THE 'TRUTH' ABOUT THE TOXICITY OF THIMEROSAL

[BASED ON THE FDA-RECOGNIZED, ADULT-RAT, CHRONIC-TOXICITY STUDY REPORTED IN:
MASON MM, CATE CC, BAKER J. ***CLINICAL TOXICOLOGY***, 1971; **4**(2): 185-204. TOXICOLOGY AND CARCINOGENESIS OF VARIOUS CHEMICALS USED IN THE PREPARATION OF VACCINES (MASON ET AL. 1971)]

In 1971, Mason et al. reported, *among other results*, their findings from chronic toxicity/carcinogenicity studies using adult rats of both sexes that utilized a 1-year dosing period and a 2-year overall study interval[1].

One of the chronic toxicity studies evaluated the chronic toxicity of Merthiolate (Thimerosal [49.6% mercury by weight]).

This study injected several groups of rats twice weekly for a year with varying levels of Thimerosal (i.e., 1.0, 0.3, 0.1 and 0.03 mg of Thimerosal/kg) dissolved in sterile saline along with two control group of rats ("Negative Control" and "Vehicle Control"), where:

a. The "Vehicle Control" group was injected twice weekly with sterile saline,

b. The "Negative Control" received no injections, and

c. The nominal volume injected into each rat each time was 0.25 mL for all the groups that were inoculated with either Thimerosal or, for the "Vehicle Control" group, sterile saline.

Thus, the nominal twice-weekly mercury levels dosing levels in the test groups were 0.50 mg/kg, 0.15 mg/kg, 0.05 mg/kg, and 0.015 mg/kg.

Based on the preceding, the respective nominal averaged Thimerosal 'daily dose' equivalents were: 0.28_{57}, 0.08_{5771}, 0.02_{857}, and 0.008_{5771} mg of Thimerosal/kg/day; and the corresponding mercury 'daily dose' equivalents were: 0.14_{16}, 0.04_{2246}, 0.01_{416}, and 0.004_{2246} mg of mercury/kg/day[2].

On page 191, lines 5-11 below the table, the Mason et al. 1971 observed:

> "It was during the last five months that the mortality increased. In the negative and vehicle controls the range varied between 5.8% to 8.3% while in test-drug groups it varied from 4.0% to 9.0%. Thimerosal was highest with 9.0%, while benzethonium chloride and ethylene chlorohydrin both had a mortality of 7.5%. There was a fairly even distribution of deaths except for the bronchopneumonia seen in the Thimerosal-treated rats (fuller details later)". [Emphasis added.]

Then, on page 194, under the heading "Drug-Related Organ Pathology", the researchers reported (emphasis added):

> " During the examination of about 2000 rats, a great variety of pathology was observed. The most frequent of these were mild changes in the liver, kidneys, heart, and lungs. Only in the Thimerosal-treated animals were the lesions in the lungs numerous or severe enough to warrant comment (see Table 6). Here only disease incidence in the high dose of each compound is recorded. The three compounds chosen had the highest incidence of bronchopneumonia and in comparison with the controls it is evident that Thimerosal had a damaging effect on the lung or its defense apparatus. Since the death rate in this group paralleled the deaths in the other compounds, it must be concluded that the damage was

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[1] "Experimental Procedure. The project was begun in three stages.
1. An initial toxicologic study to determine the acute lethal dose
2. A supplementary study to determine the maximum tolerated dose.
3. The final four-dose-level study to determine carcinogenicity of the compounds in animals treated for at least one year and held another year for observation". [Emphasis added; Mason et al. 1971, page 186]

[2] Thus, the doses administered were effectively 3.5 times the average daily dose – indicating a design that minimized the ration of the peak dose to the average daily dose.

slight, continuous, and perhaps cumulative. The incidence of pneumonia within the four dose levels of the Thimerosal group was dose-related".

The bronchopneumonia findings for the controls and the highest level of Thimerosal were depicted by the authors in their "Table 6" (Mason et al. 1971, page 195):

"Table 6
Incidence of Bronchopneumonia (18 months)[a]

Treatment group	Total number of animals	No. of animals with bronchopneumonia		Percentage of animals with bronchopneumonia	
		Gross pathology	Histopathology	Gross pathology	Histopathology
Negative control	120	5	16	4%	13%
Vehicle control	120	2	19	3	8
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Thimerosal	80	39	48	49	60

[a] High level compounds compared with vehicle and negative controls". [Emphasis added for Thimerosal]

Unfortunately, the "Gross Pathology" instances and percentages were not published for the lower Thimerosal levels.

