

**RADIATION PROTECTION**

**HUMAN ALIMENTARY TRACT MODEL  
FOR RADIOLOGICAL PROTECTION**

**A draft document by a Task Group of Committee 2 of The International  
Commission on Radiological Protection**

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**DRAFT DOCUMENT**

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## PREFACE

A Task Group was appointed by Committee 2 to review the dosimetric model of the gastrointestinal tract used in ICRP *Publication 30* (1979) and recommend revisions. The revised model described in this publication is applicable to children as well as adults. The new model will be used in future ICRP publications giving dose coefficients for radionuclide intakes following either occupational or environmental exposures. It will also be used in publications concerned with the interpretation of bioassay measurements.

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## GLOSSARY OF TERMS

This glossary is presented in two parts: the first relates to terms used in radiological protection and radionuclide dosimetry; the second relates to anatomical and physiological terms.

### ***Dosimetry and Biokinetics***

#### **Absorbed dose**

the physical dose quantity given by

$$D = d\varepsilon/dm$$

where  $d\varepsilon$  is the mean energy imparted by ionising radiation to the matter in a volume element and  $dm$  is the mass of the matter in the volume element. The SI unit for absorbed dose is joule per kilogram ( $\text{J kg}^{-1}$ ) and its name is gray (Gy).

#### **Absorbed Fraction ( $AF(T \leftarrow S)_R$ )**

the fraction of energy emitted as a specific radiation type  $R$  in a specified source region  $S$ , which is absorbed in a specified target tissue  $T$ .

#### **Alimentary tract transfer factor $f_A$**

the alimentary tract transfer factor,  $f_A$ , is defined as the fraction of activity entering the alimentary tract that is absorbed from the gut in the absence of both radioactive decay losses and endogenous input to the tract.

#### **Committed Effective Dose ( $E(\tau)$ )**

the sum of the products of the committed equivalent doses in organs or tissues and the appropriate organ or tissue weighting factors ( $W_T$ ), where  $\tau$  is the integration time in years following the intake. The integration time is 50 y for adults and from intake to age 70 y for children.

#### **Committed Equivalent Dose ( $H_T(\tau)$ )**

the time integral of the equivalent dose rate in a particular tissue or organ that will be received by an individual following intake of radioactive material into the body, where  $\tau$  is the integration time in years following the intake. The integration time is 50 y for adults and from intake to age 70 y for children.

#### **Dose Coefficient**

committed equivalent dose in organ or tissue  $T$  per unit intake  $h_T(\tau)$  or committed effective

dose per unit intake  $e(\square)$ , where  $\square$  is the time period in years over which dose is calculated (i.e.) 50 y for adults and  $(70-t_0)Y$  for children. Note that elsewhere the term "dose per unit intake (SvBq<sup>-1</sup>)" is used for dose coefficient.

### Effective Dose (E)

the sum of the weighted equivalent doses in all tissues and organs of the body, given by the expression:

$$E = \sum_T w_T H_T$$

where  $H_T$  is the equivalent dose in tissue or organ, T, and  $w_T$  is the weighting factor for tissue T.

### Equivalent Dose ( $H_T$ )

the equivalent dose,  $H_{T,R}$ , in tissue or organ T due to radiation R, is given by:

$$H_{T,R} = w_R D_{T,R}$$

Where  $D_{T,R}$  is the average absorbed dose from radiation R in tissue T and  $w_R$  is the radiation weighting factor which is based on the quality of the radiation emitted by the source. Since  $w_R$  is dimensionless, the unit is the same as for absorbed dose, J kg<sup>-1</sup>, and its name is Sievert (Sv). The total equivalent dose  $H_T$ , is the sum of  $H_{T,R}$  over all radiation types

$$H_T = \sum_R H_{T,R}$$

will be replaced by radiation weighing dose

### Gray (Gy)

the special name for the SI unit of absorbed dose: 1 Gy = 1 J kg<sup>-1</sup>

### HATM

the ICRP human alimentary tract model

### HRTM

the ICRP human respiratory tract model (ICRP, 1994)

### Organ Dose

the tissue or organ average absorbed dose  $D_T$  is given by

$$D_T = \varepsilon_T / m_T$$

where  $\varepsilon_T$  is the total energy imparted in a tissue or organ T and  $m_T$  is the mass of the tissue or organ.

### Radiation weighting factor ( $w_R$ )

the radiation weighting factor is a dimensionless factor to derive the equivalent dose from the

absorbed dose averaged over a tissue or organ and is based on the quality of radiation and its relative biological effectiveness (ICRP, 1991)

**SAF**

specific Absorbed Fraction : Absorbed fraction in a tissue divided by the mass of the tissue

**Source region (S)**

region within the body containing the radionuclide. The region may be an organ, a tissue, the contents of the gastrointestinal tract or urinary bladder, or the surfaces of tissues as in the skeleton and the respiratory tract.

**Specific Effective Energy (SEE( $T \leftarrow S$ )<sub>R</sub>)**

the energy, suitably modified by the radiation weighting factor, imparted per unit mass of a target tissue,  $T$ , as a consequence of the emission of a specified radiation,  $R$ , from transformations occurring in the source region  $S$  expressed as  $\text{Sv}(\text{Bq s})^{-1}$ .

**Sievert (Sv)**

the special name for the SI unit of equivalent dose and effective dose:  $1 \text{ Sv} = 1 \text{ J kg}^{-1}$

**Target Tissue**

tissue or organ in which radiation is absorbed

**Transfer compartment**

the compartment introduced for mathematical convenience into most of the biokinetic models used in this report to account for the translocation of the radioactive material through the body fluids from where they are deposited in tissues.

**transfer coefficients**

Fractional transfer of compartmental content per unit time.

**Transit times**

the transit time of an atom in a region of the tract is the length of time that it resides in that region. The transit time of a substance in a region is the mean of the distribution of transit times of its atoms.

**Tissue weighting factor ( $w_T$ )**

the factor by which the equivalent dose in a tissue or organ is weighted to represent the relative contributions of that tissue or organ to the total detriment resulting from uniform irradiation of the body



**Uptake**

activity that enters to the body fluids from the respiratory tract, alimentary tract or through the skin.

**Physiology****Acinus:**

groups of pancreatic cells which are single layers of pyramidal cells containing zymogen granules. The term acinus refers to the shape which resembles a berry.

**Alimentary tract:**

the tube from mouth to anus in which food is digested.

**Alimentation**

the intake, digestion and absorption of nutrients.

**Amino acids:**

biological acids which contain an amine group (NH<sub>2</sub>) and are the basic unit of proteins. In the process of digestion, proteins, which are large polypeptides, are broken down to smaller peptides, and ultimately to their constituent amino acids.

**Appendix (Vermiform appendix) :**

a small blind-ended projection from the caecal region of the large intestine. It is highly vascularised and is characterised by the preponderance of lymphoid tissue and small numbers of crypts in its epithelial lining.

**Bile :**

bile is produced and secreted by the liver, stored in the gall bladder, and then released into the duodenum. Bile is a complex mixture of organic (bile acids, phospholipids, cholesterol, bilirubin, immunoglobulin A) and inorganic solutes (Na, K<sup>+</sup> Cl, Ca<sup>2+</sup>). It helps digestion by emulsifying lipids and also contains excretory materials.

**Bolus :**

“rounded mass” of food in the oesophagus or intestinal contents which stimulates sensory stretch receptors to initiate the peristaltic reflex of the oesophageal or intestinal wall responsible for the movement of alimentary tract contents.

**Brunner's glands :**

situated in the duodenum in the sub-mucosa below the villi. These glands secrete mucus and bicarbonate in response to the passage of chyme from the stomach; the bicarbonate neutralises acid from the stomach.

**Cardiac Sphincter :**

close to the heart or cardia. Muscular sphincter controlling the opening between the stomach and the esophagus (gastroesophageal).

**Caecum :**

large cul-de-sac at the beginning of the large intestine, continuous with the ascending colon

**Colon :**

the colon (*adj colonic*) is the largest part of the large intestine and can be regarded as comprising four regions: ascending, transverse, descending and sigmoid. It is the final site of fluid and electrolyte absorption in addition to absorption of short chain fatty acids. The presence of bacteria in the colonic lumen is important for the digestion of dietary fibre.

**Chylomicron :**

intracellular chylomicrons are formed in intestinal epithelial cells to facilitate the passage of fatty acids which are enveloped by a hydrophobic coating made up of protein, phospholipid and cholesterol. Chylomicrons which are particularly small (hence micro) are absorbed via the lacteals and then pass into the general circulation via the lymphatic system.

**Chyme :**

the product of digestion in the stomach – a smooth fluid which passes to the small intestine where further digestion occurs.

**Crypts:**

crypts of Lieberkühn are invaginations of the epithelium lining the small and large intestines, containing a number of different cell types including undifferentiated stem cells which are near the crypt base. In the small intestine, the crypts lie below the villi (around 5-7 crypts per villus). There are no villi in the large intestine.

**Deglutition :**

process of swallowing which is under both voluntary and involuntary control.

**Digestion :**

process of breakdown, absorption and utilisation of ingested material which is initiated in the mouth by mastication and salivary secretions and continues along the length of the

gastrointestinal tract. Involves the breakdown of large insoluble food molecules into soluble constituents that can be absorbed through the intestinal epithelium.

**Duodenum :**

the duodenum is the initial part of the small intestine which begins at the pylorus and is around 25 cm long. It is devoid of mesentery and contains Brunner's glands as well as ducts which allow entry of pancreatic and hepatic secretions.

**Enteroendocrine cells:**

small minority of cells found on the epithelium of the stomach, small and large intestine in both villi and crypts. They contain secretory vesicles which contain bioactive amines (5-hydroxytryptamine – enterochromaffin cells) or peptides (D cells – somatostatin, N cells – neurotensin etc). Endocrine cells may produce more than one peptide or amine.

**Exocrine gland :**

formed by epithelial cells which form an infolding of an epithelial layer to form a tube. They may be either simple or compound. The glands secrete in an outward direction into the "milieu exterieur" such as in the pancreas (enzymes), liver (bile) and intestine (mucus).

**Faeces :**

eliminated waste products of digestion. Faeces contain material from sloughed intestinal cells, microorganisms and excretory materials, as well as undigested food materials.

**GALT :**

Gut Associated Lymphoid Tissue which includes Peyer' patches, intra-epithelial lymphocytes, and isolated lymphoid follicles (ILF).

**Goblet cells :**

differentiated intestinal epithelial cells which may be capable of division, located in crypts and on villi. These cells synthesise and secrete mucins which are of primary importance in maintaining the barrier between the intestinal mucosa and the luminal environment. They increase in frequency from the jejunum to the ileum. The colon has a high density of goblet cells.

**Hormone :**

some functions of the alimentary tract are regulated by mediators acting as hormones (endocrines). These hormones are polypeptides, produced by endocrine cells scattered throughout the intestinal epithelium. They include gastrin, secretin, cholecystokinin and gastric inhibitory protein, and their actions include control of secretions, epithelial cell division rates, and intestinal motility.

**Ileum :**

the third and final region of the small intestine. It is continuous with, and difficult to delineate from, the jejunum, although villi are shorter and less numerous and Peyer's patches are larger and more numerous.

**Jejunum :**

the second region of the small intestine, following from the duodenum and continuous with the ileum. The villi are larger and more numerous than in the ileum and there are circular folds (valves of Kerkring) which are large. These folds retard the digesta and provide an increased area for absorption. This section of the small intestine has the largest absorptive surface area in addition to a thick muscular wall.

**Large intestine:**

the large intestine is around 1m long in the adult. It begins at the ileocaecal valve and consists of the caecum and appendix; the ascending, transverse, descending and sigmoid colon, and the rectum.

**Liver :**

the liver is the largest organ in the abdominal cavity. It performs a multitude of metabolic functions in connection with homeostasis, alimentation and defense. It serves both as an exocrine gland, secreting bile through a system of ducts into the gall bladder and hence into the duodenum, and as an endocrine gland, synthesizing a variety of substances that are released directly to blood. It receives blood flowing from the intestinal tract via the hepatic portal vein as well as blood from the general circulation via the hepatic artery.

**M Cells :**

or microfold cells, are specialised epithelial cells occurring in the domed luminal surface of Peyer's patches, which are aggregates of lymphoid tissue, forming part of the Gut Associated Lymphoid Tissue (GALT). These cells have very few microvilli and are able to transport macromolecules and other luminal contents non-selectively in bulk. They act as antigen sampling cells, transporting these molecules to underlying leucocytes.

**Micelle :**

molecular aggregates (e.g. bile acid – long chain fatty acid) which have a hydrophobic surface with a lipophilic core. Absorption of fats are facilitated by the formation of micelles.

**Mucus :**

a protective viscoelastic, lubricant layer which covers the entire gastrointestinal tract which protects the underlying epithelial surface. Mucus composition varies in the different regions of

the gastrointestinal tract (gastric versus colonic, for example), depending on the mucin content.

**Mucins:**

mucins are synthesised and stored in goblet cells and are secreted throughout the gastrointestinal tract. They are high molecular weight glycoproteins comprising core peptides and oligosaccharides.

**Neutral Fat :**

fats are organic salts or esters, composed of three fatty acids combined with a glycerol molecule to form a triglyceride.

**Oesophagus ;**

tubular part of the alimentary tract that connects the mouth and stomach. British texts write oesophagus while American ones write esophagus. Sphincters exist at both ends, the upper oesophageal sphincter which prevents entry of air into the oesophagus and the lower sphincter which prevents reflux of gastric contents.

**Pancreas :**

a gland containing two types of secreting cells: the endocrine cells which secrete hormones into the blood; and the exocrine cells which secrete digestive enzymes and juices into the pancreatic duct which joins with the bile duct from the liver to empty into the duodenum.

**Paneth cells :**

these cells are found at the base of crypts (not in all species) in the small intestine, and possess an apical membrane with multiple short microvilli. These cells contain membrane-bound granules which contain high activities of lysozyme which has bacteriolytic activity. Defensin-like peptides – termed cryptidins are also secreted by these cells. In species where Paneth cells are present (man, rodents, ruminants) they increase in number from the duodenum to the ileum.

**Peristalsis :**

the process of sequential contraction and relaxation of circular muscles in the oesophagus and other regions of the alimentary tract that propel material aborally. During digestion in the small intestine, most contractions are segmenting to achieve mixing rather than the coordinated contractions required for peristalsis but bursts of peristalsis occur periodically.

**Pharynx :**

the pharynx, situated behind the nasal cavities, mouth and larynx, is a connecting tube. The upper region above the soft palate, the nasopharynx, connects to the nasal passages. The

mid region, the oropharynx, connects to the mouth. The laryngeal region connects to the larynx and also continues behind the larynx to the oesophagus.

**Portal vein :**

the portal vein conveys blood from the stomach, small intestine, colon, pancreas and spleen, to the liver. This allows the liver first-pass control of the entry of nutrient molecules into the general circulation.

**Pylorus :**

aboral end of the stomach close to the duodenum which comprises the pyloric antrum (storage), pyloric canal, and the pyloric sphincter which regulates release of chyme into the duodenum.

**Rectum**

continuous with the sigmoid colon. It stores faeces prior to defecation. The rectal mucosa has both longitudinal and horizontal folds.

**Rugae**

large folds in the stomach lining caused by folding of the submucosal connective tissue, present when the stomach is contracted but obliterated when the wall is stretched as a result of gastric distension.

**Salivary Glands**

these are exocrine glands which secrete saliva containing both organic (mucus, amylase) and inorganic ( $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$  and  $\text{HCO}_3^-$ ) constituents. They are the parotid (near the ear), sublingual (under tongue) and submandibular (under the mandible) glands.

**Segmentation movements :**

most of the contractions of the small intestine are of this type and serve to constantly mix the chyme and bring it into contact with the intestinal epithelial wall for digestion and absorption.

**Small intestine:**

comprises the duodenum, jejunum and ileum.

**Sphincter :**

a ring of muscle occurring at various points along the alimentary tract, that can occlude the tube and control the movement of the contents.

**Stomach :**

enlarged section of the alimentary tract which receives and temporarily stores food. Acid and enzymes are secreted into the lumen for digestion of ingested material which is then broken to form chyme. The stomach is divided into three sections: the fundus, corpus and antrum.

**Stem cells :**

undifferentiated cells, located at the base of intestinal crypts and in the basal layer of stratified epithelium. These cells maintain proliferative activity and differentiation occurs during subsequent cell divisions. (They are referred to as pluripotent stem cells because of their ability to give rise to different cell types).

**Sugars :**

sugars are carbohydrates. Simple sugars such as glucose, fructose and lactose are monosaccharides; they are the soluble products of digestion. Disaccharides are also soluble sugars (sucrose, for example). The main carbohydrate constituents of food are the insoluble storage polysaccharides, starch (plants) and glycogen (animals).

**Tongue :**

muscular structure in the mouth which plays an important part in chewing, swallowing, tasting and speaking. Its surface is dotted with papillae which give the tongue its rough surface. Also on the surfaces of the tongue are a number of taste buds or receptors.

**Tonsils :**

these structures found in the oral cavity – pharynx and are part of the Gut Associated Lymphoid Tissue (GALT). They are lymphoid structures, containing T and B cells.

**Trypsin and chymotrypsin :**

digestive enzymes, secreted by the pancreas, that hydrolyse peptide bonds of polypeptides and proteins.

**Villi :**

villi are projections of the small intestinal mucosa into the lumen. They are covered by epithelial cells which possess many microvilli on the luminal membrane which again increases the absorptive surface area. Villi are broad in the duodenum, tall leaf-like structures in the jejunum and short finger-like processes in the ileum. Within each villus is a capillary arteriole and a venule which surround the central lacteal (lymphatic vessel). In addition each villus is supplied by nerve fibres and smooth muscle fibres which allow the villus to move back and forth in the chyme to facilitate absorption.

# 1. INTRODUCTION

## 1.1. The purpose of this report

5 (1) This report provides a new model for the human alimentary tract that replaces the model  
for the gastrointestinal tract adopted by ICRP in *Publication 30* (ICRP, 1979). The  
Publication 30 model was developed specifically to calculate doses to workers, either from  
the direct ingestion of radionuclides or following their inhalation as particles with subsequent  
escalation from the lungs to the alimentary tract. The model took account of transit of  
10 ingested materials through four regions of the alimentary tract: the stomach, small intestine,  
upper large intestine and lower large intestine. The absorption of radionuclides to blood was  
specified by values of fractional uptake ( $f_1$ ) from the small intestine.

(2) This replacement was motivated by a number of developments:

- 15 • More extensive and reliable data on gut transit of materials have become available  
using new techniques such as non-invasive scintigraphic procedures.
- Information has become available on the location of sensitive cells and retention of  
radionuclides in different regions of the alimentary tract.
- The 1990 recommendations of ICRP introduced specific risk estimates and tissue  
20 weighting factors,  $w_T$ , for radiation-induced cancer of the oesophagus, stomach and  
colon (ICRP, 1991), requiring dose estimates for each of these regions. The  
*Publication 30* model did not include the oesophagus and treated the colon as two  
regions – upper and lower large intestine.

25 (3) The *Publication 30* model, although intended for the calculation of doses for the  
occupational exposure of adults, has been applied to calculate dose coefficients for  
members of the public, including children. Thus, in *Publications 56, 67, 69, 71 and 72*  
(ICRP, 1989, 1993, 1995a,b, 1996), dose coefficients for infants and children were  
calculated by scaling the *Publication 30* model to take account of the smaller mass of the gut  
30 in children. Increased intestinal absorption of radionuclides by infants was also taken into  
account but age-dependent differences in transit times were not included.

(4) The new human alimentary tract model (HATM) is applicable to children and adults under  
all circumstances of exposure. It considers the movement of radionuclides throughout the  
35 alimentary tract from ingestion to elimination. It takes account of sites of radionuclide  
absorption and retention in the alimentary tract and routes of excretion of absorbed



radionuclides into the alimentary tract. Doses are calculated for sensitive cells in each region: mouth, oesophagus, stomach, small intestine and colon.

## 1.2. Model used in ICRP Publication 30

5

(5) In 1966, Eve reviewed data on the transit of materials through the alimentary tract and other parameters necessary to calculate doses (Eve, 1966). Transit times were based largely on information from clinical studies using barium meals. Reference was also made to studies using materials labelled with iron-59 or lanthanum-140. These data provided the  
10 basis for the dosimetric model of the alimentary tract developed by Dolphin and Eve (Dolphin and Eve, 1966) and applied in ICRP *Publication 30* (1979). It is a catenary model with four compartments: the stomach, small intestine, upper large intestine and lower large intestine. The absorption of materials to blood is taken to occur in the small intestine. The transfer rate coefficients for movement of intestinal contents are equal to the reciprocal of the mean  
15 residence times, taken to be 1 hour for the stomach, 4 hours for the small intestine, 13 hours for the upper large intestine and 24 hours for the lower large intestine. These values were based on observed ranges of 25 - 120 minutes, 1 - 7 hours, 6 - 22 hours and 15 - 72 hours, respectively.

(6) In the *Publication 30* model, doses are calculated separately for the mucosal layer of each of the four regions considered. For penetrating radiations, the average dose to the wall of each region is used as a measure of the dose to the mucosal layer. For non-penetrating radiations, the specific absorbed fraction for the mucosal layer is taken to be equal to  $0.5v/M$  where  $M$  is the mass of the contents of that section of the tract and  $v$  is a factor between 0  
25 and 1 representing the proportion of energy reaching sensitive cells. The factor of 0.5 is introduced because the dose at the surface of the contents will be approximately half that within the contents for non-penetrating radiations. For electrons,  $v$  is taken to be 1. For  $\alpha$  particles, a value of 0.01 is used on the basis of an acute toxicity study in rats in which the  $LD_{50}$  for ingested yttrium-91 was estimated as about 12 Gy, while an absorbed dose to the  
30 mucosal surface of more than 100 times greater from  $^{239}\text{Pu}$  had no effect (Sullivan et al., 1960).

(7) The absorption of radionuclides to blood was specified by values of fractional absorption from the small intestine, termed  $f_1$  values. Values for workers were initially recommended in  
35 *Publication 30* (1979, 1980, 1981 and 1988). For some radionuclides, more than one  $f_1$  value was given, to apply to different chemical forms of the element that might be

encountered (eg. plutonium nitrate and oxide). For members of the public  $f_1$  values were recommended for radionuclides in diet in *Publications 56, 67, 69, and 71* (1989, 1993, 1995a,b), for the standard age-groups considered in these publications: infants (3 months), 1, 5, 10 and 15 year-old children, and adults (generally 20 y). The  $f_1$  values given for infants were greater than at older ages (unless  $f_1 = 1$  in adults, eg. caesium), in recognition of human and animal data showing greater absorption of radionuclides (and stable elements) in the immediate postnatal period. Greater intestinal permeability in the immediate postnatal period is considered to be a general phenomenon (NEA, 1988, ICRP, 1989). A number of factors, including the milk diet, may contribute to this increased availability of elements for absorption but the pinocytotic activity associated with the uptake of intact gamma globulins from milk (Brambell, 1970; Clarke and Hardy, 1971) is thought to have an important role (Fritsch et al., 1988; Harrison et al., 1987). Animal and human data show that absorption is greatest immediately after birth and decreases progressively over the suckling period.

(8) Most recently, consideration has been given in *Publication 88* to changes in absorption and  $f_1$  values during pregnancy (ICRP, 2001); for physiologically essential elements, such as calcium and iron, uptake of the ingested element can increase during pregnancy. This also applies to chemically similar elements – for example, to strontium because of its similarity to calcium. Infant  $f_1$  values have been applied, in *Publication XX*, to radionuclide ingestion in breast milk after intakes by the mother either during lactation or during or before pregnancy. It was assumed that the infant  $f_1$  values applied throughout the suckling period, taken to be for the first 6 months of life.

### 1.3. The need for a new model

(9) The 1990 recommendations of the ICRP gave revised estimates of radiation risks, based largely on reassessments of the incidence of cancer in the survivors of the atomic bombs at Hiroshima and Nagasaki (ICRP 1991). Specific risk estimates for cancer of the oesophagus, stomach and colon were included and the overall estimate of fatal cancer risk was estimated as  $0.04 \text{ Sv}^{-1}$  for workers and  $0.05 \text{ Sv}^{-1}$  for the general public in the 1990 recommendations (ICRP, 1977, 1991). For uniform whole-body exposures to low LET radiations, cancers of the alimentary tract were estimated to account for 45% of the total risk of radiation-induced fatal cancer in *Publication 60* (ICRP, 1991). The HATM includes the oesophagus, stomach and colon as specified target tissues.

(10) Since the development of the ICRP *Publication 30* (1979) model, a considerable body

of data has become available on the transit of materials through the different regions of the gut (see chapter 6). These data were obtained using non-invasive techniques and include studies of differences between solid and liquid phases, age- and gender- related differences and the effect of disease conditions. These data have been used to determine default transit rates for the defined regions of the alimentary tract for the age-groups given in ICRP *Publication 56* (1989): that is, 3 month-old infants, 1, 5, 10 and 15 year-old children, and adults.

(11) The ICRP *Publication 30* (1979) model assumes absorption to blood takes place solely in the small intestine and takes account neither of retention of radionuclides in different regions of the gut nor of transit of retained radionuclides through intestinal tissue. For some radionuclides, retention in the small intestine of adults has been shown and may contribute substantially to local doses (Roth et al., 1998). The increased absorption of radionuclides observed in the immediate postnatal period is associated with high levels of intestinal retention in some mammalian species (Inaba et al., 1984; Sullivan et al., 1987; Fritsch et al., 1988). Retention of radionuclides in the mouth has also been reported (Bhattacharyya et al., 1985; Renaud-Salis et al., 1990; Métivier, 1998). The HATM allows the calculation of doses from retained radionuclides in the limited number of cases for which data are available. While the absorption of most radionuclides to blood will be confined to the small intestine, absorption may also occur in other regions in some cases. For example, iodine absorption occurs in the stomach as well as the proximal small intestine (Berkovski, 1999). The new model makes allowance for the possibility of absorption in the mouth, stomach and large intestine as well as the small intestine. However, it should be noted that specific information on regional absorption is currently limited and absorption of most elements is assumed to occur solely from the small intestine.

(12) An important development in the new model is the calculation of doses to sensitive cells in the different regions of the alimentary tract. Doses to the oral cavity are considered as doses to skin. The location of sensitive epithelial stem cells in other regions is considered separately; that is for the oesophagus, stomach, small intestine and colon. Doses from radionuclides in the gut lumen, retained radionuclides and radionuclides in transit to blood are considered.

#### 1.4. Model development

(13) Approaches to the improvement of the *Publication 30* model have been considered in a

number of publications (Stubbs, 1992; Simko and Nosske, 1996; Poston et al. 1996a,b; Métivier, 1998), including the use of age and gender related transit data, consideration of radionuclide retention in the wall, and the calculation of absorbed energy in target layers within the wall. Stubbs (1992) reviewed transit data for adults, according to age and gender, and developed a model for describing movements through the stomach, small intestine and large intestine. A combination of linear and exponential terms was used to best describe movement through the regions. Thus, for example, liquid emptying from the stomach is well represented as an exponential loss, while movement to the small intestine after consumption of solids is better described as a linear process. Simko and Nosske (1996) highlighted the possible importance of retention of radionuclides in the wall of the small intestine during absorption. They also suggested that, in addition to direct absorption to blood, absorption to the lymphatic system should be taken into account. Poston et al. (1996a, b) developed a revised model for the calculation of photon and electron absorbed fractions at different depths into the wall of the stomach, small intestine and large intestine. For photons, the inclusion of track structure for electrons did not provide improved dose estimates when compared with the simpler approach used for *Publication 30*. For electrons, however, comparisons showed that the *Publication 30* approach might result in substantial overestimates of absorbed fractions.

(14) The approaches adopted in this report build on those considered above. A more comprehensive review of transit data has been undertaken in order to provide transit values for all regions of the alimentary tract, considering different age groups. As in the model proposed by Stubbs (1992), separate values are given for the movement of solids and liquids from stomach to small intestine; separate values are also given for solid and liquid transit to the stomach. However, although the validity of the kinetic models of Stubbs (1992) was recognised, it was considered sufficient for the purposes of this report to represent all movement between regions as first-order processes (see chapter 6).

(15) As suggested by Simko and Nosske (1996), the possibility of retention of radionuclides in the wall of the small intestine is allowed for in the model, as is possible retention and absorption in other regions. However, the lymphatic system is not included in the model. No published evidence has been found of significant accumulation of radionuclides in mesenteric lymph nodes, as would be expected if proposed mechanisms of particulate uptake involve lymphatic drainage. Thus, movement of particles to regional lymph nodes is known to occur following inhalation and deposition in the lungs (ICRP, 1994) and after wound contamination (NCRP, 2004) but does not appear to be an important contributor to the uptake of materials from the alimentary tract. The lymphatic transport of lipid-bound radionuclides may occur,

resulting in their entry into blood via the thoracic duct. However, it was considered sufficient for the purposes of this report to assume that all absorption results in radionuclide entry into blood.

5 (16) The calculation of doses to target regions within the wall of the different alimentary tract regions, following the approach of Poston et al. (1996a, b), is considered to be of central importance in this new model. In each case, the targets for cancer induction are taken to be the stem cells of the epithelial lining. These are the basal cells of the stratified squamous epithelium of the mouth and oesophagus, a small number of cells in the base of each crypt in the small and large intestines, and cells at an intermediate position in the gastric pits of the stomach (see chapters 2 and 4).  
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### 1.5. Structure of the report

(17) Chapter 2 provides an outline of information on the anatomy and physiology, sufficient for the purposes of understanding the approaches adopted in subsequent chapters. Chapter 3 introduces the subject of radionuclide behaviour in the alimentary tract in terms of their absorption, principally from the small intestine, possible retention in the alimentary tract, and secretion of systemic activity into the tract as a route of excretion. The possibility of absorption in regions other than the small intestine is discussed. Age-related changes in absorption are addressed, particularly the increased absorption observed in newborn animals. Retention in different regions is also considered, again referring to high levels of retention in neonates. Chapter 3 ends with examples of the behaviour of specific radionuclides, used later in the report to give examples of doses and to examine the effects of the assumptions made. Comprehensive information on radionuclide behaviour and associated model parameter values will be given in forthcoming publications on dose coefficients for workers and members of the public.  
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(18) Chapter 4 gives a brief summary of information on radiation effects, for cancer induction and deterministic effects. However, the main purposes of the chapter are to consider the location of target cells for cancer induction in the different regions of the alimentary tract, and other implications of risk data for model structure, including the approach taken to the partition of the large intestine.  
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(19) Chapter 5 describes the features of the new biokinetic model and its increased complexity in relation to the *Publication 30* model. The application of the model to the examples given in Chapter 3 is discussed. Chapter 6 provides a review of transit data and  
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gives default transit times for the different regions and for different ages. Chapter 7 gives morphometric data used in dosimetry, including age-related dimensions, depths of target layers, and the simplifying assumptions made for the purposes of dosimetric modelling. It also discusses dosimetric approaches and gives age-related specific absorbed fractions (SAFs). Chapter 8 gives examples of the results of dose calculation for the examples given in Chapters 3 and 5, illustrating the effect of age on doses to different regions and the effect of assumptions regarding retention in different regions. It also gives a brief overview of variability and uncertainties in dose calculation. Finally, it concludes with an overview with the key features of the model.

(20) Annexes A and B were developed with the Reference Man Task Group and provide review on the embryology, anatomy and physiology and derived physiological model which was used for defining the dosimetric model. Annex C provides reference values for anatomical and physiological features of the alimentary tract. They are consistent with reference values given in *ICRP Publication 89* (ICRP, 2002). Annex D provides a selective review of data on radionuclide absorption and retention in the gut, including consideration of mechanistic aspects and the role of chemical speciation in determining the behaviour of radionuclides. Annex E gives information on variability and uncertainties. Annex F gives specific absorption values (SAFs).

NOTE THAT ANNEXES ARE NOT INCLUDED IN THIS CONSULTATION DOCUMENT

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## 2. ANATOMY AND PHYSIOLOGY OF THE ALIMENTARY TRACT SYSTEM

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### 2.1. Introduction

(21) These chapters provides a brief description of the structure and function of the alimentary tract and associated organs, intended to be sufficient to enable the reader to understand the material presented in subsequent chapters. The main morphometric parameter values used in the model are given in Chapter 7. Detailed descriptions of the development, anatomy and physiology of the alimentary system, in support of model development and dose calculations, are given in Annexes A and B.

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### 2.2. General features

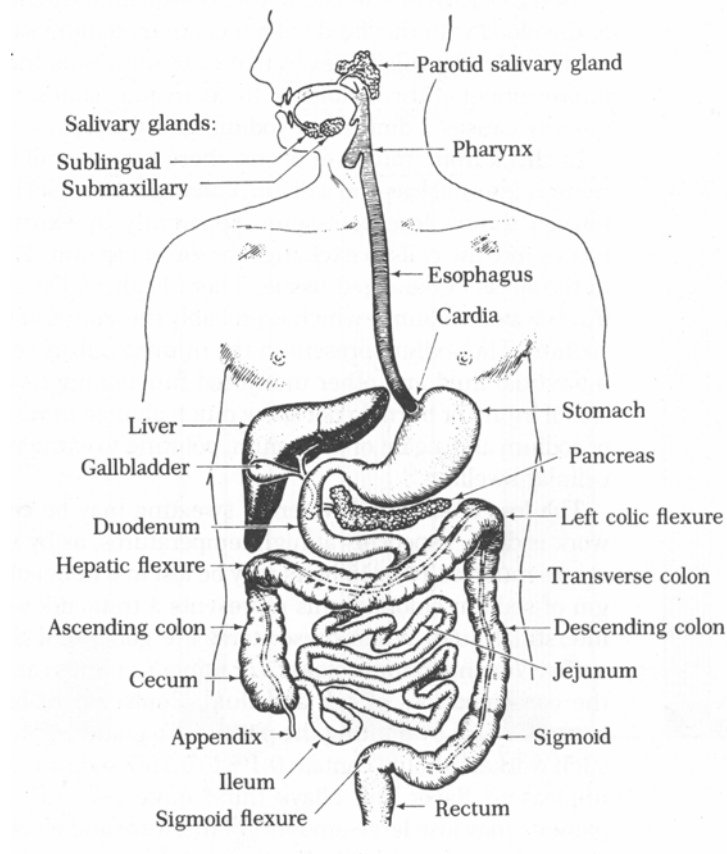
(22) The alimentary tract (Figure 2.1), also described as the digestive or gastrointestinal tract, is by definition primarily concerned with the intake, digestion and absorption of nutrients which may be termed *alimentation*. It comprises the oral cavity, including the mouth, teeth, salivary glands and pharynx, the oesophagus, the stomach, the small intestine, including duodenum, jejunum and ileum, the large intestine, including ascending, transverse and descending colon, rectum and anus. Two associated organs, the pancreas and liver, also play more general systemic roles in the body but are included in the alimentary tract system.

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(23) The alimentary tract is formed by a folding of the embryonic disc into a tube during the 3<sup>rd</sup> and 4<sup>th</sup> week of development. The epithelium lining of this tube will also form some accessory organs such as salivary glands, lungs, liver and the biliary tract and pancreas. The respiratory system is also derived from the alimentary tract and the pharynx is shared by the two systems.

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**Figure 2.1.** General structure of the human alimentary tract system with associated structures (Orten and Neuhaus, 1982).

- 5 (24) The alimentary system has a number of primary functions:
- Motor functions : intake of nutrients, storage, mixing and transport of the ingested material from mouth to anus, helped by secretion of lubricants (mucus).
  - Digestive function : secretion of enzymes in the mouth, stomach and small intestine, from glands in the epithelial lining (stomach, small intestine) and associated glands (salivary, liver, pancreas).
  - Absorptive function : essentially located in the small intestine.
  - Excretion function : liver and biliary tract and the distal part of the alimentary canal.
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- (25) Additional important functions are:
- 15   ▪ Defensive and immunological system to protect the body from colonisation by bacteria and viruses or from penetration by antigens.
  - Contains a microbial population, which produce vitamins and could have a role in the speciation of the elements.
- 20 (26) Essentially, the alimentary tract is an epithelium lined muscular tube capable of

propelling ingested material through a series of different physiological environments created by its secretory and absorptive epithelia. In these compartments, food already broken down mechanically is broken chemically into smaller molecules which can be absorbed by epithelial cells. The absorbed molecules then pass into the vascular system for circulation within the body. As the interior surface of the alimentary tract is continuous at the mouth and anus with the external surface of the body, material within its lumen can be regarded as outside the body, actually entering it in the form of small molecules and ions traversing the epithelial lining of the tract.

