MEHLMANMEDICAL

HY EQUATION QUESTIONS

FOR USMLE STEP 1

HY Equation Questions for USMLE Step 1

Concept……………………………………………………………………………………..……..Question #

1. A group of epidemiologists and geneticists is studying the frequency of alleles *A* and *a* in a population. They find that the population is in Hardy-Weinberg equilibrium. The frequency of the allele *A* is 0.12 and the frequency of the allele *a* is 0.88. Which of the following represents the percentage of heterozygous individuals in this population:

   a) 1.44%
   b) 10.56%
   c) 21.12%
   d) 33.00%
   e) 77.44%

The correct answer is c.

The Hardy-Weinberg equation is: $p^2 + 2pq + q^2 = 1$.

The Hardy-Weinberg principle states that allele and genotype frequencies will remain constant from one generation to the next in the absence of external influences. The two alleles, *A* and *a*, have frequencies of p and q, respectively. For an *AA* genotype to occur, the allele *A* needs to occur twice (each with the frequency of p). The frequency of an *AA* genotype is, therefore, $p * p$ or p^2, while the frequency of the *aa* genotype is $q * q = q^2$. The other two outcomes are genotypes *Aa* and *aA*, represented by $p * q$ and $q * p$, respectively. Both of these represent heterozygotes for the trait in question so the frequency of heterozygotes is $p * q + q * p = p * q + p * q = 2pq$. The sum of the frequencies of all the possible genotypes is 1 (100% of the population has one of those genotypes). Also $p + q = 1$ because every locus will have either the allele *A* or the allele *a* so the sum of their probabilities is 1. Note that Hardy-Weinberg equation also equals $(p + q)^2$.

In this case, $p = 0.12$ and $q = 0.88$.

Therefore, $p^2 = 0.0144 = 1.44\%$ is the *AA* frequency, $q^2 = 0.7744 = 77.44\%$ is the frequency of *aa*, and $2 * 0.12 * 0.88 = 0.2112 = 21.12\%$ is the frequency of *Aa*.

2. A group of researchers is studying a population that is in the Hardy-Weinberg equilibrium. It is discovered that 4% of individuals are affected by an autosomal recessive condition. Which of the following represents the percentage of the population that does not carry the recessive gene:

   a) 20%
   b) 32%
   c) 64%
   d) 80%
   e) cannot be calculated

The correct answer is c.

The Hardy-Weinberg equation is: $p^2 + 2pq + q^2 = 1$.

The Hardy-Weinberg principle states that allele and genotype frequencies will remain constant from one generation to the next in the absence of external influences. The two alleles, *A* and *a*, have frequencies of p and q, respectively. For an *AA* genotype to occur, the allele *A* needs to occur twice (each with the frequency of p). The frequency of an *AA* genotype is, therefore, $p * p$ or p^2, while the frequency of the *aa* genotype is $q * q = q^2$. The other two outcomes are genotypes *Aa* and *aA*, represented by $p * q$ and $q * p$, respectively. Both of these represent heterozygotes for the trait in question so the frequency of heterozygotes is $p * q + q * p = p * q + p * q = 2pq$. The sum of the frequencies of all the possible genotypes is 1 (100% of the population has one of those genotypes).

In this case, 4% of the population is affected (homozygous for the recessive allele), represented by q^2. We can easily calculate that if $q^2 = 0.04 \Rightarrow q = 0.2$.

Since $p + q = 1$, we can calculate that $p = 1 - 0.2 = 0.8$.

The recessive gene is not carried by those homozygous for the dominant gene, represented by p^2, or 0.64 = 64%.

The unaffected carriers are represented by $2pq = 2 * 0.8 * 0.2 = 0.32$ = 32%.

3. A group of researchers is studying the genetics of a population that is in the Hardy-Weinberg equilibrium. They discover that 1% of the population is born with sickle cell anemia. In a population of 10,000, which of the following best represents the likely number of individuals who are unaffected but have increased resistance to malaria:

    a) 900
    b) 1,000
    c) 1,800
    d) 8,100
    e) 9,000

The correct answer is c.

The Hardy-Weinberg principle states that allele and genotype frequencies will remain constant from one generation to the next in the absence of external influences. The two alleles, *A* and *a*, have frequencies of p and q, respectively. For an *AA* genotype to occur, the allele *A* needs to occur twice (each with the frequency of p). The frequency of an *AA* genotype is, therefore, p * p or p^2, while the frequency of the *aa* genotype is q * q = q^2. The other two outcomes are genotypes *Aa* and *aA*, represented by p * q and q * p, respectively. Both of these represent heterozygotes for the trait in question so the frequency of heterozygotes is p * q + q * p = p * q + p * q = 2pq. The sum of the frequencies of all the possible genotypes is 1 (100% of the population has one of those genotypes). Also p + q = 1 because every locus will have either the allele *A* or the allele *a* so the sum of their probabilities is 1. Note that Hardy-Weinberg equation also equals (p + q)^2.

The individuals heterozygous for the sickle cell gene are expected to have increased resistance to malaria. According to the Hardy-Weinberg equation, 2pq represents heterozygous individuals. 1% of the population has sickle cell anemia, meaning they are homozygous (q^2).

If q^2 = 0.01, we can calculate that q = 0.1. Since p + q = 1; p = 0.9.

2pq = 2 * 0.9 * 0.1 = 0.18 = 18%.

18% of the population is heterozygous and likely has increased resistance to malaria. The number of such individuals is 18% of 10,000, or 0.18 * 10,000 = 1,800.

4. It is determined that the incidence of a rare X-linked recessive disorder is 1/10,000 males. Based on this figure, which of the following represents the gene frequency of this mutation:

    a) 1/10,000
    b) 1/1,000
    c) 1/500
    d) 1/100
    e) cannot be calculated

The correct answer is a.

The Hardy-Weinberg principle states that allele and genotype frequencies will remain constant from one generation to the next in the absence of external influences. The two alleles, *A* and *a*, have frequencies of p and q, respectively. For an *AA* genotype to occur, the allele *A* needs to occur twice (each with the frequency of p). The frequency of an *AA* genotype is, therefore, p * p or p^2, while the frequency of the *aa* genotype is q * q = q^2. The other two outcomes are genotypes *Aa* and *aA*, represented by p * q and q * p, respectively. Both of these represent heterozygotes for the trait in question so the frequency of heterozygotes is p * q + q * p = p * q + p * q = 2pq. The sum of the frequencies of all the possible genotypes is 1 (100% of the population has one of those genotypes). Also p + q = 1 because every locus will have either the allele *A* or the allele *a* so the sum of their probabilities is 1. Note that Hardy-Weinberg equation also equals (p + q)^2.

Males only have a single X chromosome. Therefore, the incidence of the disease in the male portion of the population is equivalent to the frequency of the gene in the population. That differs from the autosomal recessive conditions where the probability that one is a homozygote for the recessive allele is q^2, where q is the frequency of the gene in the population. The frequency of an X-linked recessive disease in females is still q^2 as females have two X chromosomes.

5. A group of epidemiologists is studying cystic fibrosis (CF) in a population in Europe. The incidence of cystic fibrosis is found to be 1/3,600. Which of the following best represents the predicted incidence of heterozygous carriers of the CF mutation in that population:

   a) 1/3,600
   b) 1/1,800
   c) 1/60
   d) 1/30
   e) cannot be calculated

The correct answer is d.