However, based on the group sizes (Mason et. al. 1971, page 189, **Table 2**), the probable number of rats with a gross pathology of bronchopneumonia in the lower dosing levels was, based on the authors' statements that there was a clear dose-dependent relationship at all 4 levels of Thimerosal:

a. ~ 11 gross infections in the 60 adult rats (30 males and 30 females) dosed at the "0.3 mg of Thimerosal/kg of weight/twice weekly" level;

b. ~ 5 gross infections in the 40 adult rats (20 males and 20 females) dosed at the "0.1 mg of Thimerosal/kg of weight/twice weekly" level, and

c. ~ 2 gross infections in the implied[3] "20" adult rats (10 males and 10 females) at the "0.03 mg of Thimerosal/kg of weight/twice weekly" level.

and the corresponding background incidences (estimated from the "Vehicle Control" group, where there were 2 cases of gross pathology of bronchopneumonia in 120 "Vehicle Control"[4] rats or ~ 1.67 %) were:

- 1.33 for the group of 80 dosed at the 1.0 mg of Thimerosal/kg of weight/twice weekly level (background for highest Thimerosal level, which implies that the net response of 39 - 1.33 ≈ 37.67, which is ≈ 28 times background);
- 1.00 for the group of 60 dosed at the 0.3 mg of Thimerosal/kg of weight/twice weekly level (background for "**a.**"; implies net response of 12 – 1 ≈ 11, which is ≈ 11 times background);
- 0.67 for the group of 40 dosed at the 0.1 mg of Thimerosal/kg of weight/twice weekly level (background for "**b.**"; implies net response of 5 – 0.67 ≈ 4.33, which is ≈ 6.5 times background); and

[3] The number is implicit because, though the table entry for 0.03-dose group size is blank, the study design called for a total of 200 rats in the test arm for each compound evaluated.

[4] The "Vehicle Control" group was used because it was treated the "same" as each test group.

- "0.33" for the implicit group of 20 dosed at the 0.03 mg of Thimerosal/kg of weight/twice weekly level (background for "**c.**"; implies net response of 2 – 0.33 ≈ 1.67, which is ≈ 5 times background).

From the guesstimated numbers of bronchopneumonia cases with gross pathology for the 0.3, 0.1, and 0.03 mg of Thimerosal/kg/twice weekly data (12, 5, and 2, respectively) and the numbers of rats in each group, 60, 40, and implicitly 20 respectively, we can approximate the percentage versus dose as:

"**Percentage with bronchopneumonia in a given group is roughly equal to:**

(40.8 % [~~$^2/_{\neq}$ day~~]/mg of Thimerosal per kg) x ('n' mg of Thimerosal per kg/[~~$^2/_{\neq}$ day~~]) + 8.2 %" **[1]**

and construct the following putative table[5] based on equation **[1]** and the "Gross Pathology" findings:

Level of Thimerosal in mg/kg	No. of Rats in the Test Group for That Thimerosal Level	Reported or (Guesstimated) No. of Rats with Bronchopneumonia	Reported or (Est.) %. of Rats with Bronchopneumonia	Computed % of Rats with Bronchopneumonia (% = 40.8% x level + 8.2%) [diff {Reported or Estimated} – calc%]]
1.0	**80**	**39**	**49**	**49** [+0.0%]
0.3	**60**	(~12)	**(~20)**	**20.4** [+0.4%]
0.1	**40**	(~ 5)	**(~12.5)**	**12.3** [-0.2%]
0.03	**20**	(~ 2)	**(~10)**	**9.4** [-0.6%]
0.00	**120** **120**	**2** **5**	**1.7** [actually, 1.7 & 4.2]	8.2 [+6.5 & +4%]

After the one year of dosing and up to two years of observation, the "SUMMARY" findings for Thimerosal included the following statements (see Mason et al. 1971, pages 202-204):

1. "After 18 months, ... Thimerosal at ... highest dose level showed decreased weight gains as compared with the controls of ... 22%" [page 203, paragraph 2, lines 6-9];
2. "The only remarkable histopathology was related to a late bronchopneumonia which developed in many of the Thimerosal-treated animals. It was clearly a dose-related finding" [page 203, paragraph 3, all];
3. "Thimerosal had numerous injection site indurations and was second highest with fibromas" [page 203, paragraph 4, lines 7-8]; and
4. "Testicular tumors were found in most of the males that lived to 18 months. These are interstitial cell tumors peculiar to the Fischer rat. It is noteworthy that Thimerosal caused a dose-related inhibition of these tumors" [Mason et al. 1971, page 203, paragraph 6, all]. [Emphases (bolding and underlinings) added.]

