MAXIMUM PERMISSIBLE URINARY CONCENTRATIONS: THEIR RELATIONSHIP TO ATMOSPHERIC MAXIMUM ALLOWABLE CONCENTRATIONS

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There are two approaches to the determination of maximum permissible concentrations in urine (M.U.C.'s). The first is the direct method of comparing the concentration of toxic substances with the incidence of symptoms of intoxication. The second is the indirect approach of considering the worker as a sampling device and relating the urinary excretion to the atmospheric concentration to which the worker is exposed. In this case the M.U.C. will, in general, be the urinary concentration which corresponds to the atmospheric maximum allowable concentration (M.A.C.). I will employ this second approach.

Let us consider briefly three factors:

(1) collection of sample;
(2) calculation of results;
(3) relationship of M.U.C.'s to M.A.C.'s.

COLLECTION OF SAMPLE

Time of collection

The best time to collect a urine sample for evaluation of an industrial exposure depends on the excretion pattern of the substance in question. The time of day at which the specimen is obtained is important for some substances, immaterial for others, as shown by the data of *Table 1*.

Table 1. Diurnal variation in urinary excretion: average results

Substance	*Ref.*	*Morning sample*	*Evening sample*
Benzene	1	29	53
Toluene	2	300	1300
Fluoride	3	2·3	10·0
Lead	4	0·15	0·16
Mercury	4	0·12	0·08

Thus, if we are evaluating benzene exposure by the urine sulphate test, or toluene by hippuric acid excretion, we will find the highest concentration of the respective metabolites in specimens taken at the end of the exposure period. On the other hand, with lead and mercury it makes little difference whether morning or evening samples are taken. Is this because these elements are stored in the body for relatively long periods, while the organic compounds are rapidly metabolized? If so, why should we find so much variation with fluoride, which, like lead, is stored in the bones?

Size of sample

The minimum size of the sample to be collected depends in part on the sensitivity of the analytical method. It is necessary to have a sufficient sample in order to obtain results that are significant. On the other hand, it is frequently much easier to secure a specimen representing a single voiding, such as 100 ml, than a sample of 500 ml. Moreover, in the case of substances with a marked diurnal variation in excretion rate, such as benzene, the concentration of metabolite may be substantially greater in a specimen representing the last two hours of exposure than in a larger one.

CALCULATION OF RESULTS

From the medical profession we inherit the tradition of calculating urinary excretion in terms of 24-hour output. This method of expressing results is unsatisfactory for industrial exposures for three reasons:

(a) collection of 24-hour samples is difficult, as is the collection of smaller samples representing definite times of secretion;

(b) excretion per unit time inevitably depends to some extent on body weight, and probably on other factors, such as degree of physical exertion of subject;

(c) total excretion is also affected by the fluid balance, as can be seen from the typical data of *Table 2*.

Table 2. Effect of urine volume in 24-hour lead extraction[4]

Volume of urine (ml)	*Lead excreted* (mg/day)
900	0·09
2080	0·15
1290	0·15
900	0·09

On the other hand, if we go to the other extreme, and determine the mg of toxic agent per litre of urine, the dependence of the result on fluid balance is even greater, although the variation is in the opposite direction, as indicated in *Table 3*.

In this particular series, the lead concentration in spot samples varies twenty-fold when the concentration of the urine is changed by varying the fluid intake.

Table 3. Effect of specific gravity of urine on lead concentration[4]

Specific gravity	*Lead concentration* (mg/l.)
1·025	0·17
1·010	0·04
1·002	0·01
1·021	0·20

In my opinion the best method of expressing urinary excretion is to relate the concentration of toxic substance or metabolite to the concentration of some other component of the urine. Thus, in the urine sulphate ratio, the benzene metabolite, conjugated sulphate, is related to the total sulphate concentration in the urine. A more general method is to use the concentration of total solids (as measured by the specific gravity[5]), or the concentration of creatinine, as a reference point. In *Table 4*, the lead results of *Table 3* are shown when calculated by these methods.

