</tr>
<tr>
<td>% dermal uptake</td>
<td>0</td>
<td>79</td>
</tr>
</tbody>
</table>

NA, systemic dermal uptake of lead assumed to be zero.

With the peri-oral region. Thus if the worker makes an average of five hand–mouth contacts per hour, which is probably a relatively high frequency and we assume a contact area of 10 cm² (5% of the palmar surface) for each exposure event, the mass transfer to the peri-oral region would be ~40 000 µg over an 8 h day. It seems reasonable to apply a transfer efficiency of ~10% to allow for incomplete transfer of contamination from the peri-oral region to the gastrointestinal tract and by taking into account the typical absorption efficiency for the gut of ~15%, the estimated ingestion uptake would be ~600 µg.

For this particular scenario, ~46% of the aggregate exposure is due to uptake from the ingestion route. Clearly this balance would change if airborne concentrations were reduced, e.g. by applying local exhaust ventilation to the process or by improving the level of respiratory protection. For example, if the inhaled concentration was reduced to 250 µg m⁻³ then, assuming the skin loading and hand–mouth activity remain the same, the ingestion route would contribute ~80% of the total. This simplistic scenario assumes that reduced airborne levels have no effect on dermal contamination and skin loading rates (and hence ingestion uptake), which may not be the case. However, this particular scenario illustrates the importance of maintaining good personal hygiene for work with toxic metals such as lead where there is potential for relatively high skin contamination levels.

Taking a similar hypothetical case for pesticide exposure, it is assumed that a worker is involved in spraying a chlorpyrifos containing product inside residential properties to exterminate termite infestations. The task takes 1 h and the worker wears a protective overall, but no gloves or respirator. The work is in a hot, confined environment and the worker occasionally stops to wipe away sweat from his/her face during the job. If we assume that he/she washes the contamination from his/her skin at the end of the job we can compare the relative contribution by all exposure routes. Since it is known that chlorpyrifos will permeate through unbroken skin, it will be necessary to consider all three main routes of exposure for this scenario.

A study by Cattani et al. (2001) suggests that we could expect an airborne concentration of ~5 µg m⁻³ for this scenario with a skin loading rate of the order of 13 µg cm⁻² h⁻¹. Using a default absorption factor of 100% for chlorpyrifos by inhalation, the inhaled dose would be ~6 µg. For the ingestion route, if we assume 10 hand–mouth contacts, with an average contact area of 10 cm² per event, we estimate a mass transfer of 1300 µg to the peri-oral region. Assuming a transfer efficiency of 10% from the peri-oral region to the gastrointestinal tract, the ingested mass would be 130 µg. If absorption through the gut is assumed to be 93% (Griffin et al., 1999), the ingested uptake would be 120 µg.

Speak to workmates. The dermal permeation rate for inorganic lead compounds is very low so we have assumed this route of exposure provides a negligible contribution to aggregate uptake (IPCS, 1995).

Taking into account the protective effect of the respiratory protection it is estimated that the inhaled concentration of lead would be ~100 µg m⁻³. Based on an inhaled volume of 10 m³ per 8 h shift, the inhaled mass of lead (intake) could be ~1000 µg. Studies suggest that between 50 and 70% of inhaled lead will be absorbed into the blood, depending on particle size (IPCS, 1994). If we use the higher absorption figures in our exposure scenario we would estimate an inhaled uptake of 700 µg of lead.

The worker’s ingestion exposure may be estimated from the mass loading of lead contaminant on the skin, together with the frequency and area of contact
Given a dermal deposition rate of 13 μg cm\(^{-2}\) h\(^{-1}\), this might be considered as an infinite supply when compared with a flux of \(\sim 0.5\) μg cm\(^{-2}\) h\(^{-1}\) for chlorpyrifos (Griffin et al., 1999). Consequently the dermal uptake over an hour is estimated as 1900 μg, assuming an exposed skin area for the hands of 960 cm\(^2\). The dermal route contributes over 93% of the total body burden, the ingestion route \(\sim 6%\) and the inhaled route <1%. Clearly the dermal exposure route in this case is the most significant and control measures should be targeted at reducing skin contact with the pesticide, but inadvertent ingestion provides an important additional source of exposure. If the pesticide worker was prone to bite his/her fingernails then his/her ingestion exposure could be a much bigger proportion of the total.

