DIALYZER DYNAMICS
TESTING YOUR UNDERSTANDING

NANT – DIALYSIS BOOT CAMP

WEDNESDAY, MARCH 18TH, 2015

LAS VEGAS, NEVADA

JOHN SWEENY

"SEEING" THE DIALYSIS PROCESS

- AS HUMAN BEINGS, WE ARE LIMITED IN OUR ABILITY TO OBSERVE THE PROCESSES OCCURRING INSIDE A DIALYZER
- WE CAN STILL UNDERSTAND WHAT IS HAPPENING IN THE DIALYZER THANKS TO SCIENTIFIC EXPERIMENTATION, MODELING, AND APPLICATION OF THESE PROCESSES FOR BENEFIT OF THE ESRD PATIENT (THANK YOU, DR. ALBERT L. BABB, CHEMICAL ENGINEER)
- HOW WELL DO YOU "PICTURE" THE DIALYSIS PROCESS? FOLLOW ALONG AND FIND OUT

HOLLOW FIBER VS. A RED CELL

- PICTURE A HOLLOW FIBER WITH A RED CELL INSIDE. IF A BEACH BALL REPRESENTS THE INSIDE DIAMETER OF THE HOLLOW FIBER WHAT SIZE WOULD A RED CELL BE?
- A) THE SIZE OF A VOLLEYBALL
- B) THE SIZE OF A BASEBALL
- C) THE SIZE OF A PING PONG BALL
- D) THE SIZE OF A MARBLE

HOLLOW FIBER VS. RED CELL

- THE DIAMETER OF THE AVERAGE BEACH BALL IS ABOUT 16 INCHES = 41 cm
- THE DIAMETER OF A HOLLOW FIBER IS 200 MICRONS
- THE DIAMETER OF A RED CELL IS 7 MICRONS WHICH MEANS A RED CELL'S DIAMETER IS ABOUT 28X SMALLER THAN A HOLLOW FIBER'S DIAMETER
- 41cm/28 = 1.46 cm = 14.6 mm
- ANSWER: D) A MARBLE WHO'S STANDARD SIZE IS 15 mm

  NOTE: A PING PONG BALL IS 40 mm IN DIAMETER

MEMBRANE THICKNESS VS. PORE SIZE

- PICTURE A PIECE OF MEMBRANE. WHICH OF THESE ITEMS BEST REPRESENTS WHAT YOU ARE PICTURING?
- A) A SLICE OF SWISS CHEESE
- B) A FINE SPONGE
- C) A WINDOW SCREEN
- D) A SLICE OF BREAD

MEMBRANE THICKNESS VS. PORE SIZE

- THE AVERAGE MEMBRANE THICKNESS IS BETWEEN 10 AND 50 MICRONS (1 TO 4 X 10^{-5} m)
- THE AVERAGE PORE SIZE IS ABOUT 100 ANGSTROMS (1 X 10^{-8} m)
- THE MEMBRANE IS ABOUT 3,000X THICKER THAN THE AVERAGE PORE DIAMETER
- THE ANSWER IS: B) A FINE SPONGE

NOTE: THE DIAMETER OF A UREA MOLECULE IS 2.6 ANGSTROMS SO IT CAN EASILY PASS THROUGH THE PORES IN A MEMBRANE.

QUESTIONS WITH AMAZING ANSWERS

- WHEN A PATIENT IS PUT ON DIALYSIS AT THE START OF A MIDWEEK TREATMENT THEIR BUN WILL BE ABOUT 80 mg/dL. HOW MANY UREA MOLECULES WOULD BE INSIDE A SINGLE HOLLOW FIBER?
- HOW FAST DOES A UREA MOLECULE MOVE IN PLASMA AT BODY TEMPERATURE?
- UREA GETS KNOCKED AROUND BY THE WATER MOLECULES. ABOUT HOW MANY COLLISIONS ARE THERE PER SECOND?

