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3. Technical Leader Forensic Toxicology (2003- 2004)
   Georgia Bureau of Investigation
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Note: All content contained in this presentation reflects the opinions of the presenter and are not the official position of GBI or the state of Georgia.

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Alcohol Distribution – Theory, Application, and Considerations

Chris Tilson, F-ABFT

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Disclosures

The speaker has no disclosures.

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Learning Objectives

1. Students will develop a fundamental understanding of the **physiological basis of alcohol distribution** and its effect on blood alcohol concentration.
2. Students will learn how to **estimate the apparent volume of ethanol distribution** from anthropometric factors in accordance **ASB recommendations**.
3. Students will learn how ethanol **distribution into** body fluids such as **serum and plasma** impact the apparent volume of distribution and their **relationship to the blood alcohol level**.

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Theory of Distribution

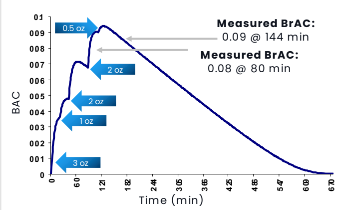
Dosed Subject Information

- 26 year old male subject
- Weight: 206 lb Height: 5'10"
- Dose 1: 3 oz @ 12:56
- Dose 2: 1 oz @ 13:16
- Dose 3: 2 oz @ 13:36
- Dose 4: 2 oz @ 14:20
- Dose 5: 0.5oz @ 14:45

Alcohol Pharmacokinetics

It is clear from the evaluation of dosed subjects that alcohol concentration is affected by:

- **Administration** of alcohol to the Body
- **Absorption** into the Bloodstream
- **Elimination** from the Body.



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Theory of Distribution

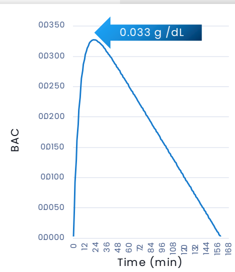
Subject (*hypothetical*)

- 220 lb male
- Dose: 3 fl oz of 80 proof liquor
  *Equivalent to **28g** of Ethanol*

Observation

- Peak BAC = **0.033 g/dL**
- Estimated blood volume: **7.5 L**
- Total Alcohol in blood: **2.475 g**

Less than 10% of the dose is accounted for in the peak BAC



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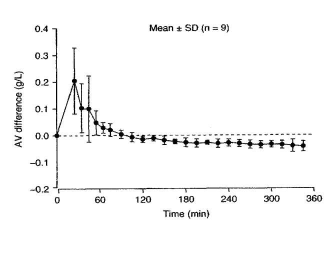
Theory of Distribution

Study
Jones, A.W., Lindberg, L. & Olsson, SG. Magnitude and Time-Course of Arterio-Venous Differences in Blood-Alcohol Concentration in Healthy Men. Clin Pharmacokinetics 43, 1157–1166 (2004). [53]

Observation
- **Arterial BAC** > **Venous BAC** during absorption.

This is attributable to alcohol distribution.



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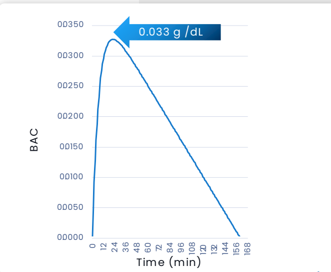
Theory of Distribution

Subject (*hypothetical*)
- 220 lb male
- Dose: ***28g*** *of Ethanol*
- Total Alcohol in blood: **2.475 g**

Other Alcohol
- Peak BAC = **0.033 g/dL** at 20 min
- Est. BAC Eliminated: 0.005 g/dL
- Est. Alcohol Eliminated: 0.375 g

~25.5 g of Ethanol unaccounted for



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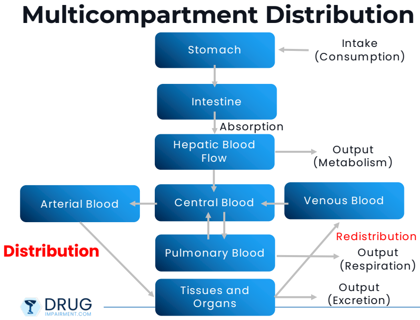
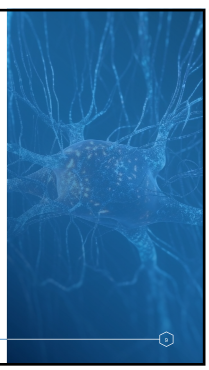
Multicompartment Distribution





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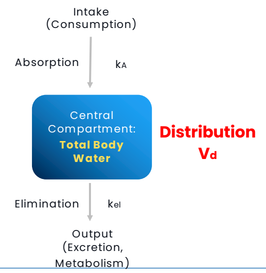
Single Compartment Distribution



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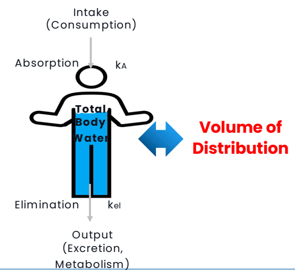
Volume of Distribution



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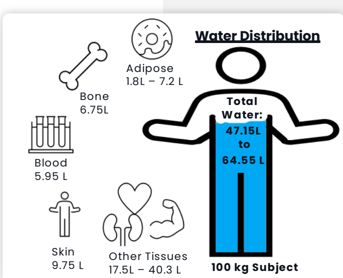
Theory of Distribution

Approximate Water Content [50,60,61]

Tissue	Water %	% of Body Weight
Adipose	18%	10%-40%
Bone	45%	15%
Skin	65%	15%
Blood	85%	7%
Other Tissue	76%	23%-53%

Total Water Content: 47% – 65% of total weight



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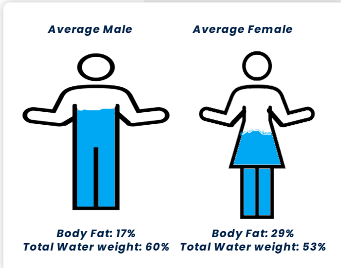
Theory of Distribution

Approximate Water Content[50,52,60,61]

Tissue	Water %	% of Weight (Male)	% of Weight (Female)
Adipose	**18%**	**17%**	**29%**
Bone	45%	15%	15%
Skin	65%	15%	15%
Blood	85%	7%	7%
Other Tissue	**76%**	**46%**	**34%**



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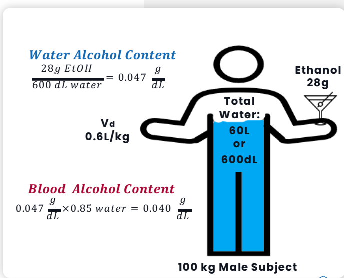
Theory of Distribution

