GASTRO-INTESTINAL ABSORPTION OF LEAD IN CHILDREN AND ADULTS:
OVERVIEW OF BIOLOGICAL AND BIOPHYSICO-CHEMICAL ASPECTS

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INTRODUCTION

The concept of biological availability as applied to the public health risks from environmental pollutants is a relatively simple one: potential human health risks associated with a substance are actualized when the substance in a bioactive form is deliverable or delivered to sites of toxic action. The specifics of the delivery are modulated by the many factors discussed in this symposium.

[Plate 1]

In the areas of nutrition and pharmacology/pharmacokinetics, assessment of bioavailability has often been the sine qua non of research effort and quantitative application. The volume of published work in these disciplines that deal with the topic is considerable and growing. Bioavailability is also implicit in the classical toxicological dictum that the dose makes the poison. The environmental epidemiology of toxic metals and metalloids, by contrast, has often given less attention to circumstances of their bioavailability. This was due in part to the absence of information on form-specific bioactivity and in part on assumption that the core element confers uniform toxicity.

Various operational definitions of bioavailability have been put forward and their focus includes entry into systemic circulation, delivery to sites of action or the extent of some effect.

[Plate 2]

Taking account of all the differing views of the topic, a generic variation of the definition by Firsov and Piotrovskii (1986) put forth for drugs, is useful:

The biological availability of a substance (nutrient, drug or human environmental toxicant) is the fraction of substance entering the systemic circulation (extent of systemic absorption) and the rate at which entry occurs.
LEAD BIOAVAILABILITY

[Plate 3]

An understanding of the bioavailability of environmental lead in human populations involves the biological aspects of lead uptake from body compartments, the biophysico-chemical behavior of different lead species in body compartments, interactive relationships of lead with other species in body compartments and toxicokinetics of lead in the human body. We are here concerned with intake/uptake of exogenous lead, but it should be kept in mind that release of lead from body stores such as the skeleton produces bioavailable lead and endogenous lead exposure.

[Plate 4]

How does one determine lead bioavailability, particularly ingested lead, in human populations? Approaches include (1) use of appropriate experimental animal models to simulate the behavior of lead species in humans, (2) validated multi-media toxicokinetic models with assumptions about intake/uptake kinetic parameters or (3) epidemiological approaches through biological monitoring, with or without reference to media-specific contributions.

GASTRO-INTESTINAL ABSORPTION OF LEAD IN HUMANS

[Plate 5]

Bioavailability of lead in the gastro-intestinal (GI) tract of humans and experimental animals is of particular interest, since ingestion is the major route of lead exposure for most risk segments of the general population. The enteric bioavailability of lead in some ingested medium, in turn, is governed by biological and biophysico-chemical factors which can operate separately or in combination.

[Plate 6]

Biological determinants include (1) inter-species differences, e.g., ruminant vs. monogastric animals, (2) stage of physiological development, e.g., children vs. young/middle-aged adults vs. the aged and (3) the molecular biology of lead uptake and transport to the systemic circulation from the gut.

[Plates 7,8,9]

The epithelial lining of the small intestine of humans and experimental animals is the anatomic and biochemical locus of lead uptake and transport from the lumen. The stomach separately plays a role in uptake mainly via transformation(s) of lead-bearing media or form-specific lead to potentially more soluble or otherwise mobile forms.
Epithelial cells on the mucosal surface, the enterocytes, are structured with finger-like projections, the microvilli. There is, overall, an enormous surface available for contact and uptake of substances from the lumen relative to epithelial cellular volume. Such cell morphology provides an optimal mechanism of uptake within the constraints of gut transit time and gut length.

Various in-vivo and in-vitro studies have been done to identify the site(s) of uptake and transport of lead. In rats and other species, lead uptake and transport occurs in the duodenum in developing and mature animals (Barton, 1884; Conrad and Barton, 1978; Edelstein et al., 1984; Flanagan et al., 1979; Henning and Cooper, 1988). In general, the more reliable in-vitro data support in-vivo results (e.g., Barton, 1984), i.e., uptake via duodenum. In other studies, experimental artifacts such as use of medium co-factors that remove lead by precipitation, limit conclusions to be drawn about regional uptake in small intestine (e.g., Blair et al., 1979; Gruden and Stantic, 1975).

[Plate 10]

Uptake of lead from duodenum to the blood stream appears to involve intracellular uptake and a saturable active transport system, with further uptake by passive diffusion also being noted (e.g., Henning and Cooper, 1988; Barton, 1984; Aungst and Fung, 1988; Mykannen and Wasserman, 1981, Flanagan et al., 1979).