THE AMAZING ANSWERS

- WHEN A PATIENT IS PUT ON DIALYSIS AT THE START OF A MIDWEEK TREATMENT THEIR BUN WILL BE ABOUT 80 mg/dL. THE NUMBER OF UREA MOLECULES INSIDE A SINGLE HOLLOW FIBER WOULD BE 163 QUADRILLION MOLECULES. (163,000,000,000,000,000 = 1.63×10^{17})
- A UREA MOLECULE MOVES IN PLASMA AT BODY TEMPERATURE AT A SPEED OF 359 m/sec. WATER MOLECULES MOVE AT 590 m/sec.
- UREA GETS KNOCKED AROUND BY THE WATER MOLECULES. THERE ARE ABOUT 36 TRILLION (36.000,000,000,000) COLLISIONS PER SECOND.
- THE DISTANCE A UREA MOLECULE MOVES BETWEEN COLLISIONS IS 10^{-11} METERS (ABOUT 10% OF THE DIAMETER OF AN ATOM) AND IS CALLED THE MEAN FREE PATH

MEAN FREE PATH (MFP) VS. DIFFUSION

- THE AVERAGE DISTANCE A PARTICLE WILL HAVE MOVED FROM ITS STARTING POINT IS THE SQUARE ROOT OF THE NUMBER OF MEAN FREE PATHS TAKEN TIMES THE LENGTH OF THE MEAN FREE PATH
- FOR 100 MEAN FREE PATH STEPS, THE AVERAGE DISTANCE TRAVELED WILL BE 10 X MFP
- IF THE RATE OF MFP STEPS IS KNOWN PER SECOND AS WELL AS THE MFP DISTANCE, THEN THE TIME IT TAKES TO GO A CERTAIN DISTANCE CAN BE DETERMINED

HOW LONG WILL IT TAKE A UREA MOLECULE TO MOVE FROM THE CENTER OF A HOLLOW FIBER TO THE MEMBRANE WALL?

- MFP = 10^{-11} m, 3.6 X 10^{13} MFP/SECOND, HOLLOW FIBER DIAMETER = 200 µm
- A) 3 MILLISECONDS
- B) 3 SECONDS
- C) 3 MINUTES
- D) 0.05 HOURS

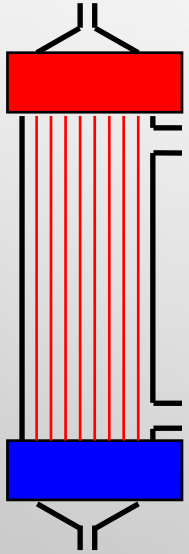
UREA HOLLW FIBER DIFFUSION TIME

- DISTANCE TO TRAVEL = 100 μm = 10^{-4} m
- NUMBER OF MFP = 10^{-4} m/10^{-11}m = 10^{7} MFP
- (NUMBER OF MFP)^{2} = 10^{14} = 100 TRILLION
- 100 TRILLION/ 36 TRILLION/SECOND = 2.77 SECONDS
- THE ANSWER IS : B) 3 SECONDS

UREA TIME AND DISTANCE

DISTANCE	TIME
1 μm	0.28 msec
10 μm	0.0277 sec
100 μm	2.77 sec
1 mm	4.6 min
1 cm	7.7 hr
10 cm	1 month
1 m	8.8 years

THE CONCEPT OF EXTRACTION RATIO



ARTERIAL BUN = 80 mg/dL

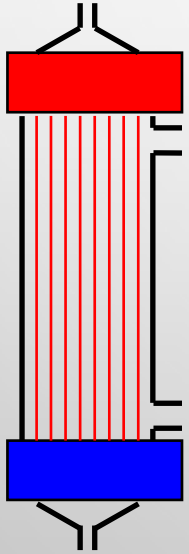
Blood Flow Rate =
Q_B = 400 mL/min

VENOUS BUN = 20 mg/dL

- WHAT IS THE EXTRACTION RATIO FOR THIS DIALYZER?

  - A) 20
  - B) 0.20
  - C) 0.75
  - D) 240 mL/min

EXTRACTION RATIO (ER)



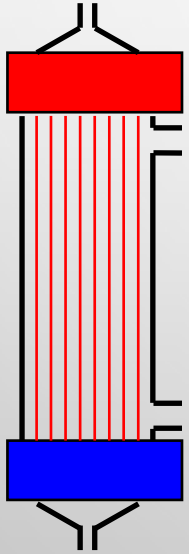
ARTERIAL BUN = 80 mg/dL

Blood Flowrate = Q_B = 400 mL/min

VENOUS BUN = 20 mg/dL

- EXTRACTION RATIO IS DEFINED AS THE RATIO OF THE BUN REMOVED DIVIDED BY THE TOTAL BUN ENTERING THE DIALYZER
- ER = $(ART_{BUN} - VEN_{BUN})/ART_{BUN}$
- ER = (80 – 20)/80 = 60/80 = 0.75
- THE ANSWER IS: C) = 0.75