The Hardy-Weinberg principle states that allele and genotype frequencies will remain constant from one generation to the next in the absence of external influences. The two alleles, *A* and *a*, have frequencies of p and q, respectively. For an *AA* genotype to occur, the allele *A* needs to occur twice (each with the frequency of p). The frequency of an *AA* genotype is, therefore, $p * p$ or p^2, while the frequency of the *aa* genotype is $q * q = q^2$. The other two outcomes are genotypes *Aa* and *aA*, represented by $p * q$ and $q * p$, respectively. Both of these represent heterozygotes for the trait in question so the frequency of heterozygotes is $p * q + q * p = p * q + p * q = 2pq$. The sum of the frequencies of all the possible genotypes is 1 (100% of the population has one of those genotypes). Also $p + q = 1$ because every locus will have either the allele *A* or the allele *a* so the sum of their probabilities is 1. Note that Hardy-Weinberg equation also equals $(p + q)^2$.

Assuming the population is in a Hardy-Weinberg equilibrium, the frequency of carriers is 2pq. Considering that the disease is rare and p is close to 1, we can simplify it to say that the frequency of carriers is approximately 2q. Since the incidence of the disease is 1/3,600, it means that the frequency of people who are homozygous for the recessive gene (or q^2) is 1/3,600. That means that $q = 1/60$. The frequency of carriers is, therefore, $2q = 2 * 1/60 = 1/30$.

In X-linked recessive disorders, the incidence of the disease in males is approximately the same as the frequency of the gene in question as males only have 1 X chromosome.

6. A healthy 30-year-old male undergoes a pre-employment physical exam. Among other tests, a blood pressure measurement and echocardiography are done. His blood pressure was determined to be 130/80 mmHg. The heart rate was 70 beats per minute. The end systolic volume was found to be 45 mL, while the end diastolic volume was found to be 120 mL. Which of the following best represents the mean arterial pressure in this patient:

   a) 105 mmHg
   b) 120 mmHg
   c) 97 mmHg
   d) 130 mmHg
   e) 80 mmHg

The correct answer is c.

The mean arterial pressure is calculated as: MAP = 2/3 diastolic + 1/3 systolic blood pressure (due to relative lengths of systole and diastole - the diastole lasts approximately twice as long as systole). 2/3 * 80 + 1/3 * 130 = 97. 130 is the systolic blood pressure and 80 is the diastolic blood pressure. If the relative lengths of systole and diastole were equal, then the mean arterial pressure would be the mean of the two pressures (105 mmHg) but that is not the case.

7. A healthy 47-year-old man is undergoing echocardiography testing. It is determined that his end-systolic volume was 50 mL and his end-diastolic volume was 120 mL. His heart rate was 75 beats per minute and his blood pressure was 120/80 mmHg. Which of the following represents the stroke volume in this patient:

    a) 50 mL
    b) 70 mL
    c) 120 mL
    d) 3750 mL
    e) 5250 mL

The correct answer is b.

The stroke volume (SV) is calculated as: end diastolic volume - end systolic volume and represents the volume of blood that the heart pumps in each beat. The end diastolic volume is the volume of blood in the heart at the end of diastole (once the filling of the heart has finished). The systolic volume is the amount of blood that remains in the heart at the end of systole (after expelling the SV of blood into the arterial system has finished). Therefore EDV = SV + ESV. In this case it is 120 mL - 50 mL = 70 mL. The cardiac output is the volume the heart pumps per minute. It is calculated as SV * HR (in this case it is 5250 mL/min) as HR represents the number of times the stroke volume is pumped.

8. A 56-year-old male is being evaluated for dyspnea. His blood pressure is 130/80 mmHg, his heart rate is 77/min and his oxygen saturation rate is 96%. ECG reveals no significant changes. An echocardiogram is performed. It is found that the end systolic volume in this patient is 55 mL and the end diastolic volume is 125 mL. Which of the following represents the ejection fraction in this patient:

    a) 12%
    b) 31%
    c) 44%
    d) 56%
    e) 69%

The correct answer is d.

Ejection fraction represents the proportion of the end diastolic volume that the heart pumps out in a beat (represented by stroke volume, SV). The stroke volume (SV) is the volume of blood that the heart pumps in each beat. The end diastolic volume is the volume of blood in the heart at the end of diastole (once the filling of the heart has finished). The systolic volume is the amount of blood that remains in the heart at the end of systole (after expelling of the blood into the arterial system has finished). One can also look at this as follows: at the end of diastole, the volume of blood in the heart is the end diastolic volume. The pumping out of the stroke volume is the systole and at the end of it, the end systolic volume remains in the heart. Therefore EDV - SV = ESV. We can calculate that the stroke volume in this patient is 70 mL (EDV - ESV). The ejection fraction is then calculated as SV/EDV = 70/125 = 56%.

9. A 55-year-old male is taking part in a research study at the cardiology department. As part of the study, he is undergoing a complete cardiac evaluation. His blood pressure was found to be 120/90 mmHg and his heart rate was 80/min. Echocardiography showed end-systolic volume of 60 mL and the end-diastolic volume of 120 mL. Which of the following represents the total peripheral resistance in this patient:

   a) 0.0208 mmHg/mL/min
   b) 0.025 mmHg/mL/min
   c) 0.0208 mmHg/mL
   d) 0.025 mmHg
   e) cannot be calculated

The correct answer is a.

The basic physics of fluid mechanics can be applied to blood vessels as well. Remember that pressure equals flow * resistance. Pressure in this case is the MAP, the flow (the amount of blood that passes through) equals the cardiac output and the resistance is the TPR.

Therefore, the total peripheral resistance is calculated from the following equation:

MAP = CO * TPR => TPR = MAP/CO.

The mean arterial pressure is calculated as: MAP = 2/3 diastolic + 1/3 systolic blood pressure (due to relative lengths of systole and diastole - the diastole lasts approximately twice as long as systole). The CO is the total amount of blood the heart pumps per minute and equals the volume of blood pumped per beat times the number of beats per minute (CO = SV * HR).

In this patient the MAP is 100 mmHg and the CO is SV * HR = (120 mL - 60 mL) * 80/min = 60 mL * 80/min = 4,800 mL/min. TPR = 100 mmHg/4,800 mL/min = 0.0208 mmHg/mL/min.

10. A 55-year-old male is referred for an echocardiogram for an evaluation of dilated cardiomyopathy. His ejection fraction is determined to be 40% and his end diastolic volume is 170 mL. His heart rate is 85 and blood pressure is 105/60 mmHg. Which of the following best represents the total peripheral resistance in this patient:

    a) 0.0087 mmHg/mL/min
    b) 0.013 mmHg/mL/min
    c) 1.3 mmHg/mL
    d) 0.882 mmHg/min
    e) 0.882 mmHg/mL/min

The correct answer is b.

The pressure equals flow * resistance. Pressure in this case is the MAP, the flow (the amount of blood that passes through) equals the cardiac output and the resistance is the TPR.

Therefore, the total peripheral resistance is calculated from the following equation:

MAP = CO * TPR => TPR = MAP/CO.

MAP = 2/3 * diastolic pressure + 1/3 * systolic pressure = 2/3 * 60 mmHg + 1/3 * 105 mmHg = 75 mmHg.