(27) The glands lining the tract supply the water, enzymes and chemical environment required for digestion and the movement of material through the tract. Small glands are present in the wall of the tract, eg. gastric glands of the stomach, while larger glands are connected to the tract by secretory ducts. These larger glands are the major oral salivary glands (parotid, submaxillary and sublingual) and the pancreas and liver.

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(28) The motility of the alimentary tract depends on muscles within its wall controlled by the autonomic nervous system and, in the case of the mouth and anus, on skeletal muscles under voluntary motor control.

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### 2.3. Alimentation

(29) The breakdown of solid ingested material is started in the mouth by the mechanical action of the teeth and the tongue (mastication). These actions greatly increase the surface area of the materials and mix them with secretions from the salivary glands which begin the process of digestion. After swallowing (deglutition), and rapid transport to the stomach via the oesophagus, gastric digestion proceeds by the action of acidic, enzymic secretions from numerous gastric glands, which also secrete protective mucus. Passing through the pylorus into the first part of the small intestine, the duodenum, the semi-fluid products of gastric digestion encounter alkaline fluids produced by liver, pancreas and duodenum. Bile salts emulsify liquid masses by tension active action, and the pancreatic secretions contain a wide variety of enzymes capable of hydrolysing many classes of macromolecules. Digestion proceeds throughout the considerable length of the small intestine (up to 3 to 4 m), accompanied by absorption of the resulting small molecules such as amino acids, monosaccharides, triglycerides, nucleotides together with vitamins and minerals by the specialised epithelial cells (enterocytes) lining the small intestine. These molecules are transferred from the enterocytes into the capillary network. The rate of such movements

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depends on the surface area of absorptive membrane bordering the intestinal lumen. The specialised absorptive region of the small intestine has a very large surface area due to a combination of intestinal length, folding of the wall and the presence of villi and microvilli (see below).

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(30) The alimentary tract also transports water and electrolytes across its wall. As the enzymes and lubricants are all in aqueous solutions or suspensions, large quantities of water and ions, especially sodium and chloride, are released into the tract. These are selectively resorbed through specialised absorptive cells which are especially numerous in the more caudal parts of the small intestine, the colon and rectum. Absorptive cells in the intestine reabsorb bile salts and other secreted materials, and absorb vitamins produced by the symbiotic bacteria in the colon. The large intestine has numerous mucus glands which lubricate the passage of the increasingly solidified faecal material moving through it. Finally, faeces are stored and then expelled under voluntary control via the colon and rectum.

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#### **2.4. Vascular supply and drainage**

(31) The arterial supply of both ends of the tract is shared with that of the surrounding regional structures. This applies to the oral cavity, pharynx and thoracic oesophagus, and to the lower two-thirds of the rectum and the anal canal. The rest of the tract receives a very rich blood supply, consistent with its secretory and absorptive roles. Three major branches of the abdominal aorta serve the abdominal oesophagus, stomach, small and large intestines, liver, spleen and pancreas (Figure 2.2). Similar distinctions apply to venous drainage. Thus, the proximal and distal ends of the tract share drainage with surrounding structures, leading to return of blood directly to the general circulation, while blood from the majority of the tract flows directly to the liver via the hepatic portal vein. As shown in Figure 2.2, the liver receives a large volume of nutrient-rich blood via the portal vein as well as a smaller volume of oxygenated blood via the hepatic artery. Hepatocytes in the liver control the entry of nutrients into the general circulation via the hepatic vein. They also remove toxic substances from the blood, some of which (after detoxification) are excreted in bile into the duodenum. The liver also contains a smaller population of Kupffer cells, which are part of the reticuloendothelial system and are capable of engulfing bacteria and other foreign materials by phagocytosis.

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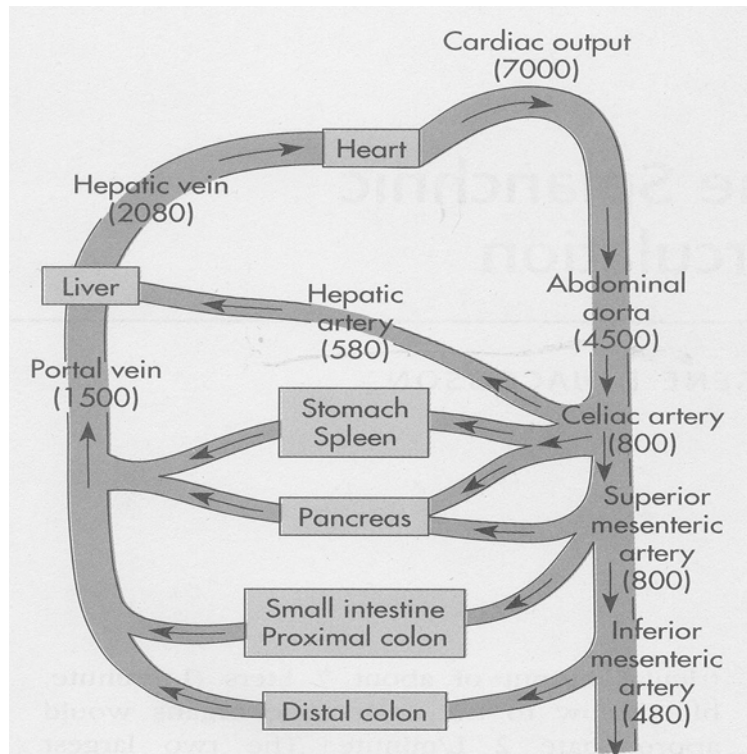


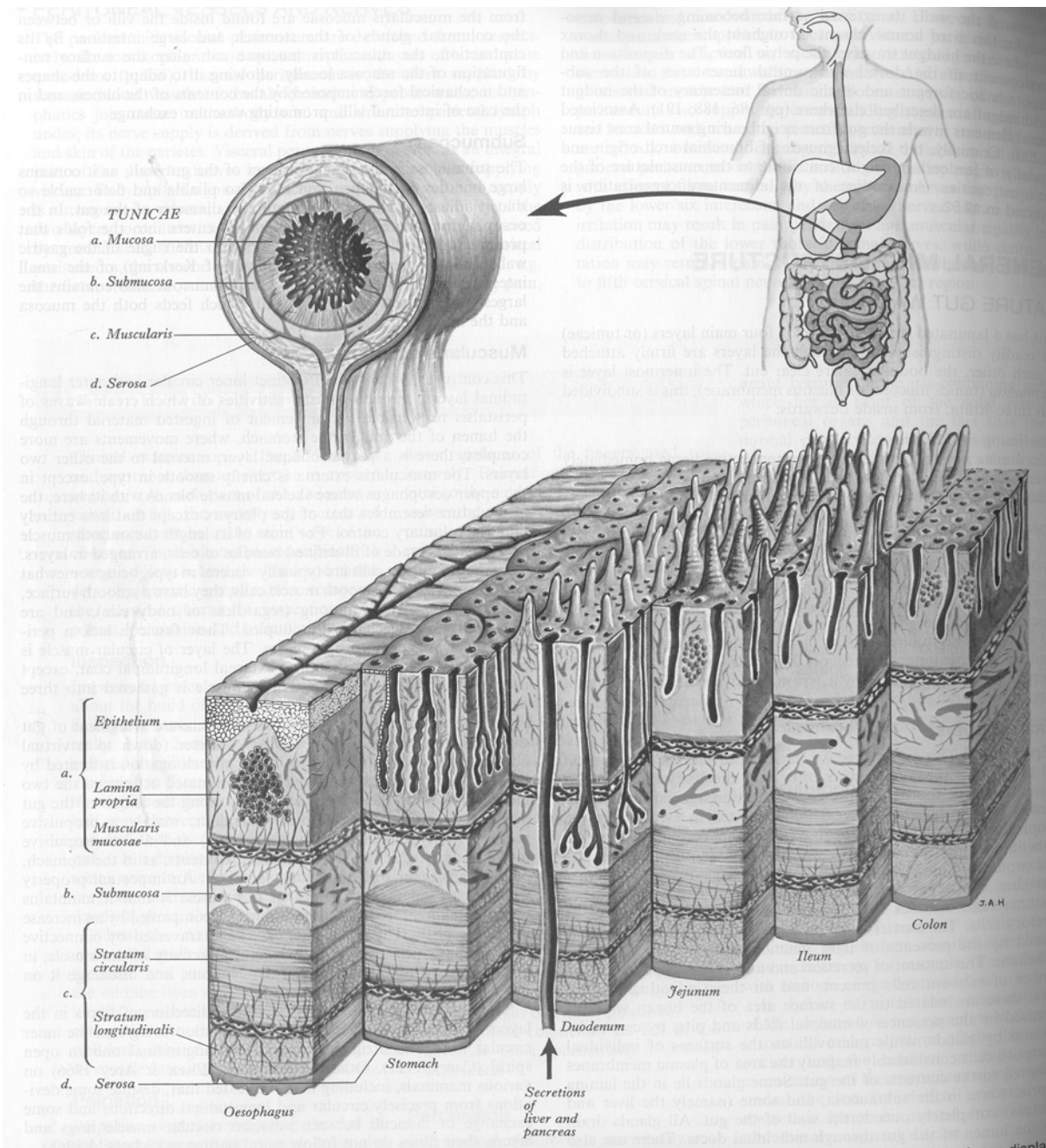
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**Figure 2.2.** The major blood vessels and organs supplied with blood in the splanchnic circulation. Figures in brackets are approximate blood flow rates (ml/min) for an adult at rest. (From Gastrointestinal Physiology, 2000)

(32) As is the case for all organs of the body, vascular drainage of the alimentary tract is accompanied by lymphatic drainage. The small intestine has particularly rich lymphatic drainage which forms an accessory transport system for the transfer of lipids from the site of absorption (see below). Lymph conveyed from the stomach, and small and large intestines, through a series of converging lymphatic vessels, empties through the thoracic duct into venous blood entering the heart. Throughout the lymphatic system, there are large numbers of lymph nodes, containing phagocytic cells and lymphocytes, providing an important line of defence against microorganisms which might otherwise enter the circulation by this route.

## 2.5. Microanatomy of the alimentary tract

(33) The hollow tube of the alimentary canal, extending from the pharynx to the anus, is made up of four concentric layers. From the lumen outward, these layers are the mucosa, submucosa, muscularis, and adventitia or serosa, as described below (Figure 2.3). The oral cavity and oropharynx also have a mucosal lining.



**Figure 2.3.** The general arrangement of the alimentary canal and cross-section of the component regions. (From Gray's Anatomy, 1995)

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(34) The *mucosa*, or mucous membrane, has three components throughout the tubular region of the tract: a superficial epithelium, an underlying stroma composed of a vascularized, highly cellular, reticular connective tissue (lamina propria), and a thin layer of smooth muscle (*muscularis mucosae*). The epithelium functions as a barrier and the site of secretion and absorption. The protective function against mechanical, thermal and chemical injury is most evident in the oesophagus and terminal part of the rectum, where the

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epithelium is thick and stratified, and is covered in mucus which acts as a protective lubricant, as also in the oral cavity and pharynx. Elsewhere in the gut the epithelium is simple, comprising a single layer of either cuboidal or columnar cells, and includes cells for absorption and various types of secretory cells. The barrier function and selectivity of absorption is assisted by the presence of tight junctions over the entire epithelium. The surface area of the epithelium is increased by the presence of mucosal folds and pits (plicae and rugae), by crypts, by villi and by glands, while microvilli on the surface of individual absorptive cells considerably increase the area of plasma membranes presented to the contents of the gut. Some glands lie in the lamina propria and some in the submucosa, and the liver and pancreas lie outside the wall of the gut. All glands drain into the lumen of the gut through individual ducts. There are also scattered endocrine cells within the epithelial lining.

(35) Lymphoid tissue is found throughout the mucosa of the alimentary tract, referred to as gut-associated lymphoid tissue (GALT). This includes masses of lymphoid tissue situated mainly in the lamina propria, but sometimes expanding into the submucosa. They contain B and T lymphocytes and related cells involved in the immune defence of the gut wall. In addition to organised nodules of lymphoid tissue, there are disseminated populations of lymphocytes within the lamina propria and epithelial base. Organised nodules include the lymphoid ring of the tonsils, and the particularly prominent nodules in the small intestine, called Peyer's patches, and in the appendix.

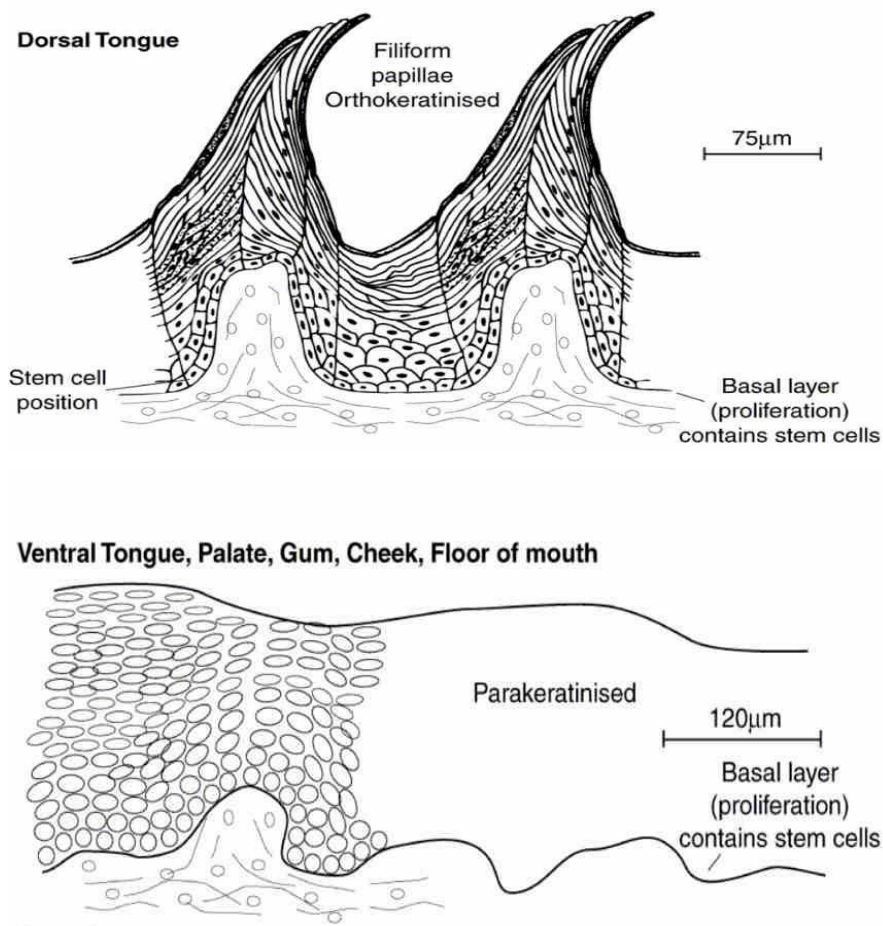
(36) The *submucosa* is a fibrous layer that in some places contains accumulations of lymphatic tissue as well as glands that extend from the mucosa. The submucosa is a vascular service area containing large blood vessels that send finer vessels into the layers that represent the specific organ functions, the mucosa and the muscularis. The *muscularis* contains two or more layers of muscle that is smooth in all parts except the upper oesophagus and the anal sphincter. Contractions of the inner, circular layers constrict the lumen, and contractions of the outer, longitudinally arranged layers shorten the tube. At the various sphincters and valves along the length of the tube, the layer of circular muscle is greatly thickened. The *adventitia* of the tract is composed of several layers of loose connective tissue, alternating between collagenous and elastic tissue.

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## 2.6. Epithelia of the alimentary tract

(37) It is the stem cells of the epithelial lining of the alimentary tract that are regarded as the targets for radiation-induced cancer (see Chapter 4). The epithelial layer is constantly renewed by cell division and differentiation, originating from stem cells located in the basal layer of the epithelium of the oral cavity, pharynx and oesophagus, and in the crypts in other regions. The depth of the stem cells from the intestinal lumen varies between regions.



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**Figure 2.4.** Illustrations of cross-sectional dimensions of the epithelial lining of the mouth – stratified squamous epithelium: A. dorsal tongue, B. ventral tongue, palate, gum, cheek and floor of mouth. Published courtesy of Professor Chris Potten, Epistem Ltd.

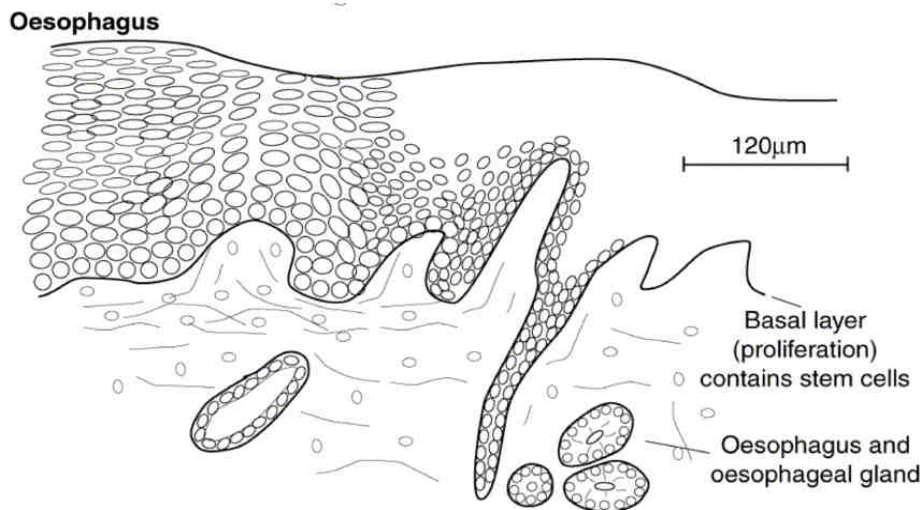
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### *Oral cavity, pharynx and oesophagus*

(38) The epithelial lining of the oral cavity, pharynx and oesophagus is a thick layer of protective tissue, many cells deep, classed as stratified squamous epithelium. In some regions of the oral cavity, as in the example of the tongue (Figure 2.4), the epithelium may be

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keratinised like skin; that is, the hardened outer layers of keratinocytes protect against abrasion and water loss. Elsewhere, the stratified squamous epithelium is non-keratinised, as in the oesophagus (Figure 2.5).



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**Figure 2.5.** Illustration of the cross-sectional structure and dimensions of the oesophageal stratified squamous epithelium. Published courtesy of Professor Chris Potten, Epistem Ltd.

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### *Stomach*

(39) The gastric epithelium is a single layer of cells, a simple or unilaminar epithelium, that lines numerous glandular indentations into the stomach wall, the gastric pits (Figure 2.6). Differentiated epithelial cells within the gastric pits secrete hydrochloric acid (Oxyntic cells), digestive enzymes (Zymogen cells) and mucus. The putative position of the stem cells is shown in Figure 2.6.

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### *Small and large intestines*

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(40) The simple single layer of columnar epithelium lining the small and large intestines forms the lining of the crypts in both regions and the covering of the villi of the small intestine. This is illustrated in Figures 2.7 and 2.8.

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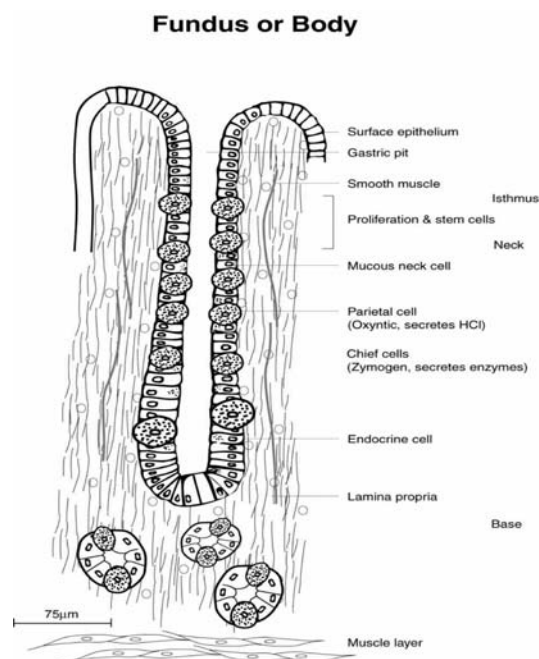
(41) The villi vary in height and form in different regions of the small intestine. Under the epithelial covering of each villus, within the highly cellular connective tissue of the lamina propria, there is a rich capillary network and a central lymphatic vessel or lacteal. The epithelial cells of the villus are mainly absorptive enterocytes, with surface microvilli to

increase the surface area for uptake of nutrients. Interspersed between the enterocytes are goblet cells that produce and secrete mucus.

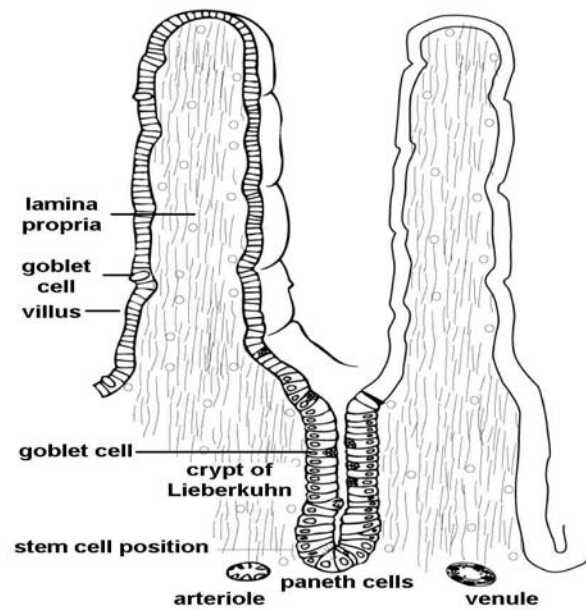
(42) At the bases of the villi are simple tubular invaginations that extend as far as the underlying muscularis mucosae but do not penetrate it. The stem cells that give rise to and constantly renew the epithelial layer of cells are positioned at the base of the crypts, immediately above a group of specialised Paneth cells. Cell division results in a constant movement of cells up the crypts and villi, with cells ultimately lost from the tips of the villi into the lumen of the intestine. The precise function of the Paneth cells is not known, although they secrete an anti-bacterial lysozyme.

(43) The epithelium overlying lymphoid nodules in the intestine, including the Peyer's patches of the small intestine, is characterised by the presence of microfold or membranous epithelial (M) cells. These cells typically possess a reduced number of shortened, irregular microvilli or microfolds on their apical surface. They act as antigen sampling cells, transporting luminal antigens to the underlying lymphoid tissue.

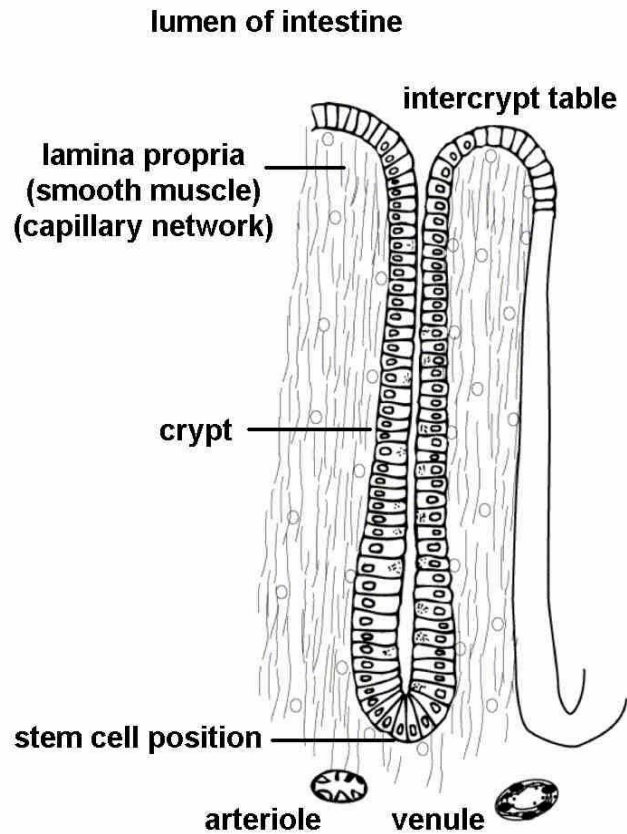
(44) In the large intestine, deep, straight crypts penetrate into the lamina propria from a luminal intercryptal plate; there are no villi. The stem cells are in the base of the crypts; there are no Paneth cells. As in the small intestine, cell division leads to a constant flow of cells up the crypts, with loss of cells in the large intestine from the intercryptal plate.



**Figure 2.6.** Illustration of the cross-sectional structure and dimensions of a typical gastric gland in the stomach, lined with a single layer of columnar epithelial cells. Published courtesy of Professor Chris Potten, Epistem Ltd.



5 **Figure 2.7.** Illustration of the cross-sectional structure of the epithelial lining of the small intestine, showing villi and crypts. Published courtesy of Professor Chris Potten, Epistem Ltd.



**Figure 2.8.** Illustration of the cross-sectional structure of the epithelial lining of the large intestine, showing crypt and stem cell position. Published courtesy of Professor Chris Potten, Epistem Ltd.

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## 2.7. References

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### 3. ABSORPTION, RETENTION AND SECRETION OF RADIONUCLIDES IN THE HUMAN ALIMENTARY TRACT

5

#### 3.1. Introduction

(45) Doses delivered to regions of the alimentary tract from radionuclides within it depend not only on rates of transfer through the lumen (see Chapter 6) but also on the extent of their absorption to blood and distribution to other tissues. Absorption takes place very largely in the specialised absorptive region of the small intestine (SI). High levels of absorption can lead to lower doses to the large intestine. However, the alimentary tract is also a route of excretion and, depending on the radionuclide, variable proportions of the absorbed systemic activity will enter the tract and pass through the large intestine. In addition, regions of the alimentary tract can receive doses from radionuclides carried in blood or deposited in tissues after absorption. The extent of absorption of individual radionuclides is dependent on the chemical properties of the element as well as the specific chemical form of the intake. Similarly, the extent of secretion of systemic activity into the tract and hence excretion is dependent on the chemical form of the element in blood and tissues. The possible retention of radionuclides in the tissues of the alimentary tract may also result in increased doses. Thus, for example, there is evidence of retention of radionuclides on the surface of teeth, and retention in the wall of the small intestine.

(46) Information on radionuclide absorption, retention and secretion is obtained largely from animal experiments, supported by more limited data from human studies. It is important to recognise that there are uncertainties associated with the available data and the application of animal data to radionuclide behaviour in humans. In addition, there may be considerable variation between individuals in, for example, the absorption of an element or radionuclide from the alimentary tract to blood. Thus, while it is normal practice to use single values for such biokinetic parameters for the purposes of dose estimation, this is done in the knowledge that ranges apply in terms of uncertainty on central values and of variability between individuals.

(47) This chapter outlines the processes of radionuclide absorption, retention and secretion. The chapter ends with specific examples used later in the report to illustrate the use of the new biokinetic model and the dosimetric approaches adopted, including the effect on doses of the different assumptions made and the effect of uncertainties. Annex E gives

further information on radionuclide behaviour in the alimentary tract. However, a comprehensive review of radionuclide behaviour is not within the scope of this report. Element specific information and parameter values for the HATM will be given in forthcoming publications on dose coefficients for workers and members of the public. The information given on radionuclide behaviour in forthcoming publications will in most cases refer to comprehensive reviews undertaken previously for the purposes of calculating dose coefficients for workers (ICRP, 1979, 1980, 1981) and members of the public (ICRP, 1989, 1993, 1995a, b). In all but a few cases, information is only available on total absorption from the alimentary tract, assumed to be from the small intestine, and on the extent of faecal excretion. However, for a limited number of elements and their radioisotopes, more information will be presented and used in the calculation of doses, as illustrated by the examples given in this chapter.

## 3.2. Radionuclide absorption

### 3.2.1. Types of intake

(48) Absorption is the process that leads to the transfer of radionuclides from the alimentary tract to blood and hence to other body tissues. Radionuclides may enter the alimentary tract directly as a result of their ingestion or indirectly after inhalation and mucociliary escalation of particles from the respiratory tract to the oropharynx and oesophagus (ICRP, 1979, 1989, 1995b). The chemical form of the radionuclide entering the alimentary tract will vary according to the type of exposure. For example, occupational exposures may involve ingestion of inorganic forms of radionuclides not normally present in the environment. Environmental exposures mainly involve ingestion of radionuclides incorporated into food materials, bound to organic constituents of food, and/or inorganic forms present in food and/or water. In each case, changes in chemical form are likely to occur during digestive processes, beginning in the mouth, but principally occurring in the stomach and small intestine. These changes in chemical form or speciation will determine the availability of the radionuclide for absorption and hence the extent of uptake through the intestinal epithelium to the bloodstream.

(49) For radionuclides deposited in the respiratory tract (RT) following inhalation, clearance occurs as two competing processes, absorption to blood and particle transport largely by mucociliary clearance. In the HRTM (ICRP, 1994), it is assumed that material removed by particle clearance is swallowed and enters the alimentary tract. In considering absorption from the alimentary tract, it was considered in ICRP *Publication 71* (1995b) that,

for environmental exposure, the radionuclides might typically be present as minor constituents of the inhaled particles, and that therefore absorption to blood would depend on dissolution of the particle matrix, as well as the element and chemical form. This may also apply to the direct ingestion of particles containing radionuclides.

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### **3.2.2. Absorption in small intestine**

(50) Generally, the absorption of radionuclides occurs together with the absorption of nutrients in the small intestine. Absorption may involve passive diffusion or active transport through the single layer of epithelial cells lining the small intestine. The extent of absorption of radionuclides will depend on the element and its chemical form. Thus, for example, the behaviour of tritium as tritiated water follows body water with essentially free passage from the alimentary tract to blood (ICRP, 1989). Caesium ions behave similarly to  $K^+$  and are rapidly absorbed (ICRP, 1989). Calcium (II), iron (III) and related elements are absorbed by active transport mechanisms that respond to physiological demand. In contrast, isotopes of the actinide elements, while showing some similarities to Fe(III) in their behaviour in the body, are very poorly absorbed (<0.1% of ingested amounts) (ICRP, 1989).

(51) In addition to the passage of ions and molecules across the microvillus membrane, materials including macromolecules and small particles may also enter epithelial cells by pinocytosis – engulfment at the cell surface into small vesicles which are internalised. This may occur in the normal epithelial absorptive cell and has been demonstrated in the lymphoid M cells of Peyer's patches (Bockman and Cooper, 1971; Joel *et al.*, 1978, 1984; Owen, 1977). The available evidence suggests that while this is not an important contributor to uptake in adults, in neonates it provides a mechanism for the acquisition of passive immunity by the uptake of antibodies from milk, also allowing uptake of other materials including radionuclides (see below). Because the epithelial layer is being constantly replaced by cell division in the crypts, any material entering the absorptive cells but not transferred to the bloodstream will be lost into the lumen: the time taken for cells to traverse the length of the villi in humans is about 6 days and approximately 17 million cells/day are shed into the intestine (see below and 3.3. Radionuclide retention). Passage of particles through tight junctions between epithelial enterocytes in the small intestine has also been studied as a route of entry into blood or lymph. Although there is little direct information regarding the fate of particles entering the body this way, current understanding of the nature of these junctions suggests that this is not an important route of uptake.



### 3.2.3. Absorption from other regions

(52) Although the small intestine is the predominant site of absorption of nutrients and other substances, there is evidence that absorption of some elements and their radioisotopes can occur in other regions of the alimentary tract, including the mouth, stomach and colon. Absorption from stomach can occur for highly lipid-soluble substances, such as alcohol and some weak acids. The large intestine is known to absorb water and electrolytes such as sodium and chloride (see Annex D).

(53) Absorption from the oral cavity is unlikely to be a major contributor to total absorption. Studies using rats have shown substantial absorption of carrier-free  $^{18}\text{F}$  and  $^{125}\text{I}$  from the mouth but only after artificially prolonged periods of retention (Gabler, 1968; Patten *et al.*, 1978). Thus, the absorption of administered  $^{125}\text{I}$  was 7% after 1 hour, 13% after 2 hours and 24% after 3.5 hours. The absorption of  $^{18}\text{F}$  was 7% after 2.5 hours (Patten *et al.*, 1978).

(54) Although the stomach is not generally considered to be an absorptive organ, there is evidence that some elements, including iodine, copper and mercury, can be absorbed to some extent from the stomach (Van Campen and Mitchell, 1965; Sasser *et al.*, 1978). Van Campen and Mitchell (1965) demonstrated substantial absorption of  $^{64}\text{Cu}$  through the ligated rat stomach. In similar studies, Wagner (1962) showed that 50% of a 29  $\mu\text{g}$  dose of fluoride was absorbed from the ligated rat stomach within 1 hr and only 16% remained after 5 hr. Eisele and Mraz (1981) reported uptake of  $^{95}\text{Nb}$  from the ligated stomach of rats of about 1% after 4hr, greater than measured for the duodenum, jejunum, and ileum (<0.2% in each case).

### 3.2.4. Absorption in infants

(55) There is evidence from animal experiments and some supporting human data that absorption of many elements is substantially greater in newborn mammals than in adults. A number of factors, including the milk diet, may contribute to this increased availability of elements for absorption, but the pinocytotic activity associated with the uptake of intact gamma globulins from milk (Brambell, 1970; Clarke and Hardy, 1971) is thought to have an important role (Sullivan, 1980; Harrison *et al.*, 1987; Barton, 1987). The acquisition of passive immunity by this process occurs in many mammalian species including mice, rats, hamsters, dogs and cattle. However, prenatal transfer of antibodies, through the yolk sac or placenta, also occurs in some species and has been considered to be the predominant, or only, mechanism in man and other primates, rabbits and guinea pigs. Nevertheless, it would

appear that the alimentary tract of these species, while possibly being impermeable to gamma globulin molecules, is not fully mature and does allow the passage of large molecules and polymers (Udall *et al.*, 1981; Lecce and Broughton, 1973). Human neonates fed cows' milk may develop circulating antibodies to cows' milk proteins, suggesting that these molecules can reach the circulation intact. Limited studies on human neonates using small polymers and saccharide molecules have shown increased absorption during the first few days of life (Fagan *et al.*, 1981; Beach *et al.*, 1982). Fritsch *et al.* (1992) suggested that closure in the neonatal primate may not be achieved before birth but at times up to several weeks or even months later. Although these processes are thought to play an important part in the high levels of absorption observed in newborn mammals, it is thought that other maturational and dietary changes will influence levels of absorption in infants and the duration of increased absorption.

(56) Data on the effect of age and other factors on the intestinal absorption of radionuclides have been reviewed by ICRP in order to specify values of fractional absorption, for use in the calculation of age-related dose coefficients for members of the public (ICRP, 1989, 1993, 1995a,b) (Table 3.1.). Dose coefficients were given for radioisotopes of 31 elements, considered of potential importance in terms of public exposures, and for a number of age groups including 3 month old infants and 1 year old children. Animal data supported by limited human data show that absorption is greatest immediately after birth and decreases progressively over the suckling period. Thus, it is considered likely that adult values of absorption will apply in many cases to intakes by weaned infants later in the first year of life. Nevertheless, the approach adopted has been to specify infant values of absorption for the 3 month old infant that are taken to apply as averages over the first year of life. Uncertainties in values of fractional absorption and consequences for the calculation of effective dose have been described by Harrison *et al* (2001).

**Table 3.1.** Comparison of transfer fraction for adults and infants as used in ICRP Publications (ICRP, 1989, 1993, 1995 a and b).

Element	Adult	Infant
H, C, Cs, S, Mo, I	1	1
Se	0.8	1
Zn, Tc, Po	0.5	1
Te, Sr*, Ca*	0.3	0.6
Ba*, Ra*, Pb*	0.2	0.6
Co*, Fe*	0.1	0.6

Sb	0.1	0.2
Ru, Ni, Ag	0.05	0.1
U	0.02	0.04
Zr, Nb	0.01	0.02
Ce, Th, Np, Pu, Am	0.0005	0.005

\*Intermediate values for 1, 5, 10, 15y old children: Sr, Ca, Pb, 0.4: Co, Ra, Ba, 0.3: Fe, 0.2

### 5 3.2.5. Factors influencing absorption

#### Speciation

(57) The influence of the chemical form of the ingested radionuclide on absorption and the nature of the diet at the time of ingestion are only partially understood. Both factors may influence the speciation, i.e., the chemical form of the radionuclide in the alimentary tract and therefore its availability for absorption. For example, evidence suggests that absorption of actinide elements depends on both the mass ingested and the redox conditions in the intestinal lumen. The pentavalent forms of neptunium and plutonium are known to be transferable to blood in relatively high quantities, although animal studies have shown that this only occurs at unrealistically high concentrations (Sullivan *et al.*, 1983a; Métiévier *et al.*, 1983; Harrison *et al.*, 1984). Lower absorption at lower concentrations was attributed to reduction to tetravalent forms that are readily hydrolysed and therefore poorly absorbed.