EXTRACTION RATIO (ER)



ARTERIAL BUN = 100 mg/dL

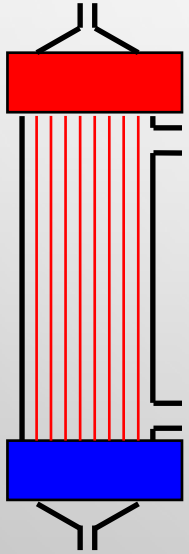
Blood Flow Rate =
Q_B = 400 mL/min

VENOUS BUN = ?? mg/dL

- WHAT HAPPENS TO THE EXTRACTION RATIO IF THE BUN IS INCREASED AT THE DIALYZER INLET?

- A) IT INCREASES
- B) IT DECREASES
- C) IT REMAINS THE SAME

EXTRACTION RATIO (ER)



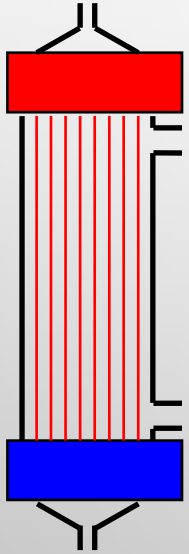
ARTERIAL BUN = 100 mg/dL

Blood Flow Rate = Q_B = 400 mL/min

VENOUS BUN = 25 mg/dL

- C) = IT REMAINS THE SAME
- THIS MEANS THE CONCENTRATION LEAVING THE VENOUS END OF THE DIALYZER WILL BE 25 mg/dL
- $ER = (ART_{BUN} - VEN_{BUN})/ART_{BUN}$
- $VEN_{BUN} = ART_{BUN} (1 - ER)$
- $VEN_{BUN} = 100 (1 - 0.75) = 25$ mg/dL

EXTRACTION RATIO (ER)



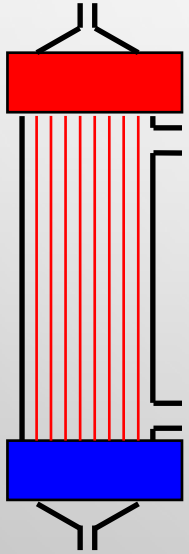
ARTERIAL BUN = 80 mg/dL

Blood Flow Rate increased or decreased

VENOUS BUN = ?? mg/dL

- WHAT HAPPENS TO THE ER IF THE BLOOD FLOW RATE IS INCREASED OR DECREASED?
- A) AS Q_B INCREASES, ER INCREASES
- B) AS Q_B INCREASES, ER DECREASES
- C) AS Q_B DECREASES, ER INCREASES
- D) AS Q_B DECREASES, ER DECREASES
- E) ER REMAINS THE SAME

EXTRACTION RATIO (ER)



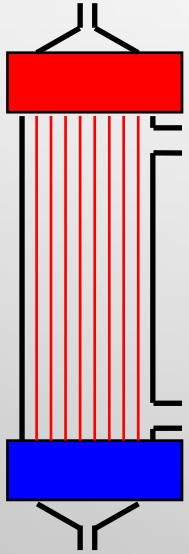
ARTERIAL BUN = 80 mg/dL

Blood Flow Rate increased or decreased

VENOUS BUN = ?? mg/dL

- B) AS Q_B INCREASES, ER DECREASES
- C) AS Q_B DECREASES, ER INCREASES
- THE WAY TO THINK OF THIS IS THAT AT HIGHER FLOW RATES THE BUN SPENDS LESS TIME IN THE DIALYZER AND HENCE HAS LESS TIME TO DIFFUSE OVER TO AND THEN THROUGH THE MEMBRANE
- IT'S JUST THE OPPOSITE FOR LOWER BLOOD FLOW RATES

EXTRACTION RATIO (ER)



