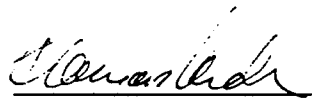


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ESTIMATES OF EXPOSURE TO ANILINE,
BENZIDINE, BETANAPHTHYLAMINE AND
O-TOLUIDINE

STUDY S094

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Re analysis bladder cancer study

To assign exposure rankings to aniline, o-toluidine, betanaphylamine and benzidine to the study population the first exposure assessment used information contained in the plant history to model exposures. While this information provided an estimate of exposure, the ERB recommended that several analyses be performed which included dividing the rankings into quartiles, separating the assessment into a skin or air component only and dividing these into quartiles to provide the final exposure rankings. An additional assessment was also made which estimated an exposure based on a more refined dose estimate using the initial assessment data, available air monitoring data and other information on absorption rates.

BACKGROUND INFORMATION ON THE FOUR CHEMICALS:

Aniline- reported skin absorption rate is 0.2 to 1.2 mg/cm²/hr. Use a value of 0.7 mg/cm²/hr for calculations. Vapor pressure is 0.67 mm Hg at 25 °C

Benzidine - Shah and Guthrie ¹ applied 1 mg/kg of radioactive benzidine to shaved skin of rats, found at 24 hours, approximately 50 % was not removed by washing. 3,3' dichlorobenzidine showed a similar absorption pattern (at 1 hour 6%, 8 hour 23% and 24 hours 49% absorbed). Aldrich et.al. ² studied Direct Black 38 (a benzidine based dye) found at 144 hours, rabbits that 10% was absorbed, rats about 0.2%. Benzidine is similar in structure to ODA that has an absorption fraction of 6% is absorbed through the skin, with 1% being eliminated, 5% remaining at the absorption site. Use an absorption fraction of 25% for an 8 hour shift. Meigs et. al. ³ indicated that an 8 hour exposure to 0.018 mg/m³ benzidine resulted in 0.026 mg/l excretion in the urine. Sciarini and Meigs ⁴ about 10 -20 % of the benzidine is recovered as the free compound and the mono and diacetylbenzidine, Prior work by Meigs found 10 % of benzidine administered was recovered unchanged. On the basis of the above work approximately 30% of a dose is measured by the urine tests employed at the site.

Melting point is 115-120 °C

¹ Shaw P.V. and Guthrie F.E., Dermal absorption of derivations in rats, Bull Environ Contam Toxicol, 31:73-78, 1983

² Aldrich F. D., Busby W. F., Fox J. G., Excretion of radioactivity from rats and rabbits following cutaneous application of two c14- labeled A20 dyes. J. Toxicil Environ Health, 18:347-355, 1986

³ Meigs J. W., Sciarini, L.J., and Van Sandt, W. A. Skin penetration by diamines of the benzidine grop, Arch Ind Hyg 9:122-32, 1954

⁴ Sciarini, L.J. and Meigs J. W., The biotransformation of benzidine II. Studies in mouse and man, Arch Environ Health 2:423-428, 1961

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Betanaphthylamine - an aqueous solution (0.013%) applied to rat tails, resulted in approximately 10% absorption (when scrubbed with benzene indicating that material was on the surface and easily removed). ⁵ Use a value of 10% absorption.

Melting point is 111-113 °C

O-toluidine - O-toluidine applied in an aqueous polyethylene glycol solution for six hours resulted in approximately 14% of dose absorbed⁶ (measured at end of 24 hour period). In first 12 hours, 63% of dose excreted in urine, 15% in 12- 24 hour time period. Metabolites were amino-m-cresol and N-acetyl amino-m-cresol (25 and 43% of absorbed dose. O-toluidine was about 8% of the metabolite. For o-toluidine, 17.5 mg/liter urine will result in 10% methemaglobin, defined as mild cyanosis. For p-toluidine, 0.4 mg will give the same response.