RELEVANT EXPOSURE METRICS FOR INGESTION

Exposure measurements must be practicable and related to the risk to the individual. It is not practical to measure the mass of a contaminant hazardous substance passing through the gastrointestinal wall and so it is necessary to focus on earlier stages in the process of uptake and intake. We believe the conceptual compartmental model that we have elaborated provides a sound basis to consider the possibilities for measurement.

The first compartment to offer some information about exposure potential is the level of contamination on surfaces. This is a measure that describes the exposure environment of the person and is similar in concept to the measurement of room air concentration of a chemical in relation to personal exposure. Although it is a valuable descriptor of environmental contamination, it does not provide a good indication of exposure. A standardized form of wiping the contaminated surface with a swab may be a suitable approach to assess the mass of contaminants on surfaces. We have not considered the strategy for selecting surfaces to sample, but clearly this is an important consideration.

The next relevant measure is the amount of contamination on the hand. There is much experience in undertaking this type of measurement for dermal exposure studies, although there is an important conceptual difference between the two measures. For dermal exposure it is most relevant to measure those parameters that are related to the flux of chemical through the skin, e.g. the concentration of the contaminant, whereas for ingestion the mass of the contaminant on the hands is more important. A wipe system may also be appropriate to assess the mass of a chemical in the skin contaminant layer, although an absorbent patch would not. It may also be important to measure the mass of a contaminant in inaccessible locations such as under fingernails.

The next compartment to consider is the peri-oral area of the face. We hypothesize that some of the contaminant in the peri-oral area will eventually transfer to the mouth and so it is a more direct measure of ingestion exposure than either surface or hand contamination. In addition, we believe that there may be a good correlation between the amount of a hazardous substance ingested by direct hand-to-mouth contacts and the indirect hand-to-peri-oral-to-mouth route. The mass of contaminant in the peri-oral area may therefore be a good surrogate for all routes of exposure by inadvertent ingestion. The peri-oral contamination could again be assessed by wiping the skin on this area of the face.

The contents of the mouth compartment might intuitively be expected to be the best measure of ingestion exposure, but it must be remembered that there is a considerable flux of saliva through the mouth that will wash contamination away. Also, physico-chemical properties of the contaminant such as water solubility may also influence residence time in the mouth. However, it is likely that the flow of saliva through the mouth is not uniform and there will be a proportion of contaminant that has a longer residence time and so measuring the contamination in the mouth may provide useful information. Two approaches to assess the mouth compartment are a mouthwash and saliva spit samples.

For all of these measures it is important to collect relevant contextual data along with the measurements. The conceptual model also helps us to define the contextual parameters that should be measured, e.g. the number of transfer events by each route, the characteristics of the process involved, the type of materials and perhaps the duration and area of contacts.

Finally, it is important to recognize that biological monitoring has an important role in assessing aggregate exposure by all routes—inhalation, skin contact and ingestion. Measurements of the concentration of substances or their metabolites in urine can provide useful data to assess inadvertent ingestion, but only in conjunction with measures of external exposure by all relevant routes.

CONCLUSIONS

The main aim of this review was to evaluate the importance of inadvertent ingestion exposure to hazardous substances from work activities. We concluded that the key substance groups likely to pose a risk to health from inadvertent ingestion are metals, pesticides, pharmaceuticals, some infectious agents, radionuclides and some high molecular weight materials that evoke allergic responses. Not all substances in these groups will have the potential to be taken up through the gut but many will and for them, this route of exposure will add to the risks to
health. Many of the substances we identified in these categories are carcinogens or suspected human carcinogens and so any additional exposure is particularly important to control.

We estimate that approximately one in six of the UK’s working population may be involved in tasks where inadvertent ingestion exposure could contribute to their total body burden. Exposure to metals, pathogens and pharmaceuticals made up approximately three-quarters of the work tasks that we identified as being at risk of significant ingestion uptake. Bystanders may also be at risk from inadvertent ingestion of these hazardous substances. However, assessment of the ingestion route has received little attention, advice on hand washing before breaks and separating eating and drinking from work are often the only control measures put in place. In our experience, these practices are often not enforced and not recognized as important in reducing total body burden to the hazardous substance. We believe that it is not sufficient to assume that encouragement of good hygiene practice will eliminate inadvertent ingestion exposure.