(58) It has been shown that incorporation of radionuclides into food, which contains complexing agents such as citrates, phytates and other organic acids, may lead to greater absorption than ingestion of inorganic forms of an element. This factor should be considered when extrapolating the result of animals studies performed with inorganic forms of elements to humans ingesting radionuclides in mixed diets containing a variety of potential complexing agents. For example, Sullivan *et al.* (1983a) showed that the absorption of  $^{238}\text{Pu}$  administered to rats as the nitrate was increased by up to a factor of 20 when fed with diets supplemented with milk or orange juice. Studies in rodents and primates have shown that binding of Pu and other actinides to citrate and phytate results in increases in absorption, compared with values for Pu nitrate, of up to factors of 5 – 10 (see Annex D). In each case, the greatest values of Pu absorption corresponded to around  $10^{-3}$  of the amount ingested. In contrast, the absorption of technetium was decreased by incorporation into food to around 0.5, compared with values of about 0.8 for Tc administered as pertechnetate, in studies using

rats, guinea pigs and sheep (Sullivan *et al.*, 1983b; Gerber *et al.*, 1989). A low value of around 0.1 was also obtained in a volunteer study of absorption of <sup>99</sup>Tc from lobster flesh (Hunt *et al.*, 2001; Harrison and Phipps, 2001). Further examples of the effect of chemical form on radionuclide absorption are given in 3.5 and Annex 3.

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### **Fasting**

(59) The absorption of radionuclides from drinking water might be increased when ingested after a period without food. Thus, for example, fasting has been shown to increase the absorption of actinide elements, including Pu (NEA, 1988). James *et al.* (1985) measured absorption in human volunteers given Pb acetate in water to be about 0.65 after a 12 hour fast compared with about 0.4 when taken with a substantial meal. Heard and Chamberlain (1982) showed that fasting values of absorption of about 0.4 – 0.5 could be reduced to about 0.1 – 0.2 by giving Pb with tea, coffee or beer rather than water.

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### **Physiological stages**

(60) For physiologically essential elements and their radioisotopes, absorption may be increased during periods of increased demand - during pregnancy and lactation in female adults, and during periods of increased growth in children. This also applies to chemically similar elements – for example, to strontium because of its chemical similarity to calcium. Human data on Ca absorption reported by Allen (1982) show an increase in absorption from about 0.3 before pregnancy to about 0.5 at 5 – 6 months after conception. Cross *et al.* (1995) measured changes in absorption during pregnancy in a group of 10 women, from 0.36 before pregnancy to values of 0.40, 0.56 and 0.62 towards the end of the first, second and third trimesters, respectively. Consideration was given in *Publication 88* (ICRP, 2001) to changes in absorption during pregnancy for the physiologically essential elements, calcium and iron, and related elements.

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## **3.3 Radionuclide retention**

(61) Retention occurs when radionuclides are bound to tissues within regions of the alimentary tract. While radionuclide retention is generally low and may be ignored in most cases, there is some experimental evidence of retention on teeth, and retention within the mucosa of the small intestine. Retention in the small intestine is pronounced in newborn animals and is associated with increased levels of absorption (see above).

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### 3.3.1. Retention on teeth

(62) Retention on teeth as a result of deposition on tooth surfaces after radionuclide ingestion has been shown to occur in experimental studies of a number of elements, including radium, cadmium, lead, tin, polonium, strontium and plutonium (see Annex D). Mechanisms of deposition are not well understood, although it is postulated that it is the consequence of the adsorption of the element on the tooth enamel. Consequently, retention on teeth might depend strongly on the speciation of the radionuclide but, as with the absorption processes, only few data are available and therefore no clear conclusion can be drawn at this stage.

(63) Experiments using beagle dogs showed that ingestion of 48 to 1330 kBq/day of  $^{90}\text{Sr}$  for 18 months resulted in a greater incidence of melanoma and carcinoma of the oral mucosa, than animals receiving  $^{90}\text{Sr}$  by intravenous injection (Book *et al.*, 1982). These results suggest that greater doses were received by the oral mucosa after ingestion than intravenous injection of  $^{90}\text{Sr}$  and, because of the rapid transit of ingested materials through the mouth (Chapter 6), retention would be required for this to occur. However, no direct information was provided on the possible sites or extent of retention.

(64) Bhattacharyya *et al.* (1985) reported detailed findings of the retention of  $^{109}\text{Cd}$ ,  $^{210}\text{Pb}$  and  $^{236}\text{Pu}$  on the teeth of mice after ingestion in drinking water. In each case, comparisons were made between the tissue distribution observed in these mice and in corresponding groups given the radionuclides either by gavage into the stomach or by intravenous injection. The results obtained showed clear evidence of retention in the mouth, and on teeth in particular.

(65) Comparisons of the behaviour of Pu(VI) and Pu(IV) ingested as the bicarbonates in drinking water showed substantial levels of retention on teeth and in the mouth for Pu(VI) but lower levels for Pu(IV). Analyses of teeth showed retention of 0.5% of the ingested activity of  $^{236}\text{Pu}$ (VI) and about 0.02% for  $^{236}\text{Pu}$ (IV), measured at 6 days after ingestion. To demonstrate that this retention was due to surface adherence, surface measurements of alpha activity were made, showing that retention was confined to the exposed portions of teeth and was absent from the roots. *In vitro* tests with mouse teeth immersed in  $^{236}\text{Pu}$ (VI) bicarbonate solution showed that 15% of the  $^{236}\text{Pu}$  was adsorbed onto the teeth after 5 hours. The addition of small amounts of bone ash (hydroxyapatite) to solutions of both Pu(VI) and Pu(IV) in bicarbonate solutions resulted in nearly complete removal of Pu from these solutions. In addition to the retention on teeth observed after ingestion of  $^{236}\text{Pu}$ (VI) and  $^{236}\text{Pu}$ (IV),

measurements also showed a lower level of retention on other mouth surfaces, accounting for about 0.03% and 0.01% of the ingested activity, respectively. Comparisons with the distribution of  $^{236}\text{Pu}$  after gavage or intravenous injection showed that the distribution of Pu absorbed from the alimentary tract was the same for ingestion in drinking water and gavage and the same as after systemic administration.

(66) Bhattacharyya *et al.* (1985) also showed retention of  $^{109}\text{Cd}$  and  $^{210}\text{Pb}$  in the heads of mice, attributable mainly to surface adherence to teeth, after administration of  $^{109}\text{Cd}(\text{II})$  chloride and  $^{210}\text{Pb}(\text{II})$  nitrate in drinking water. At 60 hours after administration of  $^{109}\text{Cd}(\text{II})$ , retention was about 0.2% and 0.4% of the ingested activities, respectively. As for Pu, the distribution of  $^{109}\text{Cd}$  and  $^{210}\text{Pb}$  between other tissues for the different routes of administration showed that the distribution of Cd and Pb absorbed from the alimentary tract was the same as the distribution after systemic injection. Other data on the behaviour of ingested Cd and Pb are less clear but provide some support for the suggestion of retention on teeth (Nomura, 1980; Cleymaet *et al.*, 1993; Wesenberg, 1983).

(67) For Pu, Renaud-Salis *et al.* (1990) conducted an extensive and detailed study of the absorption of tissue distribution of  $^{238}\text{Pu}$  in rats after chronic administration of Pu(IV) or Pu(VI) bicarbonates in drinking water over an 85 day period. They showed that retention on teeth represented from up to 97% of the total Pu(IV) or Pu(VI) retained in the body, with no effect of administered mass. This deposition on teeth corresponded to a half time of retention to about 2-4 weeks. However, while retention on teeth remained constant at this level during and after chronic ingestion of Pu(IV), the level of retention after administration of Pu(VI) fell by an order of magnitude during the ingestion period. The authors postulated that the presence of different proportions of both monomeric (ionic) and polymeric (hydrolysed and polymerised) forms of Pu may account for the difference in behaviour, relating to the greater stability of Pu(VI) ions at neutral pH. The inconsistent results of Bhattacharyya *et al.* (1985) and Renaud-Salis *et al.* (1990) regarding the behaviour of Pu(IV) or Pu(VI) may relate to differences in ingested mass; masses of  $^{238}\text{Pu}$  in the latter study were from 50 – 1500 times greater than in the former study.

### **3.3.2. Retention in the wall of the small intestine**

(68) In general, there is a lack of evidence on possible retention of radionuclides in the gut wall, other than in newborn animals (see below). However, studies comparing the time-course of the retention and excretion of iron and uranium after oral and intravenous

administration suggest that some retention in the intestinal wall may occur, either during a period of prolonged absorption, or temporarily prior to loss into the gut lumen.

(69) Werner *et al.* (1987) studied absorption and retention of Fe as an example of an essential element. Comparison of whole body retention of  $^{59}\text{Fe}$  in human volunteers after either oral or intravenous administration and whole body retention of a  $^{51}\text{Cr}$  non-absorbable marker after oral administration provided evidence of temporary retention of about 20% of the ingested  $^{59}\text{Fe}$ . The author's interpretation of the results obtained were that, of about 40% total uptake by the absorptive enterocytes of the small intestine, about half passed directly through the lamina propria to the capillary network of the villi. It was suggested that the other half may be incorporated by macrophages lying under the epithelial layer and subsequently transferred to goblet cells in the epithelium and excreted back into the lumen of the intestine. The data presented were consistent with a half-time of intestinal retention of about 3 days. The proposed mechanism is consistent with observations of iron secretion by goblet cells (Refsum and Schreiner, 1980), but there is no direct evidence for the involvement of macrophages. Werner *et al.* (1987) referred to, but did not present, data showing that the extent of temporary uptake of iron within the intestine was dependent on iron status, and suggested that it forms part of the mechanisms operating to regulate iron absorption. They also suggested that similar mechanisms may apply to other essential elements and also to some non-essential elements, particularly those sharing absorptive pathways with essential elements.

(70) Leggett and Harrison (1995) noted that some studies show a prolongation in the pattern of urinary excretion of U after oral intake compared with that typically seen after intravenous injection of uranyl nitrate. For example, Larsen *et al.* (1984) compared urinary excretion of U in the baboon after gavage of  $^{233}\text{U}$  and intravenous injection of  $^{236}\text{U}$ . The results indicated that at three days after administration, less than 50% of the total taken up from the alimentary tract had been excreted in urine compared with about 80% after systemic administration. It was concluded by Leggett and Harrison (1995) that these baboon data and the urinary excretion data from U absorption studies on human volunteers (Hursh *et al.*, 1969; Wrenn *et al.*, 1989; Harduin *et al.*, 1994) are consistent with the assumption that U passes through the intestinal wall with a half-time of 1–3 days and behaves the same as directly injected U once it reaches blood. However, it is also conceivable that U absorption is rapid but that the chemical form reaching blood results in a rate of urinary excretion that is slower than after intravenous injection of uranyl nitrate.

(71) Lang and Raunemaa (1991) have investigated the behaviour of neutron-irradiated, simulated Chernobyl UO<sub>2</sub> particles after intragastric administration to rats. Measurements by whole body autoradiography showed no evidence of absorption of <sup>141</sup>Ce, <sup>144</sup>Ce, <sup>103</sup>Ru, <sup>95</sup>Zr and <sup>95</sup>Nb to other tissues. The results suggested greater intestinal retention of <sup>95</sup>Nb than the other nuclides after one day by about a factor of two (6% of administered activity cf. 2-3%). The authors suggested that <sup>95</sup>Nb may be preferentially released from the particle matrix and concluded that particles were not transported across the intestinal epithelium.

### 3.3.3. Retention in the small intestine of neonates

(72) High levels of retention of radionuclides in the small intestine of neonates have been shown to be associated with high levels of absorption in a number of mammalian species (Sullivan *et al.*, 1984; Fritsch *et al.*, 1988; NEA, 1988). The extent of intestinal retention in different species appears to be related to the extent of pinocytotic activity, although Fritsch *et al.* (1992) also suggested that in primates the prevalence of enterocytes with developed apical canalicular systems and their association with sub-epithelial macrophages may be important factors.

(73) Very high levels of intestinal retention have been observed in rats and pigs, species that exhibit high levels of pinocytotic activity, particularly in the distal small intestine (Sullivan *et al.*, 1987), with substantially lower values reported for retention in guinea pigs and primates. Thus, for example, Harrison and Fritsch (1992) showed that retention of <sup>238</sup>Pu in the small intestine of rats and guinea pigs, at 5 days after administration as the nitrate to 12 day old animals, accounted for about 40% and 0.03% of the ingested activity, respectively. Lataillade *et al.* (1992) measured <sup>238</sup>Pu retention in baboons at four days after ingestion as the citrate as about 1.5% after administration at 50 days of age, falling to about 0.1% and 0.02% after administration at 66 and 129 days of age. Fritsch *et al.* (1992) reported that short-term intestinal retention of Pu in baboons was similar to the observed level of absorption to blood, measured as deposition in other tissues. In guinea pigs, retention has been shown to decrease with a half-time of 6.5 days (Fritsch *et al.*, 1990). In studies with isotopes of thorium, uranium, protactinium, neptunium, americium, curium, and einsteinium in a number of species, Sullivan *et al.* (1987) showed that intestinal retention accompanying increased absorption was a general phenomenon, although there were quantitative differences between elements.

(74) Autoradiographic studies with <sup>238</sup>Pu show that for rats (Figure 3.1), as for pigs, the high levels of intestinal retention are confined mainly to the epithelial cells (Fritsch *et al.*,



1988; Sullivan *et al.*, 1987; Harrison and Stather, 1996). The kinetics of loss have been considered to be a dynamic process involving the normal migration and sloughing of epithelial cells from the tips of villi. In guinea pigs (Figure 3.1), baboons and macaca, lower levels of Pu are retained mainly in macrophages beneath the epithelial layer, towards the tips of villi (Sullivan *et al.* 1987, Fritsch *et al.*, 1988; Harrison and Stather, 1996). Fritsch *et al.* (1992) estimated that 95% of retained Pu in the small intestine of baboons was located in the tips of the villi but that about 5% was in the vicinity of the crypts.



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**Figure 3.1.** Autoradiographs showing the retention of  $^{238}\text{Pu}$  in the villi of the small intestine of newborn rats (A) and guinea pigs (B) after administration as the nitrate (from Harrison and Stather, 1996).

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### 3.4. Radionuclide secretion

(75) Secretions of the gastrointestinal tract are digestive enzymes and mucus produced by the salivary glands, the epithelial cells of the gastrointestinal mucosa, the pancreas, and the liver. Most digestive secretions are formed only in response to the presence of food in the alimentary tract, and the quantity secreted in each segment of the tract is the amount needed for proper digestion. Radionuclides are excreted from the body in intestinal secretions. The resulting faecal excretion, together with urinary excretion are the main routes of radionuclides losses from the body.

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(76) Biliary secretion is known to be a particularly important excretion pathway for a number of elements and then radionuclides and has been incorporated explicitly in the physiologically based models for plutonium, americium, and several other elements (ICRP, 1993). For other elements activity removed from systemic regions is taken to be excreted in either faeces or urine according to a constant ratio (ICRP 1994). Additional information describing secretion into the alimentary tract will be given in forthcoming publications on dose coefficients for workers and members of the public, together with element-specific models, systemic models.

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(77) The rate of transfer of radionuclides into the alimentary tract in specific secretions other than bile is generally difficult to quantify. However, such transfers have been postulated for a number of elements on the basis that endogenous faecal excretion cannot be accounted for entirely by the rate of loss of activity via the liver. In the ICRP's physiologically based models for plutonium and other elements, endogenous faecal excretion is accounted for, in part, by a transfer from blood to the upper large intestine that represents collective non-biliary secretion of activity into the alimentary tract. (ICRP, 1993 and 1995)

(78) Some elements with apparently low rates of biliary secretion, including barium and radium, show high total rates of excretion into the gastrointestinal tract as indicated by a rapid loss from the systemic pool and high rate of faecal excretion. In the physiologically based models for barium and radium given in ICRP *Publication 67* (1993), losses from the systemic circulation are accounted for largely as a direct transfer from blood to the upper large intestine representing unspecified secretions.

(79) Transfer from blood to the upper large intestine, which represents most of the right colon, have been used in ICRP models to account for gastrointestinal secretions for which there is presumably no reabsorption to blood. This is in contrast to assumptions regarding biliary secretion of radionuclides; in this case, the radionuclide is assigned to the contents of the small intestine and thus is available for reabsorption to blood at the same rate as assumed for the initial input of the radionuclide into the small intestine.

(80) Transfer of systemic activity through secretions into the alimentary tract has been estimated in considerable detail for the alkali metals potassium, rubidium, and caesium (Leggett and Williams, 1986, 1988; Leggett *et al.*, 2003). Estimates for caesium are summarized in Table 3.2. The estimates are given in terms of transfer coefficients, defined as fractional transfers of the steady-state content of a donor compartment per unit time. For example, if plasma contained 0.1 Bq of caesium under steady-state conditions, then a transfer coefficient of  $1.935 \text{ d}^{-1}$  from plasma to the oral cavity contents in saliva indicates a daily transfer of  $1.935 \text{ d}^{-1} \times 0.1 \text{ Bq} = 0.1935 \text{ Bq d}^{-1}$ . For all secretions other than bile, the donor compartment is assumed in these calculations to be plasma, even though there may be a brief residence of caesium in intermediate tissues (e.g., salivary glands in the case of transfer of caesium from plasma to saliva). For bile, the donor compartment is assumed to be the liver.

**Table 3.2.** Estimated rates of secretion of caesium into contents of the alimentary tract (Leggett *et al.*, 2003).

Compartment receiving Cs	Source	Substance	Daily flow of substance (g)	Cs transfer coefficient (d <sup>-1</sup> )
Oral cavity contents	Plasma	Saliva	1200	1.935
Stomach contents	Plasma	Gastric juices	2000	2.581
Small intestine contents	Plasma	Secretions	2000	0.645
	Plasma	Pancreatic juices	1200	0.387
	Liver	Bile	700	0.116
	Plasma	Brunner's gland secretions	50	0.016
Right colon contents	Plasma	Secretions	60	0.02

5

### 3.5. Examples used in this report

(81) This section summarises information on selected radionuclides, used later in the report to illustrate the application of the biokinetic model when different types of information are available. These examples are used to show the effect of different assumptions on dose estimates, and to compare doses calculated using the new model and the *Publication 30* model. The radionuclides are:

- <sup>90</sup>Sr, <sup>106</sup>Ru and <sup>239</sup>Pu, to illustrate the *default case* in which information is available only on total absorption, assumed to be from the SI, at different ages;
- <sup>115</sup>Cd to illustrate the effect of *retention on teeth* on dose to the oral mucosa;
- <sup>55</sup>Fe and <sup>235</sup>U to illustrate the effect of *retention in the SI wall* in adults
- <sup>239</sup>Pu to illustrate the effect of *retention in the SI wall* in neonates

(82) As discussed in 3.1, all estimates of biokinetic parameter values are subject to uncertainties, according to the quality of the available data and the extent of reliance on animal data. In the case of absorption of ingested radionuclides to blood, Harrison *et al.* (2001) have published an assessment of uncertainties in absorption for selected elements and considered the effect on uncertainties in dose estimates. The approach adopted is discussed in more detail in Chapter 8 and by Leggett *et al.* (1998, 2001). The level of confidence in individual absorption values was estimated in terms of lower and upper bounds, A and B, such that there is judged to be roughly a 90% probability that the true central value is no less than A and no greater than B. The uncertainty ranges given by Harrison *et al.* (2001) are included below, for the standard case examples of Sr, Ru and Pu, and the effect of these ranges on uncertainties in dose estimates is discussed in Chapter 9.

### 3.5.1. Default case – information available on total absorption and excretion via the alimentary tract

#### 5 Strontium

(83) Due to the presence of Sr isotopes in fall-out material and its long-term retention in bone as a Ca analogue, the metabolism of Sr has been the subject of a number of human volunteer studies. Similar absorption values were obtained from studies in which inorganic forms of radiostrontium were administered orally in solution (Spencer *et al.*, 1960; Suguri *et al.*, 1963; Shimmins *et al.*, 1967) and from experiments where known quantities of radiostrontium incorporated in food were ingested (Fujita, 1966; Carr, 1967). In each case, mean values were between 0.1 and 0.3, averaging about 0.2. LeRoy *et al.* (1966) measured the absorption of Sr from real and simulated fall-out and after administration of <sup>85</sup>Sr chloride. Ten volunteers ingested samples of local fallout, largely comprising siliceous soil constituents (40-700 μm particles). The estimated absorption averaged 0.03 with a range of 0 - 0.09. For simulated fallout prepared as glass microspheres (30-40 μm), the estimated fractional absorption was 0.16 (range 0.06 - 0.25), with a value of 0.17 (0.08 - 0.34) after administration as the chloride.

(84) A number of factors have been found to increase absorption, including fasting and low dietary levels of Ca, Mg and P; milk diets and vitamin D may also increase absorption. Spencer *et al.* (1972) showed that overnight fasting increased absorption from about 0.25 to 0.55. McAughey *et al.* (1994) also reported a fractional absorption of 0.55 (0.38 - 0.72) for 4 volunteers after an overnight fast compared with 0.11 in a single volunteer ingesting Sr after breakfast. A decrease in Ca content of the diet from 30 - 40 to 0 - 10 mg d<sup>-1</sup> kg<sup>-1</sup> increased Sr absorption from an average of 0.2 to 0.4 (Shimmins *et al.*, 1967).

(85) Results from animal studies are generally similar (Coughtrey and Thorne, 1983) to those from volunteer studies. Results for the absorption of Sr administered as the titanate (SrTiO<sub>3</sub>) to rats show low levels of absorption of about 0.01 (McClellan and Bustad, 1964).

(86) Results obtained by Widdowson *et al.* (1960) suggested that absorption of strontium in 7 day old infants fed with cows' milk was greater than 0.7. Bedford *et al.* (1960) reported that absorption in 5-15-year-old children was the same as in adults. Taylor (1962) obtained absorption values of  $0.95 \pm 0.004$ . (SE, n=31) for 14-18 day old rats and  $0.74 \pm 0.024$  (SE, n=5) for 22 day old animals.

(87) The fractional absorption, values used in *Publication 67* (ICRP, 1993) for ingestion of Sr by members of the public were 0.3 for adults, 0.6 for 3 month old infants and an intermediate value of 0.4 for children. Harrison et al. (2001) proposed confidence intervals of 0.1 (A) to 0.4 (B) for adults, 0.1 – 0.5 for 10 year old children and 0.15 – 0.75 for 3 month old infants. For the purposes of illustration, these values are applied in this report to absorption from the small intestine, with no delay in transfer to blood; that is, no retention in the SI wall.

(88) The excretion of Sr via the alimentary tract is modelled explicitly by a systemic biokinetic model for the alkaline earth elements, developed by Leggett *et al.* (1982, 1992) and adopted by ICRP (1993). Data for human subjects receiving radiostrontium by intravenous injection indicate that secretions into the alimentary tract account for 20-25% of endogenous loss of strontium on average (Leggett, 1992). Data from animal studies indicate that biliary secretion accounts for only a small portion of the total secretion of strontium or its physiological analogue, calcium, into the alimentary tract (Lengemann, 1963; Wiseman, 1964). In the ICRP's biokinetic model for strontium (ICRP, 1993), secretion of systemic strontium into the contents of the alimentary tract is represented, for simplicity, as a transfer from blood plasma to the contents of the upper large intestine (see Chapter 5).

### **Ruthenium**

(89) Measurements of the absorption of Ru in male volunteers after ingestion of chloro-complexes of Ru(III) and Ru(IV) gave values of about 0.01 and a similar value was obtained for absorption from contaminated clams (Yamagata *et al.*, 1969); values for nitrosyl Ru(III) were about three times greater.

(90) Results from a number of studies of the absorption of  $^{106}\text{Ru}$  administered as the chloride to mice, rats, rabbits, guinea pigs, chickens, cats, dogs and monkeys, including values for fasted animals, were in the range of 0.03 - 0.06 (Burykina, 1962; Thompson *et al.*, 1958; Furchner *et al.*, 1971; Bruce and Carr, 1961; Stara *et al.*, 1971). Values for  $^{106}\text{Ru}$  administered as the oxide to rats and rabbits were in the range of 0.003 - 0.03. Bruce and Carr (1961, 1963) measured the absorption of Ru administered in the form of nitrosyl derivatives. Both nitrato and nitro- complexes of nitrosyl Ru are formed during dissolution in nitric acid in the reprocessing or U fuels. The nitro-complexes are probably more important because they are more resistant to hydrolysis in neutral and alkaline conditions. Results obtained for the nitrato-nitrosyl complex in rats and rabbits were 0.06 and 0.13, respectively. A value of 0.04 was reported for the absorption of Ru administered to rats as a nitro-nitrosyl.

(91) Few data are available on the absorption of ruthenium in young animals. Matsusaka *et al.* (1969) reported absorption of about 0.07 in newborn mice given  $^{106}\text{Ru}$  as the chloro-complex in dilute HCl compared with less than 0.01 in 21 day-old and adult animals. Inaba *et al.* (1984) measured the absorption of  $^{103}\text{Ru}$  administered as the chloride as 0.08 in 5 day-old rats and 0.05 in adults.

(92) The ICRP (1989)  $f_1$  values for Ru ingested by members of the public were 0.05 for adults and 0.1 for 3 month-old infants. The value for adults was also applied to children from one year of age. Harrison *et al.* (2001) proposed confidence intervals of 0.005 (A) to 0.1 (B) for adults, 0.005 to 0.15 for 10 year old children and 0.005 to 0.2 for 3 month old infants. For the purposes of illustration, these values are applied in this report to absorption from the small intestine, with no delay in transfer to blood; that is, no retention in the SI wall.

(93) Data on laboratory animals indicate that secretion of ruthenium into the alimentary tract accounts for 20-50% of total excretion of systemic ruthenium (Thompson *et al.*, 1958; Runkle *et al.*, 1980; Snipes, 1981). The main sites of secretion of ruthenium have not been determined. In the ICRP's current systemic biokinetic model for Ru (ICRP, 1989, 1993), secretion into the alimentary tract is represented as a transfer from blood to the contents of the upper large intestine.

### **Plutonium**

(94) Three studies of the absorption of Pu in humans have been reported. In the first, concentrations of fall-out Pu in autopsy samples of bone, liver and lung from five male residents of Lapland were compared with corresponding concentrations in tissues of persons who had lived in southern Finland (Mussalo-Rauhamaa *et al.*, 1984). The dietary intake of Pu by the Lapps was derived mainly from reindeer meat, especially liver, and was about 10 - 15 times greater than that in southern Finns. The authors used the data to calculate an  $f_1$  of  $8 \times 10^{-4}$ , a value which they recognized to be based on insufficient sample analyses and uncertain assumptions concerning the exposure of the two groups to inhaled Pu. Hunt *et al.* (1986, 1990) have carried out two studies of the absorption of  $^{239/240}\text{Pu}$  and  $^{241}\text{Am}$  by eight volunteers, six men and two women, who consumed winkles collected on the Cumbrian coast near to the Sellafield nuclear-fuel reprocessing plant. The reported  $f_1$  values for Pu ranged from  $2 \times 10^{-5}$  to  $5 \times 10^{-4}$ , with a median of  $1 \times 10^{-4}$  and a mean of  $2 \times 10^{-4}$  ( $\pm 1$  SD), suggesting 90% confidence limits of about  $8 \times 10^{-5}$  to  $4 \times 10^{-4}$ . Ham and Harrison (2000) reported measurements of the absorption of  $^{244}\text{Pu}$  administered in citrate solution to five male volunteers. The  $f_1$  values obtained, based on comparisons or urinary excretion of  $^{244}\text{Pu}$  after oral and intravenous

administration, were  $1.3 \times 10^{-4}$ ,  $2.4 \times 10^{-4}$ ,  $7.8 \times 10^{-4}$ ,  $8.9 \times 10^{-4}$  and  $1.2 \times 10^{-3}$ , with a mean value of  $6 \times 10^{-4}$ .

(95) Animal data on the absorption of Pu in species including rodents, pigs, dogs and primates has been extensively reviewed (ICRP, 1986; Harrison, 1991). The chemical form ingested is an important factor affecting absorption. The lowest values obtained are for the oxide, ranging from about  $2 \times 10^{-4}$  in the rat (Sullivan, 1980) to about  $3 \times 10^{-8}$  in the pig (Smith, 1970). These large differences are probably a reflection of the solubility of the oxide preparation, which is affected by the method of production (Mewhinney *et al.*, 1976), the proportion of small particles present (Stather *et al.*, 1975) and the specific activity of the isotope (Fleischer and Raabe, 1977). Mixed Pu-sodium oxides contain a higher proportion of very small particles (about 1 nm diameter) and a greater soluble fraction than the pure oxides (Stather *et al.*, 1975) and suspensions of  $^{238}\text{Pu}$  oxide are more prone than those of  $^{239}\text{Pu}$  oxide ( $6.27 \times 10^8$  and  $2.25 \times 10^6$  kBq  $\text{g}^{-1}$ , respectively) to radiolytic breakdown to small particles (Fleischer and Raabe, 1977). Comparisons of the behaviour of inhaled Pu oxide and mixed U/Pu oxides in rats and baboons showed that although solubility in the lung was low in each case, transfer of Pu to liver and bone was about two to three times greater for the mixed oxide (Lataillade *et al.*, 1995).

(96) The range in values of uptake for Pu administered to animals as the nitrate, chloride or bicarbonate is not as large as for the oxide. In general, the results are between  $10^{-4}$  and  $10^{-5}$ . Fasting has been shown to increase absorption by up to an order of magnitude. For example, absorption in mice fasted for 8 hours before and 8 hours after the administration of  $^{236}\text{Pu}$  bicarbonate was about  $10^{-3}$  compared with  $2 \times 10^{-4}$  in fed animals (Larsen *et al.*, 1981). High values of  $10^{-3}$  to  $2 \times 10^{-3}$  have been reported for uptake of  $^{237}\text{Pu}$  nitrate given as a single dose to rats and mice (Sullivan, 1981; Sullivan *et al.*, 1982). These results were taken as evidence of increased absorption at low masses. However, in experiments to determine the effect of chronic ingestion at low concentrations, a value of  $3 \times 10^{-5}$  was obtained for the nitrate in rats (Weeks *et al.*, 1956) and  $10^{-5}$  for the bicarbonate in hamsters (Stather *et al.*, 1981). It would appear that in general ingested mass and valence are not important factors affecting absorption. However, at high masses of Pu(V), absorption may be increased by an order of magnitude as demonstrated by Métivier *et al.* (1985) in studies using baboons.

(97) The absorption of Pu administered to animals as organic complexes or incorporated into food materials is generally greater than for inorganic forms (ICRP, 1986). For example, most of the reported values for Pu citrate are in the range  $6 \times 10^{-5}$  to  $6 \times 10^{-4}$  compared with the range of  $10^{-5}$  to  $10^{-4}$  for the nitrate. An organic form of importance in reprocessing is Pu-



tributylphosphate for which Métivier *et al.* (1983) measured absorption in rats as about  $10^{-4}$  to  $2 \times 10^{-4}$ .

5 (98) There is strong evidence from animal experiments to conclude that Pu absorption from the gastrointestinal tract may be increased by at least an order of magnitude in the human neonate (see 3.2), but that any increased absorption would probably decrease rapidly during the first few days or weeks of life (ICRP, 1986; Harrison and Fritsch, 1992; Fritsch *et al.*, 1992). The age by which absorption of Pu might decrease to adult levels is not known, but animal studies indicate that adult values may be reached by about the time of weaning.

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(99) ICRP (1993)  $f_1$  values for Pu ingested by members of the public are  $5 \times 10^{-4}$  for adults and  $5 \times 10^{-3}$  for 3 month old infants. The adult value is also applied to children from one year of age. Harrison *et al.* (2001) proposed confidence intervals of  $1 \times 10^{-4}$  (A) -  $1 \times 10^{-3}$  (B) for adults and children, and  $1 \times 10^{-4}$  to  $1 \times 10^{-2}$  for 3-month-old infants. For the purposes of  
15 illustration, these values are applied in this report to absorption from the small intestine, with no delay in transfer to blood; that is, no retention the SI wall.

(100) The excretion of Pu via the alimentary tract is explicitly modelled by the systemic biokinetic model for the actinide elements, developed by Leggett and colleagues (Leggett and  
20 Eckerman, 1984; Leggett, 1985, 1992) and adopted by ICRP (1993). On the basis of data on human subjects injected with tracer amounts of Pu (Langham *et al.*, 1950; Newton *et al.*, 1998) and measurements on Pu workers at times remote from intake, it has been estimated that faecal excretion typically accounts for 25-40% of total excretion of systemic Pu over a period of months or years after uptake of Pu to blood (Leggett, 1985, 2003; ICRP, 1993; Khokhryakov *et al.*,  
25 *et al.*, 2004). Data on rodents indicate that biliary secretion of Pu is an important source of endogenous faecal excretion of Pu but is not the only source (Ballou *et al.*, 1972). Kinetic analysis of human injection data (Langham *et al.*, 1950; Newton *et al.*, 1998) indicate that endogenous faecal excretion of Pu can be represented reasonably well as the sum of two feeds from systemic pools. One of these feeds roughly parallels the activity of Pu in blood while the second lags behind the blood content. In the ICRP's systemic biokinetic models for  
30 Pu (ICRP, 1993), these two feeds are assumed to represent secretion from blood directly into the intestinal contents (assumed for simplicity to occur in the upper large intestine) and transfer from the liver to the contents of the small intestine in bile, respectively. The model predicts that these two sources contribute nearly equally to endogenous faecal excretion of Pu over a period  
35 of months or years after uptake of Pu to blood.

### 3.5.2. Retention on teeth

#### Cadmium

5 (101) As discussed in 3.3, Bhattacharyya *et al.* (1985) reported detailed findings of the retention of  $^{109}\text{Cd}$ ,  $^{210}\text{Pb}$  and  $^{236}\text{Pu}$  on the teeth of mice after ingestion in drinking water. In each case, comparisons were made between the tissue distribution observed in these mice and in corresponding groups given the radionuclides either by gavage into the stomach or by intravenous injection. The results obtained showed clear evidence of retention in the mouth,  
10 and on teeth in particular. The example of Cd is pursued here because  $^{115}\text{Cd}$  retained on teeth will deliver dose to the target cells within the oral mucosa, assumed to be the basal layer of the squamous epithelium (see Chapters 2, 4 and 7).

(102) Bhattacharyya *et al.* (1985) measured retention of about 0.2% of ingested  $^{109}\text{Cd}(\text{II})$  on  
15 teeth at 60 hours after administration. No information is available from this study on the duration of retention of  $^{109}\text{Cd}$  or the other nuclides on teeth. Results obtained by Renauld-Salis *et al.* (1990) for the retention of  $^{238}\text{Pu}$  on rats' teeth, after administration as Pu(VI) in drinking water, can be taken to suggest half-times of retention of 2 – 4 weeks, although results for Pu(IV) suggested longer retention. However, it seems unlikely that retention times  
20 in rodents would apply to humans, given recognised differences in oral hygiene. For the purposes of illustration in this report, it is assumed that 0.2% of ingested  $^{115}\text{Cd}$  is retained on teeth with an arbitrary half-time of retention of 1 week.

(103) Cadmium was not considered among the 31 elements for which radionuclide dose  
25 coefficients have been given for members of the public. Ingestion of isotopes of Cd by workers was considered in *Publication 30* (ICRP 1980). The  $f_1$  values adopted for ingestion of inorganic forms of Cd was 0.05, on the basis of measurements of absorption in mice, rats and goats. Greater values of 0.06 – 0.25 were reported by Rahola *et al.* (1972) for absorption of Cd by volunteers given Cd in calves' liver. The effects of assumptions regarding absorption  
30 are not pursued in this report; the illustrative calculations in Chapters 8 and 9 assume absorption of 0.05 from the small intestine.

### 3.5.3. Retention in the SI wall

35 **Iron**

(104) As discussed in 3.3, Werner *et al.* (1987) studied absorption and retention of Fe in human volunteers, as an example of an essential element. Comparison of whole body retention of  $^{59}\text{Fe}$  after either oral or intravenous administration and whole body retention of a  $^{51}\text{Cr}$  non-absorbable marker after oral administration provided evidence of temporary retention of about 20% of the ingested  $^{59}\text{Fe}$ . The authors interpretation of the results obtained were that, of about 40% total uptake by the absorptive enterocytes of the small intestine, about half passed directly through the lamina propria to the capillary network of the villi. It was suggested that the other half may be incorporated by macrophages lying under the epithelial layer and subsequently transferred to goblet cells in the epithelium and excreted back into the lumen of the intestine. The data presented were consistent with a half-time of intestinal retention of about 3 days.