For an OT analysis in urine, a dose of 220 mg (5 ppm inhalation for a day) would yield an OT urine level of 20 mg/liter (220 mg*excretion rate of .6* prevalence of 0.08/ 500 cc urine volume = 0.02 mg/cc= 20mg/l)

Vapor pressure is 1 mm at 40 °C.

BASIC ASSUMPTIONS USED

Contact amount:

Clothes- report from meeting in Basel ⁷ Dr. Babel reports that a suit a man wore in the operating area (benzidine is ground, dried and weighed), 3 g. was extracted. A freshly washed suit had 0.167 g. of base. This gives an estimate of the amount of benzidine that could be found on a workers' clothing.

In 1934 clothes are being washed once a week. ⁸ There is no record of this changing until the new plant is constructed which requires daily changes starting in 1951.

Contact area:

For hands use a value of 300 cm², the approximate area of two palms.
For immersion into a liquid use a value of 850 cm², the area of two hands.

⁵Zorn,H., Zentralbl. Arbeitsmed. Arbeitsschutz, 21(2) 56-7, 1971 (CA75:9643)

⁶Unpublished Haskell data.

⁷ Exchange and Experiences on questions of Industrial Hygiene, October 10-11, 1951, Basel :Notes of Dr. Schobel

⁸ Regulations for the control of Industrial bladder Disease in the Dye Works, 3/14/34

For body contact use an area of 1000 cm², area approximating the front of the thighs and stomach (contact with a surface by leaning into it). On the basis of the Babel data, 3 g. of material on a suit of clothes would if it all were located in the above area be at 3 mg/cm². Since the amount of material available for absorption would be reduced from this figure, use a value of 1 mg/cm² for an estimate of the amount of material available for absorption.

Air levels:

Betanaphthylamine:

Air monitoring data for alpha-naphthylamine in 1939 in the hydrogen reduction building averaged 18 mg/m³. For betanaphthylamine, data from 2/40 was 0.2 to 0.9 mg/m³ at the flaker, and other areas in the building. Samples for alpha naphthylamine taken by the flaker and at the press at the same time were 2.6 and 2.9 mg/m³ in Hydrogen reduction.

Betanaphthylamine analysis in urine from the time period was 0.18 mg/100 cc urine from operators in the sulphonation house, and 0.24 in the amination group (time period is March through May, 1940)

With an average urine output of 2 liters/day, dose would be estimated to average 3.6 and 4.8 mg average/ day with the assumption that it does not accumulate in an organ to an appreciable extent.

O- toluidine:

Average data from 1983 0.16 mg/m³.

Area samples from the continuous process in 1975 at the filters averaged 0.27 to 0.56 ppm, 1.2 to 2.5 mg/m³.

Average data at the drumming booth in 1978 was 0.8 mg/m³.

Area samples at the bakers (CB-1) in 1979 showed during loading OT - 0.077 mg/m³ average, during charging- 0.024mg/m³, and after charging- 0.023 mg/m³.

Average of samples in the NOMEX building in 1975 were 2.3 mg/m³.

In August 1976, the average is 0.18 mg/m³

In 1977 122 area samples averaged 0.05 mg/m³.

Personal monitoring data in 1981-84 averages 0.25 mg/m³.

In 1953 analysis of urine in production of DOTTU showed average OT in the urine of 2.4 mg/l. In the ONA-naphthanil building, the average was 0.74 (103 measurements). No betanaphthylamine was found in these samples.

Aniline

Repauno air data for an operator 8 hour TWA in 1979-80 period is 0.16 ppm = 0.6 mg/m³

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Cyanosis cases:

1934 18 of 37 caused by o and p toluidine.

1935 23 of 35 associated with o and p toluidine

1950 Aniline is mentioned as one of the main causes of cyanosis in Azo.

1954 aniline causes 4 of 18 cases.

1955 9 of 25 cases due to OT.

1958 expand benzidine control program to OT workers in benzidine #1 bldg.

1962 increase in abnormal urines for benzidine double 1960 value.

1965 improving control abnormal in #1 0%, in #2 24% (abnormal is greater than 0.1 mg/liter).

