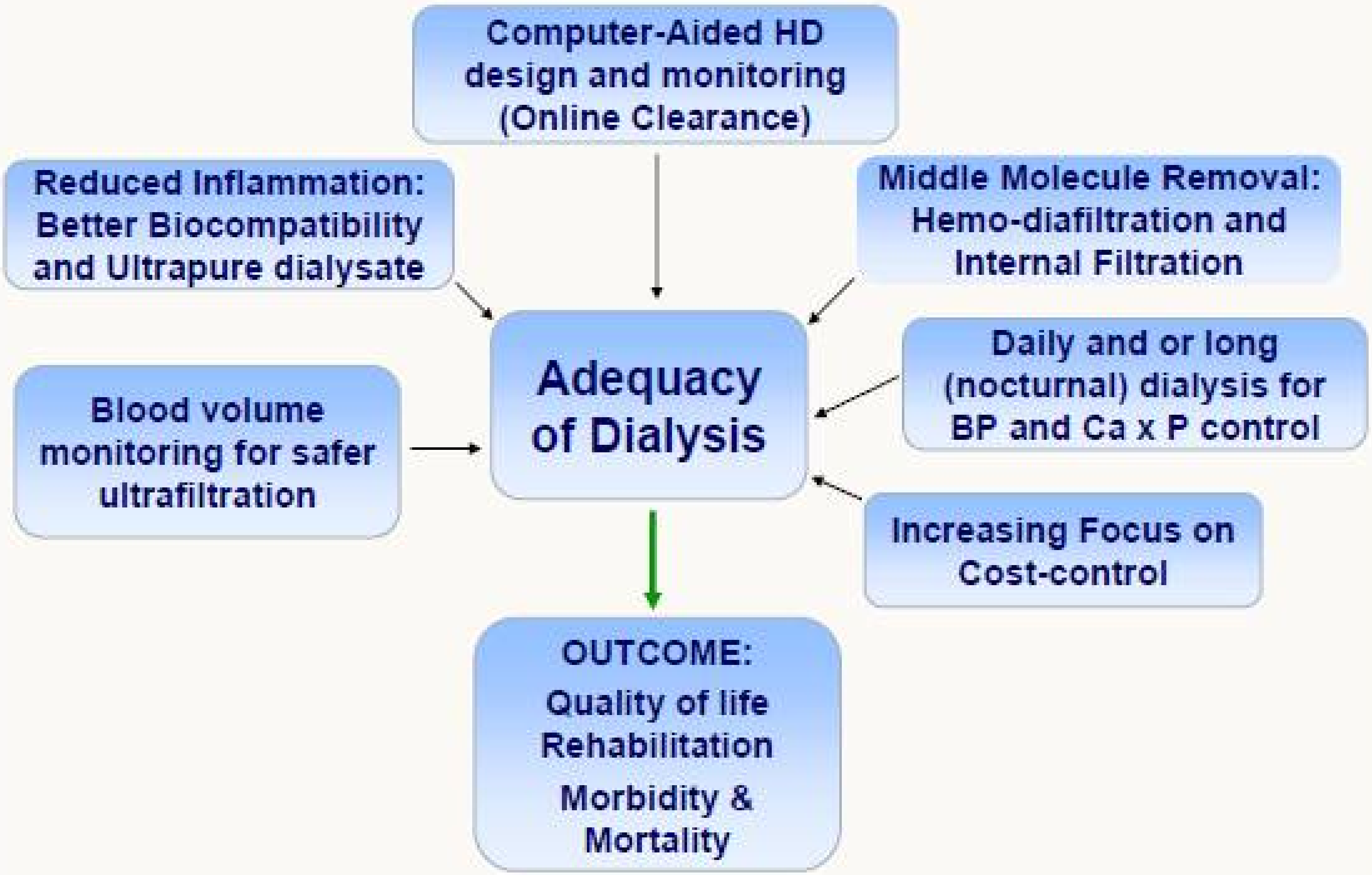
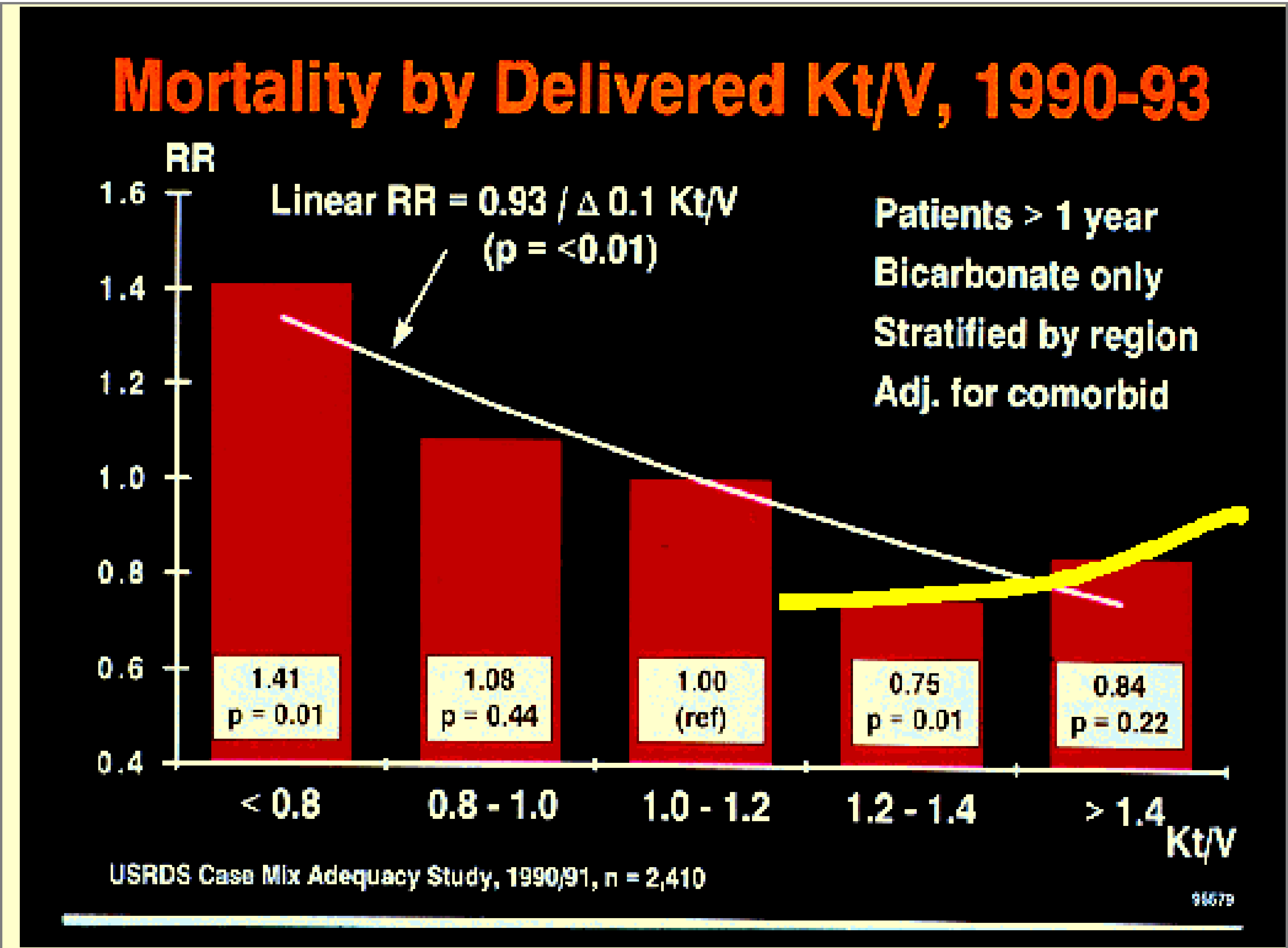
HEMODIALYSIS ADEQUACY

Dialysis Adequacy is very important.

- Urea clearance in a person is about 130cc/min.
- Urea clearance is 200 L /24h
- 60% of Body weight in everyone contain of water, so the 70 kg person has 40 Lit fluid.
- Daily adequacy in a normal person is(200/40) = 5.
- In everyday, all of body fluid cleared from urea 5 period.
- Weekly adequacy in a normal person is(7×5)=35.
- In A renal failure person who dialysis 3 times in a weak, his adequacy must be 1.2 at least.
- Weekly adequacy with 3 times dialysis is(3×1.2)=3.6, it is about 1/10 or 10%of normal kidney.