Based on all of the preceding statements, it is clear that chronic dosing of Thimerosal for 12 months caused several long-term adverse health effects related to the Thimerosal dosing, including, *in the order they were reported*:

- Significant weight loss beginning 6 months after the injection of the Thimerosal ceased,

[5] Alternatively, the intermediate numbers of instances may have been 10, 4 and 1 for percentages of 16.7%, 10% and 5% with a least signal at the 0.03 level of 2 times background for "Vehicle Control" and a line of: %gross bronchopneumonia cases = 45 % /mg of Thimerosal per kg) x ('n' mg of Thimerosal per kg) + 4 % **[2]** with calculated % = 49% at 1.0 level, "17.5%" [+1%] at 0.3 level, "8.5%"[– 1.5%] at 0.1 level, "4.3%" [– 0.7%] at 0.03 level and "4%" [+2.3% & -0.2%] at intercept, respectively. Given all of these calculations, the number of gross instances of bronchopneumonia at the 0.3 level was: 10 – 12; the number at the 0.1 level was: 4 – 5; and the number at the 0.03 level was 1 – 2.

- Dose-related incidence of bronchopneumonia in all 4 test groups,
- Numerous injection site indurations and 2nd highest levels of fibromas – indicative of significant localized adverse reactions at the injection site, and
- Dose-related inhibition of the growth of the "interstitial cell tumors peculiar to the Fischer rat" – a clear indication of damage to the ability of these cells to replicate.

Thus, it is clear that, *based on all of the statements made*, the 0.008571 (effectively, 0.0086) mg/kg level was the lowest observed adverse effect level (LOAEL) level at which an adverse effect (dose-related bronchopneumonia) was reported in this chronic adult-rat toxicity/carcinogenicity study (performed under Contract Number Ph43-67-676 for the Division of Biologics Standards, NIH) by Mason et al. and subsequently published in the journal ***Clinical Toxicology*** in 1971.

Based on the FDA-recognized Mason et al. (1971) study of chronic toxicity in rats using injected Thimerosal, after appropriately correcting the observed $LOAEL_{\text{injected Thimerosal, adult rat}}$ of "0.0086 mg/kg/day" or,"8.6 µg/kg/day" for:

- The recognized minimum inter-species factor of 10 for rats compared to humans,
- The recognized minimum 10-fold factor needed to address population diversity, and
- The accepted (by researchers, the EPA and the FDA) factor of 10 to account for the established higher susceptibility to mercury poisoning in the developing child,

and converting the reported/observed LOAEL into an NOAEL, with no safety factor, that no-safety-factor $NOAEL_{\text{injected Thimerosal, developing child}}$ is clearly: < 0.0086 µg Thimerosal/kg/day.

The similarly derived, no-safety-factor value for adults, $NOAEL_{\text{injected Thimerosal, human adult}}$, is clearly: < 0.086 µg Thimerosal/kg/day.

Given the preceding realities, even a 0.25-mL dose of a Thimerosal-preserved influenza vaccine (nominally, 100 µg Thimerosal/mL) injects the child with 25 µg of Thimerosal – a dose that exceeds the no-safety-factor $NOAEL_{\text{injected Thimerosal, developing child}}$ of < 0.0086 µg Thimerosal/ kg/day on the day of injection unless the developing child were to weigh more than 2,907 kg (6,409 pounds [3.2 tons])!

For the fetus and children over three years of age where 0.5 mL of vaccine (50 µg of Thimerosal) is injected into the pregnant woman or the child, that dose is not safe unless the fetus or the child weighs > 5,814 kg (12,818 pounds [6.4 tons])!

Thus, even when no "safety factor" is included, it is clear that no Thimerosal-preserved vaccine is safe to inject into a child or pregnant woman, (or, for that matter, man or non-pregnant woman unless he or she weighs more than 581 kg [1,282 pounds {0.64 ton}])!

Further, for the dose of Thimerosal that might be truly safe to give to a developing child who is susceptible to mercury poisoning, we would need to include at least a safety factor of 10, which would require the nominal $NOAEL_{\text{injected Thimerosal, developing child}}$ to be: less than 0.00086 µg Thimerosal/kg/ day (< 0.86 nanograms [ng] of Thimerosal/kg/day)[6].