Subject (*hypothetical*)

- Dose: 28 g ethanol
- Weight: 100 kg
- Avg Male: **60% water** by weight or
- Actual V_d: **0.6** L of water / kg of weight
- Total Body Water: 60L

Alcohol Distribution

- Water Alcohol Content = **0.047 g/dL**
- Blood Water Content = 85% by volume
- Blood Alcohol Level: **0.040 g/dL**



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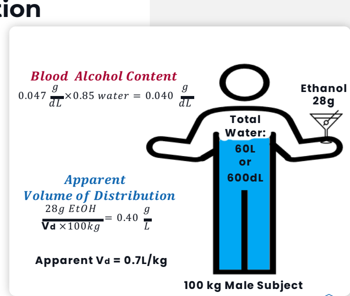
Theory of Distribution

Subject (*hypothetical*)

- Dose: 28 g ethanol
- Weight: 100 kg
- BAC: **0.04 g/dL** or **0.4 g/L**

Alcohol Distribution

- Actual Volume of Distribution = **60L**
- Actual V_d = **0.6 L/kg**
- Apparent Vol of Distribution = **70L**
- Apparent V_d from BAC = **0.7 L/kg**



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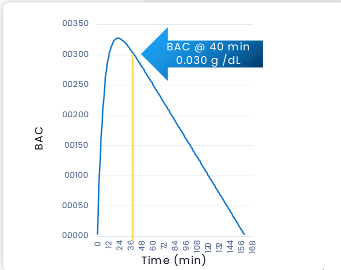
Theory of Distribution

Subject (*hypothetical*)

- 220 lb male / 100kg
- Dose: ***28g** of Ethanol*
- Distribution Volume: 60L
- Apparent V_d from BAC = **0.7 L/kg**
- BAC from Dose: **0.040 g /dL**

Alcohol Pharmacokinetics

- Post absorptive BAC = **0.030 g/dL**
- Time Post Dosing: 40 min
- Elim Rate: 0.015 g/dL/hr
- Est. BAC Eliminated: **0.010 g/dL**
- Total BAC : **0.040 g/dL**



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Theory of Distribution

BAC from Measured Results

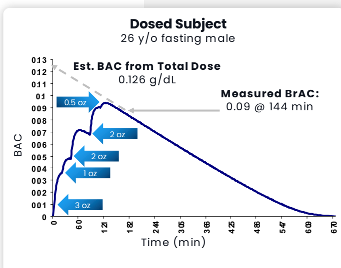
- BrAC at 144 min: **0.090 g/dL**
- **Average Elim Rate: 0.015 g/dL/hr**
- Est. BrAC elim: 0.036 g/dL
- **Est. BAC from Total Dose: 0.126 g/dL**

BAC from Distribution Model

- **Total Dose**: 8.5 oz of 80 proof liquor
- **Total Ethanol: 79.3 g** over 110 minutes
- **Subject Weight**: 206 lb or **93.52 kg**
- **Avg Vd male: 0.7 L/kg**

$$BAC\ from\ Dose\ g/L = \frac{79.3g}{0.7\ {}^{L}/_{kg} \times 93.52\ kg}$$

- **Est. BAC from Total Dose: 0.121 g/dL**



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Theory of Distribution - Summary

In Summary Alcohol …

- Conforms to a one compartment model of Distribution
- Distributes evenly throughout the Total Body Water
- The total body water (TBW) represents the volume of distribution for alcohol
- The apparent volume of distribution for ethanol in blood is 15% higher than the TBW.

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Theory of Distribution - Summary

In Summary the Volume of Distribution…

- For alcohol in blood is expressed as **Vd** and is measured in **L/kg** of total weight.
- Is primarily dependent upon the **body fat percentage** of the subject
- Thus it is **correlated with:**
  - BMI
  - Sex
  - Age
  - Ethnicity
- These factors should be considered when **applying a Vd to estimate BAC.**

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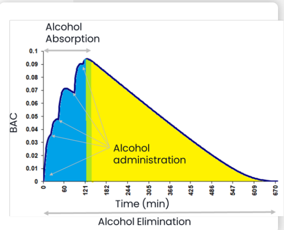
Distribution - Applied

Alcohol Pharmacokinetics

Alcohol Concentration is the product of:

- Administration
- Absorption
- **Distribution**
- Elimination



Calculating Alcohol Concentration

$$BAC = \frac{Amount\ Administered \times Fraction\ Absorbed}{Distributed\ Volume} - Amount\ Eliminated$$

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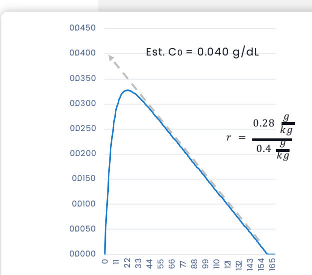
Distribution - Applied

Alcohol Pharmacokinetics

For the hypothetical example at right:

- Subject weight: 100 kg
- Dose: **28 grams or 0.28 g/kg**
- Est. C_0 : **0.040 g/dL or 0.4 g/L**
  Note: Widmark measured BAC in g/kg
- Calculated Widmark **r: 0.7**



Widmark's Formula [62,63]

$$BAC\frac{g}{kg} = \frac{Amount\ (g)}{r \times weight\ (kg)} - Elimination\ Rate\ (\beta) \times time\ (hr)$$

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Distribution - Applied

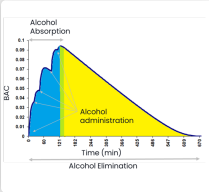
Widmark's Formula

$$BAC\frac{g}{kg} = \frac{Amount\ (g)}{r \times weight\ (kg)} - Elimination\ Rate\ (\beta) \times time\ (hr)$$

Widmark's Findings

For a population of 20 men and 10 women the **average r value** was:

- **0.68 for men**
- **0.55 for women**



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Distribution - Applied

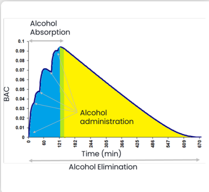
Widmark's Formula Modified

$$BAC\frac{g}{dL} = \frac{Amount\ (g)}{V_d\left(\frac{L}{kg}\right) \times weight\ (kg) \times 10dL/L} - Elim.\ Rate\ (\beta) \times time\ (hr)$$

Converting r to Vd

It should be noted that the specific gravity of blood at 37°C is approximately 1.055 g/mL[9]

Thus, **Widmark rho factors will differ from measured V_d** values by about 5%



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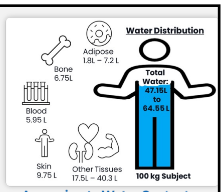
Distribution - Applied