We think it is likely that one of the main reasons that the ingestion route is under-reported is that there are no standardized metrics for measuring and characterizing exposure. In the absence of measurement we have little information to say when this route is important. There is some circumstantial evidence to suggest the importance of ingestion exposure at work for metals and infectious agents. However, development of appropriate monitoring methods for inadvertent ingestion of hazardous substances is an important prerequisite for a proper systematic investigation of this route of exposure.

There has been some progress in evaluating the ingestion of chemicals in non-occupational scenarios. While levels of exposure and uptake in such environmental scenarios are likely to be orders of magnitude lower than in occupational settings, the fact that a small fraction of the body burden in such situations comes from inhalation has encouraged those involved to focus more on developing methods to characterize dermal and ingestion routes. Models that use details of micro-activity, finger, hand and object mouthing frequency and transfer between the various exposure compartments are central to our understanding of non-occupational ingestion of hazardous substances. We need to recognize that there is a wealth of scientific material available in environmental exposure assessment and we should develop ways to utilize this in occupational exposure assessment.

We have identified a number of possible measurements that could be used to characterize inadvertent ingestion of hazardous substances. These range from peri-oral wipes, saliva samples, mouth-rinses, hand-wipes or under-nail scrapings. Just as we have seen in inhalation and dermal sampling, it is unlikely that one method will prove suitable for all types of hazardous materials. For example saliva sampling may not be a good measure of that day’s ingestion exposure to a chemical with a long half-life in the body and is endogenously secreted in extracellular fluids such as saliva. In this case the material measured in the mouth compartment would be a mixture of that day’s ingestion exposure (i.e. transferred from the workplace to the mouth) and the mass that was being endogenously produced. Similarly, substances that are rapidly absorbed through the skin or are volatile would not be suitable for skin wiping and are probably therefore less important for uptake by ingestion.

There is a need for research to examine the behavioural characteristics that increase or decrease the frequency of hand and object-to-mouth activity, both within and between people. The published research on children in relation to non-occupational exposures and our initial observations in the workplace seem to indicate that there are complex interactions between the individual’s activity, the requirement and frequency of hand-use to perform tasks, external stressors, and the presence of respiratory protective equipment or spectacles on the face. Young children may have greater hand-to-mouth activity than adults or older children, although the data are equivocal in this respect. We know from inhalation and dermal monitoring that behavioural factors can play a very important part in determining exposure levels. Kromhout et al. (1993) showed that as many as two-thirds of workers with the same job tasks have exposure level differences spanning more than 10-fold. Most of these differences in exposure will be due to differences in worker behaviour. We consider it likely that we will see at least this level of variability when examining occupational or bystander ingestion exposures, although behaviour may be even more important for ingestion because of the central role of hand-to-mouth actions. Understanding the behavioural influences controlling ingestion exposure will allow us to target interventions to reduce risks from this route.

We believe that ingestion exposure is primarily from hand-to-mouth contact. Key to our understanding of this process are the parameters that influence transfer of a material from a surface or object to the hand and then transfer from the hand to the mouth or peri-oral area. These factors can be subdivided into the following groups: surface factors, material factors, vehicle factors, hand factors and peri-oral factors. The characteristics of a surface (e.g. rough/smooth; impervious/porous) will have a bearing on how readily the material can be removed during contact with the hand. The physical properties of a material will play a major role in the transfer. Similarly, the vehicle that the material is contained within will determine the degree of transfer, e.g. a highly viscous fluid may transfer more easily from surfaces to the
peri-oral area. The condition of the hand and peri-oral skin may also regulate transfer. Dry-skin may be less able to retain contamination than skin that is moist. Sweating may also influence retention and transfer of a substance. All of these parameters require study and we need to increase our understanding of how they impact the ingestion exposure. This investigation might best, or at least initially, be undertaken by controlled laboratory investigations. When exposure measurements are made, information about such explanatory variables should also be collected.

We believe that this review has provided a rigorous examination of the importance of the ingestion route of exposure in occupational settings. With the success of control measures to reduce inhalation and dermal exposure, the fraction of total body burden arising from the ingestion route may increase. This may be particularly true where the interventions are focused on modifying the source rather than changing the process of the work environment or in reducing the mass of material taken up through the skin. Further research is needed, both in terms of exposure measurement method development and to increase our understanding of how inadvertent ingestion of workplace hazardous substances takes place.

REFERENCES