Table 4. Urinary lead concentration adjusted for specific gravity or creatinine[4]

Specific gravity	*Lead found* (mg/l. (1·024 sp. gr.)	(mg/g creatinine)
1·025	0·16	0·62
1·010	0·09	0·53
1·002	0·12	0·55
1·021	0·23	1·05

It is seen that the fluctuation, while substantial, is much less than when no adjustment is made.

RELATIONSHIP OF M.U.C. TO M.A.C.

If we compare the values which have been suggested as M.U.C.'s with the corresponding atmospheric M.A.C.'s, we arrive at some interesting results. In *Table 5* such comparisons are made for a few industrial hazards.

Table 5. Comparison of urinary M.U.C.'s and atmospheric M.A.C.'s

Substance	M.U.C. (mg/l.)	M.A.C. (mg/m³)	M.U.C./M.A.C.
Arsenic	1·0	0·25	4·0
Fluoride	5·0	2·0	2·5
Mercury	0·3	0·1	3·0
Tritium*	250	70	3·5

* Values for radioactive isotopes are given in microcuries or micromicrocuries.

These are all substances that are excreted freely in the urine, and this is reflected in the relatively high values of the ratios of M.U.C. to M.A.C. It would be surprising to find this ratio exceeding 5, since this would represent, for an average man, a daily excretion of more toxic substance than is present in 5 cubic metres of air (based on an average daily output of 1 litre of urine of 1·024 specific gravity).

In *Table 6* are listed similar data for some additional hazards.

Table 6

Substance	M.U.C. (mg/l.)	M.A.C. (mg/m³)	M.U.C./M.A.C.
Lead	0·20	0·20	1·0
Polonium*	250	600	0·4
Strontium-90*	300	600	0·5
Uranium	0·05	0·05	1·0

* Values for radioactive isotopes are given in microcuries or micromicrocuries.

With these hazards, the ratio M.U.C./M.A.C. is of the order of unity or a little less. In the case of lead, this is probably related to the fact that lead is not excreted as freely as mercury, for example. On the other hand, the data available indicate that uranium is excreted rather freely.

Table 7 lists suggested values of M.U.C. for substances for which relatively meagre data are available. These are based, for the most part, on single reports comparing urinary and atmospheric concentrations.

Table 7. Tentative M.U.C.'s and M.U.C./M.A.C. ratios

Substance	*Ref.*	M.U.C. (mg/l.)	M.A.C. (mg/m³)	M.U.C./M.A.C.
Cadmium		0·1	0·1	1·0
Chromium (CrO_3)	6	0·05	0·1	0·5
Selenium		0·1	0·1	1·0
Vanadium	7	0·05	0·1	0·5

Of these substances, there is evidence that selenium is excreted freely, and possibly a higher M.U.C. would be in order. On the other hand, the values suggested for the other three elements may be too high.

Finally in *Table 8*, data are presented for four organic solvents.

Table 8. M.U.C.'S and M.A.C.'s for organic solvents

Solvent	*Ref.*	M.U.C. (mg/l.)	M.A.C. (mg/m³)	M.U.C./M.A.C.
Benzene	8	100	80	1·2
Methanol	9	5	260	0·02
Toluene		1000	1400	0·7
Trichlorethylene	4	300	540	0·55

Here, again, in three of four cases the M.U.C./M.A.C. ratio is of the order of one.

It seems reasonable to postulate that, in general, the toxic substances which are excreted the most readily in the urine are the ones best evaluated by urine analysis. Thus we would expect that, other things being equal, M.U.C.'s for the substances in *Table 5* would be more useful than for those of *Table 7*, or for methanol, the only substance given where the M.U.C./M.A.C. ratio is much less than 0·5.

Preparation of this paper was made possible by a Research Grant from the U.S. Public Health Service (RG-5503).

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