(105) The fractional absorption of 0.2 obtained by Werner *et al.* (1987) compares with a value of 0.1 used by ICRP (1995a) for adult members of the public. However, as discussed in *Publication 69* (ICRP 1995a), iron absorption can vary substantially depending on a number of factors, including the amount of Fe in the diet, the chemical form ingested and the nature of other dietary constituents, and the Fe status of the individual. Iron deficiency is associated with increased absorption; increases during pregnancy and lactation are discussed in 3.2. In normal adults, values of 0.01 – 0.07 have been reported for Fe absorption from vegetable foodstuffs, while values of 0.1 – 0.2 are more typical of Fe absorption from meat and fish. Werner *et al.* (1987) did not give details of Fe status and chemical form administered but it is likely that the Fe was administered after a period of fasting, a standard procedure adopted by these authors.

(106) For illustrative purposes in this report (see chapter 8), the parameter values of Werner *et al.* (1987) are used without change. That is, it is assumed that total uptake into the SI wall is 0.4 of ingested  $^{55}\text{Fe}$ , that 0.2 is absorbed to blood and that the remaining 0.2 is returned from the SI wall into the gut lumen. It is assumed that this retention is confined to the villi.

### 30 **Uranium**

(107) As discussed in 3.3, Leggett and Harrison (1995) noted that the baboon data of Larsen *et al.* (1984) and urinary excretion data from U absorption studies on human volunteers (Hursh *et al.*, 1969; Wrenn *et al.*, 1989; Harduin *et al.*, 1994) are consistent with the assumption that U passes through the intestinal wall with a half-time of 1 – 3 days and behaves the same as directly injected U once it reaches blood.

(108) Information on the absorption of U is available from studies involving direct measurements of absorption in human volunteers, dietary balance data for several different human groups, and measurements of absorption in a variety of laboratory animals (Harrison and Leggett, 1995; ICRP, 1995a). On the basis of these data, an  $f_1$  value of 0.02 was used in  
 5 *Publication 69* (ICRP, 1995a) for adult members of the public. Harrison *et al.* (2001) proposed confidence intervals of 0.006 (A) - 0.03 (B). For illustrative purposes in this report, SI absorption of 0.02 is assumed and the effect of slow passage through the SI wall with a half-time of 2 days is examined. It is assumed that the temporary retention in the SI wall is confined to the villi.

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### **Plutonium**

(109) As discussed in 3.3, studies using different mammalian species have shown retention of radionuclides in the wall of the small intestine of newborn animals, associated with increased  
 15 absorption during this period of development. Species differences in the extent and location of retention relate to differences in the acquisition of passive immunity (Harrison and Fritsch, 1992; Fritsch *et al.*, 1992). Retention in humans is likely to resemble that observed in guinea pigs and primates – that is, relatively low levels of retention, mainly within villi, beneath the epithelial layer – rather than rats and pigs, with high levels of retention in the epithelial  
 20 enterocytes of the villi.

(110) Lataillade *et al.* (1992) measured retention of  $^{238}\text{Pu}$  retention in baboons at four days after ingestion as the citrate as about 1.5% after administration at 50 days of age, with lower values at greater ages (see 3.3). Similarly, Fritsch *et al.* (1992) reported that short-term  
 25 intestinal retention of Pu in baboons was similar to the observed level of absorption to blood tissues. From autoradiographic studies they estimated that 95% of retained Pu in the small intestine of baboons was located in the tips of the villi but that about 5% was in the vicinity of the crypts. The data for primates do not provide reliable information on the time-course of retention but studies using guinea pigs, with a similar pattern or retention in sub-epithelial  
 30 macrophages, have shown a decrease in retention with a reported half-time of 6.5 days (Fritsch *et al.*, 1990).

(111) For illustrative purposes in this report, it is assumed that uptake into the SI wall in human infants corresponds to 0.02 of ingested  $^{239}\text{Pu}$ , that absorption to blood is  $5 \times 10^{-3}$  (as  
 35 in ICRP, 1989) and that the half-time of retention in the wall is 1 week. It is further assumed that 95% of the retained  $^{239}\text{Pu}$  is located in the villi and that 5% is located in the lamina propria surrounding the crypts (see Chapters 2 and 7).

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## 4. RADIATION EFFECTS

### 4.1. Introduction

5 (94) The risk of cancer is the main concern following low dose irradiation of the  
alimentary tract as a result of environmental or occupational ingestion of  
radionuclides. The main purposes of this chapter are to: (1) define the location of  
target cells for cancer induction in the different regions of the gut, (2) explain the  
10 approaches taken to dose averaging within the regions, and (3) provide a brief  
summary of sources of information on radiation risks. In addition to the risk of  
cancer, some consideration is given to risks of acute and late gross tissue damages  
at higher doses, for which the target cells may include some differentiated cell types  
as well as stem cells. The epithelial lining of the alimentary tract in which cancers  
15 arise exhibits a number of specialised forms relating to functional requirements in the  
different regions. The main types are stratified squamous epithelium of the mouth  
and oesophagus and a single cell layer of epithelium, originating in crypts, in the  
stomach, and small and large intestines (see Chapter 2). Stem cell location and  
tissue organisation differ between regions.

20 (113) In the HATM developed in this report, doses are calculated separately for the  
mouth, oesophagus, stomach, small intestine, right colon, left colon and  
rectosigmoid colon. Within these regions, average dose throughout the target layer  
is considered, assuming uniform distribution of target cells in relation to the  
radionuclide source within the lumen or retained in the wall. Because risk estimates  
25 are given for the colon as a whole, doses from the right, left and rectosigmoid colon  
are summed as a mass weighted average. The rectum is considered as part of the  
rectosigmoid colon rather than separately, largely because of difficulties in  
specifying radionuclide residence times.

30 (114) Information on risks of radiation-induced cancers of the alimentary tract are  
derived from studies of populations exposed to external radiation, including the  
survivors of the atomic bombings in Japan (UNSCEAR, 2000). UNSCEAR reviewed  
the largely negative or equivocal results on human alimentary tract cancer induction  
by internal radionuclide exposure. Most information on effects of ingested  
35 radionuclides is for high dose acute effects in animals. For cancer induction by

ingested radionuclides, very limited qualitative information from animal studies is available.

## 4.2. Target cells

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(115) Cancers are generally considered to originate from stem cells, the cells which possess unlimited reproductive capacity. These are transformed by carcinogenic agents so that their differentiation patterns are altered in such a way that cell renewal predominates over differentiation, leading to growth of an abnormal cell population.

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Stem cells in stratified squamous epithelium, as in the lining of the mouth and the tongue, and the oesophagus, are taken to be located in the basal cell layer, adjacent to the basement membrane, as assumed for skin (ICRP, 1992). In the stomach, stem cells are thought to be located towards the upper regions of the gastric pits, renewing the epithelial layer by both upward flow of daughter cells towards the luminal surface of the stomach and downward flow into the gastric glands (Karam *et al.* 2003; Modlin *et al.* 2003).

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(116) Evidence for stem cell position in the small intestine was obtained from studies using short range electrons from a promethium-147 plaque to irradiate crypts in the mouse small intestine from the serosal surface towards the crypt base (Hendry *et al.* 1989). Efficient crypt sterilisation was achieved with doses calculated to cell positions 4-5 from the base, the stem-cell position above the Paneth cells. Dividing transit cells irradiated with much lower doses above the stem cell zone did not appear to contribute to repopulation of the damaged crypts. This lack of repopulation

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potential from daughter cells is in contrast to the positive contribution suggested from analyses of dose-response data obtained in other studies using high doses of penetrating irradiation in both small (Hendry *et al.*, 1992; Roberts *et al.*, 1995) and large (Cai *et al.*, 1997) intestine. It was considered possible that daughter transit cells may be recruited into the stem cell population when there is sufficient cell

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damage and death in the crypt to allow cell migration against the normal direction of cell flow, thus allowing some of these mutated transit cells to reach the stem-cell zone. This situation would be unlikely to occur in carcinogenesis after low doses when there is very little induced cell death. In a subsequent analysis, a different hypothesis was proposed, in which a secondary mechanism of injury either directly

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from damage to stem cells or indirectly from injured stromal cells, could explain the dose-response data without invoking down-migration of transit cells in the crypt (Roberts *et al.* 2003). On the basis of the above possibilities, it is considered here

that the initial stem cell population is the most likely target-cell population for carcinogenesis. A wider target cell population might be involved when considering acute effects.

5 (117) In the colon, the site where most intestinal cancers arise, the stem cells are situated at the very base of the crypts. This has been deduced from a variety of cell kinetic, mutational and regeneration studies in mouse models (Potten, 1995). Their position in man is likely to be qualitatively similar. The number of stem cells per colonic crypt in mice has been estimated to be in the range 1-8, and as colonic crypts  
10 in man are around 6 times as large in all dimensions as in mice the number of stem cells per crypt may be greater in man.

(118) It has been suggested that tumours in the human colon may originate in cells on the intercryptal plate rather than, or in addition to, stem cells at the base of the  
15 crypt (Shih *et al.*, 2001). Thus, this study indicated that most early neoplastic lesions of the colon contain dysplastic cells only at the orifices of crypts and on the luminal surface between crypts. Analysis showed loss of the *APC* gene and high expression of  $\beta$ -catenin in such dysplastic cells but not in cells with normal appearance within the crypts. Mutations in the *APC* gene are the earliest genetic alterations in the genesis  
20 of colorectal tumours and appear to be required to initiate clonal evolution, involving over-expression of  $\beta$ -catenin (Fodde *et al.*, 2001). This suggestion of target cells on the luminal surface is contentious. In normal tissue, differentiated epithelial cells on the intercryptal surface would have a very limited life-span of a few days, destined to be lost into the intestinal lumen in the normal process of cell renewal. To develop  
25 into a tumour, these dysplastic cells would need to escape this process to allow time for progression to malignancy, involving a number of mutational events (Vogelstein *et al.*, 1988; Goyette *et al.*, 1992). Although this scenario seems highly unlikely, the possibility cannot be excluded that daughter cells of the stem cells, situated at higher cell positions in the crypt, are also target cells, perhaps to a lesser degree, as  
30 considered above for the small intestine. For the purposes of this report, doses are calculated to the estimated position of the stem cells. However, in considering uncertainties in dose estimates, the possibility that cells higher in the crypts may also be targets has been addressed, including the possibility of target cells on the luminal surface(see chapter 8).

35 (119) Target cells for acute tissue damage may include a number of different cell types, perhaps relating to damage to blood vessels and other structures in the

mucosa and submucosa (see 4.4 and Chapter 2). Thus, in addition to epithelial cells, targets may include vascular endothelial cells, mesenchymal fibroblasts and other cell types. However, as discussed below (4.4), studies of the acute effects of ingested radionuclides in dogs suggest that observed effects can be related to dose delivered at the depth of the crypts in the large intestine (Cross *et al.*, 1978; Sullivan *et al.*, 1978). For the purposes of this report, the targets for all effects are taken to be the epithelial stem cells. The possibility that a wider target is involved in the case of acute damage is addressed in Chapter 8, considering doses to the large intestine because this region has the slowest transit time for its contents and hence the greatest potential doses.

### 4.3. Radiation-induced cancers in humans

(120) Evidence that ionising radiation causes cancer of the gut in humans comes from epidemiological studies of survivors of the atomic bombings in Japan (Ron *et al.*, 1994; Thompson *et al.*, 1994), patients given radiotherapy for cervical cancer (Boice *et al.*, 1985; 1988), and patients treated with radiation for benign conditions such as ankylosing spondylitis (Darby *et al.*, 1987), gynaecological disorders (Inskip *et al.*, 1990; Darby *et al.*, 1994), and peptic ulcer (Griem *et al.*, 1994). The studies of the atomic bomb survivors have followed subjects prospectively for nearly 40 years at the level of mortality (Shimizu *et al.*, 1990; Davis *et al.*, 1989) as well as incidence (Thompson *et al.*, 1994). The average whole-body dose was relatively low, about 0.23 Gy, but the distribution of doses ranged up to 4 Gy, permitting dose-response evaluations. This is the single most informative study on radiation risks, including exposures of both men and women, and children and adults. Its major limitation is that risks apply to acute brief radiation exposures and not directly to the chronic or periodic exposures experienced in daily life from environmental, occupational or medical sources.

(121) Only very limited information is available on cancer induction in the alimentary tract by ingested radionuclides. Tumours induced by internal irradiation have been observed in the gastrointestinal tract of rodents after administration of  $^{137}\text{Cs}$ ,  $^{95}\text{Nb}$  and  $^{144}\text{Ce}$ ,  $^{90}\text{Y}$ , and  $^{106}\text{Ru}$  (Casarett, 1973). Intestinal polyps in dogs and rats fed  $^{210}\text{Po}$  or  $^{144}\text{Ce}$  were also reported, mostly occurring in the large intestine with a tendency to malignant change and showing different latencies in the two species (Lebedeva 1973). UNSCEAR (2000) reviewed the mainly negative information from human follow-up studies, as summarised below.

### **Mouth**

5 (122) The oral cavity is not among the cancer sites for which the studies of the atomic bomb survivors have provided evidence of radiation sensitivity. The primary sites of most spontaneously arising tumours in western countries are the lips and tongue, although cancers of the buccal mucosa, floor of the mouth and tonsils are also seen (del Ragato *et al.*, 1985). More than 90% of oral cavity tumours are squamous cell carcinoma.

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### **Oesophagus**

15 (123) Only one of the four population studies evaluating radiation-induced oesophageal cancer reported a significant excess. Studies of cervical cancer patients and Massachusetts tuberculosis patients were negative. The A-bomb series found modest increases that were not significant. Ankylosing spondylitis patients received the highest estimated dose, 4 Gy, and were at a significantly increased risk of mortality in comparison with the general population. The relative risk at 1 Gy was estimated as 1.3 (Darby *et al.*, 1987) and absolute risk as 0.21 per  $10^4$  PY Gy<sup>-1</sup>.

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25 (124) Information on the distribution of cancers arising in the oesophagus suggests that the greatest proportions are seen in the distal region. However, ingested radionuclides have been assumed to deliver dose uniformly during their transit through the oesophagus. Dose has been averaged for the oesophagus assuming uniform distribution of target cells throughout the basal layer of the stratified squamous epithelium.

### **Stomach**

30 (125) Stomach cancer has accounted for 16% of the total excess cancer attributable to radiation in the atomic bomb survivors (Thompson *et al.*, 1994). Significant excess has occurred in 2 other series, cervical cancer patients and peptic ulcer patients. The relative risk of fatal stomach cancer at 1 Gy was estimated from the A-bomb studies as 1.2 and absolute risk as 2 per  $10^4$  PY Gy<sup>-1</sup>. UNSCEAR (2000)  
35 reviewed data for stomach cancer in patients treated with <sup>131</sup>I for hyperthyroidism. A significant excess in terms of incidence and mortality was reported in a Swedish study, with risks consistent with the estimate from the A-bomb study. However,



UNSCEAR (2000) cautioned that because of the small numbers of stomach cancers and uncertainties in the risk estimate for  $^{131}\text{I}$  exposure, it was not possible to draw conclusions about the relative effect of acute external and protracted internal radiation exposures.

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(126) Stomach cancer has been shown to be significantly increased in radon exposed cohorts of underground miners (Darby *et al.* 1995). However, there was no trend in stomach cancer mortality with the low levels of cumulative radon exposure to the stomach, and excesses of stomach cancer have been reported for other groups of miners, suggesting that factors other than radon exposure were responsible in each case. Female radium dial painters starting work after 1930 showed an increase in stomach cancer mortality (Stebbing *et al.*, 1984), but those starting work before 1930, with generally higher radium exposure, did not show an increased risk. These data do not provide convincing evidence of stomach cancer induction by alpha-emitting radionuclides.

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(127) In general, large regional differences in dose between different parts of the stomach would not be expected and it is reasonable to calculate average dose. The target is taken to be the stem cell zone, treated as a continuous uniform layer in the stomach wall (see Chapter 7).

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### ***Small intestine***

(128) The very low incidence of naturally occurring tumours and the low susceptibility for induction of cancer of the small intestine by radiation in both humans and experimental animals remain unexplained, although hypotheses based on apoptosis which deletes mutated stem cells have been proposed (Potten *et al.*, 1992). These suggest that radiation-induced TP53-dependent apoptosis in the stem cell zone in the small intestine prevents the propagation of mutated dividing progenitor cells. This is consistent with the increased frequency of cancer in *Tp53*-null mice compared to wild-type mice. In the large intestine, *Tp53* is not expressed in the stem cell zone, and *bcl-2* expression promotes cell survival and allows the development of mutated progenitor cells (Merritt *et al.*, 1995).

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(129) Dose to the small intestine has been calculated as an average throughout the length of the tube on the assumption of a constant uniform rate of transit. The target

layer is taken to be a continuous uniform layer corresponding to the stem cell zone (see chapter 7).

### **Large intestine**

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(130) Colon cancer has occurred in excess in most irradiated populations with the notable exception of cervical cancer patients (Thompson *et al.*, 1994). Conceivably, at the cytotoxic doses used to treat cancer of the uterine cervix, cell killing prevented significant cell transformation (Boice *et al.*, 1987). Estimates of relative risk (RR) at 10 Gy ranged from 1.13 to 1.67 and the absolute risk per  $10^4$  PY-Gy from 0.45 to 2.18. The only evidence that cancer of the rectum can be induced by radiation comes from the study of cervical cancer patients where the doses were very high, ranging between 30 to 60 Gy. It is possible that gross tissue damage is a necessary precursor to the initiation of rectal cancer, as appears to be the case for some other 15 types of cancer, such as bone tumours (Gössner, 2003).

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(131) Concerning internal exposures to low LET ( $^{131}\text{I}$ ) and high LET radiation (radon and radium), UNSCEAR (2000) noted that the low doses to the colon do not allow conclusions to be drawn.

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(132) Data on 957 colon cancer cases recorded to date in the 80,000 bomb survivors included in the study have been used to comment on the possibility of regional differences in risk (Preston, 2003). The point estimates tended to vary between regions. The sex-averaged ERR/Sv estimates were 0.65 (all regions), 0.16 (ascending colon), 1.4 (transverse colon), 0.67 (descending colon), and 0.78 (overlapping regions or not specified). However, these differences were not significant ( $p=0.25$ ). Hence, a constant risk is assumed for different regions of the colon.

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(133) Differences in clinical presentation and surgical management of right and left sided colon cancer are well established and recent studies have shown differences at the cytogenetic and molecular level (Richman and Adlard, 2002). Such differences may reflect different embryonic origins. Thus, the ascending colon and proximal two-thirds of the transverse colon, together with the small intestine, develop from the midgut. The distal third of the transverse colon, the descending colon, the 35 rectosigmoid colon, rectum and upper two-thirds of the anal canal develop from the hindgut.

(134) Data on the colon, particularly transit data (see Chapter 6), are often reported in terms of the right colon, left colon, and rectosigmoid. The right colon in this case is the ascending colon plus the proximal half of the transverse colon; the left colon is the distal half of the transverse colon plus the descending colon. These divisions are used in this report. In addition, the last part of the colon, the rectosigmoid colon, is taken to include the rectum, largely because of difficulties in specifying radionuclide residence times separately for the rectum. Doses have been calculated separately for each of the three regions and then summed to give an overall colon dose, calculated as a mass weighted mean. For each region, dose has been calculated as an average throughout the length of the tube on the assumption of a constant uniform rate of transit. The target layer is taken to be a continuous uniform layer corresponding to the stem cell zone. Uncertainties associated with the assumptions made are considered in Annex E.

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#### 4.4. Tissue damage

(135) The early effects of high doses of radiation, involving gross cell killing in haemopoietic, intestinal or nervous tissue, are collectively referred to as the “acute radiation syndromes” and have been extensively reviewed (Bond *et al.*, 1965; Young, 1987; UNSCEAR, 1988). Haemopoietic stem cells are more sensitive to radiation than intestinal stem cells but because of the more rapid cell division and renewal in the small intestine, sufficiently high doses (10 – 20 Gy) can cause death within 1 – 2 weeks due to breakdown of the intestinal epithelium. This destruction of the mucosal lining of the intestine results in fluid, protein and electrolyte loss, infection and haemorrhage. Survival depends on the presence of a sufficient number of stem cells to repopulate the epithelium. As discussed above (4.1), it is possible that immediate daughter cells of stem cells may retain the potential to re-establish epithelial integrity. Delayed effects, involving other cell types including vascular endothelial cells and mesenchymal fibroblasts, may be seen in the small and large intestines and in other regions of the alimentary tract. Damage includes damage to blood vessels, such as endarteritis and fibrosis, excess collagen deposition in the submucosa and strictures.

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(136) Dose-effect relationships for intestinal damage have been obtained from animal data; this is considered reasonable because different mammals respond in a similar way to irradiation of the gut (Bond *et al.*, 1965; Maisin *et al.*, 1971). Damage to the intestinal mucosa has been shown to occur at doses > 1 Gy and be

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increasingly severe at doses of 5 – 10 Gy. Data obtained from studies in which the alimentary tract of rats was exposed to X-irradiation, either *in situ* or surgically exteriorised, indicated an LD<sub>50</sub> (death of 50% of animals) of about 15 Gy for acute exposure (Sullivan *et al.*, 1959). Values of LD<sub>50</sub> of about 33 Gy for rats (25 - 41 Gy) and 40 Gy for dogs (20 - 52 Gy) were obtained in experiments in which rats ingested either <sup>106</sup>Ru/<sup>106</sup>Rh (average 1.4 MeV beta) or <sup>147</sup>Pm (average 0.06 MeV beta) and dogs were given <sup>106</sup>Ru/<sup>106</sup>Rh (Sullivan *et al.*, 1978; Cross *et al.*, 1978). The estimated dose to crypt cells in rats was the same for both <sup>106</sup>Ru/<sup>106</sup>Rh and <sup>147</sup>Pm, about 35 Gy, although the dose to the mucosal surface was about 35 times greater for <sup>147</sup>Pm than for <sup>106</sup>Ru/<sup>106</sup>Rh. This dose is comparable to a dose of about 13 Gy of external irradiation delivered acutely and is consistent with an expected reduction in effect at lower dose rate. Death was due to damage to the large intestine in both rats and dogs. Based on these data, an LD<sub>50</sub> of 35 Gy has been suggested, with a simple linear function with a LD<sub>0</sub> of 20 Gy and an LD<sub>100</sub> of 50 Gy (Pochin, 1988).

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(137) Comparisons of the toxicity of <sup>106</sup>Ru/<sup>106</sup>Rh in rats of different ages, in terms of administered activity, showed sensitivity in the order: newborn > adults > weanlings (Sullivan *et al.*, 1987). The reason for the sensitivity of the newborn is the uptake and retention of radionuclides in the mucosal cells of the intestine, particularly the proximal small intestine. This non-specific uptake of radionuclides, discussed in Chapter 3, occurs to a decreasing extent over the suckling period and distinct species differences have been observed. It would appear that at the high levels of retention observed in rats, doses of up to 100 Gy d<sup>-1</sup> may be received by cells towards the tips of the villi without evidence of mucosal injury (Sullivan *et al.*, 1987). The greater sensitivity of adults than weanlings to the effect of <sup>106</sup>Ru/<sup>106</sup>Rh was probably a reflection of greater transit times in the adult.

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(138) There are few reports of acute injury to the intestinal mucosa of humans following radionuclide ingestion. Notably, extensive internal contamination with <sup>137</sup>CsCl (>3.1 MBq) occurred in 22 persons in the Goiania accident in Brazil (IAEA, 1987). Eight individuals developed acute radiation syndrome, including symptoms such as nausea, vomiting, and watery diarrhoea during the prodromal phase. Doses received by these individuals were estimated using cytogenetic dosimetry to range between 3 and 7 Gy, accumulated over a period of 2 weeks. In 4 persons who received doses estimated between 4 and 6 Gy and who died of radiation injuries, intestinal bleeding was found at autopsy (IAEA, 1987; Brandao-Mello *et al.*, 1991).

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## 5. DESCRIPTION OF THE HUMAN ALIMENTARY TRACT MODEL

### 5.1. Introduction

5

(139) The structure of the HATM is shown in Figure 5.1. The model depicts the following processes:

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- entry of a radionuclide into the oral cavity by ingestion or into the oesophagus after mechanical clearance from the respiratory tract; sequential transfer through the contents of the oral cavity, oesophagus, stomach, small intestine, and segments of the colon, followed by emptying in faeces;
- radionuclide deposition and retention on or between the teeth and return to the oral cavity; deposition and retention in the oral mucosa or walls of the stomach and intestines;
- transfer from the oral mucosa or walls of the stomach and intestines back into the luminal contents or into blood (absorption);
- and transfer from various secretory organs or blood into the contents of certain segments of the alimentary tract (secretion).

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(140) The organs and fluids represented in Figure 5.1 by dashed boxes are not part of the HATM but are included in the schematic to show connections with the respiratory tract model or systemic biokinetic models.

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(141) First-order kinetics is assumed. This is a considerable simplification of the complex processes involved in transfer of material through the lumen of the alimentary tract (Chapter 6) but is expected to provide a reasonably accurate representation of the mean residence time of a radionuclide in each segment of the tract.

30

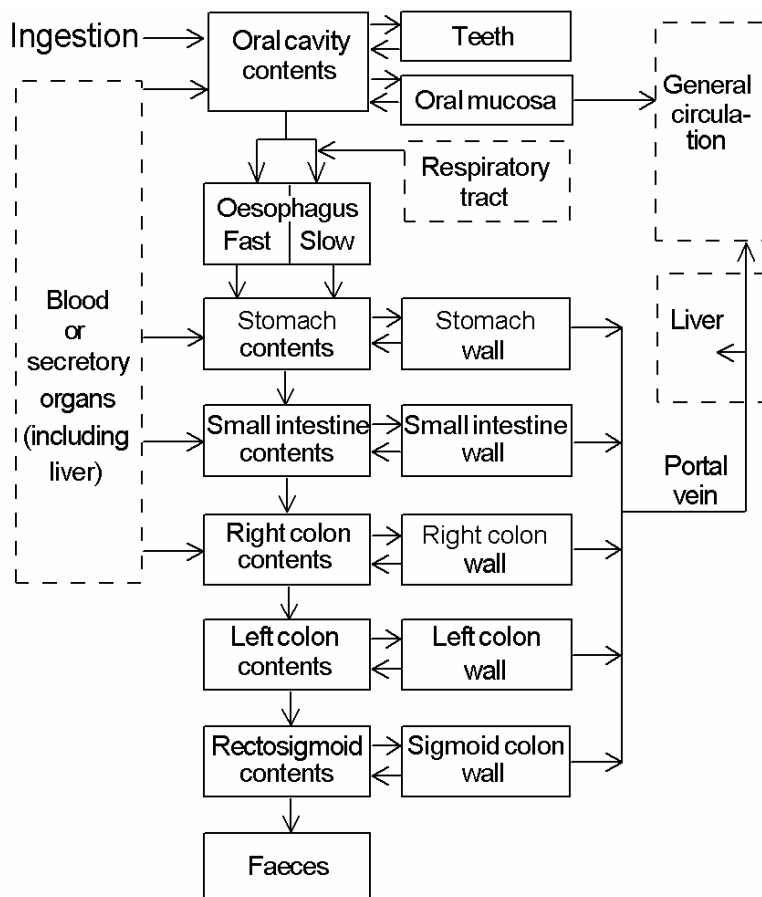
(142) For computational purposes, each parameter value of the model is represented by a transfer coefficient (also called a rate coefficient or rate constant). A transfer coefficient describes the rate of outflow of a substance from a compartment and is defined as the instantaneous fraction of the contained substance leaving the compartment per unit time. This is the common approach in biokinetic modelling.

35

(143) Parameter values of the model include both generic values and element-specific

values. The generic parameter values are those describing bulk flow of material through the lumen of the alimentary tract (see Chapter 6). The element-specific parameter values are those describing retention in or on the tissues of the alimentary tract, absorption to blood, and secretion from systemic organs or blood into the lumen of tract. (See Chapter 3 and examples in 5.4).

5



**Figure 5.1.** Structure of the HATM. The dashed boxes are included to show connections with the respiratory tract model or systemic biokinetic models.

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(144) Generic parameter values are given in Chapter 6, in the form of age-, gender-, and material-specific transit times. The transit time of an atom in a compartment is defined as the length of time that it resides in that compartment. The transit time (or mean transit time) of a substance in a compartment is the mean of the distribution of transit times of its atoms. With first-order kinetics, a transit time of T days corresponds to a transfer coefficient of 1/T per day.

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(145) Element-specific parameter values of the HATM are not given in this report except as examples of applications of the model (see 5.4). Recommendations of element-specific parameter values will be made in future ICRP reports in which the HATM is applied.

5 (146) Except where specific information is available to derive an element-specific transfer coefficient, the coefficient is assumed to be zero. As a minimum, information generally is available to derive non-zero transfer coefficients describing total absorption to blood. As discussed in section 5.4, in cases in which all absorption is assumed to take place in the small intestine and there is assumed to be no retention in the wall of the small intestine, the  
10 parameters can be calculated from an assumed absorption fraction in the same way as in the *Publication 30* model (ICRP, 1979). For some elements, there is quantitative information on absorption in segments of the tract other than the small intestine, or retention or secretion in some segments of the tract (Chapter 3).

## 15 **5.2. Main differences from the ICRP Publication 30 model**

(147) The biokinetic model differs from that of the ICRP *Publication 30* (1979) model (Figure 5.2) in the following main ways:

20 (1) In the previous model, the stomach is the point of entry of a radionuclide into the alimentary tract. The HAT model includes compartments representing the oral cavity and oesophagus to account for doses received from transit or retention of activity in the upper regions of the tract.

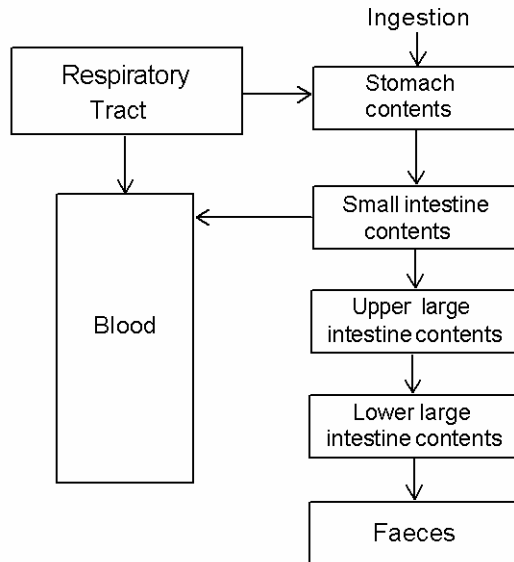
25 (2) The previous model divides the large intestine into two regions, the upper large intestine and the lower large intestine. The HAT model partitions the large intestine into three regions frequently addressed in colonic transit studies

(3) The previous model accounts only for decays of a radionuclide occurring during its transit through the lumen of the stomach and intestines. The HAT model includes compartments to account for nuclear transformations due to retention of a radionuclide in tissues of the alimentary tract in those cases where tissue retention  
30 is indicated by available information.

(4) The previous model depicts absorption of a radionuclide as occurring only in the small intestine. The HAT model includes pathways to account for absorption from the oral mucosa, stomach, or segments of the colon if specific information is available.

35 (5) ) In the previous model, the transit times through the segments of the alimentary tract are independent of age, gender, and the type of material ingested.

The HAT model provides age- and gender-specific transit times for all segments of the tract depicted in the model and, for the upper segments (oral cavity, oesophagus, and stomach), also provides material-specific transit times.



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**Figure 5.2.** Structure of the ICRP's previous model of gastrointestinal transfer (ICRP, 1979).

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### 5.3. Details of the model structure

#### 5.3.1. Transit through the lumen of the tract

(148) The transfer of material from the oral cavity to the oesophagus is represented by a single transit time that depends on the type of material entering the oral cavity. Default transit times are provided for liquids, solids, and total diet. Default values for total diet are used for unspecified material or unknown mixtures of solids and liquids.

(149) Transfer of material from the oesophagus contents to the stomach contents is described by two transfer rates. Although most of the swallowed material reaches the stomach in a few seconds, there is evidence from studies of labelled material fed by mouth that a portion of swallowed material may be cleared over a period of a few minutes and sometimes longer. This longer component of retention may also be present in the case of inhaled material transferred to the alimentary tract by mechanical transport, although it is more difficult to demonstrate experimentally in this case. Each of the two components of

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transfer from the oesophagus contents to the stomach contents is represented by a single transit time that depends on the type of material entering the oesophagus. Default transit times are provided for liquids, solids, and total diet. Values for total diet are used for unspecified material or unknown mixtures of liquids and solids. The size and retention time of the long-term component of retention in the oesophagus are highly variable and, as with other features of this model, may be adjusted in specific applications in which the default values do not appear to be appropriate.

(150) Transfer of material from the stomach contents to the small intestine contents is represented by a single transit time that depends on the type of material entering the stomach. Default transit times are provided for water or other non-caloric liquids, caloric liquids, solids, and total diet. Values for total diet are used for unspecified material or unknown mixtures of solids and liquid.

(151) After material enters the small intestine, its transit time is assumed to be independent of the type of material that initially entered the alimentary tract. Emptying of material from the contents of a segment to the contents to the next segment (e.g., small intestine contents to right colon contents) or from the rectosigmoid in faeces is represented by a single transit time.

(152) The portion of the alimentary tract extending from the caecum to the anus is viewed as consisting of three regions: right colon, left colon, and rectosigmoid. The right colon is defined as the caecum, ascending colon, and proximal half of the transverse colon; the left colon is the distal half of the transverse colon plus the descending colon; and the rectosigmoid is the sigmoid colon plus the rectum. This division of the large intestine differs from that of previous models of the alimentary tract (ICRP, 1979; NCRP, 1998) but is useful for purposes of modelling colonic transit. Because this is a standard division for diagnostic and experimental examinations of colonic transit, considerable information is available on transit times through each of these three segments. The Task Group concluded that the division of the large intestine into right colon, left colon, and rectosigmoid allows best estimates of the time-dependent distribution of ingested, inhaled, or secreted activity in the colon, based on current information (see also Chapter 6).

(153) Although the rectum serves mainly as a conduit, it also serves as a storage organ when the amount of material entering from the sigmoid colon is too small to evoke the urge to defecate or if defecation is not convenient. In the latter case, the receptors in the rectum

respond to the distension stimulus, the urge to defecate may subside, and a relatively large mass of material may be stored for some time. Due to difficulties in determining a meaningful residence time for material in the rectum, the rectum is not considered as a separate compartment.

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### **5.3.2. Retention in or on tissues of the alimentary tract**

(154) Provision is made in the model to address retention of radionuclides on the teeth or in tissues of the alimentary tract after transfer from the lumen of the tract. This is to be distinguished from systemic activity that is transferred from blood into tissues of the alimentary tract, which is not addressed in the HATM but may be included in systemic biokinetic models used in conjunction with the HATM.

(155) There is evidence of retention of some elements on the teeth after ingestion (see Chapter 3). This is depicted as a transfer from the contents of the oral cavity to the surface of the teeth and return from the teeth to the oral cavity.

(156) Provision is made to address transfer from the oral cavity contents into the oral mucosa, from stomach contents into the stomach wall, from small intestine contents into the small intestine wall, or from the contents of any segment of the colon into the wall of the corresponding segment. Activity entering the oral mucosa leaves this compartment with a half-time estimated from element-specific information. Activity leaving the oral mucosa may be assigned to the oral cavity or may be assigned partly or wholly to blood to represent direct absorption from the oral mucosa. Similarly, activity leaving the wall of the stomach, small intestine, or any segment of the colon with an element- and segment-specific half-time may be divided between the luminal contents of the corresponding segment and absorbed activity; in this case, absorbed activity is assigned to the portal vein and is available for uptake by the liver before entering the general circulation.

### **5.3.3. Absorption to blood**

(157) While absorption occurs predominantly in the small intestine, provision is made for absorption in the oral cavity, stomach, or any segment of the colon. It is known, for example, that absorption from the stomach can occur for highly lipid-soluble substances such as alcohol and some weak acids, and that substances administered as suppositories can be absorbed from the colon after movement of contents from the rectum into the sigmoid colon.

Other examples of absorption from different regions of the alimentary tract are given in Chapter 3.

5 (158) Absorption from the oral cavity is depicted as transfer from the oral cavity contents to the oral mucosa and direct transfer from the oral mucosa to blood. Absorption from any other segment of the alimentary tract is depicted as transfer from the contents to the wall of that segment, followed by transfer to blood in the portal vein with the potential for direct uptake by the liver prior to entry into the general circulation. This reflects the fact that blood flowing through the capillary beds of the stomach and intestines merge in the portal vein and is then  
10 circulated through the liver before entering the general circulation (see Chapter 2). Blood also reaches the liver from the general circulation via the hepatic artery, and all blood leaves the liver via the hepatic vein. In general, information is not available to determine whether there is significant accumulation of radionuclides in the liver during their passage to the general circulation. Because the liver is also the main route of excretion of radionuclides to  
15 the alimentary tract, there is the possibility of absorbed material passing directly back to the intestine without entering the general circulation.