Adequacy 2000 – into the future





Mortality by Delivered Kt/V, 1990-93
RR
1.6
1.4
1.2
1.0
0.8
0.6
0.4
Linear RR = 0.93 / Δ 0.1 Kt/V
(p = <0.01)
Patients > 1 year
Bicarbonate only
Stratified by region
Adj. for comorbid
1.41
p = 0.01
1.08
p = 0.44
1.00
(ref)
0.75
p = 0.01
0.84
p = 0.22
< 0.8
0.8 - 1.0
1.0 - 1.2
1.2 - 1.4
> 1.4
Kt/V
USRDS Case Mix Adequacy Study, 1990/91, n = 2,410

Dialysis dose and treatment

Why do we need dialysis today?

- **to increase life expectancy…**
- **to reduce hospitalization…**
- **to increase quality of life…**
- **to increase well-being …**

Dialysis dose and treatment

Clinical parameters of a “good dialysis“

- **patient is in a good shape and has a healthy appetite**
- **blood pressure is controlled**
- **stable lean body mass (serum albumin)**
- **good fluid balance**
- **lack of uremic symptoms**
- **control of laboratory parameters**

Dialysis dose and treatment

General recommendations

Europe:(ERA/EDTAGuidelins)

Hemoglobine > 11 g/dl

Treatment time ≥ 4 hours

Frequency at least 3 sessions per week

eKt/V ≥ 1,2 per HD-therapy (spKt/V 1,4)

Kt/V Basics

Quantification of dialysis

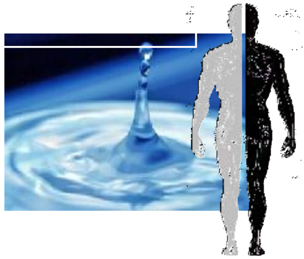
What is Kt/V?

Treatment time (t)

Clearance (K)

Kt/V

Urea distribution volume (V)



Example:

$$Kt/V = \frac{245 \text{ ml/min} * 300 \text{ min}}{54.000 \text{ ml}} = 1{,}36$$

URR

- URR stands for urea reduction ratio.
- The URR is one measure of how effectively a dialysis treatment removed waste products from the body
- expressed as a percentage.
- Blood is sampled at the start of dialysis and at the end. The levels of urea in the two blood samples are then compared

$$URR = (C_0 - C)/C_0$$

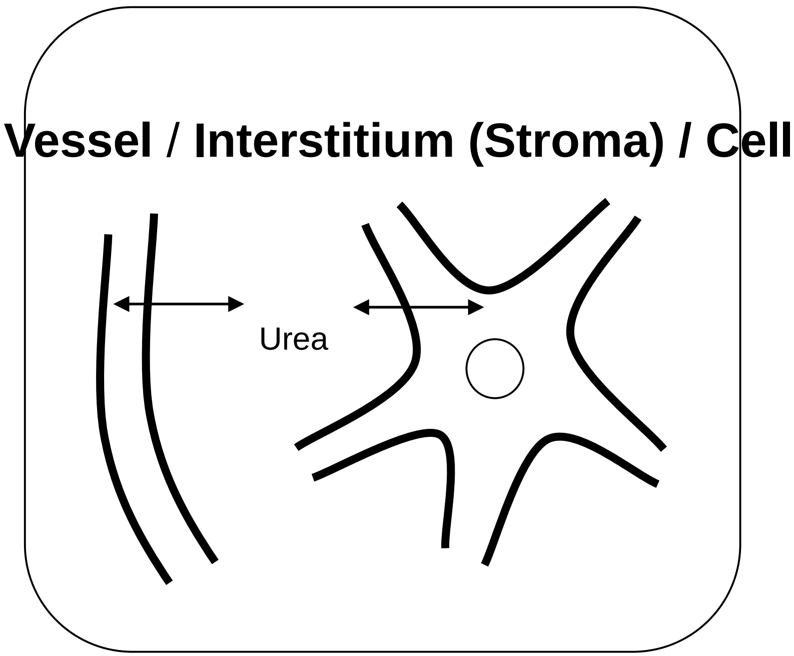
Example:

- If the initial, or predialysis, urea level was 50 (mg/dL)
- the postdialysisurea level was 15 mg/dL
- The amount of urea removed was:50 mg/dL-15 mg/dL= 35 mg/dL
- The amount of urea removed (35 mg/dL) is expressed as a percentage of the predialysisurea level (50 mg/dL).
- 35/50 = 70/100 = 70%

Kt/V Basics

Quantification of dialysis

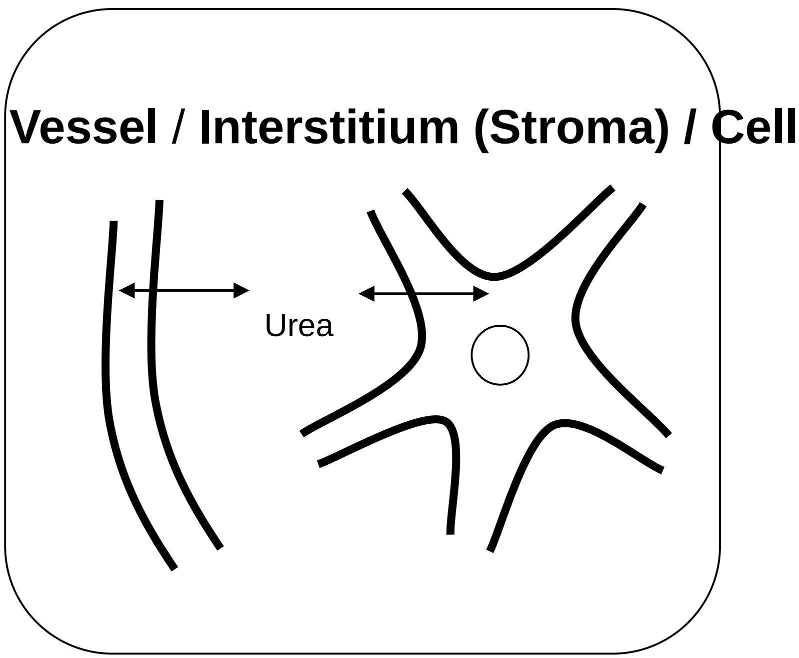
Dose calculation - background I



Single-pool model:
Ultrafiltration and urea generation are considered.

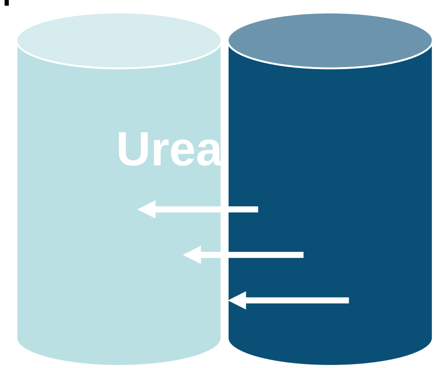
- Assumption that the body is 1 compartment

Dose calculation - background II



Double-pool model:

- Assumption that there are 2 compartments



- Rebound is taken into consideration
- (eKt/V is lower than spKt/V)

Kt/V Basics

Quantification of dialysis

Urea reduction rate [URR] $= \left(1 - \frac{C_t}{C_0}\right) \cdot 100\ (\%)$

- Most simple formula for calculating the dialysis dose

Kt/V $C_t = C_0 * e^{-\frac{K*t}{V}} = \frac{K \cdot t}{V} = -\ln\left(\frac{C_t}{C_0}\right)$

- Is used in the daily routine on the basis of the urea concentration pre and post HD

single-pool-Kt/V $= -\ln(R - 0{,}008 \cdot T) + (4 - 3{,}5 \cdot R) \cdot \frac{UF}{W}$