Widmark's Formula Modified

$$BAC\frac{g}{dL} = \frac{Amount\ (g)}{V_d\left(\frac{L}{kg}\right) \times weight\ (kg) \times 10dL/L} - Elim.\ Rate\ (\beta) \times time\ (hr)$$

Determining Vd [50]

$$Vd = \frac{0.72 \times (1 - Body\ Fat\ \%)}{0.85}$$



Approximate Water Content

Tissue	Water %	% of Body Weight
Adipose	18%	10%-40%
Bone	45%	15%
Skin	65%	15%
Blood	85%	7%
Other Tissue	76%	23%-53%

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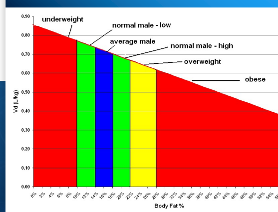
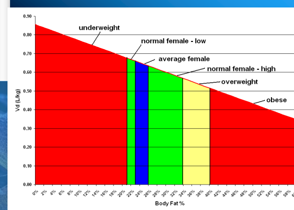
Distribution - Applied

Vd vs Body Fat - Males



Vd vs Body Fat - Females



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Distribution - Applied

Volume of Distribution [50]

$$Vd = \frac{0.72 \times (1 - Body\ Fat\ \%)}{0.85}$$

Determining Body Fat (*Gallagher* [52])

White and African American Subjects

$$Body\ Fat\ \% = 64.5 - 848 \times \frac{1}{BMI} + 0.079\ x\ age - 16..4 \times sex$$
$$+0.05 \times sex \times age + 39.0 \times sex \times \frac{1}{BMI}$$

Sex = 1 for males and 0 for Females

$$\textbf{Asian Females}\ Body\ Fat\ \% = 64.8 - 752 \times \frac{1}{BMI} + 0.016 \times age$$

$$\textbf{Asian Males}\ Body\ Fat\ \% = 51.9 - 740 \times \frac{1}{BMI} + 0.029 \times age$$

Example Calculated Vd (*Gallagher*[52])

Race	Age	Sex	BMI	Fat %	Vd
White/ Black	20	M	18.5	12.1	0.74
White/ Black	60	M	25	23.5	0.65
White/ Black	20	F	18.5	23.4	0.65
White/ Black	60	F	25	35.3	0.55
Asian	20	M	18.5	12.5	0.74
Asian	60	M	25	24.0	0.64
Asian	20	F	18.5	24.5	0.64
Asian	60	F	25	35.7	0.54

$$BMI = \frac{weight\ (kg)}{height\ (m)^2}$$

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Distribution – Applied (Gallagher[52])

Estimated Vd - Males (20-60 y/o)

White / African American

BMI: 15 -18.5 — Vd: 0.75 - 0.85
BMI: 18.5-25 — Vd: 0.65 – 0.78
BMI: 25 -30 — Vd: 0.60 – 0.69
BMI: 30 – 35 — Vd: 0.57 – 0.65

Asian

BMI: 15 -18.5 — Vd: 0.73 - 0.82
BMI: 18.5-25 — Vd: 0.64 – 0.74
BMI: 25 -30 — Vd: 0.60 – 0.65
BMI: 30 – 35 — Vd: 0.57 – 0.61

Estimated Vd - Females (20 – 60 y/o)

White / African American

BMI: 15 -18.5 — Vd: 0.65 - 0.77
BMI: 18.5-25 — Vd: 0.55 – 0.66
BMI: 25 -30 — Vd: 0.50 – 0.57
BMI: 30 – 35 — Vd: 0.47 – 0.53

Asian

BMI: 15 -18.5 — Vd: 0.63 - 0.72
BMI: 18.5-25 — Vd: 0.54 – 0.64
BMI: 25 -30 — Vd: 0.50 – 0.55
BMI: 30 – 35 — Vd: 0.47 – 0.51

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Distribution – Applied (Watson & Forrest[51,54,63,64])

Total Body Water Watson (1981)

TBW males

$$= 2.447 - 0.09516 \times age + 0.1074 \times height + 0.3362 \times weight$$

TBW females

$$= 2.097 - 0.1069 \times height + 0.2466 \times weight$$

age is in years, height in cm, and weight in kg

Total Body Water Forrest (1986)

TBW males

$$= 0.724 \times \left(weight - \frac{(1.34 \times BMI) - 12.467}{100} x\, weight \right)$$

TBW Females

$$= 0.724 \times \left(weight - \frac{(1.371 \times BMI) - 3.467}{100} x\, weight \right)$$

weight in kg

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Distribution – Applied (Ulrich, Seidl, & Maudens[63])

Volume of Distribution Ulrich (1987)

Vd males

$$= 0.715 - (0.00462 \times weight) + (0.0022 \times height)$$

height in cm, and weight in kg

Volume of Distribution Seidl (2000) [53]

Vd males

$$= 0.31608 - (0.004821 \times weight) + (0.004632 \times height)$$

Vd females

$$= 0.31223 - (0.006446 \times weight) + (0.004466 \times height)$$

height in cm, and weight in kg

Volume of Distribution Maudens (2014)

Vd males

$$= 0.8202 - (0.009 \times BMI)$$

Vd females

$$= 0.7772 - (0.0099 \times BMI)$$

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Distribution – Applied

Subject Information

Height: 5′ 10′
Weight: 175 lb
BMI: 25.076
Age: 25

Estimated Vd

Male Subject Vd: 0.59 – 0.76 L/kg
Female Subject Vd: 0.53 – 0.61 L/kg

Comparing Models Estimated Vd [52,63]

Method	Male	Female
Watson	0.69	0.61
Forrest	0.68	0.60
Ulrich	0.74	NA
Gallagher	0.69	0.57
Seidl	0.76	0.60
Maudens	0.59	0.53

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Distribution – Applied

Dosed Subject Information

Total Subjects: 241
Males: 186 Females: 55
Total Measurements: 489
Average Alcohol Concentration: 0.096

Calculation Notes

- All alcohol measurements were from BrAC measured more than 30 minutes post dose.
- An elimination rate of 0.018 g/dL/hr was assumed.

$$measured\ Vd = \frac{Dose\ (g)}{(BAC\ measured + BAC\ eliminated) \times 10 \times weight}$$

$$Vd\ Difference = Vd\ estimated - Vd\ measured$$

Comparing Estimated and Measured Vd [52,63]

Method	Vd Avg Difference	Std Dev
Widmark avg	-0.030	0.100
Watson	-0.025	0.085
Forrest	-0.007	0.095
Seidl	0.036	0.105
Gallagher	-0.016	0.088
Vd avg	-0.003	0.097
Maudens	**-0.107**	0.085