[Plates 11, 12]

There is also evidence that paracellular uptake of lead via diffusion through 'tight junctions' will occur, based on rat everted sac techniques and histochemical staining. Epithelial tight junctions have a pore diameter of 10-16 A, a negative charge density and high selectivity for cations (e.g., Morton et al., 1985).

Is this mode of uptake an artifact of experiment or is it in co-existence with intracellular transport in-vivo but restricted to cationic (vs. complexed) lead? This is possible, and supporting information exists. It is known that some uptake of iron, in low m.w. forms, is passive and occurs via tight junctions (Simpson et al., 1989) while aluminum is normally transported via tight junctions (Provan and Yokel, 1988). Aluminum uptake is markedly enhanced by citrate in animals and humans (Slanina et al., 1986; Froment et al., 1989a) while citrate imparts a similar enhancement on lead absorption (Spickett et al., 1984). Froment et al. (1989b), using ruthenium red and Ussing chamber techniques, have conclusively shown that citrate functions in Al uptake by opening tight junctions for more facile aluminum passage.
Young children, in those studies where reasonably stable exposure histories can be assumed to have existed (Ziegler et al., 1978; Alexander et al., 1973), have been shown to absorb and retain more ingested lead than do adults, 40-50% vs. 10-15% in adults. Many studies using developing vs. adult experimental animal models show the same phenomenon (as summarized in, e.g., EPA, 1986).

The basis of this difference in animals is apparently a combination of undeveloped excretory capacity for lead and enhanced lead uptake in the immature gut (e.g., Kostial et al., 1971, 1987; Pounds et al., 1978; Henning and Cooper, 1988). In the rat, many of the structural parts of the small intestine are matured at weaning, including villus and crypt density (Trehair, 1989). Furthermore, the well-known general phenomenon of pinocytosis in the sucking rat ileum (e.g., Williams and Beck, 1969) has been also identified as a significant factor in increased sucking animal uptake of lead in the gut. This involves ileal pinocytosis of lead in milk micelles (Henning and Cooper, 1988). Once pinocytized, such lead remains sequestered in the cell and contributes to body retention without contributing to lead in blood. Epithelial desquamation then results in simple elimination.

The level of ontogenic concordance in gut maturation between humans and animals in the neonate and suckling period is limited, inasmuch as the human newborn starts life with a more mature GI tract than the neonate rat (Henning, 1987). On the other hand, acid and pepsin production rates in children do not approximate adult levels until ca. two years of age (Christie, 1981; Deren, 1971) and some food proteins may be more readily taken up in infancy than later, suggesting a pinocytotic mechanism (Walker, 1985; Henning, 1987).

Limited information exists on the question of changes in Pb uptake in the aging mammalian GI tract. In human populations there appears to be a modest fall off of lead body burden owing to either metabolic or significant dietary changes (e.g., EPA, 1986) but the post-menopausal female segment of the population actually show an increase, probably owing to bone mineral changes and enhanced lead resorption from bone (Silbergeld et al., 1988). In the rat, lower oral dosing (50 ppm) with lead in aging animals is associated with an enhanced blood lead level compared to the younger adult, but this difference does not persist statistically at higher exposures (Cory-Slechta et al., 1989; Cory-Slechta, 1990).

Lead absorption from the GI tract of humans and experimental animals is markedly affected by the presence or absence of other bioactive agents in the gut, particularly certain classes of nutrients. Such interactions augment those which occur elsewhere within the body and which help to define overall lead toxicokinetics and lead toxicity in humans.
An integrated expression of such interactive behavior is the full diet effect, as seen by the impact of meal scheduling on lead uptake in the human gut. James et al. (1985), using human volunteers ingesting labeled lead (Pb-203), found that when a meal was taken 12 hours before tracer lead ingestion, label retention was ca. 62%. A similar percentage was found when meals were consumed seven hours after label ingestion on an empty stomach. Shorter periods of label-meal separation gave intermediate retentions while the lowest retention, ca. 5%, occurred with co-ingestion of meal and label. These results are in accord with a number of other studies showing the inverse link of lead uptake with levels of nutrients in the gut.