- Ultrafiltration and urea generation during dialysis are considered

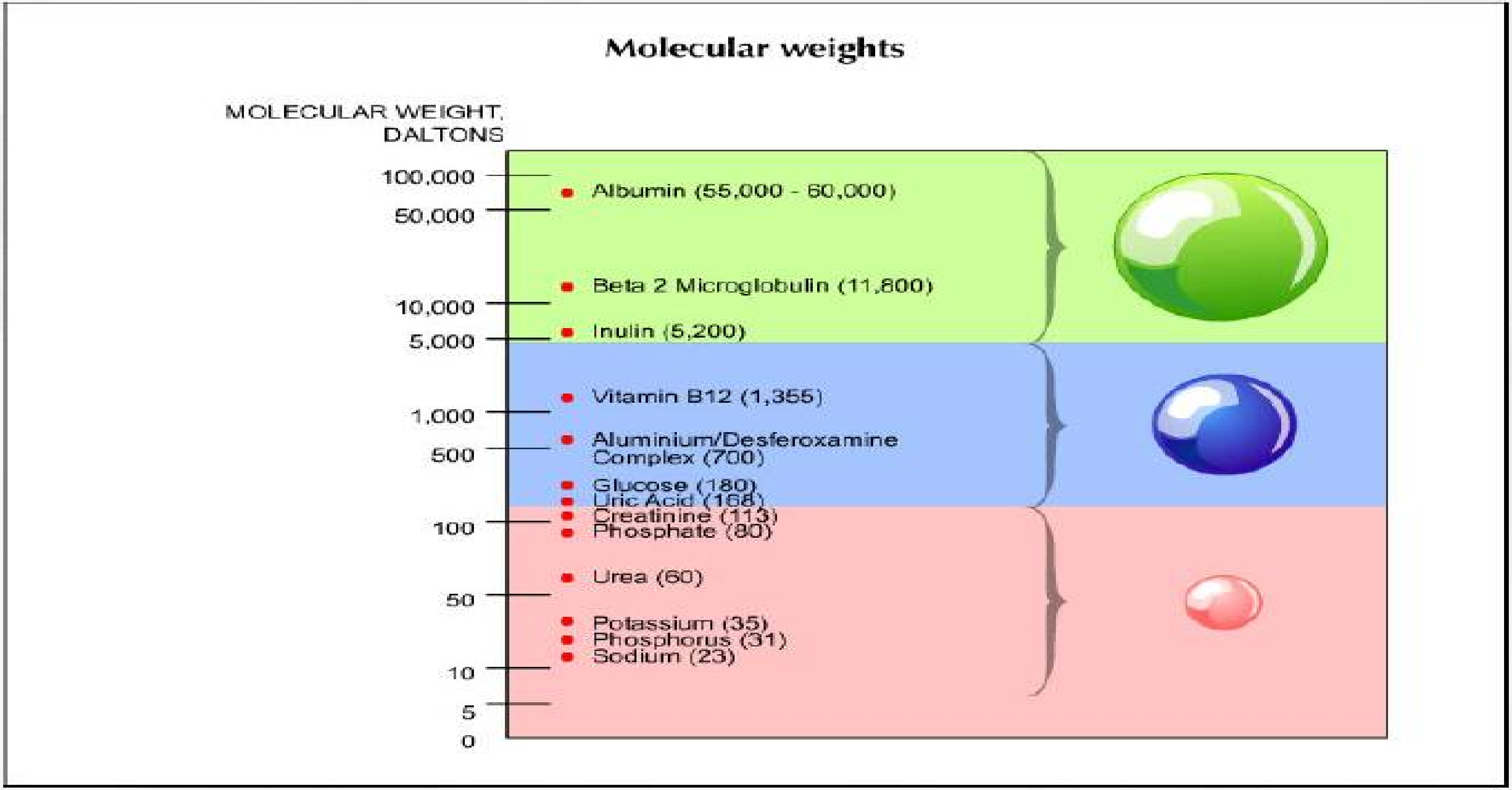
equilibrated-Kt/V [eKt/V] $= spKt/V - \frac{0{,}6}{T} \cdot spKt/V + 0{,}03$

- Urea rebound after dialysis is taken into account

TABLE 2. CATEGORIZATION OF SMALL, MIDDLE, AND LARGE MOLECULES [14]

CLASSIFICATION OF SOLUTES	MOLECULAR WEIGHT RANGE (DALTONS)
Small molecules urea (60), creatinine (113), phosphate (134)	<500
Middle molecules vitamin B12 (1355), vancomycin (1448), insulin (5200), endotoxin fragments (1000-15000), Parathromone (9425), β_2-microgobulin (11818)	500-15000
Large molecules myoglobin (17000), Retinol-Binding Protein (RBP) (21000), EPO (34000), albumin (66000), Transferrin (9000)	>15000

Adapted from Azar AT, Canaud B. Chapter 8: Hemodialysis system. In: Azar T, ed. Modelling and Control of Dialysis Systems. SCI 404. Berlin: Springer-Verlag; 2013.



Small molecules	< 300 daltons, e.g., urea, creatinine, Na+
Intermediate molecules	500 - 5,000 daltons, e.g., B12
Large molecules	5,000 - 50,000 daltons, e.g., LMW proteins - beta 2 microglobulins, cytokines, myoglobin

Improving Adequacy of Hemodialysis

It's About Life!

- *It Takes a Team*

What is Adequacy of Hemodialysis ?

- Adequacy of dialysis refers to how well we remove toxins and waste products from the patient's blood, and has a major impact on their well-being
- When we dialyze a patient, we filter out toxic particles that can affect every organ of their body

Urea and *Kt/V*

- The urea is the smallest uremic toxin (*MW* = 60 *d*)
- His measurement is easy and fast
- It is the biochemical parameter most famous in uremia
- It has a big diffusibility through natural and artificial membranes
- Its distribution volume is the same of the plasmatic water

- ***Urea is not the most important clinical marker in uremic patient***

How Do We Know if a Patient is Adequately Dialyzed?

- **Blood samples are drawn before and after the treatment. The results are compared….this is called the pre and post BUN.**

What Does This Mean?

- **URR% - Urea Reduction Ratio tells us the percentage of urea removed during the treatment**
- **KT/V - Formula utilizing dialyzer urea clearance treatment time and total body fluid.**

***K/DOQI Guidelines* Define Adequacy Dialysis as:**

- **KT/V = 1.2 or greater**
- **URR = 65% or greater**

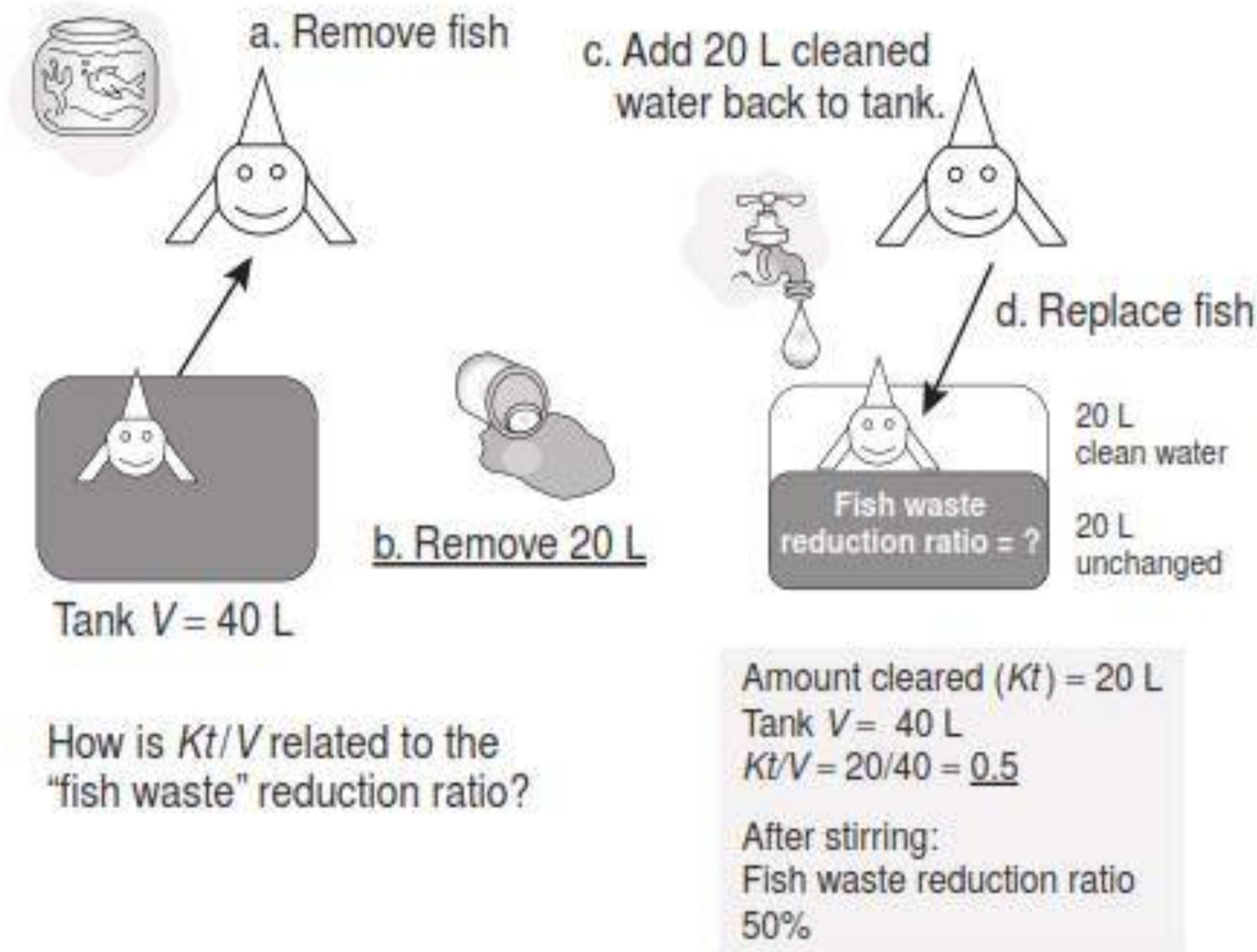


FIGURE 3.7 Fractional clearance of 50% ($Kt/V = 0.5$) in a fish tank model with the fish removed during cleaning. Note the fish waste reduction ratio is 50%, equal to the Kt/V.