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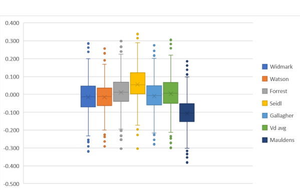
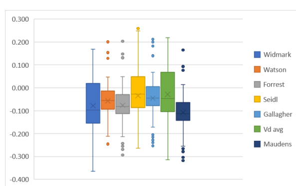
Distribution – Applied

Estimated vs Measured Vd Males



Estimated vs Measured Vd Females



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Distribution – Applied

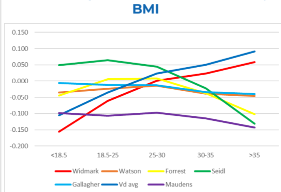
Dosed Subject Information

Total Subjects: 241
Males: 186 Females: 55
Total Measurements: 489
Average Alcohol Concentration: 0.096

Calculation Notes [53]

BMI Category		Number
Underweight	<18.5	16
Normal	18.5-25	250
Overweight	25-30	129
Obese	30-35	66
Morbidly Obese	>35	28
	Total	489

Evaluating Vd Estimation Models by BMI



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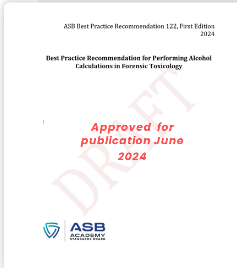
Distribution - Applied

Studies

*Maskell PD, Jones AW, Savage A, Scott-Ham M. "**Evidence based survey of the distribution volume of ethanol: Comparison of empirically determined values with anthropometric measures.**" Forensic Sci Int. 2019;294:124-131. doi:10.1016/j.forsciint.2018.10.033*


ASB Best Practice Recommendation 122, First Edition 2024

Best Practice Recommendation for Performing Alcohol Calculations in Forensic Toxicology

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Approved for publication June 2024

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Distribution - Applied

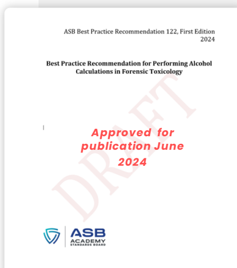
ASB Recommendations – Total Body Water

$$TBW\ males\ (Watson\ Method)$$

$$= 2.447 - 0.09516 \times age + 0.1074 \times height + 0.3362 \times weight$$

$$TBW\ females\ (Watson\ Method)$$

$$= 2.097 - 0.1069 \times height + 0.2466 \times weight$$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Distribution - Applied

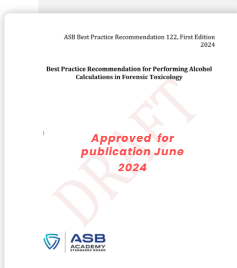
ASB Recommendations – Estimating Vd

$$Vd\ males\ (Maskell)$$

$$Vd\ \left({}^{L}/_{kg}\right) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times 0.825}$$

$$Vd\ females\ (Maskell)$$

$$Vd\ \left({}^{L}/_{kg}\right) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times 0.838}$$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Distribution - Applied

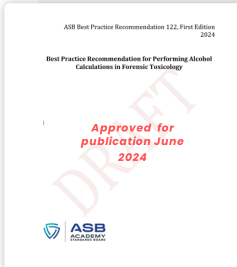
ASB Recommendations– Expressing Uncertainty

$$\textit{Vd males (Maskell and Cooper)}$$

$$Vd\ \left({}^{L}/_{kg}\right) = Vd\ {}^{+}/_{-}\ (Vd \times 9.86\%)$$

$$\textit{Vd females (Maskell and Cooper)}$$

$$Vd\ \left({}^{L}/_{kg}\right) = Vd\ {}^{+}/_{-}\ (Vd \times 15.00\%)$$


ASB Best Practice Recommendation 122, First Edition
2024

Best Practice Recommendation for Performing Alcohol Calculations in Forensic Toxicology

Approved for publication June 2024

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Distribution - Applied

ASB Recommendations – Applied

Subject: **25** y/o male
Height: 5' 10' $70in \times 2.54\ cm/in = \mathbf{177.8\ cm}$
Weight: 175 lb $175lb \times 0.454\ kg/lb = \mathbf{79.45\ kg}$

$$\textit{TBW males (Watson Method)}$$

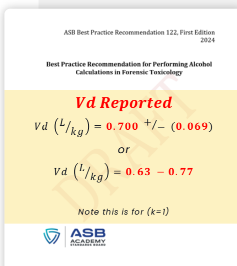
$$2.447 - 0.09516 \times \mathbf{25} + 0.1074 \times \mathbf{177.8cm} + 0.3362 \times \mathbf{79.45kg}$$

$$\textit{Vd males (Maskell)}$$

$$Vd\ ({}^{L}/_{kg}) = \frac{\mathbf{45.905(L)}}{\mathbf{79.45kg} \times 0.825}$$

$$\textit{Vd males (Maskell and Cooper)}$$

$$Vd\ \left({}^{L}/_{kg}\right) = \mathbf{0.700}\ {}^{+}/_{-}\ (\mathbf{0.7} \times 9.86\%)$$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Vd Reported

$$Vd\ \left({}^{L}/_{kg}\right) = \mathbf{0.700}\ {}^{+}/_{-}\ (\mathbf{0.069})$$

or

$$Vd\ \left({}^{L}/_{kg}\right) = \mathbf{0.63 - 0.77}$$

Note this is for (k=1)

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Distribution – Applied

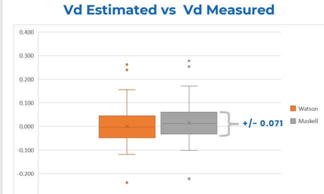
Hypothetical Subject Information

Subject: **25** y/o male
Height: 5' 10'
Weight: 175 lb BMI: 25.13

$$Vd\ \left({}^{L}/_{kg}\right) = \mathbf{0.700}\ {}^{+}/_{-}\ (\mathbf{0.069})$$

Dosed Subject Information

Total Male Subjects:	145
BMI Range :	23 – 28
Estimated Vd avg (Maskell):	0.699 L/kg
Measured Vd avg:	0.683 L/kg
Difference avg:	0.016
Difference Std Dev:	**0.071**



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Application of Distribution - Summary

In Summary Volume of Distribution …

- Can be calculated from the extrapolated BAC at time zero and the adminstered dose.
- Was reported as rho factor in the original application of the Widmark Formula
- Rho was originally derived from BAC in g/kg and must be converted to give BAC in g/dL
- Thus the modern Widmark Formula utilizes a Vd in L/kg instead of rho.