There are various categories of lead interactions applicable to GI tract behavior. While these can entail toxicant-toxicant interactions to some extent, attention has mainly been on lead-nutrient interactive behavior. Interactions can be synergistic, additive or antagonistic and in some important cases intrinsically antagonistic agents can have a functionally net synergistic effect by virtue of their deficiencies during lead exposure. This is typified by calcium-lead and iron-lead interactions.

There are many interactions with lead in the GI tract that have been described in the literature (see, e.g., EPA, 1986) but some have more obvious or recognized impacts on public health risk than others. The two nutrients that figure prominently are calcium and iron. Phosphate and vitamin D/metabolites are also important but not as fully characterized epidemiologically. Lead interactions with zinc, protein, fats, saccharides and natural chelators are known principally from studies in experimental animals.

A number of lead exposure populations have been studied in terms of their calcium status and its effect on such measures as blood lead, and this includes relevant data in the large and comprehensive Second National Health and Nutrition Examination Survey (NHANES II). Mahaffey et al. (1986) reported a statistically significant inverse association between dietary Ca intake and blood lead in the NHANES II. This large analysis is consistent with results of Ziegler et al. (1978) for infants and various investigations of the interactive relationship in high-risk children (Johnson and Tenuta, 1978; ATSDR, 1988) and adult volunteers (Heard and Chamberlain, 1982).

Numerous animal studies have described the quantitative and mechanistic aspects of Pb-Ca interactions in the mammalian gut and these have been reviewed (ATSDR, 1988; EPA, 1986; Mahaffey, 1982). Mechanisms of interaction in the gut include a ternary
interaction of Pb, Ca and phosphate (Heard and Chamberlain, 1982; Smith et al., 1978) and competitive uptake of lead on Ca carrier protein (Barton et al., 1978a), which would be an active, saturable transport process (vide supra).

The large NHANES II data base has also been analyzed in terms of iron-lead interactions in children at the ages of highest Fe deficiency. Iron status has been shown to be inversely related to blood lead, i.e., iron deficiency is associated with higher blood lead levels in this survey (Mahaffey and Annest, 1986; Marcus and Schwarts, 1987). Other reports showing this relationship and involving high-risk children have appeared (e.g., Yip et al., 1981).

As with calcium, a number of animal models of the iron-lead interaction have been described in which Fe deficiency produces more Pb uptake/retention. The Fe-Pb interaction is quite complex mechanistically, but it can be said that Fe deficiency stimulates iron absorption and this stimulation enhances lead uptake via site binding at intestinal receptors for the nutrient (Morrison and Quarterman, 1987).

Are the lead-nutrient interactions metabolically reciprocal, i.e., do alterations in levels of enteric lead affect nutrient metabolism in the same way as the reverse? At first glance, they might be expected to be so, but they are not and for good reason. Lead is non-essential and xenobiotic while elements such as iron, calcium, etc. are essential nutrients under tight homeostatic control. It is one thing for a xenobiotic agent to 'piggy back' on one part of the overall homeostatic control pathway for nutrients, as in Pb binding to carrier proteins in nutrient deficiency. Fully reciprocal behavior would require that a xenobiotic be able to effectively obliterate tight homeostatic control of nutrients. One would expect that lead would be less robust in affecting Ca or Fe uptake than the reverse.

This explains why deficiencies in Ca and Fe enhance Pb uptake but the enhancement does not persist linearly beyond repletion or excess (e.g., Mahaffey-Six and Goyer, 1970; Morrison and Quarterman, 1987). In the latter case, homeostatic control for handing adequate or excess rather than inadequate nutrient is operative, whatever the level of level present. Furthermore, lead can function to alter Ca metabolism in ways other than direct, reciprocal interaction. Fullmer and Rosen (1990) found that lead affects calcium metabolism prior to calbindin D synthesis via the cholecalciferol system in experimental animals.

[Plate 18]

In view of the above discussion, one can conclude that there are different mechanisms for GI uptake of lead in humans and
experimental animals. As summarized by Morton et al. (1985), uptake of lead can first entail the divalent Pb cation or various soluble lead complex uptake pathways. Simultaneously, some sizable fraction of divalent lead ion will be forming relatively insoluble, excretable lead complexes, e.g., hydroxide, bicarbonate or phosphate/mixed phosphate.

Uptake of lead ion by paracellular means, i.e., diffusion through 'tight junctions', has been shown in one study to be a major route under certain experimental conditions. There is supporting evidence for this in other studies of elements and their interactions with 'tight junctions.'