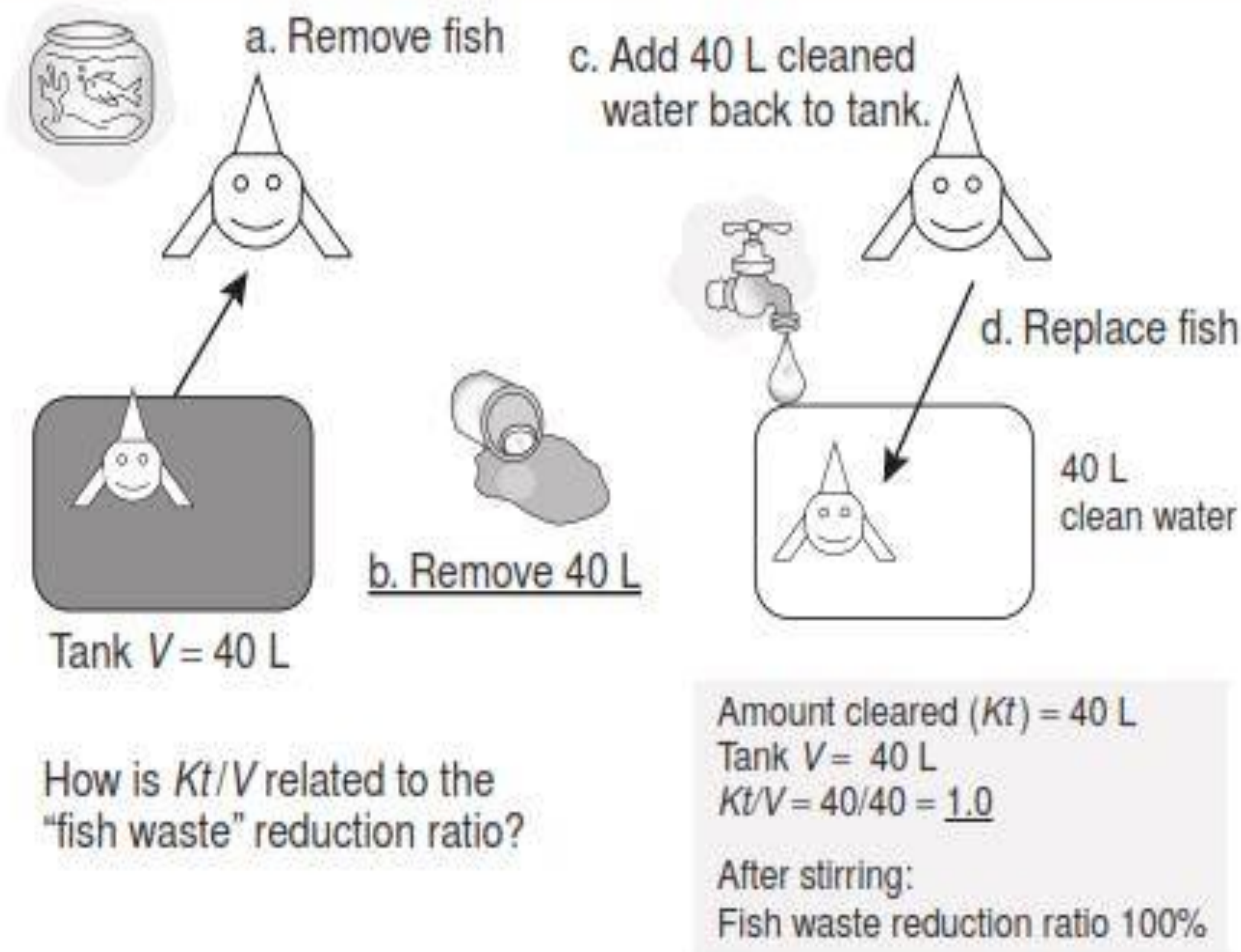


FIGURE 3.8 Fractional clearance of 100% ($Kt/V = 1.0$) in a fish tank model with the fish removed during cleaning. The fish waste reduction ratio is 100%, equal to the Kt/V.