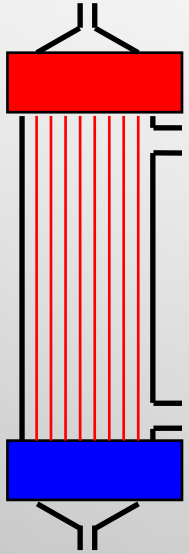
ARTERIAL BUN = 80 mg/dL

Blood Flow Rate increased or decreased

VENOUS BUN = ?? mg/dL

- IF THE ER GOES DOWN WITH INCREASING Q_B, WHY DO DOCTOR'S PRESCRIBE HIGH Q_B'S FOR THEIR PATIENTS?
- A) DOCTOR'S DON'T UNDERSTAND DIALYZER DYNAMICS
- B) FASTER IS ALWAYS BETTER
- C) THE Q_B INCREASE IS LARGER THAN THE ER DECREASE
- D) ER HAS NOTHING TO DO WITH CLEARANCE

EXTRACTION RATIO AND CLEARANCE (C_X)



ARTERIAL BUN = 80 mg/dL

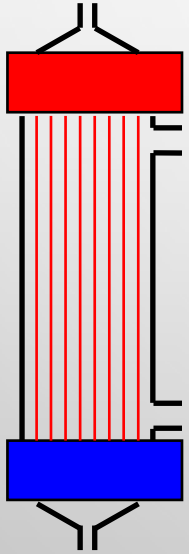
Blood Flow Rate increased or decreased

VENOUS BUN = ?? mg/dL

- C) THE Q_B INCREASE IS LARGER THAN THE ER DECREASE
- ER IS DIRECTLY RELATED TO CLEARANCE
- CLEARANCE = ER X Q_B
- REMEMBER THIS FORMULA?

$$C_X = \left(\frac{A_X - V_X}{A_X} \right) Q_B$$

EXTRACTION RATIO AND CLEARANCE (C_X)



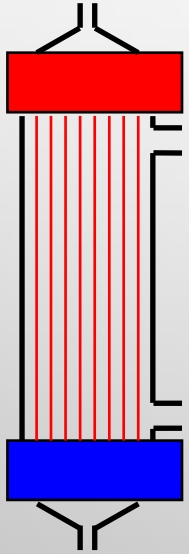
ARTERIAL BUN = 80 mg/dL

Blood Flow Rate = 200 mL/min

VENOUS BUN = ?? mg/dL

- IF THE Q_B IS REDUCED TO 200 mL/min , WE KNOW THE ER WILL INCREASE. HOW MUCH AND WHAT WILL THE CLEARANCE AND VENOUS BUN BE?
- A) ER = 0.80, VEN_{BUN} = 16 mg/dL, C_X = 160 mL/min
- B) ER = 0.90, VEN_{BUN} = 12 mg/dL, C_X = 180 mL/min
- C) ER = 0.90, VEN_{BUN} = 8 mg/dL, C_X = 180 mL/min
- D) ER = 0.96, VEN_{BUN} = 3 mg/dL, C_X = 193 mL/min

EXTRACTION RATIO AND CLEARANCE



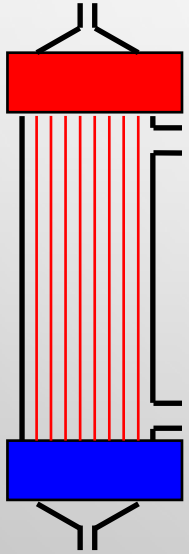
ARTERIAL BUN = 80 mg/dL

Blood Flow Rate = 200 mL/min

VENOUS BUN = 3 mg/dL

- D) ER = 0.96, VEN_{BUN} = 3 mg/dL, C_X = 193 mL/min
- THE EXACT ANSWER IS ER = 0.964, THE VENOUS BUN WOULD BE 2.9 mg/dL, AND THE CLEARANCE = 192.8 mL/min
- OK, NOW THAT YOU HAVE AN IDEA OF HOW EFFICIENT A DIALYZER CAN BE AT REMOVING UREA, WHAT ER AND VEN_{BUN} WOULD YOU EXPECT FOR:
- A) Q_B = 2000 mL/min
- B) Q_B = 20 mL/min

EXTRACTION RATIO AND CLEARANCE (C_X)



ARTERIAL BUN = 80 mg/dL

Blood Flow Rates of 2000 and 20 mL/min

VENOUS BUN = ?? mg/dL

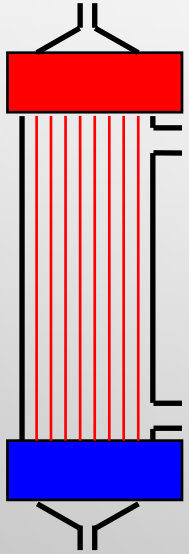
- FOR A BLOOD FLOW RATE OF 2000 mL/min:
  - ER = 0.20
  - VEN_{BUN} = 64 mg/dL
  - C_X = 403 mL/min
- FOR A BLOOD FLOW RATE OF 20 mL/min:
  - ER = 1.00
  - VEN_{BUN} = 0 mg/dL
  - C_X = 20 mL/min
- EVEN AT A Q_B OF 100 mL/min, THE CLEARANCE IS STILL 100% !!