1978 a-naphthylamine level in urine decrease from 0.22 mg/l in 77 to 0.12 mg/l.

1979 2 of 10 cyanosis due to OT

1980 1 of 2 cases due to OT.

Aniline

Reported skin absorption rate 0.7 mg/cm²/hr

Air monitoring at Repauno average for an operator 1978-82 is 0.16 ppm or 0.6 mg/m³

Therefore a dose estimate in mg/day at Repauno in 1979 is:

- air monitoring 0.6 mg/m³
- contact area of palms, leather gloves

Calculated dose is

- 0.6 mg/m³* 10 m³ = 6 mg
- 300 cm²* 0.7 mg/cm²/hr = 210 mg.

The TLV[©] was 5 ppm or 19 mg/m³ in 1979 this is equivalent to a dose for a day at the TLV of 190 mg. Thus the estimated dose is approximately equal to a TWA exposure and a reasonable estimate of exposure at that time. There is no hard data to confirm if the estimate is correct, but since the exposure estimate will be on a relative basis between jobs, plant area and year, the exposure estimates will on a relative basis be correct.

Benzidine

Absorption rate is 50%, breathing 8 hours at 0.018 mg/m³ = urine level of 0.026 mg/l (this is approximately a 30% recovery)

Recovery in urine of free benzidine and the mono/di acetylbenzidine is 10 -20%
Method used at site was crude - use 10% recovery for exposure estimates.

Therefore a dose estimate in 1918 is with an estimate of the air level at 0.5 mg/m³ and skin contact area palms and front of body at 1mg/cm² equals:

- Air = 0.5 mg/m³* 10 m³= 5 mg/day
- Skin = (300 cm²+1000Cm²)* 1 mg/cm²= 325mg/day

With 10% recovery- 325 mg dose = 33 mg in urine, for a end of shift urine level based on 33 mg/day excreted in 2 liter urine and a 500 cc end of shift urine volume equals~ 8mg or just at cyanosis level. Therefore the estimate is a reasonable approximation of the dose in 1918. No other data exists to confirm or modify this estimate.

Betanaphthylamine:

The absorption rate is 10% of what is applied to the skin. In March to May 1940 average beta-naphthylamine found in urine was 0.18 to 0.24mg/ 100 cc. This is equivalent to a dose of 3.6 to 4.8 mg with a 2 liter daily urine volume.

To estimate the dose in 1940, assume an air level of 0.5 mg/m³, for skin contact assume the area contaminated is the palms and front of body using contaminated PPE at 0.5 mg/cm² The dose is estimated at

- air = 0.5 mg/m³* 10 m³ = 5 mg
- Skin = (300+1000 cm²) * 0.5mg/cm²= 65 mg

The dose is then 5 mg + 65 mg * 10% absorption, or 11.5 mg/day. This is not very different from the measured exposure of 3.6 to 4.8 mg. There is no other data to confirm or modify this estimate.

O- toluidine

The absorption rate of a dermal dose is 14% of the applied material. It is excreted at the following rates:

- - 65% in first 12 hour
- - 15% in 12-24 hour
- O-toluidine 8% of metabolites

For O- toluidine, 17.5 mg/l urine give 10% methemoglobin, or mild cyanosis.

An estimated dose in 1919 at an air of 5 mg/m³ and skin contact with the palms and front of body at 1 mg/cm² gives a dose estimate of:

- air = 5 mg/m³* 10 m³ = 50 mg
- skin= (300+1000 cm²)* 1 mg/cm²* 14% absorption rate = 182 mg
- dose = 50+ 182 = 232mg

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Since mild cyanosis is 17.5 mg/l, a dose that gives a case of mild cyanosis would be $(17.5 \text{ mg}/8\% \text{ recovery}) = 218\text{mg}$. The estimated exposure is approximately this level and therefore a reasonable estimate. No other data was found to confirm or modify this estimate.

Final assessment:

With these estimates at single points in time, the relative exposure for other times and areas is shown in the attached tables.

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