Ejection fraction is the proportion of the end diastolic volume that the heart pumps out in a beat (represented by SV). It is calculated as SV/EDV.

EF = SV/EDV => SV = EF * EDV = 0.4 * 170 mL = 68 mL.

The CO is the total amount of blood the heart pumps per minute and equals the volume of blood pumped per beat times the number of beats per minute (CO = SV * HR).

CO = HR * SV = 85/min * 68 mL = 5780 mL/min.

TPR = MAP/CO = 75 mmHg/5780 mL/min = 0.013 mmHg/mL/min.

11. A 75-year-old male undergoes echocardiography as part of the evaluation of dyspnea. It is found that his end systolic volume is 60 mL and his end diastolic volume is 125 mL. His blood pressure is 125/80 mmHg and heart rate is 80/min. Which of the following best represents the cardiac output in this patient:

    a) 125 mL/min
    b) 65 mL/mmHg
    c) 4,800 mL/min
    d) 5,200 mL
    e) 5,200 mL/min

The correct answer is e.

The CO is the total amount of blood the heart pumps per minute and equals the volume of blood pumped per beat times the number of beats per minute (CO = SV * HR). The stroke volume (SV) is the volume of blood that the heart pumps in each beat and equals the difference between the volume of blood at the end of diastole and the volume of blood at the end of systole. Therefore EDV = SV + ESV.

Cardiac output is calculated as: CO = HR * SV = HR * (EDV - ESV).

In this case it is 80/min * (125 mL - 60 mL) = 80/min * 65 mL = 5,200 mL/min.

12. A 65-year-old patient has been hospitalized in the intensive care unit (ICU) and a Swan-Ganz catheter has been placed. It was found that his pulmonary artery oxygen content was 0.13 mL O2/mL blood. His femoral artery oxygen content is 0.18 mL O2/mL blood. The end systolic volume was 65 mL and the end diastolic volume was 130 mL. His heart rate was 95/min and blood pressure was 110/70 mmHg. Which of the following represents the oxygen consumption in this patient:

    a) 308.75 mL O2/min
    b) 308.75 mL O2/mL blood
    c) 6175 mL/min
    d) 23.40 mL O2
    e) 6175 mL O2/min

The correct answer is a.

The CO is the amount of blood the heart pumps per minute and equals the volume of blood pumped per beat times the number of beats per minute (CO = SV * HR). The stroke volume represents the amount of blood that is pumped per beat and can be calculated as the difference between the end diastolic volume and end systolic volume (as the end systolic volume is the volume that is left once SV is ejected from EDV). Oxygen consumption is the difference between the amount of oxygen leaving the lungs in the pulmonary vein and the amount of oxygen entering the lungs in the pulmonary arteries (the amount of oxygen that is consumed by the tissues). The amount of oxygen in the pulmonary veins is the pulmonary blood flow multiplied by oxygen content of pulmonary venous blood. The amount of oxygen in the pulmonary artery is pulmonary blood flow multiplied by the oxygen content of pulmonary arterial blood. The pulmonary blood flow, or the cardiac output of the right heart is equal to the cardiac output of the left heart.

Therefore, oxygen consumption can be calculated as:

O2 consumption = CO * O2 pulmonary vein - CO * O2 pulmonary artery.

Alternatively, we can calculate CO from this equation:

CO = O2 consumption / (Art. O2 content - Ven. O2 content), meaning that:

O2 consumption = CO * (Art. O2 content - Ven. O2 content).

CO can be calculated as:

CO = HR * (EDV-ESV) * (Art. O2 content - Ven. O2 content) = 95/min * (130 mL - 65 mL) * (0.18 mL O2/mL blood - 0.13 mL O2/mL blood) = 95/min * 65 mL * 0.05 mL O2/mL blood = 308.75 mL O2/min.

13. A 70-year-old female hospitalized in the ICU is being evaluated for worsening renal function after a rise in creatinine was noted. A flow meter was placed on her left renal artery and pressure probes were inserted into the left renal artery and vein. The renal blood flow was determined to be 300 mL/min. Renal arterial pressure was found to be 90 mmHg, and renal venous pressure was 10 mmHg. Which of the following represents the vascular resistance in this patient's left kidney:

    a) 24,000 mL/min/mmHg
    b) 3.75 mmHg/mL/min
    c) 3.75 mL/min/mmHg
    d) 24,000 mmHg mL/min
    e) 0.27 mmHg/mL/min

The correct answer is e.

The basic physics of fluid mechanics can be applied to blood vessels as well. Remember that pressure equals flow * resistance.

The following equation can be used:

Q = delta P / R => R = delta P / Q = 80 mmHg / 300 mL/min = 0.27 mmHg/mL/min.

Resistance can also be calculated using the Poiseuille equation:

R = 8 * vessel length * viscosity of blood / (vessel radius^4 * pi).

14. 72-year-old female is evaluated for generalized edema. Her past medical history is significant for hypertension, diabetes mellitus and aortic stenosis. Echocardiography shows that her ejection fraction has reduced significantly since her last visit. Which of the following is most likely associated with edema development in this patient:

    a) increased oncotic pressure in the capillaries
    b) increased hydrostatic pressure in the capillaries
    c) increased hydrostatic pressure in the interstitium
    d) decreased oncotic pressure in the interstitium
    e) decreased hydraulic conductance

The correct answer is b.

This patient most likely suffers from congestive heart failure (CHF). As the ejection fraction drops, the hydrostatic pressure in the capillaries rises as the heart is unable to pump the blood that enters it. The fluid movement is explained by the following formula: Jv = Kf * [(Pc - Pi) - (pi c - pi i)], where Kf is the hydraulic conductance, Pc and Pi are the hydrostatic pressures in the capillaries and the interstitium, respectively; pi c and pi i are the oncotic pressures in the capillaries and the interstitium, respectively. Elevated hydrostatic pressure in the capillary and elevated oncotic pressure in the interstitium favor the movement of fluid out of the capillaries, while elevated oncotic pressure in the capillaries and elevated hydrostatic pressure in the interstitium favor the opposite. Fluid moves from the area of the higher hydrostatic pressure towards the area with the lower hydrostatic pressure and from the area of lower oncotic pressure to the area of higher oncotic pressure. Also, by looking at the formula, we can see that increasing the capillary hydrostatic pressure and decreasing the interstitial oncotic pressure are the changes that would lead to edema formation. Kf is a constant.

15. A study is done to assess Sterling pressures in a capillary. It was determined that the Pc was 27 mmHg, Pi was -1 mmHg, pi c was 26 mmHg and pi i was 3 mmHg. Which of the following is the direction of fluid movement and the net driving force:

a) no net fluid movement
b) 3 mmHg favoring absorption
c) 3 mmHg favoring filtration
d) 5 mmHg favoring absorption
e) 5 mmHg favoring filtration

The correct answer is e.

The fluid movement is explained by the following formula:

Jv = Kf * [(Pc - Pi) - (pi c - pi i)], where Kf is the hydraulic conductance, Pc and Pi are the hydrostatic pressures in the capillaries and the interstitium, respectively; pi c and pi i are the oncotic pressures in the capillaries and the interstitium, respectively. Fluid movement out of the capillary is favored by elevated hydrostatic and decreased oncotic pressure within the capillary (and the opposite in the interstitium). Remember that fluids always move from the areas with higher hydrostatic and lower oncotic pressures to the areas with lower hydrostatic and higher oncotic pressures.