CLEARANCE VS. BLOOD FLOW

ARTERIAL BUN = 80 mg/dL Q_D = 500 mL/min

BLOOD FLOW (400 mL/min)	EXT. RATIO %	CLEARANCE (mL/min)	VENOUS BUN (mg/dL)
20,000	2	422	78
2,000	20	403	64
1,000	38	379	50
500	65	327	28
200	96	193	3
100	100	100	0

CLEARANCE VS. DIALYZER TIME

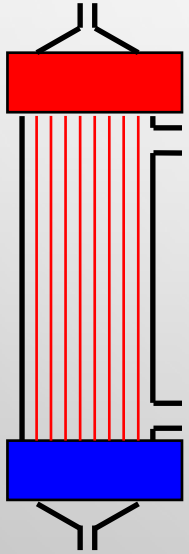


BLOOD IN (START THE CLOCK!)

BLOOD OUT (STOP THE CLOCK!)

- UREA CAN ONLY BE REMOVED FROM THE BLOOD WHILE IT"S IN THE DIALYZER. IF A DIALYZER'S BLOOD VOLUME IS 100 mL, HOW LONG DOES IT TAKE FOR BLOOD TO PASS THROUGH THE DIALYZER AT THE FOLLOWING FLOW RATES?
  - 200 mL/min
  - 400 mL/min
  - 600 mL/min

CLEARANCE VS. DIALYZER TIME



BLOOD IN (START THE CLOCK!)

BLOOD OUT (STOP THE CLOCK!)

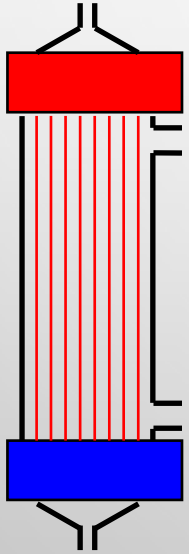
- FOR Q_B = 200 mL/min THE TIME IS 30 SECONDS (WITH A BLOOD VOLUME OF 100 mL, YOU COULD FILL 2 DIALYZERS IN A MINUTE)
- FOR Q_B = 400 mL/min, THE TIME IS 15 SECONDS
- FOR Q_B = 600 mL/min, THE TIME IS 10 SECONDS
- KEEP IN MIND, FOR A HOLLOW FIBER THAT IS 200 MICRONS IN DIAMETER, THE UREA MOLECULE ONLT HAS TO GO A MAXIMUM DISTANCE OF 100 MICRONS TO REACH THE MEMBRANE

THINKING CLEARANCE

- CLEARANCE AS BLOOD VOLUME
- LET Q_B = 400 mL/min AND C_X = 300 mL/min
  - 300 mL OF BLOOD WILL BE COMPLETELY CLEARED OF BUN AND 100 mL WILL BE UNCHANGED
  - IN ACTUALITY, ALL 400 mL WILL HAVE A REDUCTION IN BUN OF 75%
  - THE CLEARANCE RATE REMAINS CONSTANT DURING THE TREATMENT

- CLEARANCE AS BUN REMOVED
- LET ART_{BUN} = 80 mg/dL and VEN_{BUN} = 20 mg/dL
  - 60 mg/dL is removed
  - QB = 400 mL/min = 4 dL/min
  - 60 mg/dL x 4 dL/min = 240 mg/min is removed
- THE AMOUNT OF BUN REMOVED PER MINUTE WILL DROP DURING THE TREATMENT AS THE ART_{BUN} AND VEN_{BUN} DECREASE