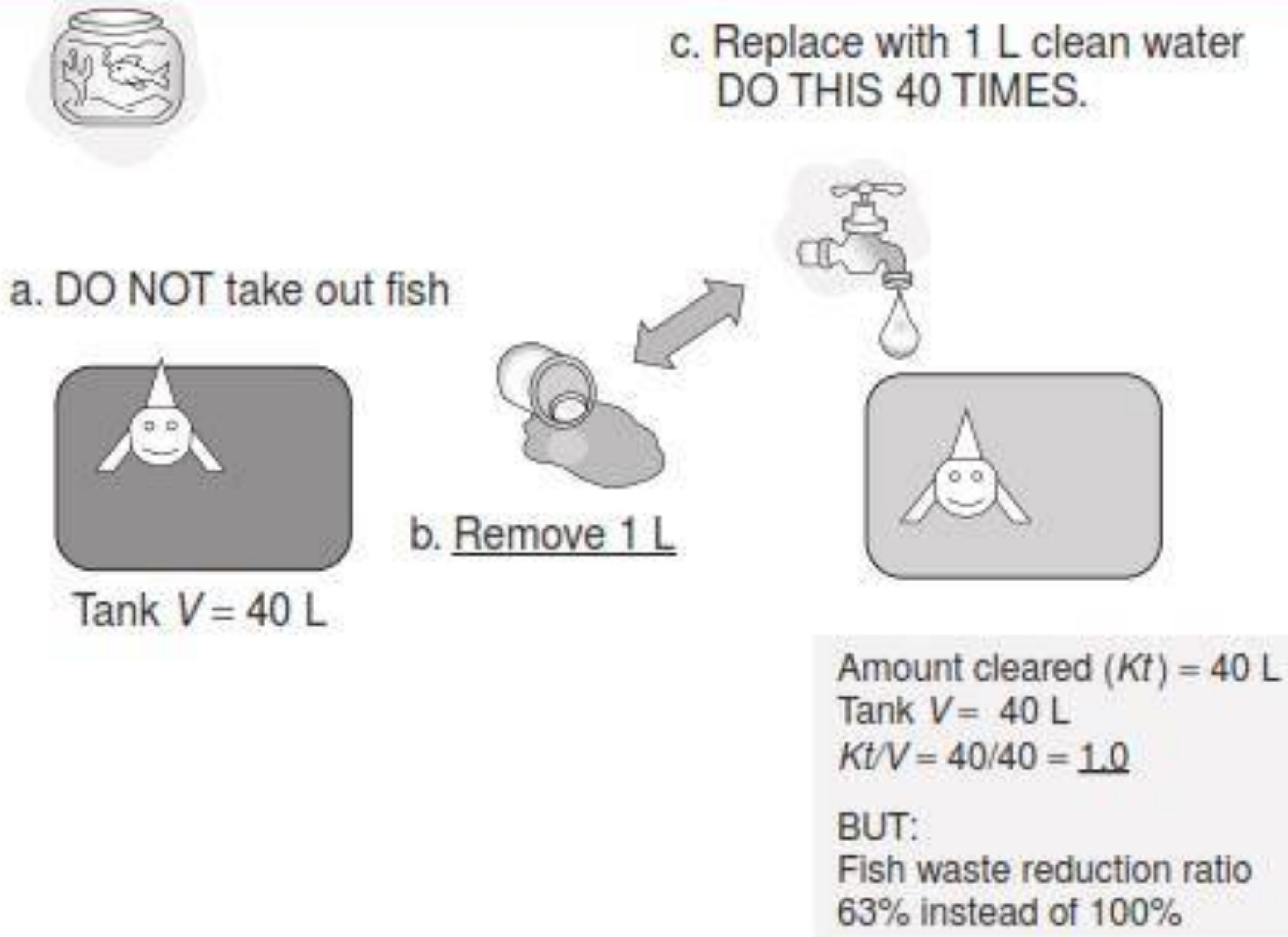
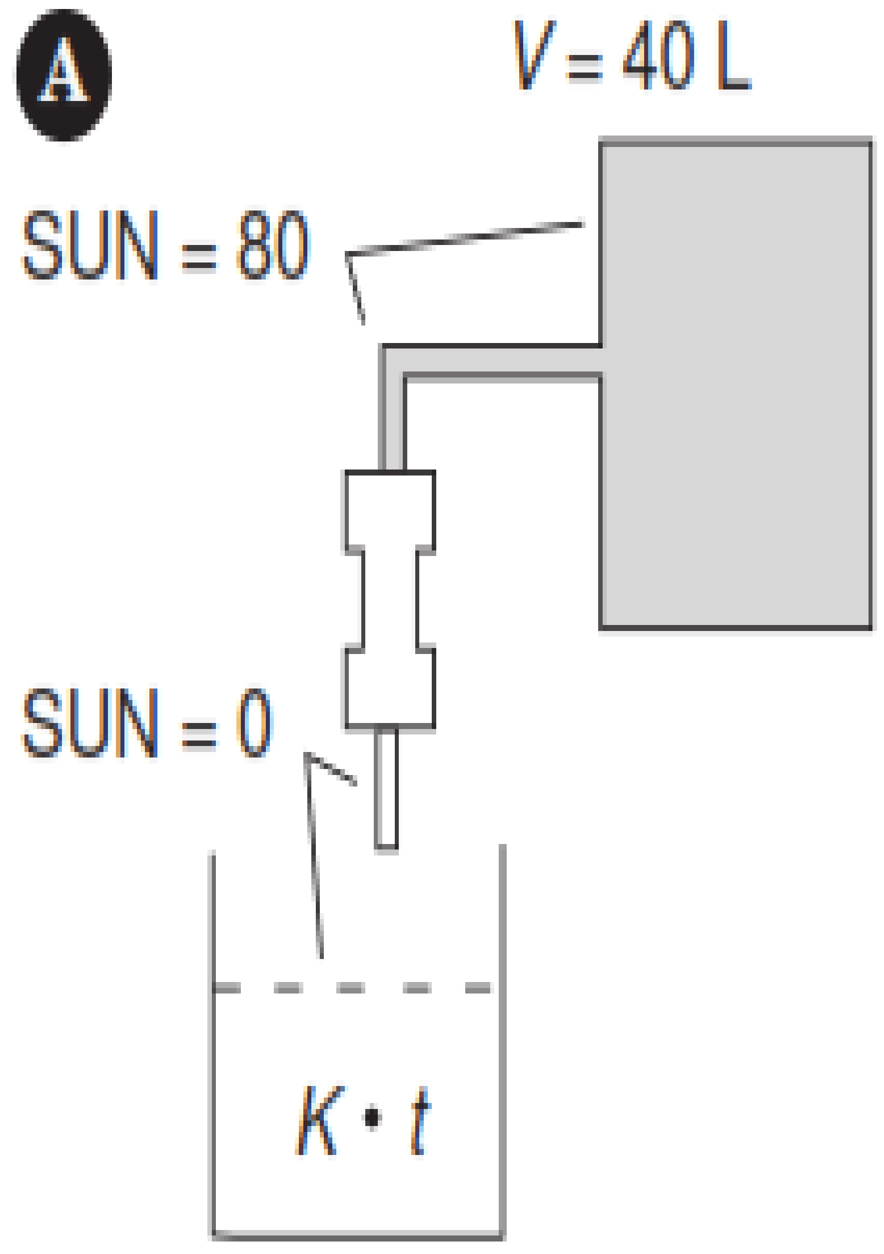
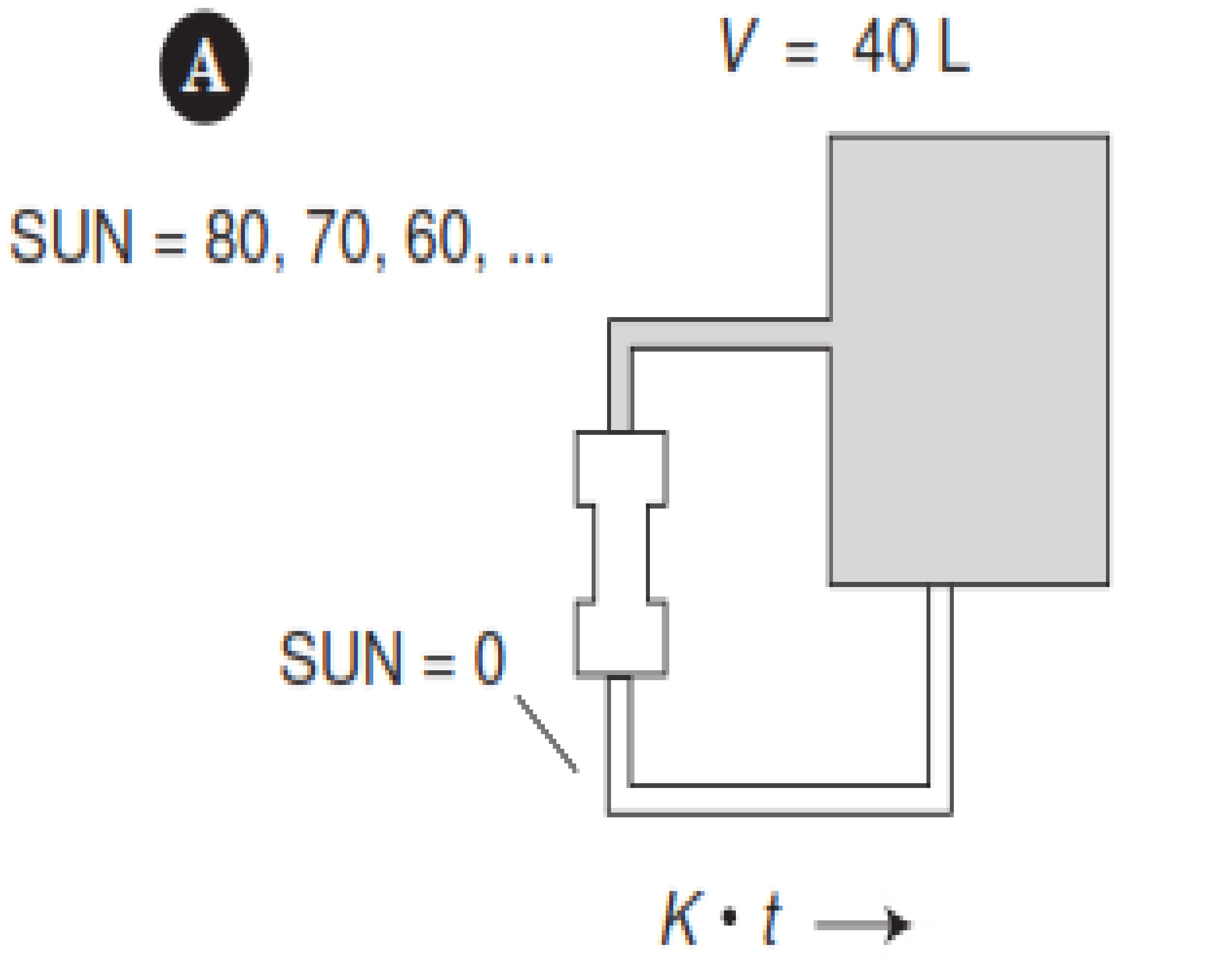


FIGURE 3.9 Fractional clearance of 100% ($Kt/V = 1.0$) in a fish tank model with the fish left in place during tank cleaning. In this situation, the fish waste reduction ratio is only 63%.