Transcellular uptake has been the mechanism that has been best studied in experimental systems and such uptake is consistent with saturable, active transport as well as some transcellular diffusion. Diffusion would perhaps involve most likely a neutral complex or other lipophilic form while binding of lead ion to receptors in the enterocyte that serve for active transport of iron and calcium. It is not clear whether 'tight junction' movement of lead would have rate-limiting character sufficient to serve as an alternative explanation of the non-linear nature of lead intake-lead uptake across a broad range of lead intake rates.

Plates 19, 20 and 21

Some biophysico-chemical factors in the human GI uptake of lead are of importance and they include solubility, particle size and heterogeneity of the physico-chemical matrix. These are factors which are not technically biological but which operate within the intake compartments to affect bioavailability in tandem with physiological parameters. These factors also are of interest in terms of the quite diverse media by which lead is ingested by exposure populations: tap water, beverages, baby foods and foods in general, lead in dusts and soils, etc.

One factor of concern in the GI handling of lead is the extent to which lead can be dissolved or otherwise mobilized with the ingestion of certain media and movement to the stomach and small intestine. This especially applies to lead viewed as being incorporated in 'inert' forms. In the case of gastric transformation(s) of ingested media and their lead content, it is important to keep a distinction between media reactivity in the human stomach and simple chemical simulations of such complex activity. The latter are relatively crude simulations of the former.

This qualification can be understood in the behavior of relatively insoluble lead sulfide. Lead sulfide, a form having a solubility product constant \((K_{sp})\) of \(3.4 \times 10^{-28}\) is extensively solubilized by gastric juice to lead chloride, \(K_{sp} = 10^{-4}\) (Healy
et al., 1982'. In the child, the basal pH of gastric juice is about 1 (Connell, 1974). In experimental animal tests of oral Pb bioavailability, a species with similar gastric pH is needed. The issue of animal models of oral Pb bioavailability in humans is discussed elsewhere in this symposium.

Most significant to the discussion, the use of lead sulfide in an ethnic preparation, the (conjunctival) eye cosmetic called "surma" in Asia and "kohl" in the Middle East, has been documented as causing elevation of blood lead to toxic levels (e.g., Ali et al., 1978 and Green et al., 1979) and overt lead intoxication (Warley et al., 1968; Fernando et al., 1981). Interestingly, "surma" is Urdu for antimony since this metalloid was the element historically used in the sulfide preparation. The recent change to lead for economic reasons accounts for the rather recent history of toxicity risk associated with use of the current formulation.

Equally important, several studies of lead isotope uptake in the human gut have been done and also indicate that the sulfide can have measurable or comparable bioavailability. Rabinowitz et al. (1980) found that lead as the sulfide, when ingested during meals or in fasting, was absorbed to the same amount as the lead chloride or cysteine complex. In fasting, this was 35% uptake. Chamberlain et al. (1978) found that the sulfide was absorbed to the same degree as the chloride with meals, but less in fasting. The difference with fasting conditions for the sulfide in the two studies may reflect differences in particle size of the sulfide (vide infra).

Particle size of lead-bearing media is an important factor in the enteric mobilization of lead. Available experimental data indicate that the smaller the particle, the more easily it will be dissolved in the stomach or elsewhere in the GI tract.

Barltrop and Meek (1979) reported that particle size of lead in several forms was a significant determinant of blood lead in rats fed the toxicant. The smaller the particle, the higher the blood lead. The most pronounced effect was seen with metallic lead, indicating that relative ease of both oxidation to the divalent state and dissolution were factors of importance.

Healy et al. (1982) found that the extent of lead sulfide solubility in-vitro was inversely proportional to particle size. Theoretically, as particle size decreases, the Noyes-Whitney dissolution law says that the substance will become soluble (Healy, 1984). These data augment a picture of higher than
expected lead exposure risk seen in (1) the higher intakes in children of lead-bearing particles less than 100 microns (Duggan et al., 1985) and (2) the fact that the smaller the particle, the higher the concentration of lead and other elements (Van Borm et al., 1988; Spittler and Feder, 1979).

REFERENCES


BIOAVAILABILITY

**Disciplinary Scope of Concept**

- Nutrition
- Pharmacology/Pharmacokinetics
- Toxicology

**Mechanistic/Functional Definitions**

- Entry intact into Systemic Circulation
- Entry/Access to Site of Action
  - Target Tissues
  - Target Organelles
- Extent of Predicted Effect(s)
BIOAVAILABILITY

Generic Definition

Biological availability of a substance (nutrient, drug, or human environmental toxicant) is the fraction of substance entering the systemic circulation (extent of systemic absorption) and the rate at which entry occurs.