CLEARANCE VS. DIALYSATE FLOW



BLOOD FLOW = 400 mL/min

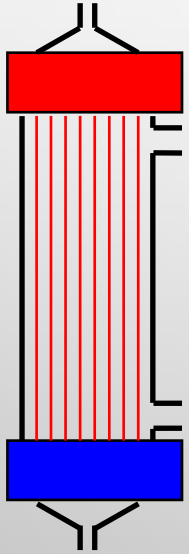
DIALYSATE FLOW = 500 mL/min

DIALYZER KoA = 945

CLEARANCE = 300 mL/min

- HOW MUCH WILL THE CLEARANCE CHANGE IF THE DIALYSATE FLOW RATE IS INCREASED TO 800 mL/min?
- A) 20%
- B) 10%
- C) 5%
- D) 0%
- E) -5%

CLEARANCE VS. DIALYSATE FLOW



BLOOD FLOW = 400 mL/min

DIALYSATE FLOW = 500 mL/min

DIALYZER KoA = 945

CLEARANCE = 300 mL/min

- THE ANSWER IS: B) 10%
- INCREASING DIALYSATE FLOW WILL INCREASE CLEARANCE
- THE CLEARANCE FORMULA IS:

$$C_X = \frac{Q_B\left(e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-1\right)}{e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-\frac{Q_B}{Q_D}}$$