A
V = 40 L
SUN = 80
SUN = 0
K • t


A
V = 40 L
SUN = 80, 70, 60, ...
SUN = 0
K • t

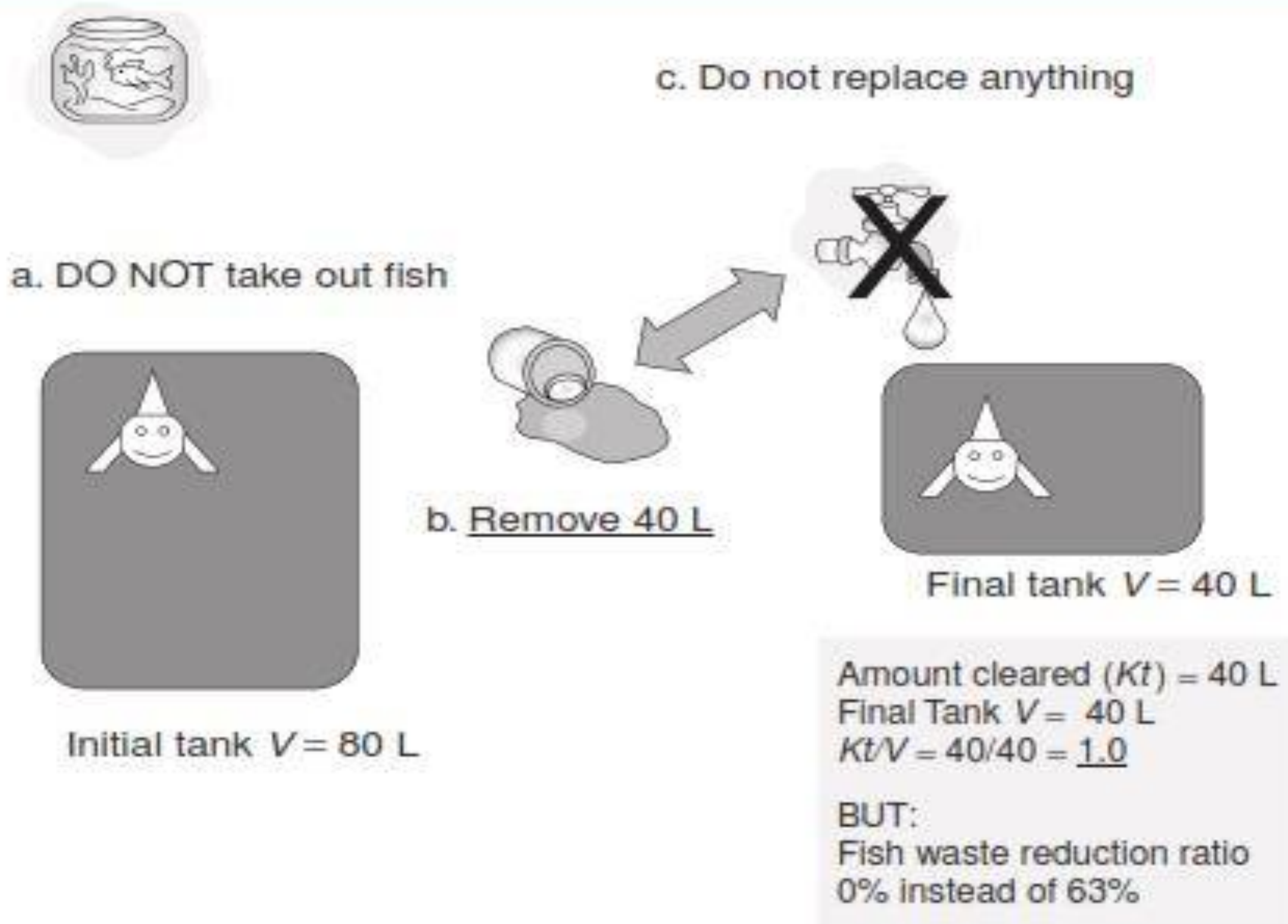


FIGURE 3.13 Effect of volume reduction on the relation between Kt/V and URR. Urea (or fish waste) removed in the process of volume contraction will not be reflected in the URR. Kt/V is calculated based on the postdialysis value for V.

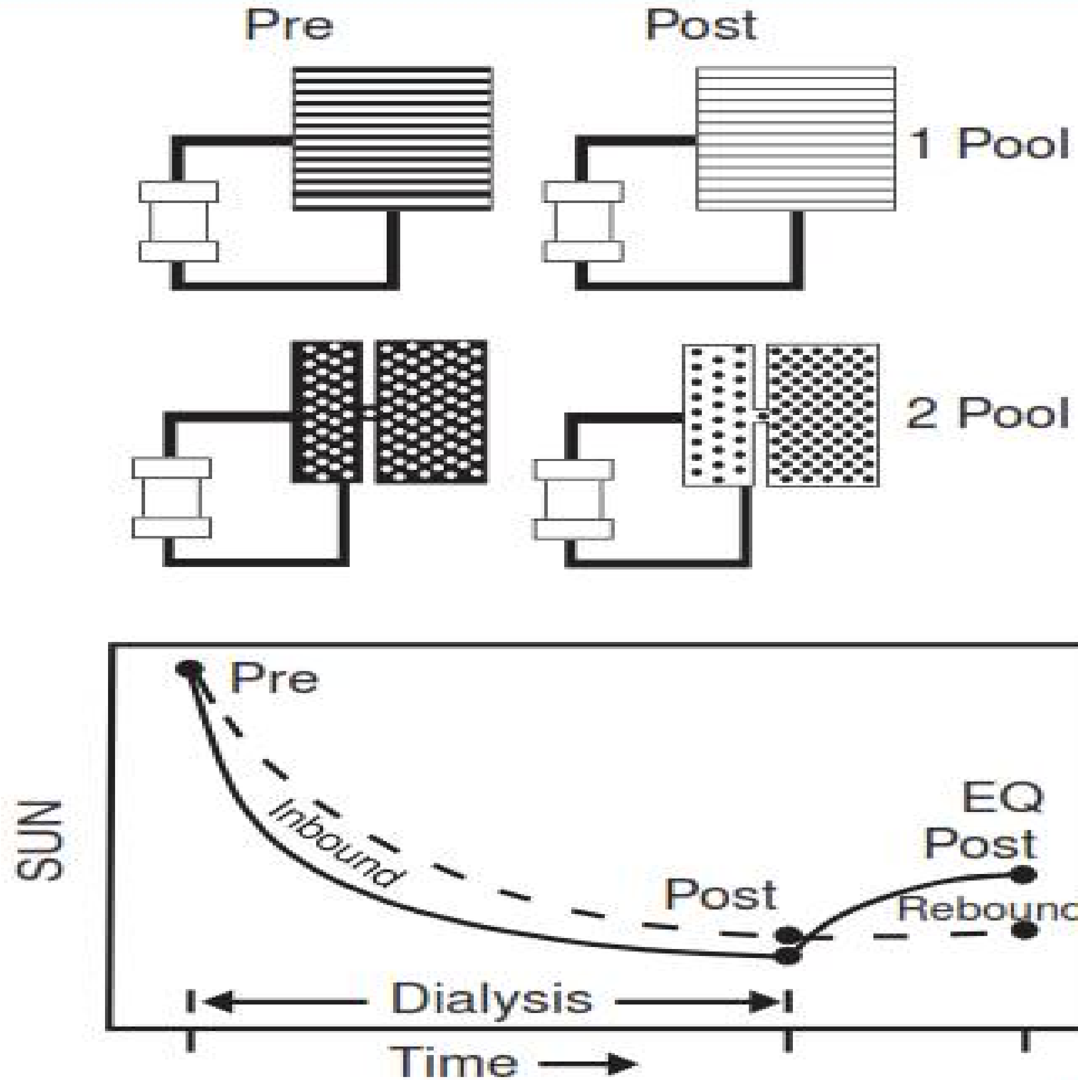


FIGURE 3.15 The effects of urea sequestration on the intradialytic fall in SUN (urea inbound) and the postdialysis increase in SUN (rebound). When there is sequestration, the intradialytic SUN level falls more quickly than expected (inbound) due to initial removal from a smaller apparent space. However, after dialysis is complete, continued entry of urea from the sequestered space to the proximal space causes urea rebound to occur. (Reproduced from Daugirdas JT. Urea kinetic modeling. *Hypertens Dial Clin Nephrol*. Available at: http://www.hdcn.com.)

Kt/V

- Gotchlater used a mechanistic analysis of these data and showed that the Kt/V of urea was an important measure of clinical outcome

- The Kt/V is mathematically related to the URR and is in fact derived from it, except that the Kt/V also takes into account extra urea removed during dialysis along with excess fluid so the Kt/V is more accurate than the URR , primarily because the Kt/V also considers the amount of urea removed with excess fluid.

- Consider two patients with the same URR and the same postdialysis weight, one with a weight loss of 1 kg during the treatment and the other with a weight loss of 3 kg. compare URR to Kt/v

The patient who loses 3 kg will have a higher Kt/V, even though both have the same URR

What are the Symptoms of Inadequate Treatment?