(159) Absorption from a given region to blood may be assumed to occur after an extremely brief residence (in effect, instantaneously), or after a more prolonged residence time in the  
20 tissues of that region. For most elements and their radioisotopes, information is not available on retention in the walls of the alimentary tract or direct uptake of absorbed activity by the liver. In such cases, absorption to blood may be depicted as rapid transfer through these compartments into the general circulation.

25 (160) The model does not account for slow transfer from the alimentary tract to blood via the lymphatic system. In most cases, this is not expected to comprise a significant proportion of total absorption to blood. While there is evidence that particles may be transported through the mesenteric lymphatic system, only transitory retention in mesenteric lymph nodes has been observed.

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(161) In the planned ICRP reports which will recommend the use of the HATM for a range of elements, information for each element will be given in terms of the alimentary tract transfer factor,  $f_A$  which replaces the  $f_1$  value of the *Publication 30* model (ICRP, 1979) and distinguishes the uses of the new and old models. Some examples of  $f_A$  are given in Table  
35 5.1. In the majority of cases, information will only be available on the total absorption of the element and its radioisotopes to blood with no information on regional absorption. As in the

Publication 30 model, the standard assumption will be that this absorption takes place entirely from the small intestine, thus in these cases the fractional transfer from SI to blood,  $f_{SI}$ , is equal to  $f_A$ . In cases where information is available on absorption from regions other than the small intestine, this will also be specified in terms of fractional absorption values. For example, if an element is known to be absorbed from the stomach as well as from the small intestine, values of  $f_{ST}$  and  $f_{SI}$  would be specified, where;

$$f_A = f_{ST} + f_{SI}.$$

(162) The transfer coefficients describing uptake from the gut to blood can be derived from  $f_{SI}$  and the transfer coefficients representing transit through the gut. The transfer coefficient for uptake from the SI to blood ( $\lambda_{SI,B}$ ) is given by:

$$\lambda_{SI,B} = \frac{f_{SI} \lambda_{SI,RC}}{1 - f_{SI}}$$

Where  $\lambda_{SI,RC}$  is the coefficient for transfer from the SI to the right colon.

(163) In cases where there is assumed to be uptake from the stomach ( $f_{ST}$ ) the transfer coefficient for uptake from the stomach is given by an equation analogous to that for SI.

$$\lambda_{ST,B} = \frac{f_{ST} \lambda_{ST,SI}}{1 - f_{ST}}$$

**Table 5.1** Examples of the fractional absorption of elements from alimentary tract to blood

Element	Fractional absorption from the small intestine, $f_A^a$ , in:	
	Infants (3 months)	Adults <sup>b</sup>
Strontium	0.6	0.3
Ruthenium	0.1	0.05
Plutonium	$5 \times 10^{-3}$	$5 \times 10^{-4}$



<sup>a</sup> $f_{SI}$  denotes absorption from the small intestine and in these examples and most cases will equal  $f_A$ , the total absorption. Values of  $f_A$  will be given in forthcoming ICRP publications. In those cases where absorption from other regions is also specified, additional fractional absorption values (eg.  $f_{ST}$ ) will also be given, together with values of  $f_{SI}$  and  $f_A$ .

<sup>b</sup>Members of the public.

#### 5.3.4. Secretion into the luminal contents

(164) Secretions into the alimentary tract originate mainly in the liver, salivary glands, the epithelial cells of the gastrointestinal mucosa, and the pancreas. In this model, secretions may be assigned to the contents of the oral cavity, stomach, small intestine, or right colon. For example, activity secreted in saliva would generally be assigned to the contents of the oral cavity, and activity secreted in liver bile or pancreatic juices would be assigned to the contents of the small intestine. However, the receptor compartment may be changed to fit the assumptions of the systemic biokinetic model applied to absorbed activity. For example, it may be assumed in the systemic model that there is no reabsorption of secreted activity, in which case secreted activity might be assigned to the contents of the right colon, assuming no absorption from this region.

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(165) When modelling secretion of a radionuclide into the alimentary tract, the source of the secreted material will depend on the systemic biokinetic model used in conjunction with the HATM. For example, a systemic biokinetic model may include a compartment representing the pancreas, in which case pancreatic secretion could be represented as transfer from the pancreas into the contents of the small intestine. In many cases it may be convenient and sufficient to assume that the secreted material originates in plasma rather than a secretory organ such as the pancreas or salivary glands.

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### 5.4. Radionuclide-specific examples of the use of the model

(166) In chapter 3, specific examples of radionuclide behaviour were discussed to illustrate the types of information that may be available, and for use later in the report to show the effect of different assumptions on dose estimates and to compare doses calculated using the new model and the ICRP Publication 30 model. The radionuclides considered in chapter 3 are:

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- $^{90}\text{Sr}$ ,  $^{106}\text{Ru}$  and  $^{239}\text{Pu}$ , to illustrate the *standard case* in which information is available only on total absorption and excretion, at different ages;
  - $^{115}\text{Cd}$  to illustrate the effect of *retention on teeth* on dose to the oral mucosa;
  - $^{59}\text{Fe}$  and  $^{235}\text{U}$  to illustrate the effect of *retention in the SI wall* for adults
- 5
- $^{239}\text{Pu}$  to illustrate the effect of retention in the SI wall for neonates

### ***Exemple of Absorption of strontium, ruthenium and plutonium***

(167) In these examples, and in most cases, no information will be available on retention in the wall of the small intestine during absorption. The transfer coefficient from the contents to the wall of the small intestine will be computed on the basis of  $f_{\text{SI}}$ , and the transfer coefficient from the wall to blood will be given a high value to correspond to rapid transfer to blood with negligible retention in the wall. Alternatively, for computational simplicity the transfer can be taken to occur directly from the contents to blood.

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### ***Exemple of Cadmium retention on teeth***

(168) On the basis of the limited data discussed in Chapter 3, the example used in this report is of fractional uptake,  $f_{\text{teeth}}$ , of  $2 \times 10^{-3}$  of ingested Cd and retention with an arbitrary half-time of 7 days. Transfer coefficients from the contents of the oral cavity to the teeth, and for removal from teeth, have been set to correspond to these values. To avoid the unnecessary complication of considering further uptake, activity removed from teeth is taken to be transferred directly to the esophagus (slow) compartment (similar to the assumption adopted for Fe in the SI wall, see below).

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### ***Retention of iron, uranium and plutonium in the wall of the small Intestine***

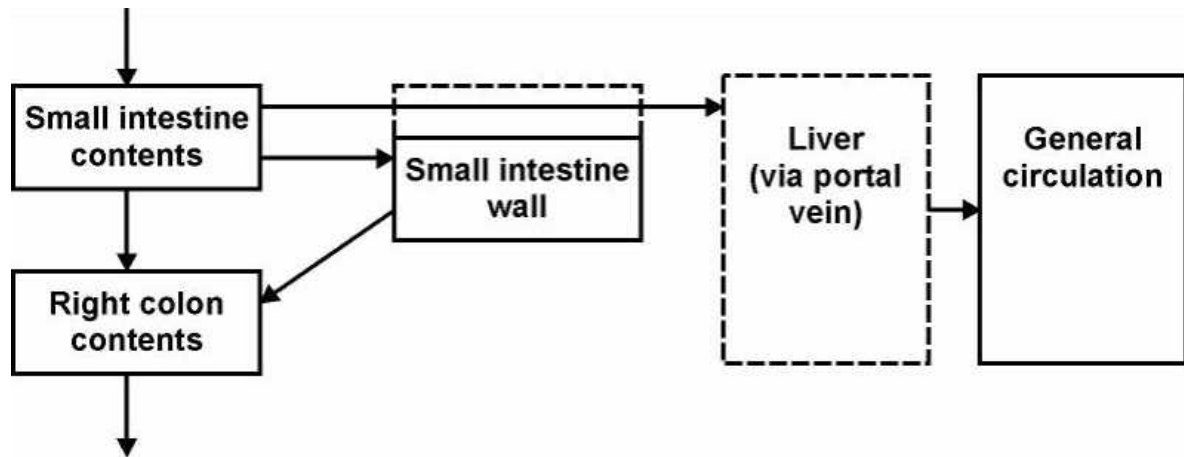
(169) For the example of iron ingested in soluble form by adults, discussed in Chapter 3, the data of Werner et al. (1987) suggest an  $f_{\text{SI}}$  of 0.2. However, while 0.2 is absorbed to blood, initial uptake into the SI wall is 0.4, of which 0.2 is absorbed directly to blood and 0.2 is retained in the SI wall with a half-time of retention of 3 days and lost into the SI contents.

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(170) To model this specific case without consideration of recycling between SI content and SI wall, requires an adaptation of the standard model. Figure 5.3 shows that absorption to blood is taken to occur directly from the contents of the small intestine, while the compartment representing the SI wall is used to account for retention in the wall followed by return back

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into the contents. To avoid the unwarranted complexity of considering further absorption to blood from this lost Fe and cyclical uptake of Fe back into the wall, Fe lost from the wall is taken to enter directly into the right colon.



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**Figure 5.3.** Specific treatment of the absorption and retention of iron in the small intestine, requiring an adaptation of the standard HAT model.

10 (171) As discussed in Chapter 3, human and primate data suggest that the absorption of uranium from the small intestine may occur with a half-time of 1- 3 days. For illustrative purposes in this report, transfer coefficients from SI contents to wall and from wall to blood are calculated on the basis of an  $f_{SI}$  of 0.02 and a retention half-time in the wall of 2 days.

15 (172) Based largely on primate data, the example of plutonium retention in the small intestine of neonates given in Chapter 3 is of an  $f_{SI}$  of  $5 \times 10^{-3}$  (as in Table 5.1), total uptake of 0.02 from contents to wall, a retention half-time of 1 week in the wall, and loss of 0.015 into the right colon.

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## 5.5. References

25 International Commission on Radiological Protection. (1979) Limits on Intakes of Radionuclides for Workers. ICRP Publication 30, Pt.1. Pergamon Press, Oxford. Ann. ICRP **2**, (3/4).

National Council on Radiation Protection and Measurements (1998) Evaluating the reliability of biokinetic and dosimetric models and parameters used to assess individual doses for risk assessment purposes. NCRP Commentary No.15. Bethesda, MD.

- 5 Werner, E., Roth, P., Hansen, Ch. (1987) Intestinal absorption of metals. In: Age-related Factors in Radionuclide Metabolism and Dosimetry. (G.B. Gerber, H. Métivier, H. Smith, Eds.) Proc. CEC Workshop, Angers, France, 1986. Martinus Nijhoff, Lancaster. pp.27-33.

## 6. TRANSIT TIMES THROUGH THE ALIMENTARY TRACT

### 6.1. Introduction

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(173) The kinetics of material in the lumen of the alimentary tract depends on its composition and location within the tract. For example, liquids usually are removed from the stomach more rapidly than solids, and water or other non-caloric liquids are removed more rapidly than caloric liquids. Gastric emptying of liquids can be described reasonably well in terms of a mono-exponential function, while solids are removed from the stomach in a nearly linear pattern. Liquids may move ahead of solids in the proximal right colon, but liquids and solids apparently transfer together through most portions of the colon in slow, highly variable mass movements.

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(174) Due to differences in emptying patterns for various materials and segments of the alimentary tract as well as individual preferences of investigators, transit data for the tract have been reported in a variety of units. For the purpose of deriving parameter values for the model developed in this document, reported transfer times through the lumen were reduced to the common basis of a transit time. The transit time of an atom in a region of the tract is the length of time that it resides in that region. The transit time of a substance in a region is the mean of the distribution of transit times of its atoms.

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(175) This chapter summarizes information on the normal movement of material through the lumen of the alimentary tract and provides default transit times representing that movement. The experimental data underlying the selected parameter values are more fully described and referenced in Annex C.

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(176) The default regional transit times given here are central estimates based on collected data for a given gender, age group, and type of material (e.g., solids, liquids, caloric liquids, or non-caloric liquids). As extensively illustrated in Annex C, transit of material through each of the major segments of the tract shows considerable inter- and intra-subject variability even under normal conditions. Extremely large deviations from the norm may result from constipation, diarrhea, unusual diet, pharmaceuticals, and a variety of diseases that affect the nervous system or increase energy requirements, for example. Thus, the default transit times given here may not be

appropriate for individual-specific applications, such as the interpretation of faecal monitoring results. In such cases the use of transit times observed for the individual would result in more accurate estimates of dose. Uncertainty and variability in transit times are considered in section 6.7.

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## 6.2. Mouth

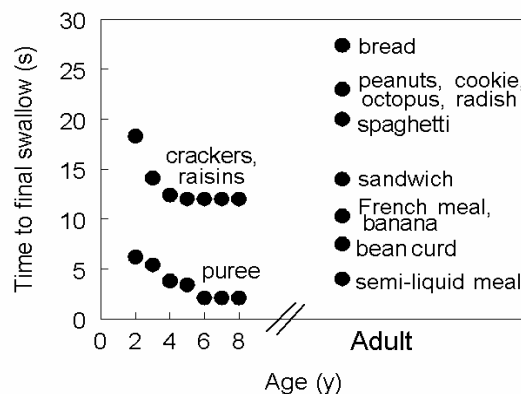
(177) Liquids generally are removed from the mouth in a single swallow in which a posterior movement of the tongue forces the material into the oropharynx. The time between intake and swallowing of a liquid usually is about 1-3 s, but liquids with a pleasing or interesting taste are sometimes held longer.

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(178) Chewing and swallowing times for solids vary with the texture of the food, the shear force required for reduction, and individual habits such as the amount of food taken into the mouth in a single bite. Solids usually are chewed for a sufficient time to reduce particles to a few cubic millimeters and are then largely removed from the mouth in a single swallow or two closely spaced swallows, but complete removal sometimes requires several swallows between periods of chewing. Available measurements indicate that hard solids typically are chewed for 20-25 s before the final swallow. The residence time in the mouth for soft solids or semi-solids depends strongly on texture and varies from a few seconds to more than 25 s (Figure 6-1; Horio and Kawamura, 1989; Guy-Grand *et al.*, 1994; Hiemae and Palmer, 1999; Hoebler *et al.*, 2000).

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**Figure 6-1.** Differences with age and food type in residence

times in the mouth. Based on data summarized in Annex C.

(179) Differences with age in food residence times in the mouth arise from changes with age in the composition of diet, gradually improved chewing skills at early ages, and anatomical changes associated with ageing. Data on sucking and swallowing rates in normal infants during feeding from a bottle (Colley and Creamer, 1958) suggest a transit time in the mouth on the order of 1-3 s. Starting at about 4 - 6 months of age there is a transition from an entirely liquid diet to increasingly textured foods and gradually improved efficiency in chewing and swallowing. For solids and semi-solids, the average time for processing food in the mouth may be higher at age 1-2 y than for older children (Figure 6-1) because the younger children often hold food in the mouth without chewing and tend to swallow several times per bite of food, whereas older children initiate chewing more quickly and often swallow only once or twice (Stolovitz and Gisel, 1991). Data for pre-teenage children suggest chewing times for solid foods similar to those observed in adults (Ingervall and Thilander, 1975; Wickwire *et al.*, 1981; Gisel and Patrick, 1988). The swallow time appears to be prolonged in elderly persons due to an increase in the pharyngeal transit time (Shaw *et al.*, 1995; Rademaker *et al.*, 1998).

(180) Default transit times for the mouth are based on the assumption that the transit time of a liquid is the time from intake to first swallow and the mean transit time of a solid is assumed to be three-quarters of the time from intake to final swallow. For liquids, the time between intake and first swallow is assumed to be 2 s. For solids, the time from intake to final swallow is assumed to be 20 s, based on a diet that includes a relatively high percentage of hard solids and/or chewy soft solids such as bread and pasta. The implied transit times are 2 s for liquids and 15 s for solids. Transit times are assumed to be independent of age after infancy because changes with age in residence times for specific foods may be largely offset by changes in diet.

**Table 6.1.** Default transit times for the mouth.

Ingested material	Transit time (s)	
	3-month Infant	Age $\geq$ 1 y
Solids	--	15
Liquids	2	2

Total diet	2	12
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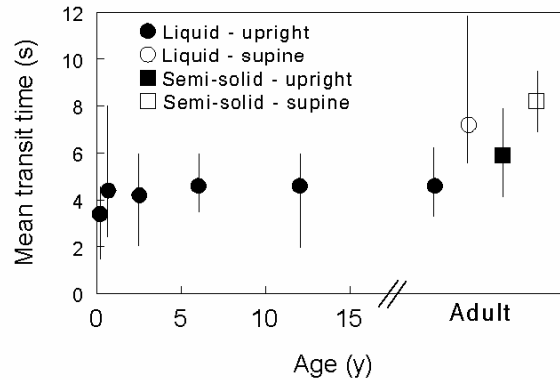
### 6.3. Oesophagus

(181) When material is swallowed, a coordinated and sequential set of peristaltic contractions produces a zone of pressure that moves down the oesophagus with the bolus in front of it. As the bolus approaches the lower oesophageal sphincter, the sphincter relaxes, allowing the bolus to enter the stomach. The rate of movement of a bolus varies with its composition and location within the oesophagus and the position of the body. Velocities ranging from about 40 cm/sec to about 1 cm/sec have been reported for different segments of the oesophagus and different conditions. The velocity of the bolus during most of the oesophageal transport usually is in the range 2-6 cm/sec, and the time required for the wave to travel from the pharynx to the stomach usually is in the range 5-12 sec. The average time required for material to reach the stomach may be slightly less than the time required for the peristaltic wave to reach the stomach, depending on the physical nature of the swallowed material and the contribution of gravity. For example, liquids swallowed by a subject in an upright position may traverse the oesophagus in less than 5 s and thus may reach the stomach before the peristaltic contraction. However, swallowed liquids may be arrested at the lower end of the oesophagus and await the arrival of the peristaltic wave before they are admitted to the stomach (Brobeck, 1979; Guyton, 1982; Johnson, 1998).

(182) Typically, transit of liquids is more rapid than that of solids, and transit of solids mixed with liquid is more rapid than that of drier solids. Esophageal transit generally is faster in the upright than the supine position (Figure 6-2).

(183) Depending on the form of the material and the amount of lubrication from saliva or other liquids, the oesophagus may not be totally emptied by the first peristaltic contraction initiated by the swallow. The distension induced by residual material initiates another peristaltic contraction, called a secondary peristalsis, in the absence of a swallow. The secondary peristalsis usually is not sensed. Several secondary contractions often are required to remove the remaining material.





**Figure 6-2.** Differences with age, food type, and body position in transit times through the lumen of the oesophagus (fast component). Symbols represent means and vertical lines represent ranges of individual observations for children and reported central values for adults. Based on data summarized in Annex C.

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(184) The portion of swallowed material remaining after the initial peristaltic wave is highly variable. Measurements involving liquids or semi-solids swallowed by supine or sitting subjects suggest that, on average, residual material may represent about 8-10% of the swallowed amount (Baulieu *et al.*, 1996; Jorgensen *et al.*, 1992; Klein and Wald, 1984, 1987; Tatsch *et al.*, 1991; Tolin *et al.* 1979). Residual material usually is largely cleared within 30-45 sec and often in a much shorter time. Dry solids ingested without water may remain in the oesophagus for several minutes and occasionally for a few hours without the subject having any sensation of the remaining material (Fisher *et al.*, 1982).

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(185) Esophageal transit of solids or liquids does not appear to be affected by gender (Lin *et al.*, 1995). There appears to be a modest increase in the average esophageal transit time for liquids during the first year of life but little if any change thereafter (Figure 6-2).

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(186) In this model, oesophageal transit is assumed to consist of two components representing relatively fast transfer of most of the swallowed amount and relatively slow transfer of residual material. Default values describing the relative sizes and transfer times of the fast and residual components are based on data for subjects in an upright position. It is assumed that transit times

for well-chewed solids are slightly greater than values for liquids and semi-solids, which are the most frequently studied materials. Default transit times for residual material are intended to represent average or typical transit times and substantially understate transit times that may occasionally occur for dry solids or pills.

5

(187) Mucus and associated material escalated from the respiratory tract (see chapters 2 and 3) enter the oesophagus via the oropharynx. It is assumed that the slow esophageal transit times for the second component of ingested material apply to the transit of all material escalated from the respiratory tract.

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**Table 6.2.** Default transit times for the oesophagus.

Ingested material	Transit time (s)			
	3-month infant		Age $\geq$ 1 y	
	Fast component (90%)	Residual material (10%)	Fast component (90%)	Residual material (10%)
Solids	--	--	8	45
Liquids	4	30	5	30
Total diet	4	30	7	40

15

#### 6.4. Stomach

(188) The kinetics of gastric emptying is affected by a number of factors, including composition of the ingested material, gender, and age. Typically, liquids are emptied from the stomach faster than digestible solids, and digestible solids are emptied faster than nondigestible solids having a dimension greater than 2 mm (NCRP, 1998).

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(189) Gastric emptying of liquids usually begins within 1-3 min of their arrival in the stomach and can be described reasonably well by a mono-exponential function, although a lag-phase of several

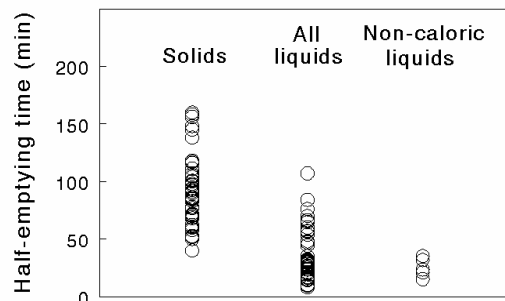
minutes has been reported for liquids of high caloric density (Gonzalez *et al.*, 2000). Removal of the solid component typically consists of an initial lag-phase of several minutes in which there is relatively slow emptying, followed by an extended phase of nearly linear emptying. Nondigestible solids are retained in the stomach until the digestible solids have been evacuated (NCRP, 1998).

5 During the latter stages of gastric emptying, a series of migrating motor complexes occurring at regular intervals move distally through the stomach, effectively sweeping the nondigestible solids into the small intestine. Normally, food is largely removed from the stomach in 2-3 h and completely removed in 5 h, but the emptying time can be affected by alcohol consumption or other factors (Suzuki, 1987).

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(190) The rate of emptying of material from the stomach is often reported as a “half-emptying time”, which refers to the time required for 50% of the ingested material to be removed from the stomach. Reported central estimates of half-emptying times for solids, all liquids, and non-caloric liquids are summarized in Figure 6-3. The data points indicated as “All liquids” represent primarily measurements of caloric liquids but also include collected data for non-caloric and unspecified liquids.

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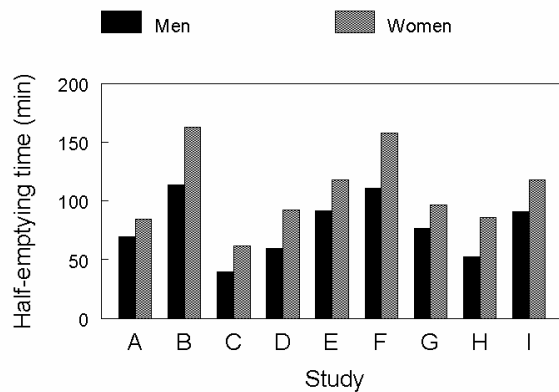
**Figure 6-3.** Comparison of reported gastric half-emptying times for solids, a variety of test liquids (including some non-caloric liquids), and non-caloric liquids in healthy adults (data tabulated in Annex C). Circles represent reported central values for different study groups.

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(191) The gastric half-emptying time depends strongly on the composition and caloric content of the ingested material and the level of nutrients in the jejunum (Naveri *et al.*, 1989; Phillips *et al.*,

1991; Vist and Maughan, 1995; Calbet and MacLean, 1997). For example, observed half-emptying times were much longer for meals with a high fat content than for meals with a high carbohydrate content (Sidery *et al.*, 1994). Observed half-emptying times for four selected foods increased in the order: mashed potatoes < bread < rice < spaghetti (Mourot *et al.*, 1988). Half-emptying times for four selected liquids increased in the order: water < non-carbonated carbohydrate-electrolyte solution < lightly carbonated carbohydrate electrolyte solution < carbonated cola (Ploutz-Snyder *et al.*, 1999).

10 (192) Results from a number of studies indicate that gastric emptying of solids is slower on average in women than men (Figure 6-4). Slower gastric emptying for women is also indicated for caloric liquids such as orange juice, but there may be little if any difference with gender in emptying of non-caloric liquids (Hutson *et al.*, 1989; Bennink *et al.*, 1998). Differences with gender in gastric emptying appear to diminish with aging due to an increase in the emptying rate in females, perhaps beginning after menopause (Hutson *et al.*, 1989; Tougas *et al.*, 2000).



15 **Figure 6-4.** Comparison of gastric half-emptying times of solids in adult male and female subjects in nine studies (data tabulated in Annex C).

20 (193) Application of various measures of central tendency (e.g., median, mean, weighted mean, or trimmed weighted mean) to the data collected in Annex C suggest a typical or central half-emptying time for solids of about 75-80 min in adult males and 100-110 min in adult females. For caloric liquids, a typical half-emptying time may be about 30-35 min in males and 40-45 min in females. For non-caloric liquids, a typical half-emptying time for either gender may be about 20-25 min.

(194) Reported gastric half-emptying times for meals in infants vary with the type of milk ingested, the maturity of the infant, and the measurement technique (Signer *et al.*, 1975; Cavell, 1982; Ewer *et al.*, 1996; Barnett *et al.*, 1999; van den Dreissche *et al.*, 1995) but average about 50-55 min (range, 15-100 min). Estimated half-emptying times of water in healthy infants average about 6 min (Lange *et al.*, 1997). Reported gastric emptying times for toddlers, young children, and adolescents generally are within the range of values determined for adults (Magazzu *et al.*, 1987; Smith *et al.*, 1990, 1993; Collins *et al.*, 1997; Chiloiro *et al.*, 1999; Gatti *et al.*, 2000). Gastric emptying may be slower in elderly persons than in young and middle-aged adults, but this has not been firmly established (Evans *et al.*, 1981; Moore *et al.*, 1983; Kupfer *et al.*, 1985).

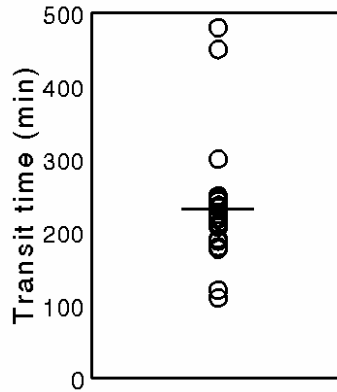
(195) Default transit times for the stomach are based on rounded central estimates of half-emptying times for solids, caloric liquids, and non-caloric liquids. It is assumed that the gastric emptying time in children of age  $\geq 1$  y is the same as that in the adult male. Based on typical patterns of clearance of liquids (nearly exponential) and solids (nearly linear) from the stomach, the transit time for liquids is estimated as 1.4 times the half-emptying time and the transit time for solids is assumed to equal the half-emptying time.

**Table 6.3.** Default transit times for the stomach.

Ingested material	Transit time (min)			
	3-month infant	Age 1-15 y	Adults	
			Males	Females
Solids	--	75	75	105
Liquid				
Caloric	75	45	45	60
Non-caloric	10	30	30	30
Total diet	75	70	70	95

## 6.5. Small intestine

- (196) Movement of material through the small intestine appears to be a nearly linear process (NCRP, 1998). Measurements of the rate of transfer of material through the small intestine generally are reported as transit times.
- 5 (197) The ileum, the distal part of the small intestine, acts as a reservoir and transfers boluses of variable sizes into the colon. Intake of a subsequent meal may stimulate transfer into the colon, but this appears to depend on the composition of the material in the ileum (Ewe *et al.*, 1989; Camilleri *et al.*, 1989; Price *et al.*, 1993; Hebden *et al.*, 1998).
- 10 (198) The transit time through the small intestine is influenced by the luminal contents. For example, fat in the small intestine induces significantly faster transit than proteins but delays ileocolonic transit (Hammer *et al.*, 1998). It has not been clearly established whether liquids and solids are transferred at the same rate through the small intestine.
- 15 (199) Reported central estimates for the transit time through the small intestine are in the range 1.8-8 h and average 3.9 +/- 1.5 h (standard deviation) (Figure 6-5). This excludes estimates based on the frequently applied hydrogen breath test, which is now regarded as unreliable (Madsen *et al.*, 1991; Wutzke *et al.*, 1997). Limited comparisons of small intestinal transit in adult males and females and in adults and children have not revealed significant differences with
- 20 gender or age in the rate of transit of material through the small intestine (Madsen, 1992; Argenyi *et al.*, 1995; Bennink *et al.*, 1999).



**Figure 6-5.** Reported small intestinal transit times in subjects without gastrointestinal disorders (data tabulated in Annex C). Circles represent central values determined in separate studies, and the bar represents the mean of these values.

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**Table 6.4.** Default transit time for the small intestine

Transit time (h)				
3-month infant	1y	5-15y	Adult male	Adult female
4	4	4	4	4

### 6.6. Colon and rectum

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(200) Flow of material in the colon is slow and highly variable. Periods of contraction between longer periods of quiescence result in mass movements of colonic material a few times during the

day (Karaus and Wienbeck, 1991). Fluids may move ahead of solids in the proximal right colon, but solids and fluids appear to move together throughout most of the colon.

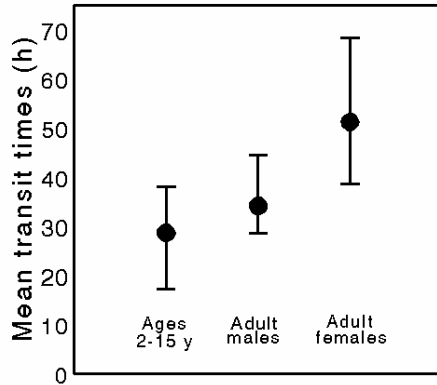
5 (201) The rectum serves mainly as a conduit but can also serve as a storage organ. Entry of material from the sigmoid colon usually evokes the rectoanal inhibitory reflex, signaling the need to defecate. The rectum serves as a storage organ when the amount of material received from the sigmoid colon is too small to evoke this reflex or when this reflex is neglected (Shafik *et al.*, 1997). The average residence time of material in the rectum cannot be estimated with much confidence.

10 (202) Reported central estimates of colonic transit times for groups of healthy adult subjects, tabulated in Annex C, range from 17 to 68 h and average 35 +/- 11 h (standard deviation). On average, the transit time through the colon is 30-40% longer in women than in men, although there is considerable overlap in individual estimates for the two genders (Figure 6-6). For example, in a study involving 80 adult males and 84 adult females, the estimated mean transit time was 30 +/- 2  
15 h (SEM) for males and 42 +/- 3 h for females, but upper 95% values were 65 h for males and 86 h for females (Meier *et al.*, 1995). Data on changes with age in colonic transit times are not definitive but suggest that the average colonic transit time is shorter in children than in adult males (Figure 6-6).

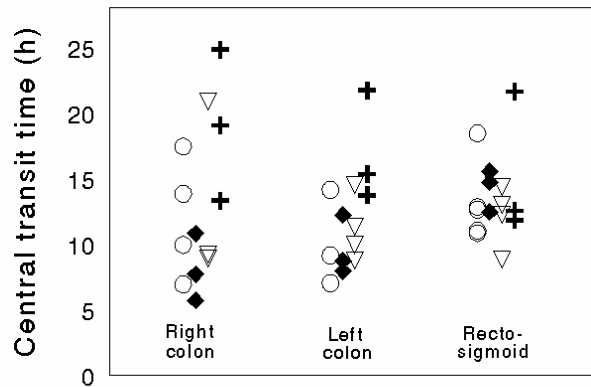
20 (203) The time to first appearance of ingested carmine red or other markers in feces (marker passage time) is used to diagnose bowel function in infants and children as well as adults. The marker passage time underestimates the mean transit time through the gastrointestinal tract but is a useful relative measure of whole gut transit and, by inference, colonic transit. Marker passage times increase noticeably during the first few months of life, particularly for infants receiving mainly  
25 breast milk (Sievers *et al.*, 1993). On the other hand, measurements of whole-gut transit in persons of all ages suggest that the colonic transit time does not change radically with age between birth and adulthood (Arhan *et al.*, 1981; Corazziari *et al.*, 1985; Saavedra *et al.*, 1989).

(204) In this model, the portion of the alimentary tract extending from the caecum to the anus is  
30 divided into three regions, right colon, left colon, and rectosigmoid, which is a standard division for diagnostic and experimental examinations of colonic transit (Bouchoucha and Thomas, 2000). Collected data on transit through the right and left colon and rectosigmoid are summarized in Figure 6-7. On average, the transit time is about the same for each of these regions, but considerable variation from this pattern has been observed in individual cases.





**Figure 6-6.** Ranges (vertical bars) and overall means (circles) of reported colonic transit times for normal children, adult males, and adult females. Based on data tabulated in Annex C.



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**Figure 6-7.** Summary of reported transit times in right colon, left colon, and rectosigmoid in normal human subjects. Circles, adults of both genders or gender not reported; diamonds, children; triangles, adult males; plus signs, adult females. Data tabulated in Annex C.

(205) Default transit times for the right colon, left colon, and rectosigmoid are based on the following central estimates and assumptions:

- in the adult male, the total colonic transit time (caecum to anus) is 36 h.
- 5 • the colonic transit time in adult females is one-third greater than that in adult males, i.e., 48 h.
- in adults, the transit time is the same for the right colon, left colon, and rectosigmoid, i.e., 12 h for each segment in males and 16 h for each segment in females.
- 10 • in males, the colonic transit time increases by about 25% (precisely, 8 h) between birth and adulthood, with the rate of increase being highest during the first year of life and more gradual thereafter.

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**Table 6.5.** Default transit times for right colon, left colon, and rectosigmoid

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Segment	Transit time (h)				
	3-month infant	1 y	5-15 y	Adult male	Adult female
Right colon	8	10	11	12	16
Left colon	8	10	11	12	16
Rectosigmoid	12	12	12	12	16

### 6.7 Uncertainty and variability

25 (206) This section provides a brief review of uncertainty and inter- and intra-individual variability in transit times through different segments of the alimentary tract. Chapter 8 considers the various

sources of uncertainty in the HATM and their effect on dose estimates.

(207) As discussed in Chapter 3 and in more detail in Chapter 8, “uncertainty” refers in this report to the level of confidence that can be placed in a given component (e.g., parameter value) or prediction of the HATM, as an estimate of the central value (usually, an arithmetic or geometric mean) in the population. “Variability” refers to quantitative differences between different members of a population under similar conditions (inter-individual variability) or within an individual under different conditions (intra-individual variability).

### 10 **6.7.1. Uncertainties associated with model formulation**

#### ***Use of first-order kinetics***

(208) Representation of movement of material through the lumen of the alimentary tract as a series of first-order transfers between well-mixed pools is a considerable simplification. For example, material traverses the small intestine in a more or less linear fashion and is transferred to the ascending colon in multi-bolus form. Flow of material in the rectosigmoid region of the colon is slow, variable, and intermittent, with periods of contraction between longer periods of quiescence resulting in mass movements of material a few times during the day.

(209) The assumption of first-order kinetics is made for computational convenience. The emptying half-time for a segment of the tract is set to reproduce central estimates of reported mean transit times of material through that segment, in the absence of radioactive decay. For relatively short-lived radionuclides, first-order kinetics can overestimate decays in the lower regions of the tract because it implies an immediate appearance of some ingested atoms in all regions of the tract. For example, an ingested radionuclide with half-life 20 min is likely to decay almost entirely between the mouth and caecum (ignoring absorption to blood) because more than 10 radiological half-lives may elapse before the first appearance of the ingested material in the right colon, but the HATM predicts on the basis of first-order kinetics that about 3% of the total decays in the alimentary tract would occur in the colon.

(210) In interpreting bioassay data, it should be kept in mind that the HATM or other first-order gastrointestinal models will not yield meaningful predictions of the faecal excretion rate during the early hours after intake due to its simplification of kinetics in the tract. For the case of ingestion of

a radionuclide by an adult male, the HATM predicts that, in the absence of absorption to blood, total faecal excretion is about 3% of the ingested amount after 12 h. The time to first appearance of ingested carmine red or other ingested markers in faeces of healthy adults (see Annex C) is typically greater than 12 h.

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(211) The HATM predicts that total faecal excretion of an unabsorbable marker would be about 22% of the ingested amount after 1 d, 69% after 2 d, 91% after 3 d, 98% after 4 d, and >99.5% after 5 d. These predictions are broadly consistent with reported data for carmen red or other markers and with more variable data on accidental intakes of radionuclides, although it appears that faecal excretion often is more nearly complete after about 3 d than the model predicts. Of course, It can be misleading to check the model against small numbers of individual cases due to substantial inter- and intra-subjects variability in the transit time. In some individual cases, nearly all of the swallowed amount appears in faeces during the first day. In other cases, 2-3 days or longer elapse before any appreciable faecal excretion of ingested material.