—Adapted from Firsov and Piotrovskii, 1986
Lead Bioavailability

- Biological/physiological factors in uptake from Pb in body compartments: pulmonary and GI tracts
- Physical and physico-chemical characteristics of lead species
- Interactive relationships of lead and other species in body compartments
- Toxicokinetics of lead uptake and distribution to monitoring media and target tissues
Assessment of Lead Bioavailability

**Experimental or Predictive Model**

- Pb balance studies (net daily Pb retention or loss)
- Experimental GI bioavailability vs. reference (AUC ratios)
- Toxicokinetic models, e.g., EPA's IU/BK Model

**Epidemiological**

- Pb levels in physiological media due to uptake of exogenous (and endogenous) Pb
- Disaggregated/aggregated regression analyses linking systemic Pb and environmental Pb levels
Gastrointestinal Absorption of Pb

- **Biological aspects**
  - Peculiar to the exposure population

- **Biophysico-chemical aspects**
  - Peculiar to the elements of lead exposure

- **Mixed biological/ biophysico-chemical aspects**
  - Lead interactions with nutrients and non-food matrix
  - *In-vivo* alterations of Pb bioavailability
  - Determination of toxicokinetic models for Pb
Biological Factors: GI Absorption of Lead

- Anatomical/ Physiological Features
  - Interspecies Differences
  - Sites of Uptake of Pb
  - Development/ senescence stage vs. extent of uptake
  - Metabolic modifiers, e.g., seasonal effects

- Nature of Lead Transport
  - Paracellular
  - Transcellular
  - Active transport
  - Passive diffusion

- Biological Factors in Lead Interactions
  - With nutrients
  - With non-food materials
Some Schematic Features of Intestinal Lining

- Lumen
- Microvilli
- Epithelial cell
- Lateral intercellular space
- Tight-junction
- Cell membrane
- Basement membrane
- Capillary network
Pb Transport From The Gut

- Anatomical Sites of Pb Uptake
  - In-vivo studies
  - In-vitro studies
  - Sites of accumulation vs. transport

- Epithelial Sites of Pb Transport
  - Transcellular transport
    - Passive diffusion
    - Active transport against gradient
    - Mixed

- Paracellular Transport

- Developing vs. Mature GI Tract
GI Regional Specificity Of Pb Uptake

- Uptake from the GI tract is mainly in the small intestine

- Studies of region specificity for Pb uptake give mixed results, reflecting design differences (e.g., transport vs. retention)

- In adult (Conrad and Barton, 1978) and suckling (Henning and Cooper, 1988) rat, Pb uptake/transport occurs in duodenum; similar data for chick (Edelstein et al., 1984) and mice (Flanagan et al., 1979)

- *In-vitro* data support *in vivo* results (Barton, 1984); other studies affected by artifacts
GI Transcellular Transport Of Pb

- Enterocytes of rat duodenum involved in active transport of Pb (Barton, 1984). Kinetic analysis indicates active transport and diffusion in chicks (Mykannen and Wasserman, 1981)

- Uptake is concentration-dependent in rats (Aungst and Fung, 1981; Henning and Cooper, 1988) and mice (Flanagan et al., 1979) and non-linear uptake is due to transport saturation and/or cytotoxicity to enterocytes

- Duodenal cells show dose-dependent Pb uptake in organelles (Parmley et al., 1979)
Paracellular Transfer of Pb in the GI Tract

- Epithelial tight junctions exist between cells in the small intestine, with pore size of 10–16 Å and selectivity for cation permeability.

- Main evidence that Pb is primarily transported via tight junctions, a passive diffusion mode, is from data of Coogan (1982) using rat everted sacs and staining techniques.
Paracellular Transfer of Pb in the GI Tract

- Some paracellular (tight junction) uptake of low m.w. Fe forms can occur (Simpson et al., 1989)

- Al is normally transported via tight junctions (Provan and Yokel, 1988)

- Pb and Al uptake is enhanced by citrate in humans and animals (Slanina et al., 1986; Spickett et al., 1984; Froment et al. 1989a)

- Rat duodenal closed loops and ruthenium red/Ussing chamber studies prove citrate serves to open tight junctions for Al (Froment et al., 1989b)
GI Uptake in Development, Adulthood and Senescence

- Children absorb and retain 40–50% of Pb in diet vs. 10–15% in adults; animal studies support this.