- **Weakness, Tiredness**
- **Loss of Body Weight**
- **Poor Appetite**
- **Nausea / Vomiting**
- **Feeling Better after Treatment**
- **Yellowish Skin Color**
- **More Infections**
- **Prolonged Bleeding**
- **Premature Death**
- **Under-Dialyzed Patients May Expire**

Hemodialysis Prescription Determines Adequacy

Hemodialysis Prescription Components:

- **Duration of Treatment**
- **Dialyzer Urea Clearance (KOA)**
- **Blood Pump Speed**
- **Dialysate Flow Rate**
- **Heparinization**
- **Access**

Duration of Treatment

- **The longer a patient dialyzes, the more blood flows through the dialyzer, allowing for more cleaning to take place…**

- ***Every Minute Counts!***

- ***Encourage Your Patients to Complete the Entire Treatment Time!***

Blood Pump Speed

- **Also known as Blood Flow Rate…Speed of the blood going through the dialyzer membrane for urea removal.**
- **The more blood passing through the dialyzer during the treatment…the *More Urea Removed*.**
- ***Verify the Blood Pump Speed***
- ***Matches the Dialysis Prescription!***
- ***Patient Should Maintain Prescribe Blood Flow Rate Throughout Dialysis Treatment!***

Dialysate Flow Rate

- The Speed which the Dialysate Flows through the Dialyzer.
- The **Faster the Dialysate Flows through the Dialyzer ….the *More Urea is Removed***. Dialysate flow rate DFR (800 ml/min –increase urea clearance by about 5%-8% -efficiency dialyzer –blood flow rate 350 ml/min) - dialysate flow rate 1.5-2 times blood flow rate
- *Verify Correct Dialysate Flow Setting!*

Heparinization

- Keeps the blood from clotting, and blocking the fibers. This allows the blood to flow freely through the fibers of the membrane, and urea can be removed.
- Adequate Heparinization will Prevent Fiber Clotting and*… More Urea is Removed!*
- *Ensure Correct Heparin Dose is Administered!*
- *Monitor Lines and Dialyzer for ClottingThroughout Treatment!*

•Vascular Access

What Can You Do To Improve Vascular Access Function?

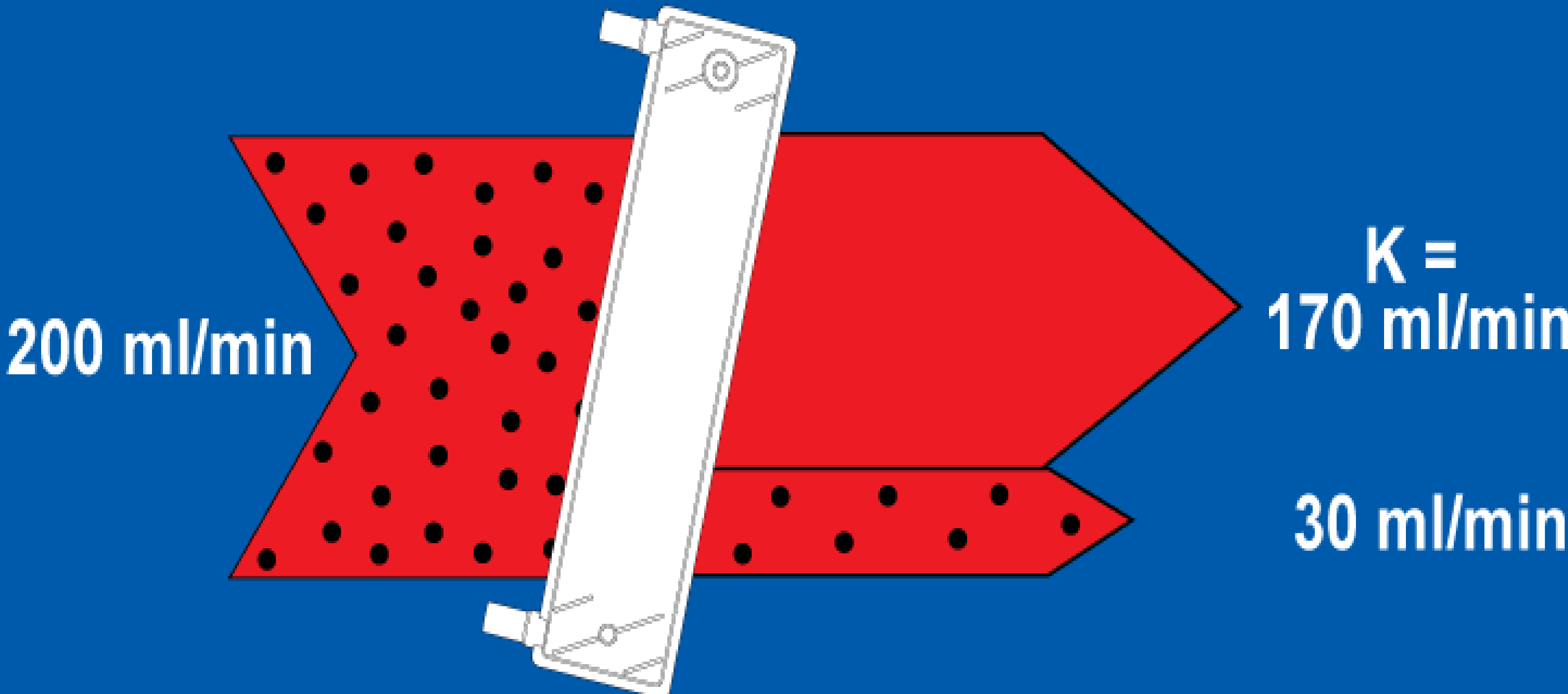
- AV Fistula is the Preferred Access
- Adequate dialysis depends on having a vascular access that works well
- Poorly functioning access causes inadequate dialysis and can lead to *premature death*
- *Become Proficient in Proper Access Cannulation*
- *Notify Physician if Access has Poor Flow and Request Surgical Evaluation of Access*
- *Thorough Access Assessment Every Treatment*
- *Monitor Arterial Pressure for Signs of Inadequate Flow (Negative pressure > -250)*
- *Monitor Venous Pressure for Signs of Excessive Pressure (Venous Pressure > ½ of Blood Flow Rate)*
- *Prompt Physician Notification of Access Problems*

Dialyzer Clearance

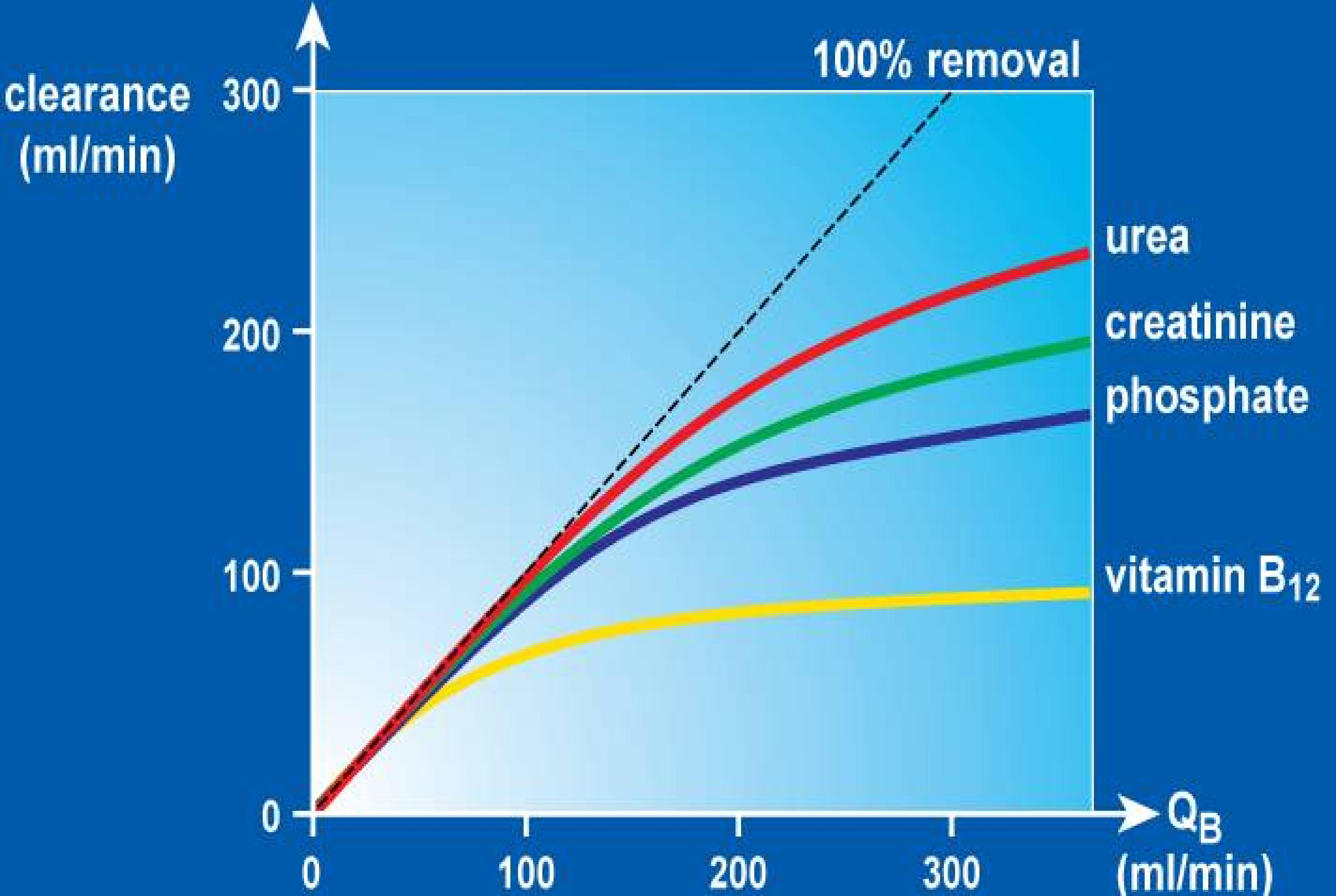
- Clearance (k) specification for dialyzers indicate the amount of a specific solute will be “cleared” from the patients blood in a given amount of time.