Higher Pc and pi i favor fluid filtration, while higher Pi and pi c favor fluid absorption. Overall, that means that the 27 mmHg + 3 mmHg were favoring filtration, while 26 mmHg + (-1 mmHg) favored absorption. The difference is the net driving force. In this case it is 30 mmHg - 25 mmHg = 5 mmHg, favoring fluid filtration.

16. A 50-year-old male is taking part in a research study at the nephrology department. He is infused with PAH to determine the renal plasma flow (RPF). His urine flow rate is 1 mL/min, his plasma concentration of PAH is 1 mg/mL and his urine concentration of PAH is 580 mg/mL. The hematocrit was found to be 42%. Which of the following represents the effective renal plasma flow in this participant:

    a) 580 mg/mL
    b) 580 mg/min
    c) 580 mL/min
    d) 1000 mL/min
    e) 1380 mL/min

The correct answer is c.

Renal clearance represents the rate at which a substance is removed from plasma. It can be calculated as the ratio of the concentration of the substance in the urine and plasma multiplied by the urine flow rate. The renal clearance of certain substances allows us to estimate some physiologic parameters. For example, inulin is freely filtered but it is neither reabsorbed nor secreted, meaning the inulin that is filtered is also cleared. Therefore, inulin clearance measures the glomerular filtration rate. Para-aminohippuric acid (PAH) is both filtered and secreted and can be used to estimate renal plasma flow. Since, volume of RBCs accounts for a significant percentage of blood volume (hematocrit), the renal blood flow can be estimated from the renal plasma flow as RBF = RPF / (1 - Hct).

As previously mentioned, the effective renal plasma flow equals the clearance of PAH. Clearance of any substance is calculated as: [U] * V / [P].

In this case, it is 580 mg/mL * 1 mL/min / 1 mg/mL = 580 mL/min.

The renal blood flow is calculated as: RPF / (1 - Hct) = 580 mL/min / (1 - 0.42) = 1000 mL/min.

17. A 45-year-old male is taking part in a research study at the nephrology department. He is infused with PAH to determine the renal blood flow. His urine flow rate is 1 mL/min and his plasma concentration of PAH is measured to be 1 mg/mL. The concentration of PAH in his urine is 620 mg/mL. The hematocrit is 45%. Which of the following represents the effective renal blood flow in this participant:

a) 620 mg/min
b) 620 mL/min
c) 1127 mg/min
d) 1127 mL/min
e) 1378 mL/min

The correct answer is d.

Renal clearance is the rate at which a substance is cleared from plasma. It can be calculated as the ratio of the concentration of the substance in the urine and plasma multiplied by the urine flow rate. Inulin is freely filtered but neither reabsorbed nor secreted, meaning the inulin that is filtered is also removed from the body. Therefore, inulin clearance can be used to measure the glomerular filtration rate. Para-aminohippuric acid (PAH) is both filtered and secreted and can be used to estimate renal plasma flow. Since the volume of RBCs accounts for a significant percentage of blood volume (hematocrit), the renal blood flow can be estimated from the renal plasma flow as RBF = RPF / (1 - Hct). The RPF is the clearance of PAH, or [U] * V / [P] = 620 mg/mL * 1 mL/min / 1 mg/mL = 620 mL/min. It follows that RBF = 620 mL/min * (1 - 0.45) = 620 mL/min * 0.55 = 1127 mL/min.

18. A 45-year-old female is taking part in a research study at the nephrology department. She is infused with PAH and inulin. Her urine flow rate was determined to be 1 mL/min. Her plasma concentration of both PAH and inulin was 1 mg/mL. The urine concentration of inulin was 150 mg/mL and the urine concentration of PAH was 610 mg/mL. Her hematocrit was 45%. Which of the following represents the glomerular filtration rate in this participant:

    a) 150 mL/min
    b) 273 mL/min
    c) 610 mL/min
    d) 1109 mL/min
    e) 1356 mL/min

The correct answer is a.

Renal clearance is the rate at which a substance is cleared from plasma. We can calculate it by multiplying the ratio of concentrations of the substance in the urine and plasma by the urine flow rate. Inulin is freely filtered but it is neither reabsorbed nor secreted so all the inulin that is filtered is also cleared, making inulin clearance an excellent marker for glomerular filtration rate. Para-aminohippuric acid (PAH) is both filtered and secreted and can be used to estimate renal plasma flow. RBCs account for a significant percentage of blood volume (hematocrit), so the renal blood flow can be estimated from the renal plasma flow as RBF = RPF / (1 - Hct).

The glomerular filtration rate (GFR) is the clearance of inulin. It is calculated as [U] * V / [P] = 150 mg/mL * 1 mL/min / 1 mg/mL = 150 mL/min. The clearance of PAH represents the effective renal plasma flow and in this patient equals 610 mg/mL * 1 mL/min / 1 mg/mL = 610 mL/min. The effective renal blood flow is calculated as RBF = RPF / (1 - Hct) = 610 mL/min / 0.55 = 1109 mL/min.

19. A 50-year-old female is taking part in a research study at the nephrology department. She is infused with PAH and inulin. The plasma concentration of both substances was 1 mg/mL. The urine concentration of inulin was 140 mg/mL, while the urine concentration of PAH was 600 mg/mL. Her urine flow rate was found to be 1 mL/min and her hematocrit was 40%. Which of the following represents the filtration fraction in this patient:

    a) 14%
    b) 23%
    c) 38%
    d) 58%
    e) 429%

The correct answer is b.

Renal clearance represents the rate at which a substance is cleared from plasma. It can be calculated as the ratio of the concentrations of the substance in the urine and plasma multiplied by the urine flow rate. Inulin, as a substance that is only filtered (and neither reabsorbed nor secreted) is an excellent marker for glomerular filtration rate while PAH (a substance that is filtered and secreted) is an excellent marker for renal blood flow. The volume of RBCs accounts for a significant percentage of blood volume (hematocrit) so the renal blood flow can be estimated from the renal plasma flow as RBF = RPF / (1 - Hct). The filtration fraction represents the proportion of the renal plasma flow that is filtered in the glomerulus (GFR/RPF).

The filtration fraction is calculated as: FF = GFR/RPF = Clearance (inulin) / Clearance (PAH).

The clearance of inulin is: C (inulin) = [U] * V / [P] = 140 mL/min.

The clearance of PAH is: C (PAH) = [U] * V / [P] = 600 mL/min.

The filtration fraction is: FF = 140 mL/min / 600 mL/min = 23%.

Hematocrit is needed when calculating the effective renal blood flow, rather than plasma flow.

20. A 75-year-old male is taking part in a clinical trial in management of chronic renal insufficiency due to long-standing diabetes mellitus. As part of the evaluation, the renal clearance of a number of substances is calculated. Which of the following represents the correct way of calculating the renal clearance of a substance:

    a) C = [P] * V * [U]
    b) C = [P] * V / [U]
    c) C = [P] * [U] / V
    d) C = [U] / (V * [P])
    e) C = [U] * V / [P]

The correct answer is e.