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#### ***Division of the tract into compartments***

(212) With the exception of the division of the colon, the compartments used to describe transfer of material through the lumen of the alimentary tract represent anatomically and functionally distinct regions of the tract. The colon has been divided in a number of different ways in different radiation protection models. The model of *Publication 30* divides the colon into the upper large intestine (ULI) and the lower large intestine (LLI), where the ULI includes the ascending and transverse colons and the LLI includes the descending colon, sigmoid colon, and rectum. A model developed for use in nuclear medicine (Stubbs, 1991, 1992; NCRP, 1998) divides the colon into the ascending colon, transverse colon, and rectosigmoid. The HATM divides the colon into the right colon, left colon, and rectosigmoid. The right colon is defined as the caecum, ascending colon, and proximal half of the transverse colon; the left colon is the distal half of the transverse colon plus the descending colon; and the rectosigmoid is the sigmoid colon plus the rectum. This division is often used for diagnostic and experimental examinations of colonic transit, and considerable information is available on transit times through each of these three segments. The Task Group concluded that the division of the large intestine into right colon, left colon, and rectosigmoid allows best estimates of the time-dependent distribution of ingested, inhaled, or secreted activity in the colon, based on modern data.

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(213) The Task Group considered whether the rectum should be represented as a separate compartment, since it is commonly assumed to function mainly as conduit rather than a storage organ. Information found in the literature indicated, however, that the rectum can serve for extended periods as a storage organ and in some cases could contain a substantial portion of the total activity in the alimentary tract. For example, Notghi *et al.* (1993) used a polymer-coated capsule to deliver  $^{111}\text{In}$ -resin into the ileocaecal region in eight volunteer subjects and at 24 hours found activity mainly in the rectum in two of the subjects. In a study involving 48 healthy volunteers (mean age 38.4 +/-15.8 SD years; 30 men, 18 women), Shafik *et al.* (1997) investigated whether the rectum serves as a storage organ as well as a conduit. Stools in the rectum were found in about two-thirds of the subjects. The subjects with an empty rectum had their last defecation 5.2 +/- 3.6 h before examination, and the subjects with a partially filled rectum had their last defecation 15.6 +/-12.9 h earlier. In view of such findings, and because of the difficulties in determining a meaningful transit time separately for the rectum, the Task Group concluded that the rectum should not be treated as a separate compartment.

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### 6.7.2 Uncertainties in measurement techniques and interpretation

(214) In the years since the development of the *Publication 30* model (ICRP, 1979), numerous investigations of the kinetics of material in the gastrointestinal tract have been conducted by improved, non-invasive techniques, such as external viewing of radio-labeled foods, liquids, or indigestible substances (see previous sections and Annex C). While the uncertainties associated with measurement techniques have been substantially reduced, the difficulties involved in determining true transit times should not be underestimated. For example, the physical characteristics of markers used in modern studies apparently can affect colonic transit times (Olmos *et al.*, 1994). Also, some methods still in common use do not appear to provide representative or reproducible results (e.g. see the discussion of the hydrogen breath test in Annex C).

(215) Uncertainties also are inherent in the assumptions and algorithms used to translate measurements into estimates of the mean transit time. For example, measurements of colonic transit frequently are based on counts of ingested radio-opaque markers in the regions of interest. It has been argued that this technique may substantially underestimate actual transit times in many cases because the experimental methods may not closely approximate the underlying assumptions of continuous ingestion of markers and attainment of steady-state by the time of

30

counting (Bouchoucha and Thomas, 2000). The extent of underestimate may vary considerably from one study to another due to differences in numbers and patterns of administration of the marker and times of measurement.

### 5 **6.7.3 Variability in transit times**

(216) Annex C describes a number of factors that can have substantial influence on transit rates of material in different segments of the alimentary tract, and several of these factors are mentioned in the present chapter. The following paragraphs summarize some of the main sources  
10 of variability in transit times and the extent of variability indicated by reported data. The reader is referred to Annex C for further details and a list of references.

(217) The time that food is held in the mouth varies from a few seconds to 30 seconds or more, depending on the composition and texture of the food, the level of hunger, personal habits,  
15 customs, and other factors. The residence time in the mouth can be increased by up to an order of magnitude by some diseases that interfere with chewing or swallowing such as poliomyelitis and encephalitis.

(218) In the HATM, esophageal transit is viewed as consisting of two components, one  
20 representing relatively fast transfer of most of the swallowed amount and one representing relatively slow transfer of a small fraction of residual material. For normal subjects, transit times for liquids are generally in the range 3-12 s for the fast component. Esophageal transit of solids varies considerably with the composition of the ingested material and the amount of fluid ingested with the solid. Transit is particularly slow for relatively dry, non-viscous solids. The portion of  
25 swallowed material remaining after the initial peristaltic wave and the time that the residual material remains in the esophagus are both highly variable. Residual material usually is cleared completely within 30-45 sec and often within a much shorter time, but capsules or solid food ingested without water may remain in the esophagus for several minutes or even hours. Transit times are increased by cold fluids and decreased by warm fluids. Esophageal transit generally is  
30 faster in the upright than the supine position, particularly for solids. Changes with age in esophageal transit appear to be modest. Esophageal transit is affected by a number of disorders of the digestive system including hiatal hernia, esophageal reflux, esophageal spasm, and esophageal diverticulosis and is particularly slow in persons with achalasia, a condition in which the lower esophageal sphincter fails to relax during the swallowing mechanism. In achalasia, the

residual component often represents half or more of the swallowed material. When achalasia becomes severe, the esophagus may not empty swallowed food for many hours.

5 (219) The kinetics of gastric emptying is affected by the composition of the ingested material, gender, age, and other factors. Typically, liquids are emptied from the stomach faster than digestible solids, and digestible solids are emptied faster than nondigestible solids having a dimension greater than 2 mm. For healthy adult subjects, reported central values for observed gastric half-emptying times range from 40 to 160 min for solids and from 8 to 107 min for liquids. The means and standard deviations of the collected central values are 91 +/- 30 min for solids and 10 36 +/-22 min for liquids. Many of the observed half-emptying times for children are within the range of values determined for adults. Reported gastric half-emptying times for meals in infants generally are in the range 15-100 min. Gastric emptying may be slower in elderly persons than in young and middle-aged adults, but findings are not entirely consistent. The rate of gastric emptying of ingested material depends strongly on its composition and the level of nutrients in the jejunum. 15 The emptying time increases nearly linearly with the caloric content of the meal and also is increased substantially by fat. The emptying time of either solids or caloric liquids is substantially greater on average in women than in men. Emptying times are altered by a number of diseases, including several diseases that affect the nervous system or alter energy requirements. Substantially altered rates are seen in cirrhosis and hypothyroidism. Emptying rates are not 20 consistently increased or decreased in diabetics but appear to be considerably more variable in diabetics than in control subjects. The gastric half-emptying time of a solid meal was almost five times longer in long-term insulin-treated diabetics with gastrointestinal, dyspeptic symptoms than in control subjects. The gastric emptying rate is altered by some pharmaceuticals.

25 (220) The transit time through the small intestine shows some variation with contents or other factors but appears to be much less variable than transit through the stomach or colon. Most reported values based on apparently reliable techniques fall in the relatively narrow range of 3-4 h. Some studies suggest faster transfer of liquids than solids in the small intestine, while others indicate that liquids and solids transit the small bowel together, which is assumed in the present 30 model. Fat in the small intestine induces faster transit than proteins but delays ileocolonic transit. Ingestion of oleic acid appears to slow the transit of material through the small intestine. Limited comparisons of small intestinal transit in adult males and females have not revealed significant differences with gender. The rate of movement of material through the small intestine may be increased moderately by diarrhea and decreased moderately by constipation, but the data are not

definitive. The transit time through the small intestine appears to be altered by some pharmaceuticals. Limited data suggest that the transit time through the small intestine may be reduced by stress and physical exercise and increased during pregnancy.

5 (221) Reported central transit times through the total colon vary by about a factor of 4 (range, 17-  
68 h) but are typically in the range 24-48 h. On average, transit times are 30-40% greater in adult  
females than in adult males and appear to be greater in adult males than in children. Results of  
studies of potential changes with adult age in colonic transit times are equivocal. Measurements of  
segmental transit times in relatively large study groups indicate upper 95% values of roughly 24 h  
10 for the right colon, 36 h for the left colon, and 40 h for the rectosigmoid. Average oro-rectal transit  
times, expected to represent mainly colonic transit, vary substantially from one region of the world  
to another, presumably due mainly to differences in dietary fibre. For example, measured oro-  
rectal transit times were longer on average for populations whose diets consisted largely of  
refined, low-fiber foods (means, 48-83 h) than for populations that ate mainly unrefined, high-fibre  
15 foods (means, 34-36 h) or mixed diets (means, 41-47 h). Transit through the colon may be altered  
substantially by constipation or diarrhea. In one study, colonic transit times of about 18 h and 5 d  
were determined for groups of subjects with diarrhea and constipation, respectively, while no  
significant difference in gastric emptying or small intestine transit was found between the two  
groups. A number of disease states affect colonic transit. Patients with progressive systemic  
20 sclerosis showed an increase in the estimated median gastric emptying time and colonic transit  
time compared with control subjects but no abnormality in the small intestine transit time. Diarrhea  
and decreased gastrointestinal transit times are common manifestations of hyperthyroidism,  
whereas constipation frequently occurs in hypothyroidism. The transit time through the colon may  
be altered substantially by drugs.

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## 7. MORPHOMETRY AND DOSIMETRY

### 7.1 Introduction

5

(222) This chapter presents morphometric data for regions of the human alimentary tract and describes the geometric models used to represent these regions for the purposes of calculating Absorbed Fractions (*AF*) and Specific Absorbed Fractions (*SAF*) for non-penetrating radiation. It also outlines methods for deriving photon *SAF* values both for the  
10 alimentary tract and other regions of the body. A mathematical description of the method of age-dependent dose calculation is presented and some example *AF* and *SAF* values for electrons and alpha particles are discussed.

15

(223) Information is given in this chapter on anatomical parameter values for newborn infants, 1, 5, 10 and 15 year-old children and adults. The data are consistent with information given in *Publication 89 on Basic Anatomical and Physiological Data for use in Radiological Protection* (ICRP, 2002). These data are used to compute values of Specific Effective Energy (*SEE*; see section 7.3.1) for the above age groups. *SEE* values for intermediate ages are derived by interpolation (linear interpolation by inverse body mass is usually used). Further information on morphometry is given in Annexes A, B and D.

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25

(224) Throughout this Chapter *source* is used to describe those regions where nuclear transformations occur, generally the contents of the lumen, or the mucosal layer of the wall of a region, and *target* is used to describe regions which contain the radiosensitive cells, ie. the salivary glands or the wall of a region.

### 7.2. Morphometry

#### 7.2.1. Oral cavity

30

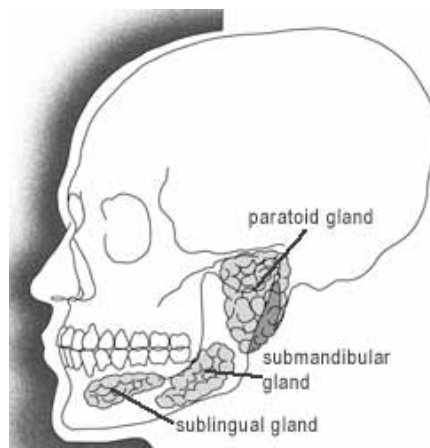
(225) For the purposes of calculating absorbed fractions, the lower portion of the head is represented by a right circular cylinder which contains the oral cavity, teeth, tongue and salivary glands. The radius of the cylinder is 6.45 cm and the total height is 13 cm. Within this cylinder the teeth are represented by a semi-circular arc of internal and external radii  
35 3.6 cm and 4.45 cm respectively. The teeth are assumed to be cubes with sides of 0.85 cm, on the basis of data showing variations in tooth height from 0.65 cm to 1.1 cm,

labiolingual width from 0.6 cm to 1.1 cm and mesiodistal width from 0.5 cm to 1.1 cm (see Annex A). The tongue is assumed to be a right-circular cylinder, 1.18 cm in depth, bounded by the teeth. The three pairs of salivary glands (parotid, submandibular and sublingual glands), are represented by ellipsoids of different axial lengths (Figure 7.1). The parotid (or paratoid) has axes of length 6, 1.8 and 4.4 cm, the submandibular (or submaxillary) has axes of 2, 3 and 4 cm, and the sublingual has axes of 1.6, 1.5 and 4 cm. The masses of the salivary glands computed from their volumes based on these dimensions, and assuming a density of  $1 \text{ g cm}^{-3}$ , are 24.9, 12.6 and 5.0 g (parotid, submandibular, sublingual) which are in good agreement with the reference masses of 25, 12 and 5 g given in *Publication 89* (ICRP, 2002).

(226) The teeth are taken to have a density of  $2.5 \text{ g cm}^{-3}$  and to be composed of 50% oxygen, 20% phosphorus and 30% calcium, representing an average of the values given for different teeth in *Publication 89* (ICRP, 2002). All other tissue in the head is taken to be soft tissue (ICRU, 1989) of density  $1 \text{ g cm}^{-3}$ . The source representing food and drink within the mouth is assumed to be water (density  $1 \text{ g cm}^{-3}$ ).

(227) The source regions of interest in the head and mouth are:

- food or liquid in the oral cavity, assumed to be a uniformly distributed layer, 5 mm in depth, lying within the oral cavity on top of the tongue, in the shape of a cylinder. The mass of food in a 5 mm layer is 20g;
- radionuclides retained on the surface of teeth (see Chapters 3 and 5) are assumed to be uniformly distributed in a thin layer ( $10 \text{ }\mu\text{m}$ ) on inner and outer surfaces – that is, adjacent to the tongue and cheeks. This is illustrated diagrammatically in Figures 7.2 and 7.3;
- The salivary glands (described above).



**Figure 7.1.** Position and shape of the salivary glands.

(228) Biokinetic models which identify salivary glands as a source region are unlikely to specify different uptakes for the different glands. Therefore values of *AF* are given in this report for the mass-weighted mean of the three pairs of the salivary glands.

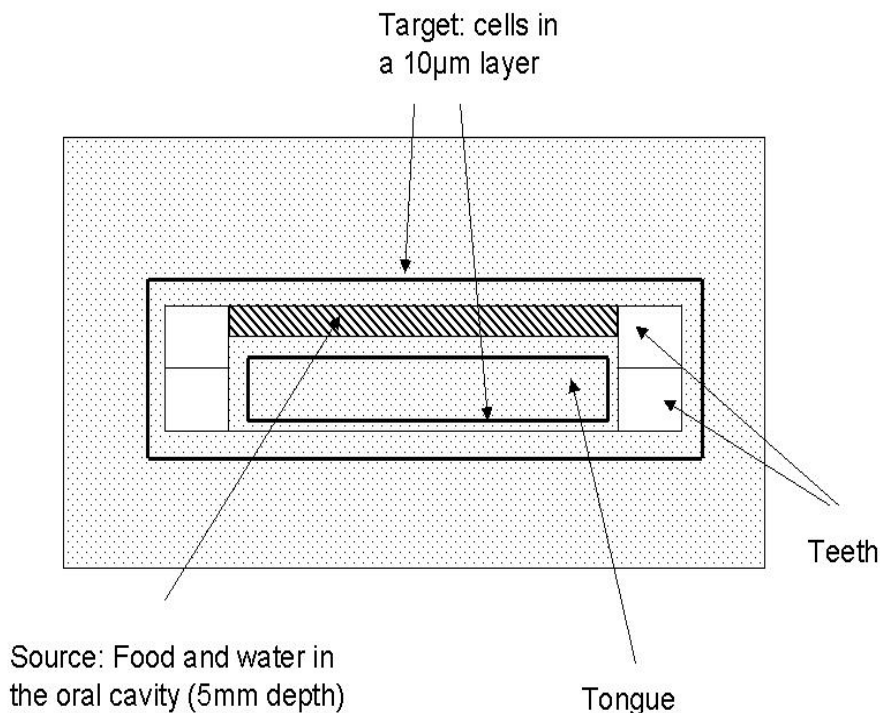
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(229) The target regions in the mouth and lower head are taken to be:

- the salivary glands;
  - the basal cells of the epithelial layer of the tongue, and inner surfaces of the oral cavity.
- As illustrated by Figure 2.4, the depth varies substantially within and between different regions in the mouth, with an overall range of about 70 – 400  $\mu\text{m}$ . For the purposes of this report, the target depth is taken to be a 10  $\mu\text{m}$  layer at from 190 to 200  $\mu\text{m}$ . This depth is assumed to apply to all age groups. In situations where information is available on retention of radionuclides in the oral mucosa, it is assumed for dosimetric purposes that the source region has activity uniformly distributed within a 200  $\mu\text{m}$  thick layer of the epithelia of the oral cavity and tongue.

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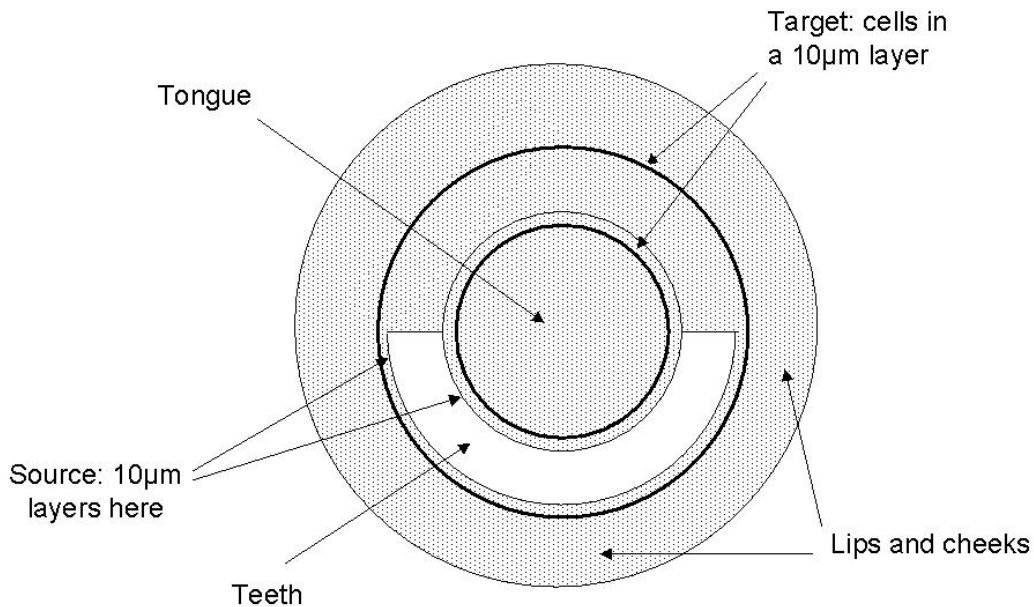
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**Figure 7.2.** The geometric model (cross-section) used to calculate values of Absorbed Fraction (*AF*) in the head and mouth, showing the source region of radionuclides in diet in relation to target regions in the tongue, and epithelial lining of the mouth.

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**Figure 7.3.** The geometric model (plan view) used to calculate values of Absorbed Fraction (AF) in the head and mouth. Food or liquids containing radionuclides are taken to be confined to a short cylinder on top of the tongue, bounded by the teeth, and the roof and back of the mouth (see also Figure 7.2). Radionuclides may, in certain cases, also be retained on teeth.

(230) Because of the schematic nature of the model for the mouth and the lack of good age-dependent data, it has not been extended to other age groups. The values of Absorbed Fraction derived from the adult model described above are taken to apply to all ages.

(231) In the ICRP Human Respiratory Tract Model for Radiological Protection (HRTM, ICRP 1994a), the oral cavity was included with the other airways of the head and neck, in a composite organ, called the “extrathoracic airways” (ET). The oral cavity was not considered explicitly in the *Publication 30* gastrointestinal model, with which the HRTM has been used up to now. However, since the oral cavity is identified in the HATM, consideration must be given to consistency between HATM and HRTM. As described in Annex F, separating the oral cavity from ET has a negligible effect on the behaviour of inhaled materials predicted by the HRTM, or on the resulting calculated doses. It is

therefore proposed that when used with the HATM, the oral cavity is not included in the ET region of the HRTM.

### 7.2.2. Oesophagus

5

(232) For the purposes of this report, transit through and doses to the pharynx are ignored and radionuclides are assumed to pass directly from the mouth to the oesophagus. Radioactive particles escalated from the respiratory tract are assumed similarly to pass directly into the oesophagus.

10

(233) The length of oesophagus, from the pharynx to the stomach, is typically in the range 23-30 cm in adult males and 20-26 cm in adult females (ICRP, 2002). Autopsy measurements on infants and children indicate an oesophageal length of about 8-10 cm at birth, 12 cm at age 1 y, 18 cm at 10 y, and 19 cm at 15 y (ICRP, 1975). The similarity in the values for ages 10 and 15 y is inconsistent with the rate of growth of the upper body during that period and suggests that the subjects may not have been representative.

15

(234) The length of the oesophagus has been determined in a number of modern studies by external imaging techniques. Reported values vary considerably, apparently due mainly to differences in the definition of “oesophageal length” in medical studies and, to a lesser extent, to intersubject variability. In a study of 51 normal adults (27 males and 24 females) from the U.S., oesophageal length, defined as the average distance from the proximal end of the upper oesophageal sphincter and the distal end of the lower oesophageal sphincter, was given as  $28.3 \pm 2.4$  cm (Awad et al., 1999).

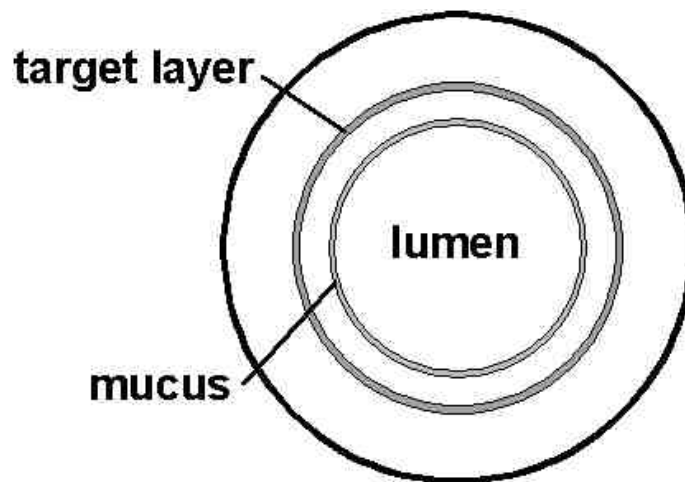
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(235) On the basis of these data, values for the length of the oesophagus were given in *Publication 89* (ICRP, 2002) as shown in Table 7.1

**Table 7.1** Reference values for length of the oesophagus (cm)

Newborn	1 y	5 y	10 y	15 y		Adult	
				Male	Female	Male	Female
10	13	18	23	27	26	28	26

30



**Figure 7.4.** Cross-section of the geometric model used to calculate Absorbed Fractions for the tubular regions of the alimentary tract. For tubular regions, the presence of mucus on the luminal surface is ignored in the calculation of Absorbed Fractions. Target cells are assumed to form a continuous layer at a defined depth from the luminal surface.

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10

(236) All tubular regions of the alimentary tract – the oesophagus, small and large intestines – are treated for the purposes of the calculation of absorbed fractions for short range radiations, as right circular cylinders. This simplification takes no account of the peristaltic waves of contraction within the walls of the various regions, that propel the contents along the tract. It also takes no account of the villi in the small intestine and internal ridges and folds in the small and large intestines (see Chapter 2 and Annex A). Each section is taken to be a right circular cylinder and the source is taken to be water uniformly filling the cylinder. Tissue comprising the walls of the regions is taken to be of density  $1 \text{ g cm}^{-3}$  and to have the composition of ICRU soft tissue (ICRU, 1989). The lengths of the sections are given in the tables of this chapter. This approach allows for absorption of energy both within the lumen and within the mucosal tissue of the wall lying between the lumen and the target region.

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(237) It is assumed that the internal diameter of the oesophagus in adults when distended by a bolus of food is 1 cm. This diameter is applied to the first (rapid) component of transit through the oesophagus (see Chapter 6), assuming that radionuclides present in food are uniformly distributed throughout the contents. For the second (slow) component of transit, it is likely that in most cases the oesophagus will not be distended. However, for simplicity, the same internal diameter is used but the second component is assumed to transit as a thin layer on the internal mucosal surface of the oesophagus (the remainder of the lumen is taken to be filled with water for the calculation of  $AF$ ).

30

(238) Little information is available on which to base estimates of changes in internal diameter of the alimentary tract regions with age. Here it is assumed for the oesophagus, as for the small and large intestines (see below), that the internal diameter in the newborn is half that in adults, with intermediate values for 1 to 10 year-old children.

5

**Table 7.2** Assumed values for the internal diameter of the oesophagus (cm)

Newborn	1 y	5 y	10 y	15 y	Adult
0.5	0.6	0.7	0.8	1	1

(239) The oesophageal wall of the adult is about 3.5 - 5.6 mm thick (ICRP, 1975). The stratified squamous epithelium lining the oesophagus, illustrated in Figure 2.5, is taken to be 200  $\mu\text{m}$  thick in the adult. The target layer is assumed, therefore, to be at a depth of 190  $\mu\text{m}$  to 200  $\mu\text{m}$ . The oesophageal wall of the newborn is thinner than that of the adult, but the epithelium thickens rapidly after birth and the depth of the target layer is assumed to be independent of age for the purposes of this report. The presence of a layer of mucus on the luminal surface of the oesophagus has been ignored. The thickness of the mucus layer, of perhaps 10 – 30  $\mu\text{m}$ , is within the range of uncertainties in the overall average depth of the basal cell target layer.

### 7.2.3. Stomach

(240) The stomach is highly variable in volume, being capable of distension to accommodate a large amount of ingested material. It is connected to the oesophagus at the cardiac sphincter and to the small intestine at the pyloric sphincter. The stomach wall exhibits numerous longitudinal folds, or rugae, when the organ is not distended with food. For the purposes of this report, it was assumed that the stomach is a simple sphere of volume 175  $\text{cm}^3$  in adults. Volumes at different ages, Table 7.3, were based on values of mucosal surface area given in *Publication 23* (ICRP, 1975). To calculate age-dependent volumes, a constant relationship was assumed between measured mucosal areas and the surface area of the reference spherical stomach (volume of 175  $\text{cm}^3$ ).

**Table 7.3** Values for the volume of the stomach ( $\text{cm}^3$ )<sup>a</sup>

Newborn	1 y	5 y	10 y	15 y	Adult
30	40	60	80	120	175

30

<sup>a</sup>calculated using values for mucosal surface area based on data given in Publication 23: 150 cm<sup>2</sup> at 3 months (applied here to newborn), 200 cm<sup>2</sup> at 1 y, 250 cm<sup>2</sup> at 5 y, 300 cm<sup>2</sup> at 10 y, 400 cm<sup>2</sup> at 15 y and 525 cm<sup>2</sup> in adults.

5 (241) The gastric epithelium is a single layer of cells, continuous with the basal layer of the stratified epithelium of the oesophagus (see Chapter 2). The lining of the stomach is indented by numerous pits that supply several million tubular glands. The glands are divided into three categories: the cardiac glands occur in the first 5-40 mm from the cardiac orifice; the pyloric glands occur near the intestine; and the gastric glands lie between these  
10 two extremities. The cells of the cardiac and pyloric glands all appear to be of the mucus type. The epithelium of the gastric glands is more diversified, containing enzyme- and acid-secreting cells as well as mucus cells.

(242) The mucosal lining of the stomach is of variable thickness but for dosimetric  
15 purposes in situations of retention of radionuclides in the stomach wall, the source region is taken to extend to a depth of 300 µm into the mucosa (see Chapter 2). Figure 2.6 illustrates the cross-section of a typical gastric gland, showing that the proliferative cells and hence target stem cells, are thought to be towards the upper luminal ends of the glands. A target depth of 60 – 100 µm is assumed here to apply at all ages, as a uniform target at this depth  
20 over the entire inner surface of the stomach.

#### 7.2.4. Small intestine

(243) The small intestine is a thin-walled tube about 3 (2.3-3.8) meters long in the adult. It  
25 extends from the pylorus of the stomach to the caecum.

(244) The values for the physiological length of the small intestine in Table 7.4 are as given in *Publication 89* (ICRP, 2002), based on data from *Publication 23* (ICRP, 1975). For both newborn infants and adults, the central estimates of the length of the small intestine  
30 are approximately 1.6 times body height. This relation is assumed to hold for ages 1-15 y and for adult females.

**Table 7.4** Reference values for the physiological length of the small intestine (cm)

	15 y				Adult			
Newborn	1 y	5 y	10 y	Male	Female	Male	Female	
80	120	170	220	270	260	280	260	

(245) The diameter of the lumen of the small intestine changes with age and varies with location within the intestine. Values in the range 1.2-2.6 cm have been estimated for the small intestine in newborn infants (ICRP, 1975). For the adult, estimates are in the range 3-6 cm for the first part of the small intestine and decrease to 1.5-2.5 cm for the last part (ICRP, 1975). Table 7.5 shows the values used in this report, taken to apply to the entire length of the small intestine.

**Table 7.5** Assumed values for the internal diameter of the small intestine (cm)

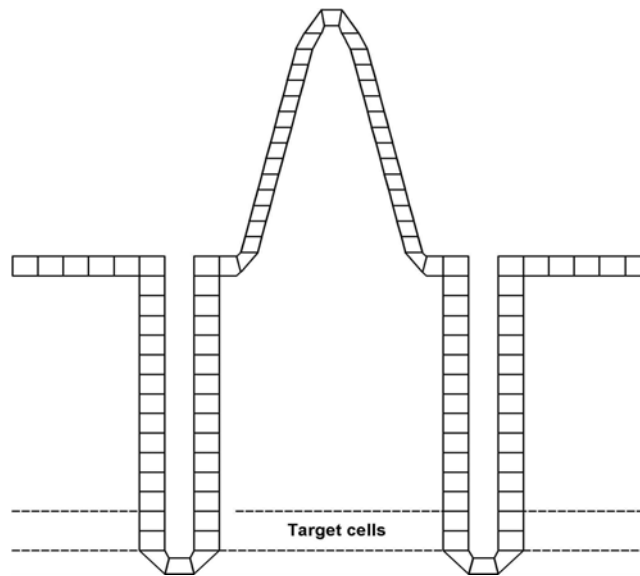
<b>Newborn</b>	<b>1 y</b>	<b>5 y</b>	<b>10 y</b>	<b>15 y</b>	<b>Adult</b>
<b>1</b>	<b>1.2</b>	<b>1.4</b>	<b>1.6</b>	<b>2</b>	<b>2</b>

(246) The lining of the small intestine possesses gross and microscopic structures for increasing the surface area available for digestive and absorptive processes (see Chapter 2). The surface is covered with numerous projections, the villi, which serve as absorptive units and which are unique to this segment of the alimentary tract (Figure 2.7). At their bases are simple tubular invaginations, called crypts of Lieberkühn, that extend to the muscularis mucosae but do not penetrate it. The villi have a single columnar epithelial cover and a core of highly cellular reticular connective tissue. The villi vary in height and form in different regions of the human small intestine. For the purposes of this report, the villus height is taken to be 500  $\mu\text{m}$  in adults and children from 10 years of age and 400  $\mu\text{m}$  for younger children, based on the ultrastructural studies of Stenling *et al.* (1984).

(247) The stem cells responsible for continuous renewal of the epithelial layer are located towards the base of the crypts, immediately above a group of secretory cells, called Paneth cells, at the base of the crypts (see Chapter 4). Potten (2002) measured the depth from the intercryptal plate to the top of the Paneth cell zone to be  $144 \pm 8 \mu\text{m}$ , scoring 11 crypts from 3 adults. The target layer is taken to be 3 cells deep, assumed here to be at a depth of 130 – 150  $\mu\text{m}$  from the intercryptal plate. This depth is assumed to apply at all ages, although there is evidence that crypts are somewhat longer in young children (Stenling *et al.* 1984; Penna *et al.* 1981).

(248) The diagrammatic cross-section in Figure 7.5 shows the location of the target cells in the epithelial layer. For dosimetric purposes, this is assumed to be a continuous layer at 130 – 150  $\mu\text{m}$  from the inner surface of a simple cylinder. Absorbed fractions for non-penetrating radiations from radionuclides in the contents of the small intestine were calculated (see section 7.3) on the assumption that activity is uniformly distributed

throughout the contents of a cylinder, ignoring the presence of the villi. This is considered to be a reasonable assumption because gut contents penetrate between the villi as far as the intercryptal plate. It is assumed that gut contents do not penetrate into the crypts against the flow of secretions from crypt cells. The presence of mucus on the luminal surface was ignored.



10 **Figure 7.5.** Diagrammatic representation of the epithelial lining of the small intestine showing the location of target cells at the base of the crypts. The target cells are assumed to be a continuous layer at 130 – 150  $\mu\text{m}$  below the intercryptal plate.

15 (249) In considering retention of radionuclides in the wall of the small intestine, the general assumption is that retention is confined to the absorptive region of the villi. This is modelled as a uniform layer of tissue above the intercryptal plate, 500  $\mu\text{m}$  thick in adults and children of 10 years and older, and 400  $\mu\text{m}$  thick in younger children. Thus, the spaces between villi, occupied by gut contents, are ignored for this purpose. In a limited number of cases, information may be available suggesting retention in deeper mucosal tissues, within the lamina propria between crypts (see eg. of Pu retention in neonates; Chapter 3). To model retention in the wall of the small intestine, other than retention in villi, uniform distribution throughout the region of the mucosa beneath the villi is assumed, to a depth of 200  $\mu\text{m}$  (base of crypts).

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### 7.2.5. Colon and rectum

(250) The large intestine, or colon, begins at the ileocaecal valve and consists of a caecum and appendix; the ascending, transverse, and descending segments; the sigmoid colon; and a terminal portion, the rectum, ending at the external orifice of the anus.

(251) Data on the large intestine, particularly data related to the motility of the luminal contents, are often reported in terms of the right colon, left colon, and rectosigmoid region or simply the rectosigmoid (see Chapters 4 and 6). This division is adopted in this report. The right colon is defined as the ascending colon including the caecum, plus the proximal half of the transverse colon. The left colon is the distal half of the transverse colon plus the descending colon. The last part of the colon, the rectosigmoid, is taken to include the rectum, largely because of difficulties of specifying residence times of radionuclides separately for the rectum.

(252) Central estimates for the physiological length of the large intestine of the newborn and adult are ~45 cm (range, 20-70 cm) and 110 cm (range, 91-125 cm), respectively (ICRP, 1975). These central estimates are used in *Publication 89* (ICRP, 2002) as reference values for newborn infants and adult. Values for ages 1-15 y are based on the assumption that the length of the large intestine is linearly related to height.

**Table 7.6** Reference values for the physiological length of the large intestine And its segments (cm)

Segment	Newborn	1 y	5 y	10 y	15 y		Adult	
					Male	Female	Male	Female
Right colon	14	18	23	28	30	30	34	30
Left colon	16	21	26	31	35	35	38	35
Rectosigmoid	15	21	26	31	35	35	38	35
<b>Total</b>	<b>45</b>	<b>60</b>	<b>75</b>	<b>90</b>	<b>100</b>	<b>100</b>	<b>110</b>	<b>100</b>

(253) The diameter of the large intestine varies along its length, reducing from caecum to rectosigmoid. The values used in this report are given in Table 7.7, based on data reviewed in *Publication 23* (ICRP, 1975). As for the small intestine, it is assumed that the internal diameters of the regions in infants are one-half the values used for adults and intermediate values are used for 1 to 10 year old children.