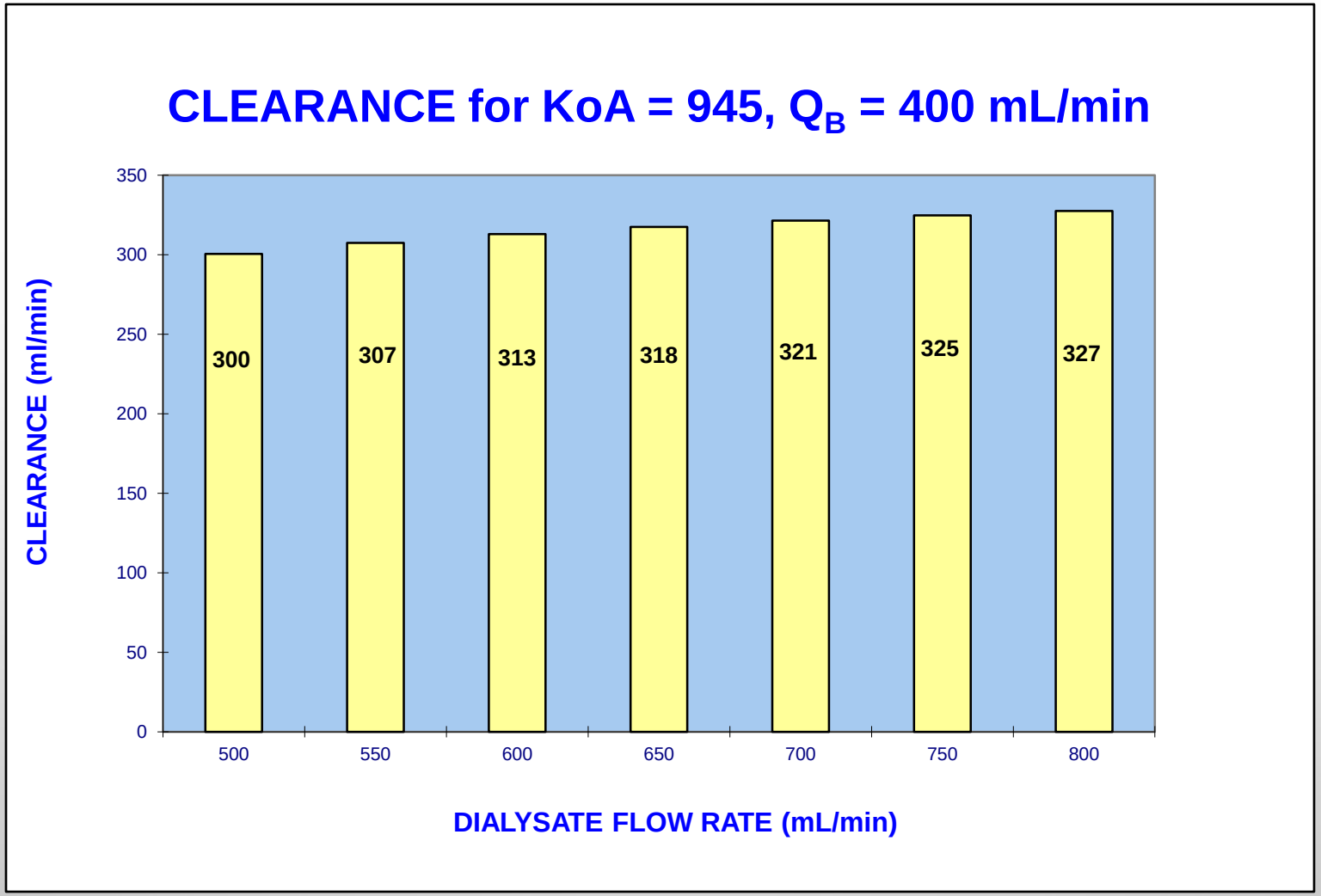
Where: C_X = Clearance of solute, X

Q_B = Blood flowrate

Q_D = Dialysate flowrate

ln = Natural logarithm = e

e = 2.718281828..


CLEARANCE for KoA = 945, Q_B = 400 mL/min
CLEARANCE (ml/min)
350
300
250
200
150
100
50
0
300
307
313
318
321
325
327
500
550
600
650
700
750
800
DIALYSATE FLOW RATE (mL/min)

NEWS BREAK: INCREASING Q_D MAY HAVE ZERO BENEFIT !

- RENAL WEEK 2010 abstract (Ward RA, et al: TH-FC038)
  - 28 patients, crossover study
  - Q_D = 600 mL/min alternating with 800 mL/min BABA ABAB
  - Q_B averaged 435 mL/min
  - Revaclear or Revaclear MAX dialyzers were used
- RESULTS:
  - 600 mL/min had Kt/V of 1.67 ± 0.04
  - 800 mL/min yielded KT/V of 1.65 ± 0.04
- Benefits of higher dialysate flow may not be true anymore, especially with today's newer dialyzers.

FINAL QUESTION !!

What did the electrician's wife say to her husband when he came home late one night ?

ANSWER

Wire Ya Insulate !

jsweeny@tampabay.rr.com

Thank you for attending. I hope you have a better "picture" of how a dialyzer works.

UREA IN BLOOD

- ASSUME A HOLLOW FIBER IS ONE FOOT LONG AND 200 MICRONS IN DIAMETER
- ITS VOLUME WOULD BE = L x πR^2 = 9.57 x 10^{-9} m^3 = 9.57 x 10^{-6} LITER
- AMOUNT OF BUN = 80 mg/dL = 800 mg/L = 0.8 g/L
- UREA"S GRAM MOLECULAR WEIGHT IS 60. BUN WEIGHT is 28
- NUMBER OF ATOMS PER LITER = (60/28) x (0.8 g/L)/60 x (6.023 x 10^{23}) = 1.71 x 10^{22} ATOMS/L
- UREAS/FIBER = 1.71 x 10^{22} ATOMS/L x 9.57 x 10^{-6} L = 16.3 x 10^{16} = E) 163 QUADRILLION ATOMS

THE VELOCITY OF UREA IS DIRECTLY PROPORTIONAL TO IT'S ENERGY

- ENERGY (E) RELATES TO SPEED BY THE FOLLOWING EQUATION:

$$E = \frac{mv^2}{2} = \frac{3K_BK}{2} \rightarrow \quad v = \sqrt{\frac{3K_BK}{m}}$$

- WHERE:
  - m = mass of urea molecule = 9.963×10^{-26} kg
  - K_B = Boltzmann's constant = 1.3805×10^{-23} J/K
  - K = Degrees Kelvin = 310 (37^oC)
  - V = velocity in m/s
- THE UREA VELOCITY IS: 359 m/s (WATER MOLECULES = 590 m/s)
- THE ANSWER IS: C) THE SPEED OF A BULLET

UREA COLLISIONS

- THE DISTANCE A PARTICLE TRAVELS WITHOUT COLLIDING WITH ANOTHER PARTICLE IS CALLED A "MEAN FREE PATH".
- FOR WATER AT ROOM TEMPERATURE, THIS DISTANCE IS ONLY 10^{-11} METER!
- THE NUMBER OF MEAN FREE PATHS COVERED BY UREA IN ONE SECOND WOULD BE:
  - 359.3 METERS/10^{-11} METER = 3.593 X 10^{13} = 36 TRILLION MEAN FREE PATHS
- SINCE EACH MEAN FREE PATH ENDS WITH A COLLISION, THEN THE NUMBER OF COLLISIONS WILL ALSO BE 36 TRILLION/SECOND (ANSWER E)