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Application of Distribution - Summary

In Summary Volume of Distribution …

- Can be estimated from $\frac{\%\,Total\ Body\ Water}{\%\,Whole\ Blood\ Water}$
- Average Vd estimates of 0.7 L/kg for males and 0.6 L/kg for females only works well for average people.
- Using the adapted Watson TBW formula should provide reasonable estimates for Vd across most BMIs
- To estimate Vd per ASB 122:
  1. Calculate TBW
  2. Convert to Vd
  3. Apply uncertainty

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Distribution - Considerations

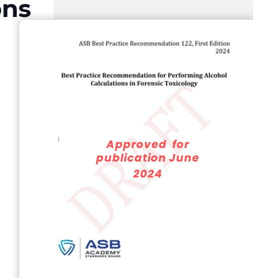
ASB Recommendations – Estimating Vd

Vd males (Maskell)

$$Vd\ (L/kg) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times 0.825}$$

Vd females (Maskell)

$$Vd\ (L/kg) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times 0.838}$$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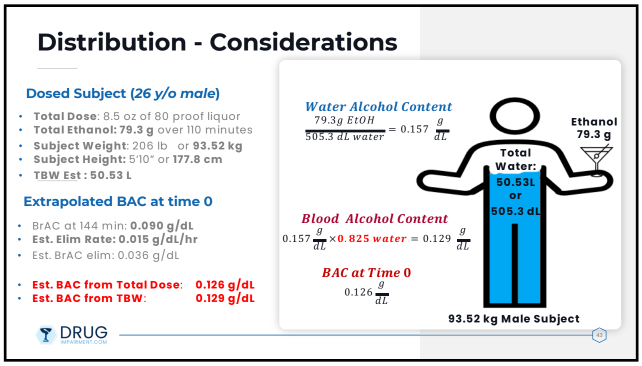
Distribution - Considerations
Dosed Subject (26 y/o male)
Total Dose: 8.5 oz of 80 proof liquor
Total Ethanol: 79.3 g over 110 minutes
Subject Weight: 206 lb or 93.52 kg
Subject Height: 5'10" or 177.8 cm
TBW Est : 50.53 L
Extrapolated BAC at time 0
BrAC at 144 min: 0.090 g/dL
Est. Elim Rate: 0.015 g/dL/hr
Est. BrAC elim: 0.036 g/dL
Est. BAC from Total Dose: 0.126 g/dL
Est. BAC from TBW: 0.129 g/dL
Water Alcohol Content
$\frac{79.3g\ EtOH}{505.3\ dL\ water} = 0.157\ \frac{g}{dL}$
Ethanol 79.3 g
Total Water: 50.53L or 505.3 dL
Blood Alcohol Content
$0.157\frac{g}{dL} \times 0.825\ water = 0.129\ \frac{g}{dL}$
BAC at Time 0
$0.126\frac{g}{dL}$
93.52 kg Male Subject
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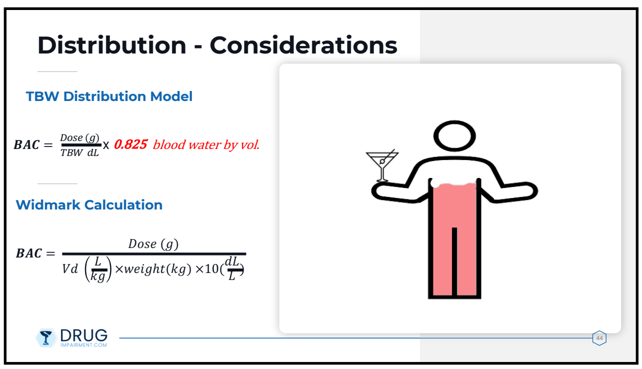
Distribution - Considerations
TBW Distribution Model
$BAC = \frac{Dose\ (g)}{TBW\ dL}$ x 0.825 blood water by vol.
Widmark Calculation
$BAC = \frac{Dose\ (g)}{Vd\ \left(\frac{L}{kg}\right) \times weight(kg) \times 10(\frac{dL}{L})}$
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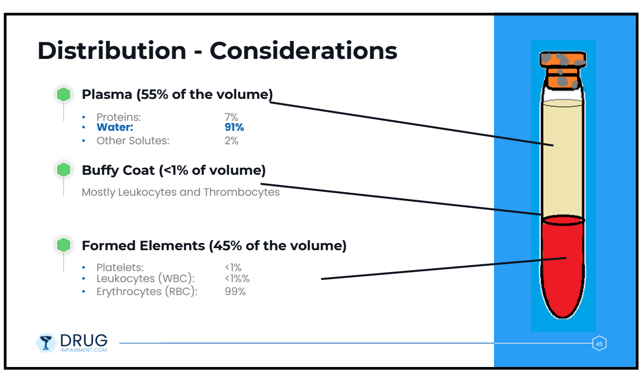
Distribution - Considerations
Plasma (55% of the volume)
Proteins: 7%
Water: 91%
Other Solutes: 2%
Buffy Coat (<1% of volume)
Mostly Leukocytes and Thrombocytes
Formed Elements (45% of the volume)
Platelets: <1%
Leukocytes (WBC): <1%%
Erythrocytes (RBC): 99%
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Distribution - Considerations

Plasma

- $Plasma\ Water\ fraction\ = plasma\ water\ \% \times \%\ of\ blood\ volume$

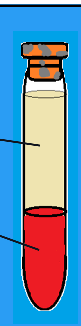
Red Blood Cells

- $RBC\ Water\ fraction\ = RBC\ water\ \% \times \%\ of\ blood\ volume$

Whole Blood Water Percent

- $WB\ Water\ Percent\ = Plasma\ Water\ Fraction + RBC\ Water\ Fraction$

Note: Hematocrit is defined as the percent of the blood volume comprised of red blood cells



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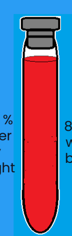
Distribution - Considerations

Measured Water Contents
Iffland et al (1999) [47]

Laboratory	N	Specimen	Mean g%	SD g%	CV%	Range
Kiel	230	Serum	90.49	0.86	0.95	87.2-93.3
		Whole Blood	78.35	1.44	1.83	74.8-82.9
		Serum/WB	**1.156**	**0.0184**	**1.59**	**1.11-1.21**
Köln	503	Serum	90.71	0.54	0.59	88.6-92.2
		Whole Blood	78.41	1.11	1,41	75.7-83.0
		Serum/WB	**1.157**	**0.0145**	**1.25**	**1.10-1.20**
Münster	100	Serum	90.75	0.61	0.67	89.1-92.8
		Whole Blood	78.14	1.28	1.63	74.9-83.3
		Serum/WB	**1.162**	**0.0187**	**1.61**	**1.08-1.20**
Combined	833	**Serum**	**90.66**	**0.66**	**0.72**	**87.2-93.3**
		Whole Blood	**78.36**	**1.23**	**1.57**	**74.8-83.3**
		Serum/WB	**1.157**	**0.0163**	**1.40**	**1.08-1.21**

Water Content expressed in (w/w), grams of water per gram of blood or serum.