Renal clearance represents the rate at which a substance is removed from plasma. It can be calculated as the ratio of the concentration of the substance in the urine and plasma multiplied by the urine flow rate. Therefore, C = [U] * V / [P], where [U] represents the concentration of the substance in the urine, V represents the renal flow rate, and [P] represents the concentration of the substance in the plasma.

21. An elderly patient with multiple co-morbidities has been hospitalized in the ICU due to a severe infection that triggered an exacerbation of his previous condition. As part of the intensive monitoring, a urinary catheter is placed, and studies of the plasma and urine are done every few hours. Which of the following would lead to a largest decrease in renal filtration fraction in this patient:

   a) increase in GFR, no change in RPF
   b) increase in GFR, increase in RPF
   c) increase in GFR, decrease in RPF
   d) decrease in GFR, increase in RPF
   e) decrease in GFR, decrease in RPF

The correct answer is d.

The filtration fraction represents the proportion of the renal plasma flow that is filtered in the glomerulus (GFR/RPF).

Since filtration fraction is calculated as FF = GFR / RPF, the largest decrease in FF would occur with the decrease in GFR and increase in RPF.

22. A 25-year-old female was brought to the emergency department with progressive weakness and altered mental status. She has recently complained to her friends about polyuria and polydipsia. Laboratory results are as follows: pH 7.25, PaCO2 43 mmHg, HCO3- 12 mEq/L. Which of the following best describes the acid-base status in this patient:

a) metabolic acidosis with respiratory compensation
b) metabolic acidosis with respiratory alkalosis
c) metabolic acidosis with respiratory acidosis
d) metabolic alkalosis with respiratory compensation
e) metabolic alkalosis with respiratory alkalosis

The correct answer is c.

This patient is most likely suffering from diabetic ketoacidosis, a form of metabolic acidosis. Healthy individuals generally respond to acid-base disturbances by compensating for them. Metabolic compensation occurs with respiratory acidosis/alkalosis and respiratory compensation occurs with metabolic acidosis/alkalosis. It is possible to calculate the expected compensation for each patient. If the measured values do not correspond to the calculated expected values, a combined disorder should be suspected.

Winter's formula is used to evaluate respiratory compensation in metabolic acidosis:

$PaCO_2 = (1.5 * HCO_3^-) + 8 +/- 2$.

In this case $PaCO_2 = 1.5 * 12 + 8 +/- 2 = 26 +/- 2$.

Since the actual $PaCO_2$ in this patient is higher than what would be expected in a compensated metabolic acidosis, the patient has likely developed respiratory acidosis on top of the metabolic alkalosis, likely due to respiratory failure.

If the $PaCO_2$ level was lower than what would be expected according to Winter's formula, the likely explanation would be a concurrent respiratory alkalosis.

23. A 65-year-old man is being evaluated in the emergency department. As part of the evaluation, the basic laboratory tests are done and they show the following: $[HCO_3^-]$ = 24 mmol/L and PCO_2 = 40 mmHg. Which of the following is the pH of this patient's arterial blood:

a) 7.25
b) 7.30
c) 7.35
d) 7.40
e) 7.45

The correct answer is d.

The pH of arterial blood can be calculated from Henderson-Hasselbach equation if we know the concentration of HCO_3^- and PCO_2. In general, Henderson-Hasselbach equation is used to calculate the ratio of pairs in buffered solutions.

$pH = pK + \log [A^-] / [HA]$.

For the bicarbonate buffer, it can be simplified to:

$pH = 6.1 + \log [HCO_3^-] / (0.03 * PCO_2) = 6.1 + \log 20 = 7.4$.

The same equation can be used to calculate the value of PCO_2 or $[HCO_3^-]$ if the pH is known.

24. A 15-year-old male is being evaluated in the emergency department. He is comatose. As part of the evaluation, the basic laboratory tests are done and they show blood pH of 7.05, Na^+ 140 mEq/L, Cl^- 100 mEq/L and HCO_3^- 15 mEq/L. Which of the following is the most likely explanation of this patient's condition:

a) diabetic ketoacidosis
b) gastrointestinal fistula
c) severe diarrhea
d) furosemide abuse
e) Addison disease

The correct answer is a.

Anion gap is the difference between the measured cations and anions in the plasma. In reality, in order for plasma to be electrically neutral, the number of cations and anions must be equal. However, fewer anions are measured compared to cations. Even if we exclude potassium from the equation, the concentration of sodium cation is still larger than the sum of the concentrations of chlorine and bicarbonate anions, accounting for the “gap”. The normal anion gap is between 6 and 12 mEq/L. Sometimes, metabolic acidosis can be caused by the addition of new anions from different acids (e.g., in ketoacidosis or lactic acidosis). In those cases, the bicarbonate anions are “replaced” by unmeasured anions and the anion gap widens. In some other cases, where no new anions are added, the bicarbonate anions are replaced by chlorine, which is measured so the anion gap remains unchanged. This is why metabolic acidosis in general can be divided into normal anion gap metabolic acidosis and high anion gap metabolic acidosis.

The causes of high anion gap metabolic acidosis can be memorized using the mnemonic MUDPILES: methanol, uremia, DKA, propylene glycol, iron, lactic acidosis, ethylene glycol, salicylates.

This patient is suffering from high anion gap metabolic acidosis. Of the answer choices provided, only diabetic ketoacidosis causes high anion gap metabolic alkalosis. GI losses of bicarbonate in the form of diarrhea and fistulas as well as Addison disease cause normal anion gap metabolic acidosis, while loop diuretics cause metabolic alkalosis.

Anion gap is calculated as $[Na^+] - ([Cl^-] + [HCO_3^-])$.

This patient’s anion gap is 140 mEq/L - (100 mEq/L + 15 mEq/L) = 140 mEq/L - 115 mEq/L = 25 mEq/L.

25. A 55-year-old male has been hospitalized after a suicide attempt. The neighbors found him unconscious next to a bottle of an unidentified substance. The laboratory tests are as follows: pH 7.01, Na+ 138 mEq/L, Cl- 103 mEq/L, HCO3- 25 mEq/L. Which of the following substances did the patient most likely take:

a) methanol
b) ethylene glycol
c) spironolactone
d) iron
e) propylene glycol

The correct answer is c.

Anion gap is the difference between the measured cations and anions in the plasma. In reality, in order for plasma to be electrically neutral, the number of cations and anions must be equal. However, fewer anions are measured compared to cations. Even if we exclude potassium from the equation, the concentration of sodium cation is still larger than the sum of the concentrations of chlorine and bicarbonate anions, accounting for the "gap". The normal anion gap is between 6 and 12 mEq/L. Sometimes, metabolic acidosis can be caused by the addition of new anions from different acids (e.g., in ketoacidosis or lactic acidosis). In those cases, the bicarbonate anions are "replaced" by unmeasured anions and the anion gap widens. In some other cases, where no new anions are added, the bicarbonate anions are replaced by chlorine, which is measured so the anion gap remains unchanged. This is why metabolic acidosis in general can be divided into normal anion gap metabolic acidosis and high anion gap metabolic acidosis.

The causes of high anion gap metabolic acidosis can be memorized using the mnemonic MUDPILES: methanol, uremia, DKA, propylene glycol, iron, lactic acidosis, ethylene glycol, salicylates.