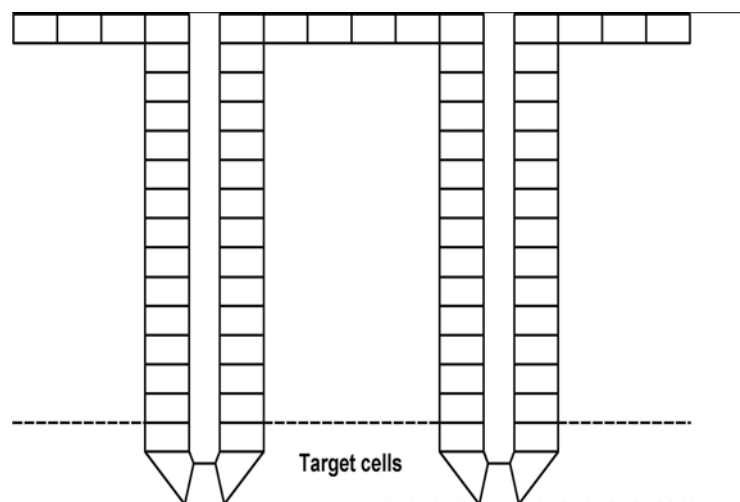


**Table 7.7** Assumed values for the internal diameter of the large intestine (cm)

Segment	Newborn	1 y	5 y	10 y	15 y	Adult
Right colon	3	4	4.5	5	6	6
Left colon	2.5	3	3.5	4	5	5
Rectosigmoid	1.5	2	2.3	2.5	3	3

(254) The mucosa of the large intestine lacks villi and has deep, straight crypts (Figure 2.8 and 7.6). Stem cells are considered to be situated at the base of the crypts; Paneth cells occur at the base of crypts in the small intestine but not the large intestine. Potten (unpublished observations) measured crypt depths of  $311 \pm 9 \mu\text{m}$  for the ascending colon (48 crypts from 1 adult),  $358 \pm 16 \mu\text{m}$  for the sigmoid colon (28 crypts, 3 adults) and  $245 \pm 10 \mu\text{m}$  for the rectum. It was assumed here that the target layer is at a depth of 280 – 300  $\mu\text{m}$  at all ages. As for the small intestine, the target cells were taken to form a continuous layer at this depth in a cylindrical tube (see Figure 7.3). In situations where retention of radionuclides in the wall of the large intestine is considered, distribution is assumed to be uniform within the mucosa to a depth of 300  $\mu\text{m}$  from the luminal surface.

(255) The rectum is divided into an upper region and the anal canal. In the anal canal, the epithelium changes abruptly from simple columnar to stratified. The rectum is treated here as part of the rectosigmoid colon for dosimetric purposes.



**Figure 7.6.** Diagrammatic representation of the epithelial lining of the large intestine showing the location of target cells at the base of the crypts. The target cells are assumed to be a continuous layer at 280 to 300  $\mu\text{m}$  below the intercryptal plate.

### 7.3. Dosimetry

(256) This section gives an overview of the dosimetric methods used in this report, explains how the Absorbed Fractions (AF) and Specific Absorbed Fractions (SAF) used in the HAT model have been computed from the geometric models described in section 7.2, and compares some of the HATM SAF values with *Publication 30* model values (ICRP, 1979).

#### 7.3.1. Dosimetric Principles

(257) To evaluate doses to target tissues, the methods of age-dependent dosimetry first described in *Publication 56* (ICRP, 1989) are applied. In short, the committed equivalent dose,  $H_T$ , in each target tissue, T, is determined by

- the total number of nuclear transformations of each radionuclide of the decay chain in the source regions, S, over a period  $\tau$  after intake of the radionuclide,  $\tau$  in general being 50 years for adults and from the time of intake to age 70 years for children;
- the energy absorbed per unit mass in the target tissue, T, suitably modified by the radiation weighting factor for each type of radiation emitted per nuclear transformation.

The equivalent dose rate,  $\dot{H}_T(t, t_0)$  at age t resulting from an intake at age  $t_0$ , in target tissue T can be expressed as

$$\dot{H}_T(t, t_0) = c \sum_S \sum_j q_{S,j}(t, t_0) \cdot SEE(T \leftarrow S; t)_j \quad (1)$$

where  $q_{S,j}(t, t_0)$  is the activity of decay chain member j present in the source region S at age t after an intake at age  $t_0$ ;  $SEE(T \leftarrow S; t)_j$  is the equivalent dose in the target tissue T per nuclear transformation in region S at age t for radionuclide j (equation 3); and c is any numerical constant required by the units of q and SEE.

(258) The committed equivalent dose in the target tissue T accumulated by age 70 y due to a single intake of a radionuclide at age  $t_0$ ,  $H_T(70-t_0)$  is:

$$H_T(70-t_0) = \int_{t_0}^{70} \dot{H}_T(t, t_0) dt = c \cdot \int_{t_0}^{70} \sum_S \sum_j q_{S,j}(t, t_0) \cdot SEE(T \leftarrow S; t)_j dt \quad (2)$$

Where  $j > 1$  are potential members of the decay chain headed by the radionuclide.

(259) For each radionuclide, the specific effective energy, SEE, at age  $t$  takes into account the contributions of each radiation emitted by the radionuclide weighted by the appropriate radiation weighting factor. The SEE quantity of Equations 1 and 2 is computed as:

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$$SEE(T \leftarrow S; t) = \frac{1}{M_T(t)} \left[ \sum_i E_i Y_i w_{R,i} AF(T \leftarrow S; E_i, t) + w_{R,\beta} \int_0^{\infty} Y(E) E AF(T \leftarrow S; E, t) dE \right] \quad (3)$$

where  $E_i$  is the energy of the  $i$ -th discrete radiation emitted by the radionuclide with intensity  $Y_i$  per nuclear transformation,  $M_T(t)$  is the mass of the target tissue  $T$  at age  $t$ ,  $w_{R,i}$  is the radiation weighting factor applicable to the  $i$ -th radiation,  $AF(T \leftarrow S; E_i, t)$  is the absorbed fraction quantity representing the fraction of the energy  $E_i$  emitted in  $S$  that is absorbed in  $T$  for an individual of age  $t$ , and  $Y(E) dE$  denotes the number of electrons in the beta or positron spectrum, with energy between  $E$  and  $E + dE$ . Information on the energies and intensities of the radiations emitted by the radionuclides considered here are contained in  
 15 *Publication 38* (ICRP, 1983) and are available, including the beta spectra, in electronic form (Eckerman *et al.*, 1994). The quotient of absorbed fraction,  $AF$ , and mass,  $M_T$ , is known as the Specific Absorbed Fraction ( $SAF$ ). Information in the literature is often available, particularly for photons, in terms of  $SAF$  rather than  $AF$ .

20 (260) In the HATM, doses are calculated separately for the right colon, the left colon, and the rectosigmoid section. Chapter 4 concludes that the relative risk of radiation effects is not significantly different in these three regions of the colon. Therefore, in this report, the dose coefficient for colon to be used in conjunction with the tissue weighting factor ( $w_T$ ) given for colon (ICRP, 1991) is calculated as the mass-weighted average of the dose coefficients for  
 25 the three sections of the colon, i.e.

$$h_{colon} = \frac{m_{rc}h_{rc} + m_{lc}h_{lc} + m_{rs}h_{rs}}{m_{rc} + m_{lc} + m_{rs}}$$

Where  $h_T$  and  $m_T$  are the equivalent dose coefficients for, and mass of, section  $T$  of the colon, and  $rc$ ,  $lc$  and  $rs$  denote right colon, left colon and rectosigmoid respectively.

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### 7.3.2. Absorbed Fractions for photons

(261) Absorbed Fractions ( $AF$ ) and Specific Absorbed Fractions ( $SAF$ ) for photons are calculated using computer models of the human body. The Medical Internal Radiation

Committee (MIRD) of the US Society of Nuclear Medicine developed a phantom in which organs were represented as simple mathematical shapes such as spheres, ellipses and cones (Snyder *et al.*, 1969). This phantom and its later derivatives (Cristy and Eckerman, 1987, 1993, Stabin *et al.*, 1995), collectively known as MIRD-type phantoms, have been used to calculate photon values of *SAF* for previous ICRP dose compendia (ICRP 1994, 1996, 2001). Recently, however, a new type of phantom has become available which offers the prospect of increased realism and accuracy in dose calculations. These phantoms are based on computed tomography (CT) or magnetic resonance images (MRI) obtained from high resolution scans of individuals. They consist of a large number of volume elements known as voxels (**volume pixels**), and are usually known as voxel phantoms.

(262) This development began about 15 years ago and a number of laboratories around the world have developed voxel phantoms for both males (Dimbylow, 1997; Zankl and Wittman, 2001; Zubal *et al.*, 1994; Saito *et al.*, 2001; Petoussi-Henss *et al.*, 2002; Xu *et al.*, 2000) and females (Fill *et al.*, 2004). Some of these phantoms have already been used for internal dosimetry (Chao and Xu, 2001; Smith *et al.*, 2001; Zankl *et al.*, 2003; Fill *et al.*, 2004).

(263) Voxel phantoms can provide more anatomically realistic models than the MIRD-type phantoms. However, a voxel phantom is a model of an individual person while, for calculating doses for application to population groups, models that are typical of average male and female members of the population are required. There are a number of approaches to deriving a typical phantom from an original individual-specific model. One such method is to change the dimensions of the original voxels (Dimbylow, 1997; Chao *et al.*, 2001, Fill *et al.*, 2004), another is to add or subtract layers of voxels to a region. Work is in progress (Zankl *et al.*, 2003; Fill *et al.*, 2004) to produce reference voxel models for radiation protection purposes. It is expected that these models will include the anatomical regions associated with the HATM. Thus, in the planned future application of the HATM to a range of radionuclides, results from the reference voxel models will be used to calculate photon doses, and information concerning the use of the HATM in conjunction with the voxel phantom will be given at that time. For the illustrative calculations given in this report, results from Cristy and Eckerman (1993) based on MIRD-type phantoms have been used.

### 7.3.3. Absorbed Fractions for electrons

(264) Absorbed Fractions for electrons have been computed using the geometric models, described in Section 7.2, which specify the source and target regions for each region of the

HATM. Activity in any source region is taken to be distributed uniformly within the region. The mass of each target region is computed from the dimensions of the geometric model and the depth and thickness of the target region (Table 7.8); a tissue density of  $1 \text{ g cm}^{-3}$  is assumed (other than for teeth, see section 7.2.1).

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(265) Absorbed Fractions for electrons have been calculated using the MCNP General Purpose Monte Carlo Code (Briesmeister, 1997). The simplified geometric models used in this report (section 7.2) to represent the various regions of the alimentary tract are specified in MCNP. A large number of computer simulations of electron transport throughout the geometric model is then carried out for a discrete initial energy using the condensed history technique (Berger, 1963). The theories of Goudsmit-Saunderson (1940) and Landau (1944) are used to predict the angular deflections and energy losses, respectively. More details about MCNP are given by Briesmeister (1997). The total energy deposited in the target region for all simulations is computed and the Absorbed Fraction is this energy divided by the total initial energy summed over all the simulations. The calculation is repeated for a number of energies; results for adult males are given in Annex G. Results for females and other age-groups will be given in future reports. The results calculated for electrons are applied to beta particles and positrons as well as to mono-energetic electrons.

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**Table 7.8.** Summary of target cells depths and masses for target each region of the HATM for adult males.

Region	Target cell depth ( $\mu\text{m}$ )	Target cell mass <sup>a</sup> (g)
Oral cavity	190-200	0.23
Oesophagus	190-200	0.091
Stomach	60-100	0.62
Small intestine	130-150	3.6
Right colon	280-300	1.3
Left colon	280-300	1.2
Recto-sigmoid	280-300	0.73

a - computed from the length and diameter of each section (or radius for stomach) and the depth and thickness of the target cells, assuming a tissue density of  $1 \text{ g cm}^{-3}$ .

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(266) In cases where the source is a 'wall region' the above approach is also used. For sections other than the small intestine, activity in the wall is taken to be uniformly distributed

throughout the mucosal layer of the section (see section 7.2). For activity in the small intestine wall, the general assumption is of uniform distribution throughout a layer corresponding to the villi (section 7.2.4). The illustrative calculations given in this report require values of  $AF$  only for the wall of the small intestine. These are therefore given in Annex G for adult males; results for walls of all regions will be given in future reports, for males and females and for all age-groups.

(267) Many of the systemic kinetic models used to describe the behaviour of activity following absorption from the alimentary or respiratory tracts specify retention in 'other tissues' or 'other soft tissues'; other systemic models specify whole body distribution. In each of these cases, the walls of the HATM regions are included as source regions, taking account of normal processes of circulation and distribution of systemic activity. Thus, the target regions of the HATM can receive doses from this activity as well as from activity in the contents of the lumen or retained in the walls during absorption. For non-penetrating radiation, including electrons and alpha particles, all tissues that constitute 'other tissues' (or 'other soft tissues' or 'whole body') are assigned the same dose; this dose is taken to apply to the all target regions of the HATM. For the compartments of relatively rapid transit, such as the mouth and oesophagus, systemic activity often contributes the main component of dose.

### Examples

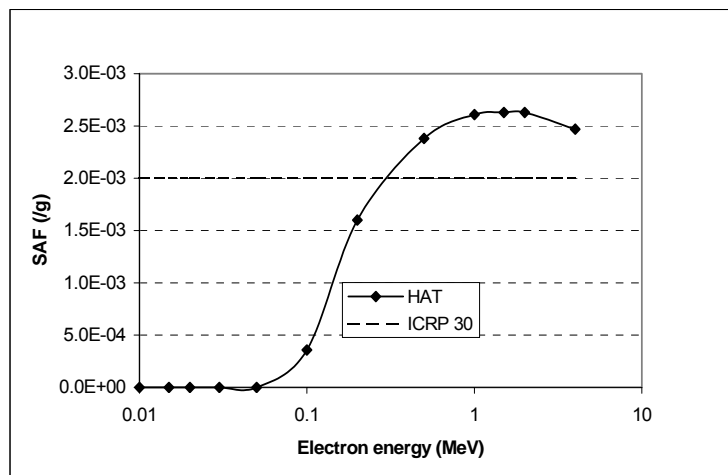
(268) These examples consider values of  $SAF$  in adult males to allow direct comparison with  $SAF$  values given in *Publication 30* (ICRP, 1979). Figure 7.7 shows the variation of  $SAF$  with electron energy for the source 'stomach contents' and the target region in the stomach wall. Above about 0.5 MeV the  $SAF$  of the HAT model is about 25% larger than the energy-independent *Publication 30* value, but decreases rapidly to much smaller values at low energies. The two approaches yield reasonably similar values of  $SAF$ , at least at moderate to high energies, because the assumed position of the target cells is relatively shallow in the stomach (depth of 60-100  $\mu\text{m}$ ) and the mass of the stomach contents used in the *Publication 30* model is similar to that used in the HATM.

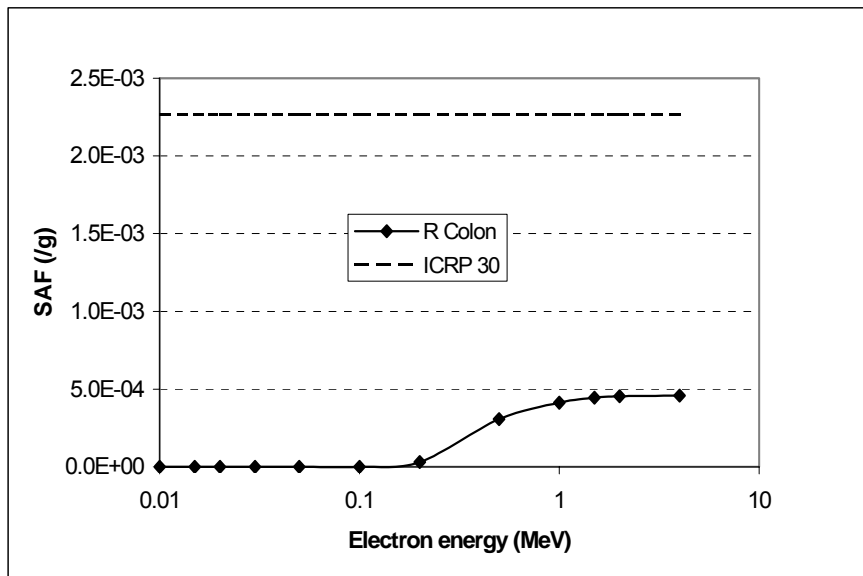
(269) Figure 7.8 shows the variation of  $SAF$  with electron energy for the source 'right colon' and compares results with *Publication 30* value for the most anatomically similar region ('upper large intestine', ULI). Above about 1 MeV the value calculated for the HATM is about a factor of five lower than the *Publication 30* value. The *Publication 30* method effectively calculated a dose at the surface of the contents of the lumen and applied this to the target cells in the wall. A relatively low mass of the ULI contents (220 g) was used in the *Publication*

30 model which results in higher values of SAF than the HATM method of calculating the energy absorbed in the target cells throughout the length of the right colon. In addition the HATM results are lower due to absorption of energy within the tissue overlying the target region. At lower energies the differences are larger, and as the energy decreases below 0.1 MeV the value of SAF for the HATM becomes zero as electrons do not possess sufficient energy to reach the target region. Similar comparisons apply to the other sections of the colon.

(270) The implication for low energy emitters is clearly that doses calculated using the HATM can be expected to be lower than *Publication 30* values. However, simple statements about the extent to which doses will be lower cannot be made for radionuclides with emissions over a wide range of energies, or in cases where systemic activity makes a significant contribution to doses to tissues of the alimentary tract. Radionuclide-specific examples of the effect of the HATM on doses, with comparisons to *Publication 30* doses, are given in Chapter 8.

**Figure 7.7.** Comparison of values of Specific Absorbed Fraction (SAF) for the HATM and the *Publication 30* model (1979) for the source in the lumen of the stomach of adult males.





**Figure 7.8.** Comparison of values of Specific Absorbed Fraction (SAF) for the HATM and the Publication 30 model (ICP, 1979) for the source in the lumen of the right colon (HATM) or upper large intestine (*Publication 30*) of adult males.

#### 7.3.4. Absorbed Fractions for alpha particles

(271) Absorbed Fractions for alpha particles are zero for all of the lumen source regions of the HATM (i.e. the 'contents' regions) due to the depth of the target cells in relation to the range of an alpha particle in tissue. Thus, when target cells are situated at a depth of greater than around 40 or 50  $\mu\text{m}$  in the wall, alpha particles emitted by important radionuclides (eg.  $^{210}\text{Po}$ ,  $^{239}\text{Pu}$ ) cannot penetrate the wall to the depth of the target region.

(272) In the simple geometric model of the stomach, some energetic alpha particles could penetrate to the target region (60 – 100  $\mu\text{m}$ ). However, taking into account the presence of a layer of mucus on the luminal surface of the stomach, around 20  $\mu\text{m}$  thick, which has been ignored in calculations for electrons, means that in practice *AF* values for alpha particles emitted in the stomach can also be taken to be zero.

(273) The source region 'small intestine wall' is generally taken to be a layer of tissue corresponding to the villi, which are situated beyond the range of an alpha particle from the target region. In cases where the source region is a wall of a section, other than the villi of the small intestine, a method of calculating values of *AF* for alpha emitters has been developed

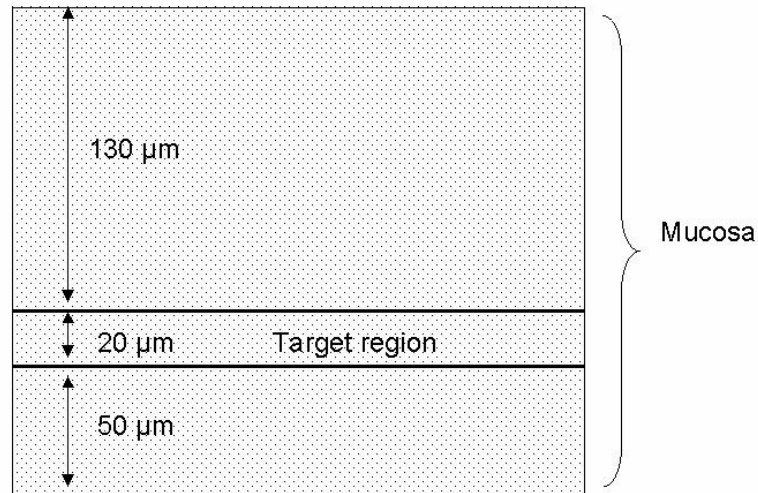


based on an algebraic relationship between stopping-power in soft tissue and alpha particle energy (Sontag, 1987). The range of alpha particles in tissue is sufficiently short for the curvature of the wall to be ignored in these calculations. The wall can therefore be treated as a rectangular section of tissue. Alpha particles are assumed to be emitted at random angles throughout the depth of the mucosal layer that is taken to be the source (see 7.2.4), ie. in the target region itself as well as the adjacent tissue assumed to be part of the source region (e.g. Figure 7.9).

(274) The comments in section 7.3.3 regarding doses to HATM target regions from systemic activity also apply to doses from alpha emissions.

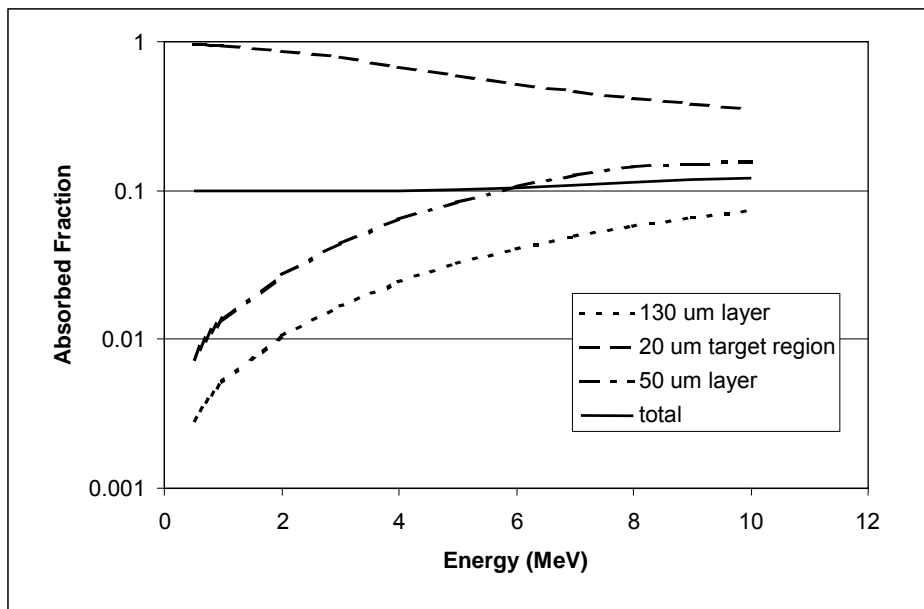
### **Example**

(275) Figure 7.9 shows the geometric model used to calculate values of  $AF$  for alpha particles in the case of retention in the small intestine in mucosal tissue underlying the villi. It is assumed that activity is distributed uniformly throughout a 200  $\mu\text{m}$  layer of tissue that includes the target cell layer at a depth of 130 – 150  $\mu\text{m}$  (see 7.2). In this example, values of  $AF$  are calculated separately for three source regions: the region corresponding to the target, and layers of mucosal tissue on both sides of this layer. Total values of  $AF$  are computed as a volume-weighted sum and the values for the separate source regions and the total are shown as a function of initial alpha particle energy in Figure 7.10. At low energies the range of the particles is very short and thus  $AF$  for emissions in the target region is one; conversely values of  $AF$  for emissions in the adjacent regions are very low. At higher energies, some of the energy of particles emitted in the target region is deposited outside the region and thus  $AF$  for this source decreases to below one; in contrast, values of  $AF$  for the adjacent regions increases as more particles penetrate into the target region. The total for the three source regions is reasonably constant, lying between 12 and 10% over the energy range 0.5 to 10 MeV. This result can be compared to a simple approach of assuming that all energy is absorbed at the site of alpha particle emission. With this assumption, the total  $AF$  would be given by the volumetric fraction of target region in the whole of the mucosa, ie. 20/200 (10%).



**Figure 7.9.** The geometric model used to calculate values of alpha Absorbed Fraction (AF) for retention in the small intestine in mucosal tissue underlying the villi (see 7.2). The source consists of three layers, including the target layer.

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**Figure 7.10.** Absorbed Fraction (AF) as a function of initial alpha particle energy for particles emitted in the three different sections of the mucosa of the small intestine wall shown in Figure 7.9., and the volume-weighted total AF.

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## 8. USE OF THE MODEL

### 8.1. Introduction

(276) This chapter includes example dose calculations which illustrate the implications of the new model in comparison to the *Publication 30* model, in terms of doses to regions of the alimentary tract and of effective dose. It illustrates the standard case in which radionuclide-specific information is available only on total absorption. It considers the application of the model to cases where information is available on retention of radionuclides on teeth or in the small intestine wall, and cases where information may be available on absorption from different regions of the tract. The scope for differences in alimentary tract doses between adult males and females and between different age-groups is also discussed. Uncertainties are assessed, considering the effect on doses of uncertainties in radionuclide absorption, location of target cells for cancer induction, transit times of materials through the lumen of the tract, and dimensions of the colon. The Chapter concludes with a brief overview of the new model and the effect of its use on estimates of dose for a number of example radionuclides. It should be noted that where doses are discussed, the values given are preliminary and for illustrative purposes only. Definitive dose coefficients calculated using the new model will be published in forthcoming ICRP reports on doses to workers and members of the public.

### 8.2. Examples of doses using the HATM

#### **8.2.1. *Default case – information available only on total absorption of the radionuclide to blood, assumed to be from the SI***

(277) The examples in this section are for acute intake of strontium-90, ruthenium-106 and plutonium-239 by adults. Preliminary estimates are given of committed equivalent doses to alimentary tract regions and committed effective doses, including doses resulting from activity in the lumen of the alimentary tract and doses arising from activity absorbed to blood and retained in body tissues.

(278) First, Table 8.1 considers ingestion of  $^{90}\text{Sr}$  and compares numbers of nuclear transformations over 50 years,  $U(50)$ , occurring in the alimentary tract regions of the new model and those of the *Publication 30* model. Using the new model, results are given for ingestion of  $^{90}\text{Sr}$  in total diet by either males or females, and for ingestion by males of  $^{90}\text{Sr}$  in solid foods, and “non-caloric” and “caloric” liquids (egs. water and cola, respectively). The calculated  $U(50)$  values given in Table 8.1 illustrate the small number of transformations occurring in the oral cavity and oesophagus, the regions included in the new model that were not included in the *Publication 30* model. This results from the rapid transit of materials from mouth to stomach, with small differences between solids and liquids (see Chapter 6). However, residence times in the oral cavity can be increased substantially in specific cases of radionuclide retention on teeth (see 8.2.2). In the absence of retention, differences in  $U(50)$  between regions of the HATM are directly proportional to transit times.

**Table 8.1.** Comparison of the number of nuclear transformations over 50 years,  $U(50)$ , in the regions of the alimentary tract predicted by the HATM and *Publication 30* model, for unit acute ingestion of  $^{90}\text{Sr}$  by adult males and females.

Region	U(50)					ICRP 30
	HATM					
	Male			Female		
	Solids	Non-caloric liquid	caloric liquid	Total diet	Total diet	
Oral cavity	15	2	2	12	12	-
Oesophagus (fast)	7.2	4.5	4.5	6.3	6.3	-
Oesophagus (slow)	4.5	3	3	4	4	-
Stomach	$4.5 \times 10^3$	$1.8 \times 10^3$	$2.7 \times 10^3$	$4.2 \times 10^3$	$5.7 \times 10^3$	$3.6 \times 10^3$
Small Intestine	$1 \times 10^4$	$1 \times 10^4$	$1 \times 10^4$	$1 \times 10^4$	$1 \times 10^4$	$1 \times 10^4$
Proximal colon <sup>a</sup>						
Right Colon (HAT)	$3.3 \times 10^4$	$3.3 \times 10^4$	$3.3 \times 10^4$	$3.3 \times 10^4$	$4.4 \times 10^4$	-
ULI (ICRP Pub 30)	-	-	-	-	-	$3.7 \times 10^4$
Distal Colon <sup>b</sup>						
Left Colon (HAT)	$3.3 \times 10^4$	$3.3 \times 10^4$	$3.3 \times 10^4$	$3.3 \times 10^4$	$4.4 \times 10^4$	-
Recto-sigmoid (HAT)	$3.3 \times 10^4$	$3.3 \times 10^4$	$3.3 \times 10^4$	$3.3 \times 10^4$	$4.4 \times 10^4$	-
LLI (ICRP Pub 30)	-	-	-	-	-	$6.6 \times 10^4$

a – the upper large intestine of the ICRP 30 model compares with the right colon in the HATM.

b – the lower large intestine of the ICRP 30 model compares with the left colon and rectosigmoid colon in the HATM.

(279) The use of the HATM increases the estimated  $U(50)$  for the stomach, compared with the *Publication 30* value, by about 15% in males and about 40% in females, reflecting the

longer mean transit times used in the new model (70 min in males and 95 min in females, compared with 60 min in *Publication 30*). There are large differences in U(50) for the stomach for solids and liquids using the HATM, with values for solids that are about 2.5 times greater than for non-caloric liquids in males, and 3.5 times greater in females, reflecting their transit times (see Chapter 6). Since the total transit time in the left colon and the rectosigmoid colon of the HATM in males is the same as that in the lower large intestine (LLI) of the *Publication 30* model, the sum of U(50) for left colon and rectosigmoid is equal to U(50) for LLI. Gender differences in colon transit times and U(50) values in the HATM are similar to those for the stomach, with values about one-third greater in females than males. In the calculation of dose coefficients this gender difference will be compounded by lower female tissue masses, but for dose assessments is likely to be reduced by lower intakes of foodstuffs by females in many situations.

(280) Figures 8.1 to 8.3 show estimates of committed equivalent doses to regions of the alimentary tract and committed effective doses for the ingestion of unit activity of  $^{90}\text{Sr}$ ,  $^{106}\text{Ru}$  and  $^{239}\text{Pu}$  by adult males, comparing doses calculated using the HATM and the *Publication 30* model. In each case, standard systemic models are used for the distribution and retention of activity absorbed to blood (ICRP, 1989, 1993). Doses to the oral mucosa and oesophagus are not available from the *Publication 30* model; for the purposes of comparison these have been assumed to be equal to the dose to a typical non-source organ such as muscle. The figures show that doses to the oral mucosa and oesophagus calculated on the basis of this assumption are very similar to doses obtained using the HATM. This is because transit through the oral cavity and oesophagus in the HATM is rapid and the main component of dose is from activity absorbed to blood, with systemic models assigning the same dose to all unspecified soft tissues. The figures show that the HATM and *Publication 30* model also give quite similar doses to the stomach and small intestine for the examples considered. For  $^{90}\text{Sr}$ , doses to these regions will be dominated in each case by doses from activity absorbed to blood, which are calculated using the *Publication 67* (ICRP, 1993) systemic model. For  $^{106}\text{Ru}$ , dose to the stomach is slightly increased using the HATM rather than the *Publication 30* model, because of the greater transit time in the HATM (70 min cf. 60 min) and similar SEE values (see section 7.3) for the two models, while dose to the SI is lower using the HATM because the transit time is unaltered and the SEE value is lower. For  $^{239}\text{Pu}$ , doses to the stomach and SI are lower using the HATM than the *Publication 30* model because doses from activity in the lumen are zero in the HATM as a result of the explicit consideration of doses to target regions. Doses to these regions from  $^{239}\text{Pu}$  shown in Figure 8.3 are solely due to systemic activity when doses are calculated using the HATM and largely from systemic activity when the *Publication 30* model is used.

(281) The largest differences shown in Figures 8.1 to 8.3 are for doses to regions of the colon. As in Table 8.1, the right colon of the HATM has been compared with upper large intestine of the *Publication 30* model and left colon and rectosigmoid have been compared with lower large intestine. For the three radionuclides considered here, colon doses calculated using the HATM are significantly lower than using the *Publication 30* model. This is largely due to reductions in SEE values, reflecting the reduced SAF values calculated for the HATM on the basis of a specified target region in the mucosal layer of the colon wall, as opposed to the simple energy-independent method of *Publication 30* (see Chapter 7); these reductions are due to loss of energy in the contents of the lumen and mucosal tissue lying between the lumen and the target region. As for other regions of the HATM, colon doses from  $^{239}\text{Pu}$  in the lumen are zero (section 7.3.4) and doses shown in Figure 8.3 are solely from systemic activity. Similar decreases in colon doses compared with the *Publication 30* model will apply generally to pure alpha emitters.

(282) The extent to which differences in equivalent doses to the tissues of the alimentary tract affects the effective dose, E, depends on the relative contribution of these tissues to E. For  $^{90}\text{Sr}$ , E is dominated by skeletal doses (bone surfaces and red bone marrow) and there is little difference in values of E calculated using the HATM and *Publication 30* model. For  $^{106}\text{Ru}$ , doses to alimentary tract regions contribute significantly to E such that the value obtained using the HATM is about half of that using the *Publication 30* model. For  $^{239}\text{Pu}$ , as for  $^{90}\text{Sr}$ , doses to alimentary tract regions make only a small contribution to E, the dominant contributors being liver and skeletal tissues.

### **8.2.2. Effect of retention on teeth**

(283) Experimental data were presented in Chapter 3 on the retention of radionuclides on teeth in rodents and dogs, referring to studies by Book *et al.* (1982), Bhattacharyya *et al.* (1985) and Renaud-Salis *et al.* (1990). The radionuclides studied were isotopes of Sr, Cd, Pb and Pu. As discussed in Chapter 3, the example used for illustrative purposes in this report is  $^{115}\text{Cd}$ , since its beta particle emissions, as well as photon emissions, will result in irradiation of the target layer in the epithelium of the oral mucosa. It is assumed, for the purposes of this example, that 0.2% of ingested  $^{115}\text{Cd}$  is retained on teeth with a half-time of 1 week (see 3.5.2). The retained activity is assumed to be situated in a 10  $\mu\text{m}$  layer on the surface of the teeth and doses have been calculated using the Specific Absorbed Fractions given in Annex G. As discussed in Chapter 7, target regions associated with the oral cavity include the salivary glands as well as the oral mucosa. While electron and



photon emissions from radionuclides retained on teeth may irradiate these targets, the same is not true of alpha particle emissions. Doses from alpha emissions from  $^{239}\text{Pu}$  retained on teeth would therefore be zero, although, as discussed above, all soft tissues receive some dose from  $^{239}\text{Pu}$  as a result of activity absorbed to blood.

(284) Table 8.2 compares doses to the oral mucosa from ingested  $^{115}\text{Cd}$  with and without retention on teeth. The assumptions regarding retention of  $^{115}\text{Cd}$  on teeth result in increased doses to the oral mucosa by nearly two orders of magnitude. However, this increase does not change the effective dose which is dominated by contributions from other tissues, principally the colon, ovaries and liver. Table 8.2 shows that the dose to the oral mucosa from retained  $^{115}\text{Cd}$  is exceeded by the colon dose by about 30%. Comparison with doses calculated using the *Publication 30* model show that, as discussed in section 8.2.1, the colon dose is reduced in the HATM, leading also to a significant reduction in the effective dose.

**Table 8.2** Illustrative dose coefficients ( $\text{Sv.Bq}^{-1}$ ) for ingestion of  $^{115}\text{Cd}$  by adult males (total diet), comparing doses to the oral mucosa using the *Publication 30* model and the HATM with and without retention on teeth.

	HATM		<i>Publication 30</i> <sup>c</sup>
	Default assumptions <sup>a</sup>	Retention on teeth <sup>b</sup>	
Oral mucosa	$1.2 \times 10^{-11}$	$1.0 \times 10^{-9}$	$1.2 \times 10^{-11}$
Colon	$1.3 \times 10^{-9}$	$1.3 \times 10^{-9}$	$1.0 \times 10^{-8}$
CED <sup>d</sup>	$3.2 \times 10^{-10}$	$3.2 \times 10^{-10}$	$1.4 \times 10^{-9}$

a- normal transit times with no retention in any regions; absorption assumed to be from the small intestine,  $f_A = 0.05$ .

b – retention of 0.2% of ingested  $^{115}\text{Cd}$  with a half-time of one week.

c- the dose to the thymus is used as a surrogate for dose to the oral mucosa, since the latter is not included in the *Publication 30* model.

d- Doses to the oral mucosa (or thymus in *Publication 30* model) are included in the calculation of mass-weighted dose to remainder tissues, in the derivation of committed effective dose (CED).

### 8.2.3. Effect of retention in the wall of the small intestine (SI)

(285) Experimental data were presented in chapter 3 on the retention of ingested iron and uranium in the small intestine in adults. On the basis of human data for  $^{59}\text{Fe}$  ingested in soluble form, Werner *et al.* (1987) concluded that absorption to blood was 0.2 of the ingested activity. This total absorption was assumed to take place from the small intestine, i.e.  $f_A = f_{\text{SI}}$ . However, while 0.2 was absorbed to blood, the data obtained were interpreted to suggest initial uptake of 0.4 and subsequent return of 0.2 into the lumen of the SI with a half-time of retention of 3 days. As discussed in Chapter 5, to model this specific case without consideration of recycling between SI contents and SI wall requires an adaptation of the standard model (see 5.4). Thus, absorption to blood is taken to occur directly from the contents of the small intestine, while the compartment representing the SI wall is used to account for retention in the wall followed by return into the contents. Activity is returned to the right colon rather than the SI, to avoid unwarranted complexity of considering recycling between SI contents and SI wall.