Whole Blood



Specific gravity 1.0581 g/mL at 37C

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Distribution - Considerations

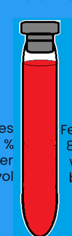
Measured Water Contents
Iffland et al (1999) [47]

Sex	N	Specimen	Mean g%	SD g%	Range
Males	692	Whole Blood	**78.15**	**1.15**	**74.8 – 83.3**
Females	141	Whole Blood	**79.37**	**1.09**	**76.3 – 82.5**

Water Content expressed in (w/w), grams of water per gram of blood or serum.

$$Water\ Content\ \%\ \left(\frac{g\ water}{mL\ blood}\right) = Water\ Content\ \%\ \left(\frac{g\ water}{g\ blood}\right) \times\ 1.0581\ \frac{g}{mL}$$

Whole Blood



Specific gravity 1.0581 g/mL at 37C

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Distribution - Considerations

Whole Blood

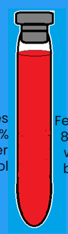
ASB Recommendations – Estimating Vd

$$Vd\ males\ (Maskell)$$

$$Vd\ (L/kg) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times 0.825}$$

$$Vd\ females\ (Maskell)$$

$$Vd\ (L/kg) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times 0.838}$$



Specific gravity 1.0581 g/mL at 37C

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Distribution - Considerations

Plasma/ Serum

Serum Tests – Estimating Vd

$$Vd\ (Serum)$$

$$Vd\ (L/kg) = \frac{Totat\ Body\ Water\ (L)}{W\ (kg) \times serum\ water}$$

$$Serum\ Alcohol\ Conc.\ (\frac{g}{dL}) = \frac{Dose\ (g)}{Vd\ \left(\frac{L}{kg}\right) \times weight(kg) \times 10(\frac{dL}{L})}$$

Specific gravity 1.0278 g/mL at 37C

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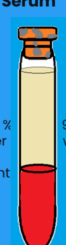
Distribution - Considerations

Serum

Measured Water Contents
Iffland et al (1999) [47]

Laboratory	N	Specimen	Mean g%	SD g%	CV%	Range
Kiel	230	Serum	90.49	0.86	0.95	87.2-93.3
		Whole Blood	78.35	1.44	1.83	74.8-82.9
		Serum/WB	**1.156**	**0.0184**	**1.59**	**1.11-1.21**
Köln	503	Serum	90.71	0.54	0.59	88.6-92.2
		Whole Blood	78.41	1.11	1,41	75.7-83.0
		Serum/WB	**1.157**	**0.0145**	**1.25**	**1.10-1.20**
Münster	100	Serum	90.75	0.61	0.67	89.1-92.8
		Whole Blood	78.14	1.28	1.63	74.9-83.3
		Serum/WB	**1.162**	**0.0187**	**1.61**	**1.08-1.20**
Combined	833	**Serum**	**90.66**	**0.66**	**0.72**	**87.2-93.3**
		Whole Blood	**78.36**	**1.23**	**1.57**	**74.8-83.3**
		Serum/WB	**1.157**	**0.0163**	**1.40**	**1.08-1.21**

Water Content expressed in (w/w), grams of water per gram of blood or serum.



Specific gravity 1.0278 g/mL at 37C

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Distribution - Considerations

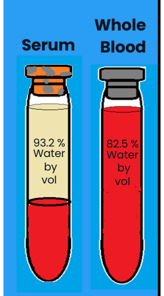
Serum Tests – Estimating Vd

Vd (Serum)

$$Vd\left(\frac{L}{kg}\right) = \frac{45.905\ (L)}{79.45\ (kg)\times 0.932} = 0.620$$

Vd (whole blood)

$$Vd\left(\frac{L}{kg}\right) = \frac{45.905\ (L)}{79.45\ (kg)\times 0.825} = 0.700$$



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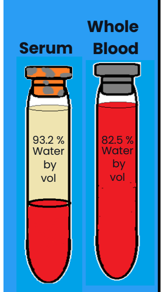
Distribution - Considerations

Serum Alcohol Concentration

$$\textit{Serum Alcohol Conc.}\left(\frac{g}{dL}\right) = \frac{56\ (g)}{0.62\ \left(\frac{L}{kg}\right)\times 79.45(kg)\times 10\left(\frac{dL}{L}\right)} = 0.114$$

$$\textit{Blood Alcohol Conc.}\left(\frac{g}{dL}\right) = \frac{56\ (g)}{0.70\ \left(\frac{L}{kg}\right)\times 79.45(kg)\times 10\left(\frac{dL}{L}\right)} = 0.100$$

$$\frac{\textit{Serum Alcohol Conc.}}{\textit{Blood Alcohol Conc.}} = 1.14$$



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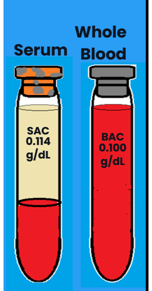
Distribution - Considerations

Measured Water Contents
Iffland et al (1999) [47]

Laboratory	N	Specimen	Mean g%	SD g%	CV%	Range
Kiel	230	Serum	90.49	0.86	0.95	87.2-93.3
		Whole Blood	78.35	1.44	1.83	74.8-82.9
		Serum/WB	**1.156**	**0.0184**	**1.59**	**1.11-1.21**
Köln	503	Serum	90.71	0.54	0.59	88.6-92.2
		Whole Blood	78.41	1.11	1,41	75.7-83.0
		Serum/WB	**1.157**	**0.0145**	**1.25**	**1.10-1.20**
Münster	100	Serum	90.75	0.61	0.67	89.1-92.8
		Whole Blood	78.14	1.28	1.63	74.9-83.3
		Serum/WB	**1.162**	**0.0187**	**1.61**	**1.08-1.20**
Combined	833	**Serum**	**90.66**	**0.66**	**0.72**	**87.2-93.3**
		Whole Blood	**78.36**	**1.23**	**1.57**	**74.8-83.3**
		Serum/WB	**1.157**	**0.0163**	**1.40**	**1.08-1.21**

Water Content expressed in (w/w), grams of water per gram of blood or serum.