This patient is suffering from normal anion gap metabolic alkalosis. Of the answer choices provided, only spironolactone ingestion causes normal anion gap metabolic alkalosis. Methanol, ethylene glycol, iron and propylene glycol ingestion all cause high anion gap metabolic acidosis.

Anion gap is calculated as $[Na^+] - ([Cl^-] + [HCO_3^-])$.

This patient's anion gap is 138 mEq/L - (103 mEq/L + 25 mEq/L) = 138 mEq/L - 128 mEq/L = 10 mEq/L.

26. A 76-year-old male has been hospitalized for severe diarrhea. On admission, he is drowsy. The laboratory tests reveal that his pH is 7.15, his Na+ level is 135 mEq/L and his Cl- is 105 mEq/L. Which of the following HCO3- values would be expected in this patient:

    a) 12 mEq/L
    b) 18 mEq/L
    c) 26 mEq/L
    d) 34 mEq/L
    e) 40 mEq/L

The correct answer is c.

This patient is suffering from acidosis. Diarrhea is a cause of normal anion gap metabolic acidosis. Anion gap represents the difference between the measured cations and the measured anions in the plasma. To preserve electroneutrality, the real concentrations of anions and cations must be equal. However, fewer anions are measured compared to cations, leading to the “gap”. The normal anion gap is between 6 and 12 mEq/L. Metabolic acidosis can be caused by the addition of new anions from different acids (e.g., in ketoacidosis or lactic acidosis), which are themselves unmeasured, widening the gap. There are also cases of metabolic acidosis where no new anions are added and the bicarbonate anions are replaced by chlorine, which is measured so the anion gap remains unchanged.

The causes of high anion gap metabolic acidosis can be memorized using the mnemonic MUDPILES: methanol, uremia, DKA, propylene glycol, iron, lactic acidosis, ethylene glycol, salicylates.

Anion gap is calculated as: $[Na^+] - ([Cl^-] + [HCO_3^-])$.

Of the answer choices provided, only answer c would give an anion gap between 6 and 12 mEq/L.

27. A 50-year-old male is taking part in a research study at the pulmonology department. It is determined that his rate of CO_2 production is 80% of the rate of O_2 consumption. His arterial PCO_2 is 36 mmHg and the PO_2 in humidified tracheal air is 150 mmHg. Which of the following represents the alveolar PO_2 in this patient:

a) 105 mmHg
b) 114 mmHg
c) 86 mmHg
d) 91 mmHg
e) cannot be calculated

The correct answer is d.

In order to calculate the alveolar PO_2 in this patient, we need to use the alveolar gas equation:

$PAO_2 = PIO_2 - PaCO_2 / R$.

R is the respiratory quotient (the respiratory exchange ratio), in this case it is 0.8 (since CO_2 production is 80% of oxygen consumption). PIO_2 in this case is 150 mmHg. $PaCO_2$ is 36 mmHg.

$PAO_2 = 150\ mmHg - 36\ mmHg / 0.8 = 150\ mmHg - 45 = 105\ mmHg$.

28. A clinical study is done at the pulmonology department to compare lung function between individuals of different ages. The researchers decide to compare the physiologic dead spaces between individuals. If all the other variables were the same, which of the following would be associated with an increase in physiologic dead space:

a) increased $PECO_2$
b) increased VT
c) decreased $PaCO_2$
d) decreased minute ventilation
e) increased respiratory rate

The correct answer is b.

Dead space refers to the volume of the airways that does not participate in gas exchange. Anatomic dead space refers to the volume of the conducting airways, whereas physiologic dead space refers to the volume of lungs that does not participate in gas exchange, usually due to a ventilation/perfusion mismatch.

Physiologic dead space can be calculated from the following equation:

VD = VT * [(PaCO2 - PECO2) / PaCO2], where VD is the physiologic dead space, VT is the tidal volume, PaCO2 is the PCO2 of the arterial blood and PECO2 is the PCO2 of mixed expired air.

From this equation, it can be concluded that an increase in VT would lead to elevated VD, assuming PaCO2 and PECO2 remained the same. If PaCO2 and PECO2 were equal, VD would be 0. The minute ventilation is TV * breaths/minute.

29. A 49-year-old male is being evaluated as part of the clinical trial at the pulmonology department. It is determined that his tidal volume is 500 mL, his respiratory rate is 15/min, his PCO2 in the expired air is 30 mmHg and his PaCO2 is 40 mmHg. Which of the following is the physiologic dead space volume in this patient:

    a) 0 mL
    b) 50 mL
    c) 125 mL
    d) 150 mL
    e) 333 mL

The correct answer is c.

Dead space is the volume of the airways that does not participate in gas exchange and can be divided into anatomic and physiologic dead space. Anatomic dead space is the volume of the conducting airways (which do not take part in gas exchange). Physiologic dead space is to the volume of lungs that does not participate in gas exchange (i.e., due to ventilation-perfusion mismatch).

The physiologic dead space can be calculated from the following equation (think of it as if trying to determine how much of the alveolar oxygen is not used to “generate” CO_2):

$V_D = V_T * [(PaCO_2 - PECO_2) / PaCO_2]$, where VD is the physiologic dead space, VT is the tidal volume, $PaCO_2$ is the PCO_2 of the arterial blood and $PECO_2$ is the PCO_2 of mixed expired air.

VD = 500 mL * [(40 mmHg - 30 mmHg) / 40 mmHg] = 500 mL * 0.25 = 125 mL.

The respiratory rate is needed to calculate the alveolar ventilation:

VA = (VT - VD) * breaths/min.

If $PaCO_2$ and $PECO_2$ were equal, VD would be 0. The minute ventilation is TV * breaths/minute.

30. A 67-year-old man with history of type II diabetes mellitus, hypertension, obesity and NYHA 3 congestive heart failure (CHF) has been hospitalized for the CHF exacerbation. Due to deteriorating function of both his left and right ventricles, he has been transferred to the intensive care unit (ICU). His cardiac output as well as pressures in the pulmonary artery and left atrium are measured. Which of the following would likely result in this largest elevation of this patient's pulmonary vascular resistance:

a) increased CO and unchanged pressure difference
b) increased CO and increased pressure difference
c) increased CO and decreased pressure difference
d) decreased CO and decreased pressure difference
e) decreased CO and increased pressure difference

The correct answer is e.

Just like in any other organ, the same principle for calculating the vascular resistance applies in the lungs as well. Remember that pressure difference = resistance * flow. The flow represents the cardiac output as the entire cardiac output and resistance is the pulmonary vascular resistance.

Pulmonary vascular resistance can, therefore, be calculated from the following equation:

PVR = (P pulm art. - P left atrium) / Cardiac Output.

Decreased CO and increased pressure difference would, therefore, lead to an increase in PVR.

31. A 35-year-old man is brought to the emergency department after suffering burns to 20% of his body following a major road accident in which his vehicle caught fire. He weighs 75 kg and his BMI is 25. Which of the following represents the amount of fluid this patient should receive over the first 24 hours:

a) 1.2 L
b) 1.5 L
c) 4.7 L
d) 6 L
e) 18 L

The correct answer is d.

The rule of 9s applies to approximate the body surface area that is covered by burns. In adults, each arm represents 9% of the body surface area, the entire head represents 9%, entire chest represents 9%, and entire abdomen represent 9% of the body surface area. Each side of each leg also represents 9% of the body surface area (in total 18% per leg) and each half of the back represents 9% (18% for the whole back). The perineal area accounts for 1% of the body surface area.