(286) The site of radionuclide retention in the small intestine is taken to be the absorptive epithelial cells of the villi. In practice, as discussed in chapter 7, this is modelled as a uniform layer of tissue above the intercryptal plate, with a height of 500  $\mu\text{m}$  in adults (see 7.2.4). The target layer for cancer induction is assumed to be at the position of the stem cells towards the bases of the crypts, at a depth of 130 – 150  $\mu\text{m}$  below the intercryptal plate.

(287) While human and animal data suggest that uranium may be retained in the intestinal wall during its absorption (Chapter 3), this possibility is not considered further here because alpha particle emissions from radioisotopes of U retained in the villi will not irradiate the target layer at the bases of the crypts.

(288) Table 8.3 shows the effect of retention of ingested  $^{59}\text{Fe}$  in the SI wall on doses to the SI, by comparing doses with and without retention. The assumptions made regarding retention in the SI wall resulted in increased dose to the SI by about a factor of two; doses to the colon are also higher due to photon cross-fire. Comparisons with doses obtained using the *Publication 30* model show that, as discussed in 8.2.1, the largest differences are lower doses to the colon using the HATM.

**Table 8.3** Illustrative dose coefficients ( $\text{Sv}\cdot\text{Bq}^{-1}$ ) for ingestion of  $^{59}\text{Fe}$  by adult males (total diet), comparing doses to the wall of the small intestine (SI) using the *Publication 30* model, and the HATM with and without retention in the villi

	HATM		<i>Publication 30</i>
	Default assumptions <sup>a</sup>	Retention in SI <sup>b</sup>	
SI wall	$2.2 \times 10^{-9}$	$4.7 \times 10^{-9}$	$1.9 \times 10^{-9}$
Colon	$3.1 \times 10^{-9}$	$3.6 \times 10^{-9}$	$5.8 \times 10^{-9}$
CED	$2.2 \times 10^{-9}$	$2.3 \times 10^{-9}$	$1.8 \times 10^{-9}$

a- normal transit times with no retention in the wall of any region; absorption assumed to be from the small intestine,  $f_A = 0.2$ , from Werner *et al.* (1987), rather than ICRP (1995) value of 0.1

b – retention in SI wall of 0.2 of ingested  $^{59}\text{Fe}$ , retained with a half-time of 3 days.

(289) Chapter 3 also discussed experimental data for various mammalian species showing that radionuclides are retained in the wall of the small intestine of newborn animals. On the basis of primate data for Pu (Lataillade *et al.*, 1992; Fritsch *et al.*, 1992), it is assumed here for illustrative purposes that absorption of  $^{239}\text{Pu}$  to blood ( $f_A$ ) in human infants is rapid and accounts for  $5 \times 10^{-3}$  of ingested  $^{239}\text{Pu}$ , but that an additional fraction of  $1.5 \times 10^{-2}$  is retained in the wall of the small intestine with a half-time of 7 days. The data also showed that most of the retained activity was located in the villi but that about 5% was retained in the vicinity of the crypts. It is assumed here that 5% of retained activity is distributed uniformly in the mucosa underlying the villi, to a depth of 200  $\mu\text{m}$ , ie. a layer of tissue beneath the intercryptal plate that includes the crypts (see 7.2.4). This information has been used to compute the number of nuclear transformations occurring in this 200  $\mu\text{m}$  layer of tissue. Using the methods outlined in section 7.3.4, the Absorbed Fraction (AF) for  $^{239}\text{Pu}$  alpha particles emitted in the mucosa has been calculated to be 0.1 On this basis, the dose resulting from  $^{239}\text{Pu}$  retention in the wall of the small intestine contributes about 20% of the total committed equivalent dose to the small intestine, with the dominant contribution (80%) due to doses to soft tissues including the SI wall from  $^{239}\text{Pu}$  absorbed to blood (see 8.2.1).

#### **8.2.4. Effect of absorption from stomach and small intestine**

(290) In the absence of specific information, the reasonable assumption is made that all absorption of radionuclides from the alimentary tract occurs in the small intestine, the region that is adapted for absorption of nutrients and essential elements (see Chapter 2 and Annex B). However, as discussed in Chapter 3, animal studies have shown that absorption of elements and their radioisotopes can occur, to some extent, in regions of the alimentary tract other than the small intestine, including the stomach. Reliable quantitative assessments of the extent of absorption from different regions under normal circumstances of radionuclide ingestion do not appear to be possible on the basis of currently available information, but studies have shown absorption from the stomach for the examples of I, F, Cu and Nb (Patten *et al.* 1978; Gabler *et al.* 1968; Van Campen and Mitchell, 1965; Eisele and Mraz, 1981).

(291) For illustrative purposes, the effect of absorption from the stomach is considered here for the example of isotopes of iodine. For most isotopes of iodine (such as  $^{131}\text{I}$  and  $^{129}\text{I}$ ), the more rapid entry of the isotope into the circulation following absorption from the stomach will have the effect of slightly increasing doses to the thyroid while decreasing doses to the stomach and small intestine. The impact on effective doses is small. For isotopes of very short physical half-life (such as  $^{132}\text{I}$ ), the assumption of uptake directly from the stomach will increase thyroid doses and effective doses. For example, the assumption that half of ingested iodine is absorbed from the stomach and half from the SI, compared with the standard assumption of complete absorption from the SI, results in an increase in thyroid dose of < 1% for  $^{129}\text{I}$  and  $^{131}\text{I}$ ; This assumption of iodine absorption from the stomach also has the effect of decreasing doses to the SI, and to the colon due to irradiation from the SI contents, by 4 - 8% for the short-lived  $^{131}\text{I}$  (half-life 8 days), but not the long-lived  $^{129}\text{I}$  (half-life  $15.7 \times 10^6$  years); effective dose is increased by < 1% for both isotopes.

#### **8.2.5 Doses to infants and children**

(292) The HATM gives age-dependent transit times for the regions of the alimentary tract (Chapter 6), as well as age-dependent dimensions (Chapter 7), while the *Publication 30* model gave transit times only for adults. The *Publication 30* model was used to calculate doses to infants and children in Publications 56, 67, 69, 71 and 72, using the adult transit times but applying age-dependent masses. In general, the shorter transit times for infants and children specified in Chapter 6 will tend to reduce doses, while the smaller tissue masses

and lumen volumes will tend to increase doses (the latter because there is less absorption of energy within the smaller contents of the lumen).

(293) Quantitative examples of the effect of age on doses calculated using the HATM are beyond the scope of the report; information on doses to children and infants will be given in future reports.

### **8.2.6. Application to ingestion of particles**

(294) The HATM can be used to calculate doses from discrete particles of high activity such as fragments of irradiated fuel (often called ‘hot particles’), as well as for the normal situation of distribution of activity throughout the contents of the alimentary tract. The consideration of realistic target cell locations in the HATM enables doses to be calculated using radiation transport calculations considering, for example, different particle sizes, densities, and elemental compositions. The particles can be taken to be at different radial positions within the lumen since this can lead to a different dose to the target cells. Calculations of this sort have been performed using a model similar to the HATM (Darley *et al.*, 2003). This approach takes into account absorption of energy within the particle. It generally yields lower doses than the *Publication 30* model, although the extent of the difference will depend on the radionuclides which provide the major fraction of the dose and the size of the particles. Darley *et al.* (2003) considered the case of possible ingestion of fragments of irradiated fuel, found in small numbers on the coast near the Dounreay Nuclear Power Development Establishment in Scotland. The principal radionuclides contained within the particles are  $^{137}\text{Cs}$  and  $^{90}\text{Sr}/^{90}\text{Y}$ , although they also contain small amounts of plutonium isotopes and  $^{241}\text{Am}$ . Darley *et al.* (2003) obtained estimates of dose to the lower large intestine that were lower than calculated using the *Publication 30* model by factors of about 30 for an adult and more than 50 for a one year-old child.

## **8.3. Uncertainties**

### **8.3.1 Definitions**

(295) In this report, “uncertainty” refers to the level of confidence that can be placed in a given component (e.g., parameter value) or prediction of the HATM, as an estimate of the central value (usually, an arithmetic or geometric mean) in the population. The uncertainty in the central value of a model feature should not be confused with the “variability” of that

feature in the population. Variability refers to quantitative differences between different members of a population under similar conditions (inter-individual variability) or within an individual under different conditions (intra-individual variability). For example, the transit time of material through the colon may differ between two persons of the same size, race, age, and gender and having identical diets (inter-individual variability) or may differ in the same person at different times due to changes in diet, state of health, or other conditions (intra-individual variability) (see Chapter 6 and Annex C).

(296) This section considers the uncertainty in some major components of the alimentary tract model. Statements of uncertainty given here are subjective judgments of the Task Group based on the quality and completeness of the underlying data. The uncertainty in a given quantity is expressed in terms of a subjective confidence interval, that is, an interval of positive values, [A,B], such that the true but unknown value is judged with reasonable confidence to lie between A and B. Here, “reasonable confidence” is defined as a subjective confidence level of 90%. That is, it is judged that there is only a small probability (about 5%) that the true value is less than A and only a small probability (about 5%) that it is greater than B.

(297) For purposes of comparing levels of uncertainty of model components that are expressed in different terms or have different orders of magnitude, it is sometimes convenient to apply the concept of an uncertainty factor (UF). An uncertainty factor for a quantity with subjective confidence interval [A,B] is defined as  $(B/A)^{1/2}$ . The quantity is considered to be known within a factor of  $(B/A)^{1/2}$  in the sense that all values in the interval are within a factor of  $(B/A)^{1/2}$  of the geometric mean of A and B. The description of uncertainties in terms of uncertainty factors is simply a convenient way of summarising conclusions regarding uncertainties in model components and has no implications with regard to the central value or the distribution of possible values of a model component.

(298) Unless otherwise indicated, the following consideration of uncertainties in anatomical and physiological characteristics of the alimentary tract refers to a young or middle-aged adult male of weight 73 kg and height 176 cm. Uncertainties are usually smaller for young or middle-aged males than for other segments of the population due to greater availability of information for this group, but there are exceptions. For example, knowledge of the retention time of material in the walls of the gastrointestinal tract is no better for young or middle-aged adult males than for other age-groups.

(299) Uncertainties are discussed in the following sections for a number of parameters of the model, considering the effect on doses of uncertainties in radionuclide absorption, location of target cells for cancer induction, transit times of materials through the lumen of the tract, and dimensions of the colon.

### **8.3.2 Uncertainty in radionuclide absorption**

(300) The uncertainty in fractional uptake from the gastrointestinal tract to blood varies considerably from one element to another. In a relative sense, uncertainties in fractional uptake are smallest for elements that are known to be nearly completely absorbed, including hydrogen (as tritium), carbon, sodium, chlorine, potassium, bromine, rubidium, molybdenum, iodine, caesium, thallium, fluorine, sulphur, and germanium. An uncertainty factor in the range 1.1-1.5 might be appropriate for each of these elements, depending on the quality and completeness of the data base for individual elements. Average uptake from the gastrointestinal tract is also reasonably well established for several frequently studied elements whose absorption is incomplete but represents at least a few percent of intake, such as copper, zinc, magnesium, technetium, arsenic, calcium, strontium, barium, radium, lead, iron, manganese, cobalt, and uranium. Uncertainty factors for these elements would also vary with the element and generally would be greater than 1.5 but no more than about 3. Relative uncertainties generally are greater for the remaining elements due to sparsity of direct observations on human subjects (e.g. ruthenium, silver), inconsistencies in reported absorption fractions (e.g. beryllium, antimony, silicon), or absorption too low to be determined with much precision under most conditions (e.g. most actinide and lanthanide elements). Absorption of a few poorly absorbed elements such as plutonium, americium, and curium has been studied under controlled conditions in human subjects, and average uptake in the adult may be known within a factor of 3 – 4 for these elements. Relative uncertainties may be greatest for several elements whose absorption has not been studied in man but for which animal data or other indirect evidence indicates absorption of at most a few hundredths of a percent, such as samarium, gadolinium, dysprosium, erbium, thulium, actinium, yttrium, and scandium. Absorption fractions for these elements are order-of-magnitude estimates. Annex E presents data on the absorption of selected elements, illustrating the types and quality of information available.

(301) As discussed in Chapter 3, Harrison *et al.* (2001) assessed uncertainties in absorption of ingested radionuclides for selected elements and considered the effect of these uncertainties on dose estimates. The available data are summarised in chapter 3 for the examples of  $^{90}\text{Sr}$ ,  $^{106}\text{Ru}$  and  $^{239}\text{Pu}$ , and A and B values relating to 90% confidence

intervals are given. Table 8.5 shows B/A and uncertainty factors, UF, for absorption ( $f_A$ ) and the effect on colon doses and committed effective doses, calculated using the HATM and current systemic models (ICRP, 1989, 1993). For  $^{90}\text{Sr}$  and  $^{239}\text{Pu}$ , uncertainties in CED values are similar to or the same as for  $f_A$  because effective doses are largely due to doses to organs/tissue from activity absorbed to blood. For  $^{106}\text{Ru}$ , colon dose is an important contributor to effective dose and the uncertainty in CED is small compared with uncertainty in  $f_A$ . Note, however, that this assessment does not take account of smaller uncertainties in colon dose due to uncertainties in transit times (see 8.3.4).

**Table 8.5.** Uncertainty Factors (UF) and ratios (B/A) of dose coefficients resulting from uncertainty in uptake from the alimentary tract ( $f_A$ ), considering ingestion by adult males.

Nuclide	$f_A$		Colon dose		CED <sup>a</sup>	
	B/A <sup>b</sup>	UF <sup>c</sup>	B/A	UF	B/A	UF
$^{90}\text{Sr}$	4.0	2.0	1.2	1.1	3.9	2.0
$^{106}\text{Ru}$	20	4.5	1.3	1.1	2.8	1.7
$^{239}\text{Pu}$	10	3.2	1.0	1.0	10	3.2

a- committed effective dose.

b- A and B values correspond to 5<sup>th</sup> and 95<sup>th</sup> percentile confidence intervals.

c-  $UF = (B/A)^{1/2}$ .

### 8.3.3 Uncertainties in the location of target regions for cancer induction

(302) Doses are calculated separately for the mucosal layer of each region of the HATM. For penetrating radiations, it is reasonable to use the average dose to the walls of each region as a measure of the dose to the mucosal layer. For non-penetrating  $\alpha$  and  $\beta$  particle emissions, the dose is dependent on the assumptions made regarding the location of target cells for cancer induction. For each region of the alimentary tract, the target has been taken to be the stem cells that are located in the basal layer of the stratified squamous epithelia of the mouth and oesophagus and within the crypts that penetrate the mucosal layer in the stomach and small and large intestines (Chapters 4 and 7).

(303) Uncertainties are illustrated here for the specific case of doses to the colon, since colon doses are generally the major contributors to alimentary tract doses (see 8.2.1). As discussed in Chapter 4, although it is generally accepted that it is the stem cells in the bases of the crypts that are the targets for cancer induction, some uncertainty has been raised by observations of dysplastic cells on the luminal surface of the colon between apparently normal crypts (Shih *et al.* 2001). Thus, as well as uncertainties in the depth of



the crypts and hence the depth of the stem cells, there is also uncertainty as to whether it is only the stem cells that should be regarded as targets.

(304) Table 8.6 compares colon doses for different assumptions of target location, normalised to the default assumption that they form a continuous layer at a depth of 280 – 300  $\mu\text{m}$  from the luminal surface of the colon. Thus, uncertainties in the depth of the crypts and hence the depth of the stem cells, represented by columns 2 and 3, result in differences of about  $\pm 10\%$  for  $^{115}\text{Cd}$  and smaller differences for the other examples considered. For  $^{234}\text{U}$  and  $^{239}\text{Pu}$ , there is no dose to the colon wall from activity in the lumen (see 8.2.1), and thus no change with changing assumptions regarding stem cell depth. Similarly, widening the target to include cells at higher positions up the crypts (200 – 300  $\mu\text{m}$ ), results in a maximum change in colon dose of about 10% for  $^{115}\text{Cd}$ . The extreme assumption that the target may include all epithelial cells from the base of the crypts to the luminal surface (0 – 300  $\mu\text{m}$ ) results in larger increase in doses. The increase by factors of about 1.5 for  $^{234}\text{U}$  and 3 for  $^{239}\text{Pu}$  are relative to the dose to the colon resulting from activity absorbed to blood (see 8.2.1). However, these increases in colon doses from  $^{234}\text{U}$  and  $^{239}\text{Pu}$  will make negligible differences to committed effective doses, which are dominated by contributions from doses to tissues and organs from activity absorbed to blood.

**Table 8.6.** Differences (%) in dose coefficients (h) for the colon, compared to the default case<sup>a</sup>, resulting from considerations of target depth in the mucosa, considering ingestion by adult males.

Nuclide	Assumed location of the target region – depth from lumen, $\mu\text{m}$			
	220 – 240	340 - 360	200-300	0-300
Fe-55	0%	0%	0%	0%
Fe-59	1%	-1%	1%	6%
Sr-90	7%	-6%	5%	21%
Ru-106	3%	-2%	2%	8%
Cd-115	13%	-9%	9%	38%
U-234	0%	0%	0%	148%
Pu-239	0%	0%	0%	317%

<sup>a</sup> default case assumes a target depth of 280 – 300  $\mu\text{m}$

### **8.3.4 Uncertainties in transit times**

(305) In the years since the development of the *Publication 30* model (ICRP, 1979), numerous investigations of the kinetics of material in the gastrointestinal tract have been conducted by improved, non-invasive techniques, such as external viewing of radio-labeled foods, liquids, or indigestible substances (see Chapter 6 and Annex C). While the uncertainties associated with measurement techniques have been substantially reduced, the difficulties involved in determining true transit times should not be underestimated. For example, the physical characteristics of markers used in modern studies apparently can affect colonic transit times (Olmos *et al.*, 1994). Also, some methods still in common use do not appear to provide representative or reproducible results (see 6.7 and Annex C).

(306) Section 6.7 of Chapter 6 provides a short review of uncertainty and variability in transit times, referring to preceding sections of Chapter 6 and the more extensive review of transit data presented in Annex C. Section 6.7 addresses uncertainty associated with modelling assumptions as well as the quality of available data. This includes discussion of the effect of the simplifying application of first order kinetics to all movements of material through alimentary tract regions. The rationale behind the choice of large intestine compartments was also explained: most available data correspond to the sub-regions of the right colon, left colon and rectosigmoid. The decision not to consider doses to the rectum separately but as part of the rectosigmoid was based on the difficulty in specifying transit times for this region, due to the paucity of information and likely high variability between individuals. Sections 6.7 discusses variability in transit times for all regions of the alimentary tract, referring to the effect of disease states as well as variability in normal healthy individuals. It is concluded that substantial errors can result from application of default parameter values to individual cases, for example in the interpretation of bioassay data, because the standard assumptions may not apply. Specific information on transit times should be used in such cases when available, as for other parameters in the model,

(307) Considering only average residence times in healthy individuals within a population, and based on the information given in Chapter 6 and Annex C, it is judged that the typical residence time of material in the mouth or oesophagus of the adult male is known within a factor of about 2. The typical residence time of material in the stomach, small intestine, right colon, left colon, or rectosigmoid colon in the adult male is judged to be known within a factor of about 1.5. On this basis effective dose coefficients and equivalent dose coefficients to the colon have been calculated for the examples of ingestion of  $^{90}\text{Sr}$ ,  $^{106}\text{Ru}$  and  $^{239}\text{Pu}$  by adult males, using transit times of 8 hours and 18 hours in each of the three

segments of the colon (the default value is 12 hours for each segment). In the cases of  $^{90}\text{Sr}$  and  $^{106}\text{Ru}$  the uncertainty factors for colon dose are 1.5 and 1.4 respectively, which are nearly the same as that for transit time, reflecting their close association. For  $^{239}\text{Pu}$ , colon dose arises solely from activity absorbed to blood, and variations in transit time have no effect on colon dose. For  $^{106}\text{Ru}$  the colon dose from activity in the contents makes an important contribution to effective dose, and thus the uncertainty in transit times leads to an uncertainty factor in effective dose of about 1.2. In contrast for  $^{90}\text{Sr}$  and  $^{239}\text{Pu}$ , colon doses contribute very little to effective doses and results are unchanged by variations in transit time.

**Table 8.7.** Uncertainty Factors (UF) and ratios of dose coefficients (B/A) resulting from uncertainty in transit times in the colon<sup>a</sup>, considering ingestion by adult males.

Nuclide	Colon dose		CED <sup>b</sup>	
	B/A <sup>c</sup>	UF <sup>d</sup>	B/A	UF
$^{90}\text{Sr}$	2.3	1.5	1.0	1.0
$^{106}\text{Ru}$	2.0	1.4	1.3	1.2
$^{239}\text{Pu}$	1.0	1.0	1.0	1.0

a- for colon transit time, B/A = 2.3 (18/8), and UF = 1.5 ( $\sqrt{2.3}$ )

b- committed effective dose.

c- A and B values correspond to 5<sup>th</sup> and 95<sup>th</sup> percentile confidence intervals.

d- UF = (B/A)<sup>1/2</sup>.

### 8.3.5 Uncertainty in anatomical features

(308) The dimensions and geometrical configurations of the structures of the tract were formerly estimated from measurements on cadavers, and those estimates often did not closely reflect conditions in the living body. More accurate determination of the geometry of the gastrointestinal tract of a living person has become possible with the advent of external visualisation techniques with high resolution. Nevertheless, it remains difficult to determine typical sizes, shapes, and relative positions of structures of the tract with high accuracy due to the considerable variability in these features from one person to another and from one body position to another in the same person.

(309) Uncertainty factors of about 1.4 are assigned to the dimensions (e.g., length and width, or internal diameter of the lumen) of most structures within the alimentary tract. However, an uncertainty factor of 2 is assigned to the internal diameter of the oesophagus,

for which the average over time is difficult to estimate in the living body. The typical internal diameter of the oral cavity appears to be known within a factor of about 1.3.

(310) An uncertainty factor of 1.4 in the length of a region leads to the same uncertainty factor in dose to the region, assuming that all other parameters remain unchanged, since the mass of the target region is proportional to the length of the region. In practice, the length of a region may be correlated with the transit time. For example, an increase in length of a region could lead to an increase in transit time by the same factor with the result that the dose is unaltered. This would tend to reduce the UF in dose to below 1.4.

(311) In order to examine the effect of uncertainty in diameter, the dose per nuclear transformation (SEE value, Chapter 7) for a 6 cm diameter section is compared with that for a 3 cm diameter section (UF of 1.4 in the parameter). Strontium-90 (mean beta energy = 0.20 MeV) and  $^{90}\text{Y}$  (mean beta energy = 0.94 MeV) are chosen to represent a range of energies. In both cases the uncertainty factor in SEE is about 1.9. In contrast to other parameters, this is a case where the uncertainty factor for the result (SEE or dose) is larger than in the parameter (diameter). This is because the UF in the cross-sectional area of the section, which is an indicator of the extent of energy absorption within the lumen, is 2 for a UF of 1.4 in the diameter. However, such uncertainties in colon dose from  $^{90}\text{Sr}/^{90}\text{Y}$  will have a negligible effect on committed effective dose which is dominated by doses to tissues from activity absorbed to blood

#### 8. 4. Key features of the HATM

(312) The main features of the HATM can be summarised as follows:

- Inclusion of all alimentary tract regions. Doses are calculated for the oral cavity, oesophagus, stomach, small intestine, right colon, left colon and rectosigmoid (including the rectum). Colon doses are combined as a mass-weighted mean.
- Age-dependent parameter values for the dimensions of alimentary tract regions and associated transit times of contents through the regions.
- Gender-dependent parameter values for adults for dimensions and transit times.
- Transit times for food and liquids, as well as for total diet, for the mouth, oesophagus and stomach.
- Default assumption that total fractional absorption,  $f_A$ , of an element and its radioisotopes to blood occurs in the small intestine, ie.  $f_{SI} = f_A$ .

- Model structure to allow for absorption in other regions, in situations where information is available.
- Model structure to allow for retention in the mucosal tissues of the walls of alimentary tract regions, and on teeth, in situations where information is available.
- Explicit calculations of dose to target regions for cancer induction within each alimentary tract region, considering doses from radionuclides in the contents of the regions, and considering mucosal retention of radionuclides when this is taken into account.

(313) The oral cavity and oesophagus will receive very low doses from ingested radionuclides in transit because of their short retention times (see Chapter 6 and 8.2.1). However, these regions were included for completeness, because a specific  $w_T$  was assigned to the oesophagus in *Publication 60* (ICRP, 1991), and because retention in the mouth, on teeth for example (see 8.2.2), can result in a substantial increase in dose to the oral mucosa. In general, the alimentary tract regions of greatest importance in terms of doses and cancer risk are the stomach and particularly the colon. While the small intestine may receive greater doses than the stomach, it is not sensitive to radiation-induced cancer and is not assigned a specific  $w_T$  value. Doses are calculated separately for the right colon, left colon and rectosigmoid. This partitioning of the colon for the purposes of dose calculations is predicated on the availability of transit time data. The rectum is taken to be part of the rectosigmoid, because of difficulties in determining transit times separately and because the rectum does not have a specific  $w_T$  value.

(314) Transit times are generally shorter in infants and children than in adults (see Chapter 6) and, on this basis, the application of the *Publication 30* model (for reference adults) in a number of ICRP publications (e.g. *Publication 72*, 1996) considering radionuclide ingestion by infants and children will have overestimated doses. In adults, mean transit times for the stomach and colon are about one-third greater in females than males. Slightly smaller masses in females (e.g. 10% lower mass of colon tissue) will compound this gender difference.

(315) It is not within the scope of this report to specify values for the fractional absorption of elements and their radioisotopes from the alimentary tract to blood ( $f_A$ ). This will be done in forthcoming publications in which doses are calculated using the HATM. In general, the values of  $f_A$  will be the same as the  $f_1$  values given previously for use with the *Publication 30* model, since in most cases there is unlikely to be sufficient new information to warrant a

revision in values. In addition, the general default assumption will be that absorption occurs solely from the small intestine, as in the *Publication 30* model; that is,  $f_{SI} = f_A$ . However, the HATM allows absorption to be specified for other regions as well as the small intestine. As discussed for the examples of isotopes of iodine (see 8.2.4), doses to alimentary tract regions and other tissues will in many cases be insensitive to assumptions regarding the site of absorption.

(316) Human and animal data suggesting or showing retention of ingested radionuclides in mucosal tissues of the walls of alimentary tract regions, principally the small intestine, can be used to specify retention in the HATM. The inability of the *Publication 30* model to take account of such retention has long been regarded as an important deficiency. However, as illustrated by calculations for examples from the few cases for which quantitative information can be derived ( $^{59}\text{Fe}$ ,  $^{239}\text{Pu}$  in neonates; see 8.2.3), inclusion of retention may not result in large increases in doses to the small intestine and increases in committed effective doses are likely to be small.

(317) An important development in the HATM is the methodology used to calculate doses in the various regions from non-penetrating alpha and electron radiations. Thus, while the *Publication 30* approach was to assume that the dose to the wall was one half of that to contents of the region, with an additional factor of 0.01 included for alpha particles to allow for their short range (see section 1.2), the HATM takes explicit account of the location of the target tissue in the mucosal layer of the wall of each region. The targets relating to cancer induction are taken in each case to be the epithelial stem cells, located in the basal layers of the stratified epithelia of the oral cavity and oesophagus and within the crypts that replenish the single cell layer epithelium of the stomach and small and large intestines (see Chapters 4 and 7).

(318) As discussed in 8.2.1 and illustrated in Table 8.8, the HATM results in substantially lower estimates of doses to the colon than obtained using the *Publication 30* model. This is because the HATM takes explicit account dose to the target region throughout the length of the colon, and of loss of energy in the colon contents and the mucosal tissue overlying the target stem cells (at a depth of 280 - 300  $\mu\text{m}$ ). This reduces energy deposition in the target tissue for electrons and results in zero dose in the target tissue from alpha particles. In the absence of retention of radionuclides in the alimentary tract wall, doses from ingested alpha emitters to all regions of the alimentary tract will be solely due to their absorption to blood and subsequent irradiation from systemic activity in soft tissues. For the stomach, the HATM and *Publication 30* approaches give more similar estimates of doses from electron-

emitting nuclides. Table 8.8 illustrates that the large reductions in colon dose obtained using the HATM compared with the *Publication 30* model, of factors of up to about 5 – 10, result generally in small changes in committed effective dose, which is dominated in most cases by doses to tissues and organs resulting from activity absorbed to blood.

(319) The most important uncertainties associated with the HATM and *Publication 30* model, in terms of effective doses from ingested radionuclides but not alimentary tract doses, are uncertainties in  $f_A$  values. As discussed in 8.3.2, uncertainty factors in  $f_A$  of 2 for  $^{90}\text{Sr}$  and 3.2 for  $^{239}\text{Pu}$  translate directly to the same uncertainty factors for committed effective doses. While uncertainties in typical transit times appear not to be large (see 8.3.4), it is recognised that variability between individuals can be substantial. The transit times used in the HATM may not be applicable in individual circumstances. Uncertainties associated with the depth of target tissues in the mucosa of the various alimentary tract regions are small (see 8.3.3); doses are generally insensitive to the assumed depth of the stem cells and the use of a wider target including lineage committed and fully differentiated cells.

(320) The HATM will be applied to the calculation of doses from the ingested radionuclides in forthcoming ICRP publications on doses to workers and members of the public. These calculations will use the parameter values given in this report, together with values of fractional absorption to blood,  $f_A$ , and additional information on sites of absorption and retention where available. The use of alternative assumptions is encouraged in situations where specific information is available.

**Table 8.8.** Comparison<sup>a</sup> of ingestion dose coefficients (both equivalent and effective) derived using the HATM with those of the ICRP *Publication 30* model.

Radionuclide	Regional doses:			Effective Dose
	Stomach	Right Colon <sup>b</sup>	Left colon <sup>c</sup>	
Fe-55	0.9	0.5	0.2	-7%
Sr-90	1.0	0.2	0.1	-6%
Ru-106	1.2	0.2	0.1	-59%
Pu-239	0.8	0.4	0.2	nil

a - equivalent dose coefficients are compared as a ratio, effective doses as a fractional change (%).

b – compared with the upper large intestine of the ICRP *Publication 30* model

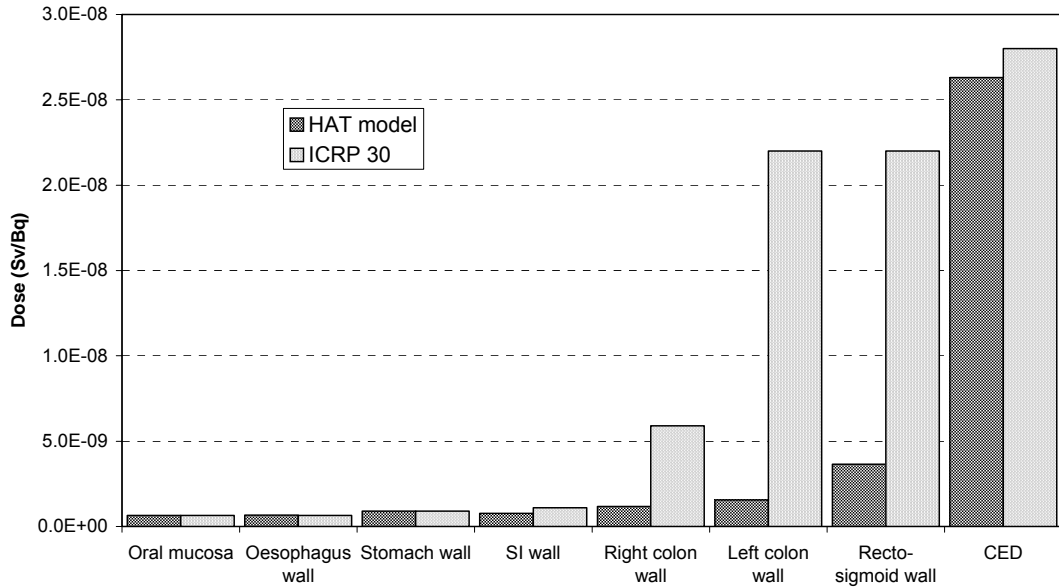
c – compared with the lower large intestine of the ICRP *Publication 30* model

## 8.6. References

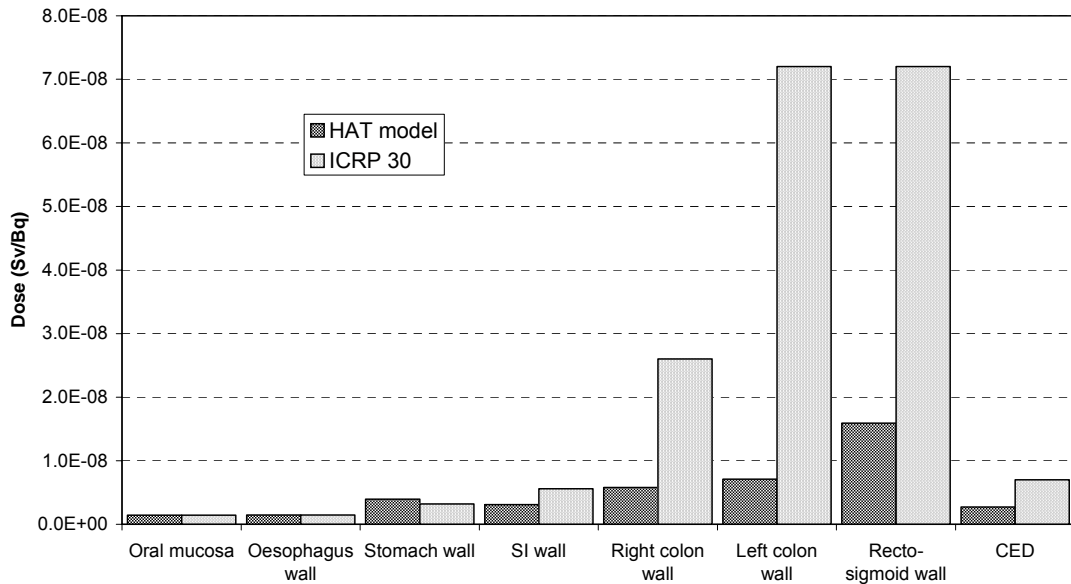
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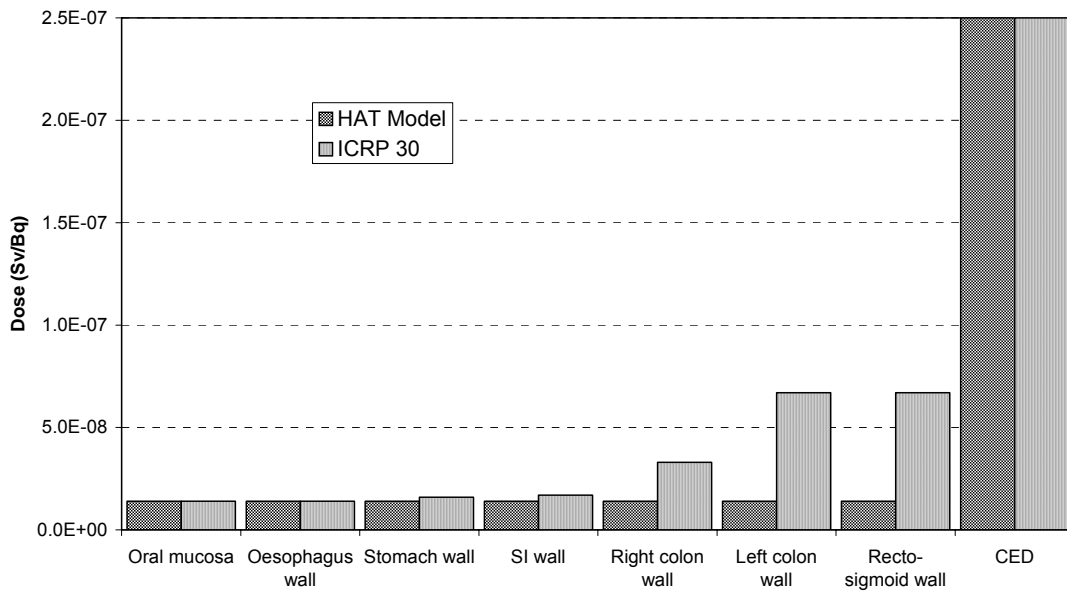
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**Figure 8.1.** Comparison of dose coefficients calculated using the HATM and the *Publication 30* model, considering single acute ingestion of strontium-90 by adult males.



**Figure 8.2.** Comparison of dose coefficients calculated using the HATM and the *Publication 30* model, considering single acute ingestion of ruthenium-106 by adult males.



**Figure 8.3.** Comparison of dose coefficients calculated using the HATM and the *Publication 30* model, considering single acute ingestion of plutonium-239 by adult males.