[6] For a 1-kg (2.2 pound) neonate, this would translate into a dose of <0.00086 µg of Thimerosal per 0.25-mL (the least volume typically injected) or < 0.0034 µg of Thimerosal/mL (<0.00000034%) of vaccine – levels that obviously indicate that Thimerosal cannot be safely added to any vaccine given to the developing child or pregnant women.

Realistically, for highly toxic bioaccumulative compounds, like Thimerosal, whose end metabolite (tissue-retained inorganic mercury) has a half-life of on the order of two decades in the human brain[7], a safety factor should be 100 or greater.

Obviously, we need better studies in animals whose sensitivity to mercury poisoning more closely resembles human sensitivity to get more exact estimates of the NOAELs for not only gross chronic toxicity but also reproductive effects, teratogenicity, and DNA damage.

For example, the Gold-Syrian hamster (*Mesocricetus auratus*), which exhibited[8] regressive neurodevelopmental symptoms similar to those seen in children (and physical weight deficits in the weights of the test individuals and their brains) when given a post-natal Thimerosal-dosing regimen mimicking that from vaccines given to U.S. children at 2, 4 and 6 months under the 2001 U.S. recommended schedule, could be used to get better estimates for the global toxicity NOAELs and perhaps the toxicity studies for the required developing animal, reproductive, male and female chromosomal damage, and multi-generational reproductive studies.

However, the present no-added-safety-factor estimates for the general toxicity NOAELs for injected Thimerosal are more than adequate to establish that Thimerosal-preserved vaccines are not safe to the requisite level, "**sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient, ...**" (as set forth in 21 CFR § 610.15(a)).

Given the fact that injected Thimerosal solutions are definitely toxic to:

- Developing humans at levels *less than* 0.01 µg of Thimerosal/kg/day (< 0.005 µg of mercury/kg/day), and
- Adult humans at levels *less than* 0.1 µg of Thimerosal/kg/day (< 0.05 µg of mercury /kg/day),

it is obvious that Thimerosal cannot safely be used as preservative in vaccines nor, for that matter, used as an in-process sterilant unless the maximum residual level does not exceed 0.001 µg [1 nanogram] of Thimerosal per dose.

Therefore, the 'Truth' About the Toxicity of Thimerosal is:

- **Thimerosal is too toxic to be used in the manufacture of any medicine without proof of safety to the "sufficiently nontoxic …" standard in 21 CFR § 610.15(a)!**
- **The use of Thimerosal, or any other organic mercury compound, as a preservative in any medicine should be banned!**
- **All Thimerosal-preserved vaccine doses should be immediately recalled and destroyed!**
- **All vaccines and other drugs containing a level of mercury from added Thimerosal or other added mercury compound that is at or above 0.05 part-per-million (ppm), or ≥ 0.000005 %, should be recalled and destroyed unless the FDA-registered**

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[7] Sugita M. The biological half-time of heavy metals. The existence of a third, "slowest" component. ***Int Arch Occup Environ Health*** 1978; **41**(1): 25-40

[8] The golden hamster exhibits regressive neurodevelopmental symptoms similar to those seen in children when given a post-natal Thimerosal-dosing regimen mimicking that from vaccines in human children at 2, 4 and 6 months under the 1999 U.S. recommended schedule. [See, Laurente J, Remuzgo F, Ávalos B, Chiquinta J, Ponce B, Avendaño R, Maya L. Neurotoxic effects of thimerosal at vaccines doses on the encephalon and development in 7 days-old hamsters. ***An Fac Med Lima*** 2007; **68**(3): 222-237.]

manufacturer can prove with at least a 100-fold safety margin in all of the appropriate applicable toxicity studies that said vaccine or other drug is safe to the "sufficiently nontoxic …" standard set forth in 21 CFR § 610.15(a)!

- **Given the evidence that Thimerosal and other mercury compounds are <u>not</u> generally safe to use in medicines <u>unless</u> their mercury level is below 0.05 ppm, the federal government should ban ALL use of Thimerosal or other mercury-based compounds in medicine!**

CONCLUDING REMARKS

Should any reader find significant factual errors in this short article, then please send the author (at paulgkingphd@gmail.com) your proposed changes to the article along with e-mail attachments that contain copies of the published documents that provide the proof needed to substantiate your claims.

Then, *as has been the case in the past*, after verifying the validity of your concerns, the confirmed significant factual errors will be appropriately corrected and a corrected document posted.

If you find spelling or punctuation errors, please also send them in so that this document can be appropriately updated and posted as a "revised draft".

Respectfully,

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