The Parkland formula is used to estimate the volume of replacement fluid that should be administered to patients with burns over the first 24 hours. It is calculated as:

V = 4 mL * weight in kg * area surface area burned.

The first half of the fluid volume is given over the first 8 hours; rest is given over the next 16 hours.

In this patient: V = 4 mL * 75kg * 20% burned = 6,000 mL = 6 L.

32. A 55-year-old patient who has suffered severe burns following an accident has been admitted to the hospital. He has suffered serious burns to the front and back of both of his legs and feet. In order to replace the fluid loss, he has had to receive 12 L of IV fluids. Which of the following represents the weight of the patient:

a) 83 kg
b) 90 kg
c) 33 kg
d) 133 kg
e) cannot be calculated

The correct answer is a.

The surface area of the body that is covered by burns can be approximated using the rule of 9's. In adults, each arm represents 9% of the body surface area, the entire head represents 9%, entire chest represents 9%, and entire abdomen represent 9% of the body surface area. Each side of each leg also represents 9% of the body surface area (in total 18% per leg) and each half of the back represents 9% (18% for the whole back). The perineal area accounts for 1% of the body surface area.

The volume of replacement fluid that should be administered to patients with burns over the first 24 hours is calculated using the Parkland formula as follows:

V = 4 mL * weight in kg * area surface area burned.

The first half of the fluid volume is given over the first 8 hours; rest is given over the next 16 hours.

Since each leg accounts for approximately 18% of the body surface area, the % surface area burned is 36.

This patient has received 12,000 mL of fluid.

Weight in kg can be calculated from the Parkland formula:

Weight in kg = V / (4 mL * surface area burned) = 83.

33. A 46-year-old patient is receiving an unknown drug intravenously. It is known that the drug is distributed into total body water. What dose of the drug is needed to obtain an initial plasma level of 4 mg/L in a patient weighing 70 kg?

a) 42 mg
b) 168 mg
c) 200 mg
d) 210 mg
e) 280 mg

The correct answer is b.

In order to answer this question, we need to determine the loading dose of the drug. The loading dose is the initial higher dose of the drug given to achieve a certain plasma concentration earlier before maintaining it with a lower, maintenance dose. It is calculated from the following equation: LD = (Cp * Vd) / F, where Cp is the plasma level, Vd is the volume of distribution, and F is the bioavailability of the drug. The loading dose is proportional to the volume of distribution because the larger the volume of distribution the more drug needs to be given to achieve the same plasma concentration. The bioavailability of the drug is the opposite. More drug needs to be given if the bioavailability is lower (i.e., drugs with low bioavailability less readily enter systemic circulation so more drug needs to be given). For drugs administered intravenously, F = 1. Since the drug is distributed in total body water, Vd is about 60% of total body weight, or 42 kg (0.6 * 70 kg). 42 kg of water is 42 L of water. Therefore, Vd = 42 L.
LD = 4 mg/L * 42 L / 1 = 168 mg.

34. A 20-year-old male hospitalized for a severe infection is receiving an IV antibiotic that distributes in total body water. He was initially given 1,800 mg of the drug. His body weight is 75 kg. Which of the following represents the plasma concentration of the antibiotic in this patient:

a) 14 mg/L
b) 24 mg/L
c) 40 mg/L
d) 45 mg/L
e) 75 mg/L

The correct answer is c.

The answer to this question can be calculated from the equation for the loading dose of the drug. The loading dose is the initial higher dose of the drug given to achieve a certain plasma concentration earlier before reducing the dosage to a maintenance dose. The loading dose is calculated as: $LD = (Cp * Vd) / F$, where Cp is the plasma level, Vd is the volume of distribution, and F is the bioavailability of the drug. The greater the volume of distribution of the drug, the more drug needs to be given to achieve the same plasma concentration, whereas more drug needs to be given if the bioavailability is lower. For drugs administered intravenously, F = 1 as all the drug enters systemic circulation. Since the drug is distributed in total body water, Vd is about 60% of total body weight, or 0.6 * 75 kg = 45 kg. 45 kg of water is 45 L of water. Loading dose is 1,800 mg.

1,800 mg = Cp * 45 L / 1 => Cp * 45 L = 1,800 mg => Cp = 1,800 mg / 45 L = 40 mg/L.

35. A drug is administered to a 75-year-old patient whose renal function has decreased by 50%. Which of the following best describes the change that would be expected in this patient:

a) t 1/2 would be shorter
b) Vd would decrease
c) loading dose would increase
d) clearance of the drug would increase
e) maintenance dose would be lower

The correct answer is e.

The patient in question has decreased renal function, meaning his renal clearance is lower. The maintenance dose of the drug is the dose of drug given to the patient to maintain a certain plasma concentration. The equation for the maintenance dose is: MD = Cl * Cp * td / F, where Cl is the clearance, Cp is the steady state concentration, td is the dosing interval and F is the bioavailability. It can be concluded from this equation that the maintenance dose would be lower if the renal clearance was lower. It also makes sense intuitively as a decrease in renal clearance of the drug indicates that more drug remains in the body for extended periods of time so lower maintenance doses would be needed to maintain a certain plasma concentration. Vd would not change. t 1/2 would increase due to decreased clearance. Note that the loading dose equation, in comparison, does not take into account the renal clearance.

36. A 50-year-old patient is started on an IV infusion of a drug at the rate of 300 mg/h. The clearance of the drug is 50 L/h. Which of the following represents the steady state concentration of the drug in question:

a) 250 mg/L
b) 75.6 mg/L
c) 60 mg/L
d) 6 mg/L
e) 3.6 mg/L

The correct answer is d.

The maintenance dose of the drug is the dose of drug given to the patient to maintain a certain plasma concentration. It can be calculated as: MD = Cl * Cp * td / F, where Cl is the clearance, Cp is the steady state concentration, td is the dosing interval and F is the bioavailability. Since the drug is given as an IV infusion, there is no need to consider the dosing interval or bioavailability so it can be simplified as: MD = Cl * Cp => Cp = MD / Cl = 300 mg/h / 50 L/h = 6 mg/L.

37. A clinical study is done to determine the characteristics of a novel drug that is distributed in total body water. Which of the following represents the total amount of the drug in a body of a 35-year-old participant whose body mass is 80 kg if the plasma concentration of the drug is 10 mg/L:

a) 480 mL
b) 480 mg
c) 640 mL
d) 640 mg
e) 800 mg

The correct answer is b.

Once a drug enters the body, it distributes within body fluid compartments. Not all drugs distribute equally (i.e., some may remain in plasma only, others may distribute in interstitial fluid, while some others may distribute in total body water). The volume of distribution is the ratio of the total amount of drug in the body and the concentration of the drug (remember, for any solution c = amount / V => V = amount / c). Therefore, Vd = amount of drug in the body / Cp => amount of drug in the body = Vd * Cp. Since water represents approximately 60% of body weight, it can be calculated that this patient has 48 kg of water in his body (0.6 * 80 kg), or 48 L of water. Therefore, Vd is 48 L. Cp = 10 mg/L. Amount of drug in the body = 48 L * 10 mg/L = 480 mg.