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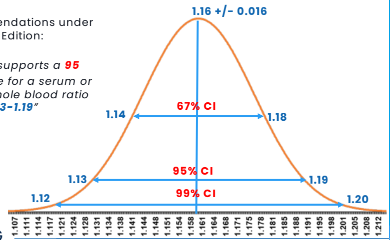
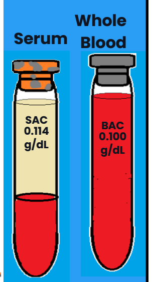
Distribution - Considerations

Serum:Whole Blood Water Ratios
Iffland [47]

ASB Recommendations under 122 1st Edition:

*"Research supports a **95 percent** range for a serum or plasma to whole blood ratio of **1.13–1.19**"*





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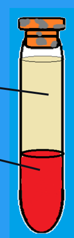
Distribution – Considerations [65]

- **Plasma**
  - $Plasma\ Water\ fraction = 91\% \times (1 - hematocrit)$
- **Red Blood Cells**
  - $RBC\ Water\ fraction = 65\ \% \times hematocrit$
- **Whole Blood Water Percent**
  - $Blood\ Water\ Percent = Plasma\ Water\ fraction + RBC\ Water\ fraction$
- **Plasma / Whole Blood Ratio**
  - $\frac{Plasma}{Blood} Ratio = \frac{Plasma\ Water\ \%}{Whole\ Blood\ Water\ \%}$
  - $\frac{Plasma}{Whole\ Blood} ratio = \frac{0.91}{0.65 \times hematocrit + 0.91 \times (1 - hematocrit)}$



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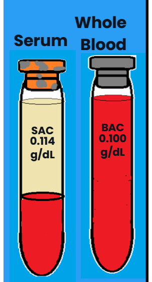
Distribution - Considerations

Hematocrit and Distribution [65]

Hematocrit (Hct)	Clinical Significance	Expected Plasma/ Blood Ratio
< 30	Possible Transfusion Needed	< 1.09
30 -35	Serious to Moderate Anemia	1.09 – 1.11
34 – 50	Normal - Women	1.11 – 1.17
39 - 54	Normal - Men	1.12 – 1.18
50 - 55	Elevated*	1.17 – 1.18
55 – 60	Erythrocytosis or Polycythemia	1.18 – 1.20

**Elevated hematocrit can be the result of living at high altitudes, chronic smoking, blood doping, dehydration, or hypoxia among other things.*



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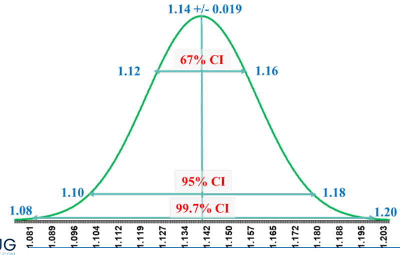
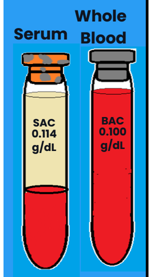
Distribution - Considerations

Serum:Whole Blood Ethanol Ratios
Winek and Carfagna (1987) [12]





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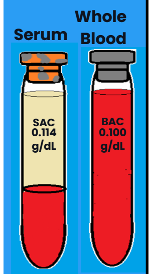
Distribution - Considerations

Serum:Whole Blood Ethanol Ratios [65]

Mean Ratio	SD	Range	Subjects	Author	Method
1.14	0.019	1.09-1.18	50	Winek	GC - Direct
1.15	0.02	1.10-1.25	134	Hak	GC - Headspace
1.16	0.13	0.88-1.59	211	Rainey	GC - Direct
1.14	0.015	1.12-1.18	14	Shajani	GC/ADH
1.12 - 1.18	NA	NA	176	Barnhill	GC/ADH
1.11	0.04	1.04 – 1.16	5	Penetar	GC - Headspace
1.14	0.041	1.04 – 1.26	235	Wigmore	GC - Headspace



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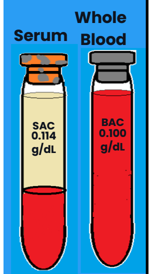
Distribution - Considerations

Serum:Whole Blood Ethanol Ratios [14]

Mean Ratio	SD	Range	Subjects	Author	Method
1.14	0.019	1.09-1.18	50	Winek	GC - Direct
1.15	0.02	1.10-1.25	134	Hak	GC - Headspace
1.16	0.13	0.88-1.59	211	Rainey	GC - Direct

$$\frac{Plasma}{Blood} Ratio = \frac{Plasma\ Water\ \%}{Whole\ Blood\ Water\ \%}$$



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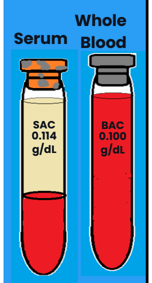
Distribution - Considerations

The Rainey Study : Biological vs Analytical Variability[14]

Category	Mean Ratio	Central 95% (k=1.96)	Central 99% (k=2.576)
Published Results	1.16:1	0.95 – 1.40	0.90 – 1.49
Est. Variation from Analytical Imprecision (7.4% CV)	1.16:1	0.99 – 1.33	0.94 – 1.38
Est. Variation from on Biological Factors (4.0% CV)	1.16:1	1.06 – 1.25	1.03 – 1.28

**Assumes no bias. Estimated biological variation is calculated based on a total population deviation of 11.4% total %CV - 7.4% analytical %CV*



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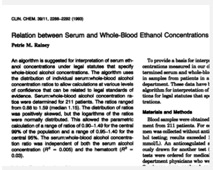
Distribution - Considerations

The Rainey Study : Biological vs Analytical Variability [14]

- *"The range of serum:whole-blood alcohol concentration ratios found in this study population was 0.88-1.59 much wider than the range of 1.09-1.18 reported by Winek and Carfagna and reflecting the effects of the greater analytical variability in our measurements."*
- *"The study of Winek and Carfagna provides the most useful data" and "should closely reflect the underlying true ratios"*
- *"The present study was carried out to conservatively determine the range of serum:whole-blood ratios that might be encountered under real clinical laboratory conditions" …"where fast turnaround is more important than pinpoint precision."*


CLIN. CHEM. 39/11, 2288–2292 (1993)

Relation between Serum and Whole-Blood Ethanol Concentrations

Petrie M. Rainey

An algorithm is suggested for interpretation of serum ethanol concentrations under legal statutes that specify whole-blood alcohol concentrations. The algorithm uses the distribution of individual serum:whole-blood alcohol concentration ratios to allow calculations at various levels of confidence that can be related to legal standards of evidence. Serum:whole-blood alcohol concentration ratios were determined for 211 patients. The ratios ranged from 0.88 to 1.59 (median 1.15). The distribution of ratios was positively skewed, but the logarithms of the ratios were normally distributed. This allowed the parametric calculation of a range of ratios of 0.90–1.49 for the central 99% of the population and a range of 0.95–1.40 for the central 95%. The serum:whole-blood alcohol concentration ratio was independent of both the serum alcohol concentration (R^2 = 0.005) and the hematocrit (R^2 = 0.03).