- Increased Pb retention in the young is due to inefficient excretion and enhanced uptake in GI tract.

- Increased Pb uptake in the suckling animal is mainly due to ileal uptake by pinocytosis of milk casein micellar Pb and cell retention.

- Aged rats had higher Pb-Bs than adults at 50 ppm diet Pb, but differences less at higher doses.
Effect of Meal Time on Pb Retention
(James et al., 1985)
Categories of Lead Interactions—GI Tract

- Lead vs. nutrients or other toxicants
- Synergistic vs antagonistic
- Experimental data vs. public health importance

- Ca and Fe are the main interactors with lead from human health perspective
- Phosphate and vitamin D/ metabolites are also important
- Zn, protein, saccharides, natural chelators have mainly been studied experimentally
Calcium-Lead Interaction: GI Tract

- Dietary Ca and Pb-B of children in the large NHANES II survey were inversely associated \( p < .028 \) (Mahaffey et al., 1986), consistent with other human studies.


- Mechanisms of interaction in the gut include (1) ternary interaction of Pb, Ca, and PO\(^4^-\); (2) competitive binding of Pb with calbindin D, involved in active Ca transport; and (3) interaction of Pb on Ca prior to calbindin D synthesis via cholecalciferol system (Fullmer and Rosen, 1990).
Iron status and Pb-B link in children has been shown in the NHANES II (Mahaffey and Annest, 1986; Marcus and Schwartz, 1987); also shown with various high-risk populations.

Various animal studies document the inverse relationship of Fe status and Pb uptake (increased uptake with Fe deficiency).

Interactive mechanisms are complex:

- Uptake of Pb is enhanced only in Fe deficiency, i.e., not simply by stimulated Fe absorption.

- Fe deficiency elevates intestinal Fe receptor capacity for active transport, increasing binding sites for Pb as well (Morrison and Quarterman, 1987).
Pb^{2+} binds to surface of intestine

Transport via tight junctions

Diffusion across gut wall

Lumen

Food
Bile
Pancreatic secretions

Gut wall secretions e.g. bicarbonate

Lipid soluble Pb complex

Insoluble Pb complexes

Excreted

Intestine wall

Specific transport systems

Pb^{2+} and soluble Pb complexes

Routes of intestinal Pb uptake (Morgan et al., 1985)
Biophysico-Chemical Factors: GI Absorption of Lead

- Lead in chemically/biochemically diverse intake media—food, water, dust/soil, etc.

- Chemical and physical forms of lead
  - Differential solubility of Pb chemical species
  - Differential solubility of Pb physical forms: pure material, particle-bound, geochemically bound, etc.
  - Particle size

- Biochemical interactions of lead and other elements in the intestinal lumen, gut wall, etc.
Environmental Sources of GI Intake of Lead

- Lead in food and beverages— all consumers
- Lead in drinking water— all consumers
- Lead in baby food — infants and toddlers
- Lead in particles swallowed from upper respiratory tract deposition— workplace exposures
- Lead in dust/ soil— young children
- Idiosyncratic— folk medicine preparations (e.g., azarcon, a lead oxide taken for GI disturbance)
GL Solubilization of Media-Variable Pb

- Pb uptake from water, beverages, and diet is assumed to entail "soluble" forms; Pb in dusts and soils requires a closer look.

- Pb mobilization in the GI tract by gastric acid hydrolysis of "inert" forms can be considerable and poorly simulated in crude bench-top tests (Healy, 1982, 1984). Gastric acid in children is ca. pH 1.0 (Connell, 1974).

- PbS (Ksp=3.4 exp-28) undergoes gastric acid hydrolysis to PbCl$_2$ (Ksp=exp-4).
# Toxicity of PbS in Ethnic Preparations

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<td>&quot;kohl&quot;</td>
<td>Kuwaiti children</td>
<td>Acute Pb poisoning</td>
<td>Fernando et al., 1981</td>
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Effect of Particle Size on GI Bioavailability

- Lead particle size is inversely proportional to uptake rate and Pb-B level (Barltrop and Meek, 1979)

- PbS of <100 micron size much more soluble in gastric juice than larger particles (Healy et al., 1982)

- Dust/soil particles of less than 100 microns or less show higher intake rate in children (Duggan et al., 1985)

- The smaller the particle, the more enriched in lead (Van Born et al., 1988; Spittler and Feder, 1979)

- With small particles, the Noyes–Whitney dissolution law says there is no theoretical limit on solubility (Healy, 1984)