38. A 25-year-old patient is being treated with a drug that distributes in the total body water. Currently, the amount of drug in his body is 600 mg and the plasma concentration of drug is 10 mg/L. Which of the following represents this patient's body weight:

a) 60 kg
b) 66 kg
c) 80 kg
d) 88 kg
e) 100 kg

The correct answer is e.

Individual drugs distribute differently between the body's fluid compartments. The volume of distribution represents to what degree the drug distributes within the body and can be calculated as the ratio of the total amount of drug in the body and the concentration of the drug (remember, for any solution c = amount / V => V = amount / c). Therefore, the volume of distribution of a drug can be calculated from the following formula:

Vd = amount of drug in the body / Cp.

In this patient, Vd = 600 mg / 10 mg/L = 60 L.

Since the drug is distributed in the total body water, the total volume of water in this patient is 60 L. The weight of 60 L of water is 60 kg. Since water represents approximately 60% of body weight, it can be calculated that his body weight is 60 kg / 0.6 = 100 kg.

39. A novel drug is being studied in a clinical trial. It is determined that the half-life of a drug is 4 h and that the Vd of a drug in one of the participants is 30 L. Which of the following represents clearance of the drug in this patient:

a) 0.18 L/h
b) 3.15 L/h
c) 5.25 L/h
d) 7.50 L/h
e) 10.71 L/h

The correct answer is c.

First-order elimination of the drug means that a constant fraction of the drug is eliminated per unit of time. Therefore, we can determine the half-life of the drug, which is the time frame in which the concentration of the drug in the body halves. The equation used to calculate the half-life of the drug is:

t 1/2 = 0.7 * Vd / Cl.

It makes sense that clearance is inversely proportional to the half-life (i.e., greater clearance means more drug is removed from the body, making the half-life shorter). The clearance of the drug can be calculated from the equation for the half-life:

t 1/2 = 0.7 * Vd / Cl => Cl = 0.7 * Vd / t 1/2 = 0.7 * 30 L / 4 h = 5.25 L/h.

40. A 40-year-old patient with a body mass of 70 kg is treated with the drug that is distributed in total body water. The drug has clearance of 10 L/h. Which of the following best represents the half-life of the drug in question:

a) 1 h
b) 2 h
c) 3 h
d) 4 h
e) 5 h

The correct answer is c.

The half-life is calculated for the drugs that follow first-order kinetics, meaning that a constant fraction of the drug is eliminated per unit of time. It represents the time frame in which the concentration of the drug in the body halves.

The equation used to calculate the half-life of the drug is:

$t_{1/2} = 0.7 * Vd / Cl$.

Since the drug is distributed in total body water, Vd is the total volume of water in the body. Since water accounts for approximately 60% of body weight, the weight of water in this patient's body is approximately 42 kg (0.6 * 70 kg). 42 kg have the volume of 42 L. Cl is 10 L/h. Therefore, $t_{1/2} = 0.7 * 42$ L / 10 L/h = 2.94 h, or roughly 3 hours.

41. A 35-year-old patient is participating in a clinical trial involving a novel drug that distributes in total body water. The plasma concentration of the drug, its clearance and half-life are measured. Which of the following represents the correct way of calculating the rate of elimination of the drug from the body:

a) clearance * plasma concentration
b) clearance / plasma concentration
c) clearance * volume of distribution / half-life
d) clearance * half-life
e) clearance * half-life / volume of distribution

The correct answer is a.

The rate of elimination can be calculated from the following equation:

Cl = rate of elimination / Cp => rate of elimination = Cl * Cp; where Cl is clearance and Cp is plasma concentration.

It makes sense that the rate of elimination of the drug is proportional to the clearance and the concentration of the drug. If there is more drug in the plasma and more plasma gets cleared, more drug will be eliminated.

42. A 40-year-old patient is treated with a novel drug that distributes in total body water. The body mass of the patient is 80 kg. It is determined that the half-life of the drug is 5 hours. The plasma drug concentration is 10 mg/L. Which of the following represents the rate of elimination of the drug:

    a) 6.72 L/h
    b) 67.2 mg/h
    c) 48 L/h
    d) 160 mg/h
    e) 40 mg/h

The correct answer is b.

The rate of elimination can be calculated from the following equation:

Cl = rate of elimination / Cp => rate of elimination = Cl * Cp; where Cl is clearance and Cp is plasma concentration.

The rate of elimination of the drug is proportional to the clearance and the concentration of the drug (the more drug in the plasma and the higher the clearance of such plasma - the more drug gets eliminated).

First-order elimination of the drug means that a constant fraction of the drug is eliminated per unit of time, making it possible to determine the half-life of the drug, which is the time frame in which the concentration of the drug in the body reduces by 50%.

The equation used to calculate the half-life of the drug is:

t 1/2 = 0.7 * Vd / Cl, where t 1/2 is the half-life and Vd volume of distribution.

Clearance of the drug can be calculated from that equation:

t 1/2 = 0.7 * Vd / Cl => Cl = 0.7 * Vd / t 1/2.

The drug is distributed in total body water, which accounts for 60% of the body weight, or 48 kg (0.8 * 80 kg). 48 kg of water have the volume of 48 L. Therefore, Vd = 48 L.
Cl = 0.7 * 48 L / 5 h = 6.72 L/h.

Rate of elimination = 6.72 L/h * 10 mg/L = 67.2 mg/h.

43. A 40-year-old man is brought to the emergency department after being found somnolent in his apartment with an empty bottle of aspirin pills. The laboratory studies show blood pH within the normal range. The HCO3- is 8 mmol/L. Which of the following PaCO2 values would most likely be seen in this patient assuming the overdose happened 6 hours ago:

a) 16 mmHg
b) 18 mmHg
c) 20 mmHg
d) 22 mmHg
e) 24 mmHg

The correct answer is a.

Salicylate intoxication in adults usually occurs following intentional overdose with aspirin. It causes respiratory alkalosis and metabolic acidosis simultaneously, resulting in a mixed acid-base disorder. The respiratory alkalosis is caused by the stimulation of the respiratory center and occurs shortly after ingestion. Respiratory stimulation leads to increased expiration of CO_2 and subsequent alkalosis development. A few hours later, a number of metabolic derangements develop, including the uncoupling of oxidative phosphorylation, leading to acid accumulation (increase in unmeasured anions) and subsequent high anion gap metabolic acidosis development. Patients who present soon after the ingestion will generally have respiratory alkalosis alone, while those who present a few hours later will typically have a mixed disorder (respiratory alkalosis with metabolic acidosis). Winter's formula is used to evaluate respiratory compensation in metabolic acidosis. $PaCO_2 = (1.5 * HCO_3^-) + 8 \pm 2$. If the value is outside of the range predicted by Winter's formula, a mixed disorder should be suspected. In this case, a patient has a combined metabolic acidosis and respiratory alkalosis. Therefore, $PaCO_2$ level in this patient would be lower than expected according to the Winter's formula. $PaCO_2 = 1.5 * 8 + 8 \pm 2 = 12 + 8 \pm 2 = 20 \pm 2$.

In a patient with compensated metabolic acidosis, the expected $PaCO_2$ would be between 18 and 22 mmHg. Patients who also have a respiratory alkalosis would have $PaCO_2$ levels lower than 18 mmHg.

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FOR USMLE STEP 1