To provide a basis for interp… centrations measured in our c… termined serum and whole-blo… in samples from patients in a… department. These data have … algorithm for interpretation of… tions for legal statutes that sp… trations.

Materials and Methods

Blood samples were obtained … ment from 211 patients. For e… men was collected without anti… hol testing; results exceeded … mmol/L). An anticoagulated … ously drawn for another test … tests were ordered for medical … department physicians who we…

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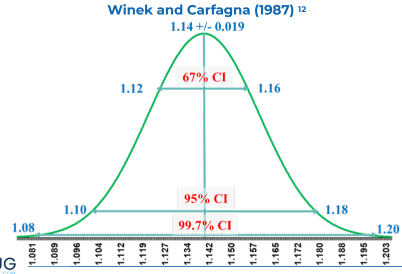
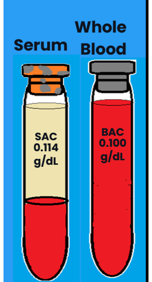
Distribution - Considerations

Serum:Whole Blood Ethanol Ratios
Winek and Carfagna (1987) [12]





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Distribution - Considerations

Serum:Whole Blood Ethanol Ratios Estimation Methods [65]

Mean Ratio	SD	Range	Confidence	Method
1.14	0.019	1.08-1.20	99.7%	**Winek** Serum: Whole Blood Study
1.16	0.016	1.12 - 1.20	99.7%	**Iffland** Water Content Study
1.15	NA	1.09 – 1.20	Estimated Range	Estimated from **Hematocrit**
1.14	0.033	1.05 – 1.22	99.7%	**Aggregate** of Measured Serum: Whole Blood Ratio Studies*

*Estimates for hematocrit values of 30 – 60.
**Excludes data from Rainey et al.

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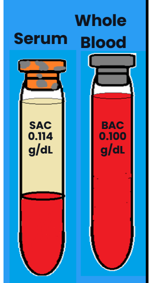

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Distribution - Considerations

Serum:Whole Blood Ethanol Ratios Applied

$Serum\ Alcohol\ Concentration\ (SAC)_{hypothetical} = 0.114\ g/dL(+/-0.005)$

Analytical Uncertainty $+/-0.005$

-0.005 → SAC: 0.109 g/dL

$+0.005$ → SAC: 0.119 g/dL

Biological Variability 99.7% Conversion Ratio Range (1.08 – 1.20)

1.20 → BAC: 0.090 g/dL

1.08 → BAC: 0.110 g/dL

$Blood\ Alcohol\ Concentration\ (BAC)_{estimated} = 0.09 - 0.11\ g/dL$

Note: Serum alcohol tests are frequently reported in mg/dL and should be converted to g/dL for simplicity.

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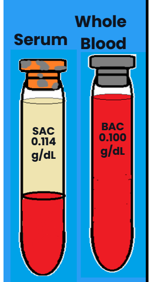

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Distribution - Considerations

Plasma:Whole Blood Ethanol Ratios [65]

Mean Ratio	SD	Range	Subjects	Author
1.10	0.034	1.03 – 1.24	17	Jones
1.14	0.018	1.09 – 1.17	50	Winek
1.11	0.037	1.04 – 1.19	5	Penetar
1.18	0.057	1.10 – 4.35	20	Payne

$Mean\ \mathbf{Plasma}:\mathbf{Blood}\ Ethanol\ Ratio_{\ Aggregate} = 1.14 +/-0.035$

$Mean\ \mathbf{Serum}:\mathbf{Blood}\ Ethanol\ Ratio_{\ Aggregate} = 1.14 +/-0.033$

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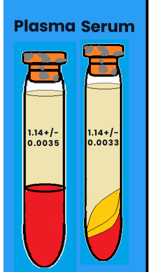

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Distribution - Considerations

In Summary …

- The apparent Vd is specific for the medium in which alcohol is being distributed.
- Due to its higher water content serum will have a lower apparent Vd than whole blood.
- Iffland et al found that serum is on average 91% water (w/w) while blood is 78% (w/w)
- This gave an average serum:blood ratio of 1.16 with a 95% range of 1.13 to 1.19

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Distribution - Considerations

In Summary …

- ASB currently recommends* applying the 95% range when estimating BAC from serum alcohol levels
- Direct studies of the serum:blood ethanol ratio show a possible range of ratios from 1.08 to 1.20.
- The observed range of ratios is the product of both analytical uncertainty and biological variability.
- When estimating a BAC from a measured SAC both these factors should be considered in the final calculation.

Note: ASB Best Practice Recommendation 122 First Edition was approved for publication June of 2024.

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For Further Information

Additional Resources

Jones AW, Tilson C.

Distribution ratios of ethanol and water between whole blood, plasma, serum, and erythrocytes: Recommendations for interpreting clinical laboratory results in a legal context.

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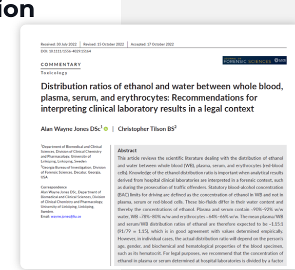

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JOURNAL OF FORENSIC SCIENCES
COMMENTARY
Toxicology

Distribution ratios of ethanol and water between whole blood, plasma, serum, and erythrocytes: Recommendations for interpreting clinical laboratory results in a legal context

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Abstract
This article reviews the scientific literature dealing with the distribution of ethanol and water between whole blood (WB), plasma, serum, and erythrocytes (red-blood cells). Knowledge of the ethanol distribution ratio is important when analytical results derived from hospital clinical laboratories are interpreted in a forensic context, such as during the prosecution of traffic offenders. Statutory blood-alcohol concentration (BAC) limits for driving are defined as the concentration of ethanol in WB and not in plasma, serum or red-blood cells. These bio-fluids differ in their water content and thereby the concentrations of ethanol. Plasma and serum contain ~90%–92% w/w water, WB ~78%–80% w/w and erythrocytes ~64%–66% w/w. The mean plasma/WB and serum/WB distribution ratios of ethanol are therefore expected to be ~1.15:1 (91/79 = 1.15), which is in good agreement with values determined empirically. However, in individual cases, the actual distribution ratio will depend on the person's age, gender, and biochemical and hematological properties of the blood specimen, such as its hematocrit. For legal purposes, we recommend that the concentration of ethanol in plasma or serum determined at hospital laboratories is divided by a factor

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