- For example, if the specs say a dialyzer has a clearance of 350 ml/min at a Qb of 400 ml/min, it means that in one minute 350 ml’s of blood will be cleared of urea, and the remaining 50 ml/min will have the same amount of urea that is started with

Dialyzer Clearance



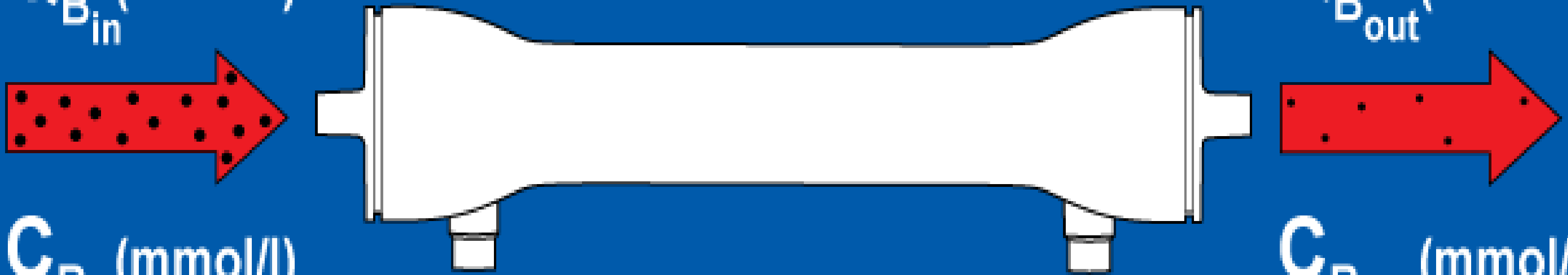
Clearance vs Blood Flow Rate



Clearance Calculation

$Q_{B_{in}}$ (ml/min)

$C_{B_{in}}$ (mmol/l)

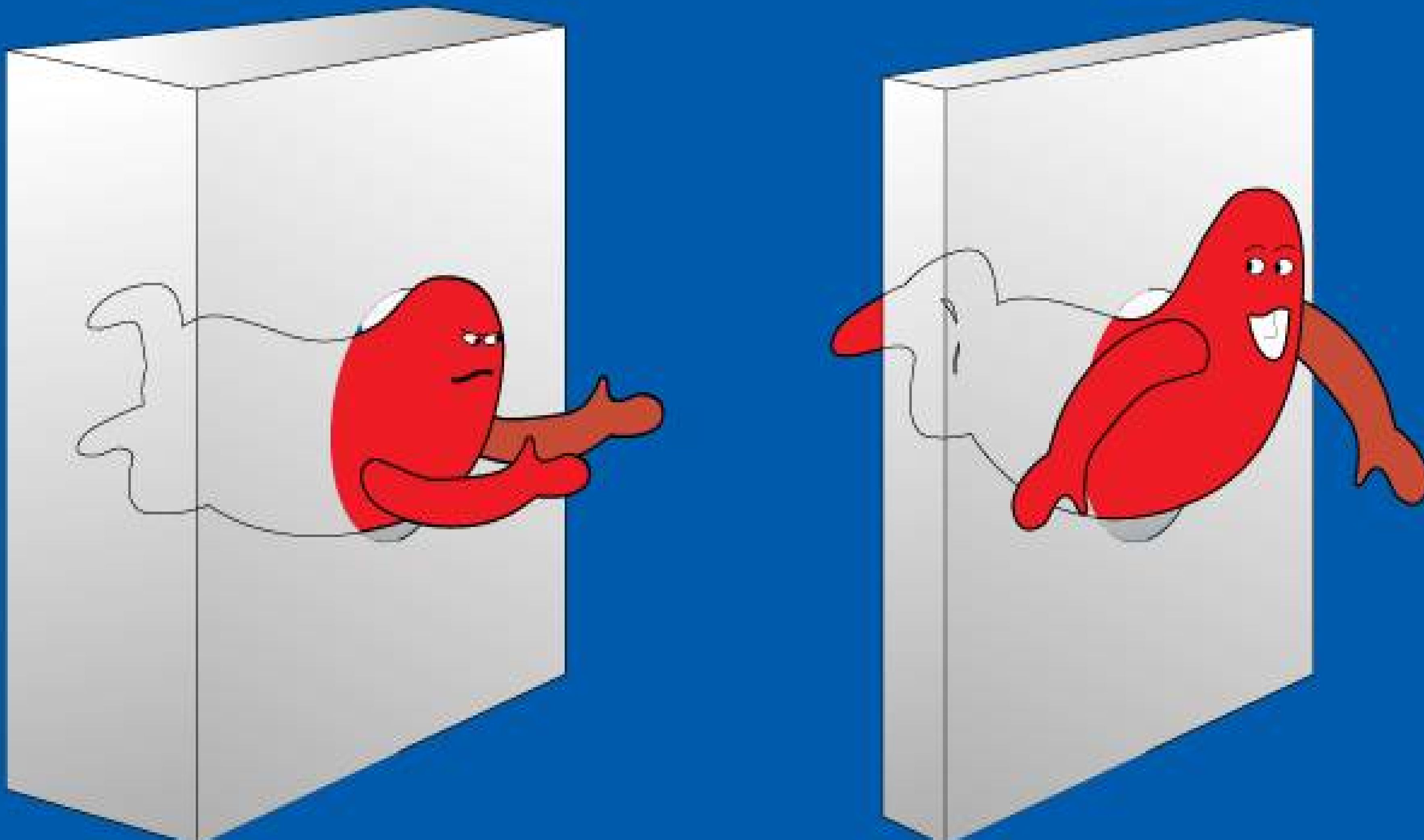


$Q_{B_{out}}$ (ml/min)

$C_{B_{out}}$ (mmol/l)

$$K = \frac{Q_{B_{in}} \times C_{B_{in}} - Q_{B_{out}} \times C_{B_{out}}}{C_{B_{in}}} \text{ (ml/min)}$$

Membrane Thickness



Mass transfer area coefficient (*K0A*):

The *K*0*A* is the **maximum theoretical clearance** of the dialyzer in **milliliters per minute** for a given solute at **infinite blood and dialysis solution flow rates**.

Dialyzers with ***K*0*A* urea values <500** should only be used for “**low-efficiency**” dialysis or for small patients.

Dialyzers with ***K*0*A* values of 500–800** represent **moderate-efficiency** dialyzers, useful for routine therapy.

Dialyzers with ***K*0*A* values >800** are used for “**high-efficiency**”dialysis, although this is a relative term; **many modern dialyzers** used routinely today have **in vitro *K*0*A* values of 1,200–1,600 mL/min**.

- **Page 79,John T. Daugirdas, Peter G. Blake, Todd S. Ing. Handbook of Dialysis FIFTH Edition 2015**

Dialyzer classification by **efficiency**

"low-efficiency" dialysis

K0A urea values <500

- F4= 365
- F5 = 475
- PES10 = 518

moderate-efficiency dialyzers

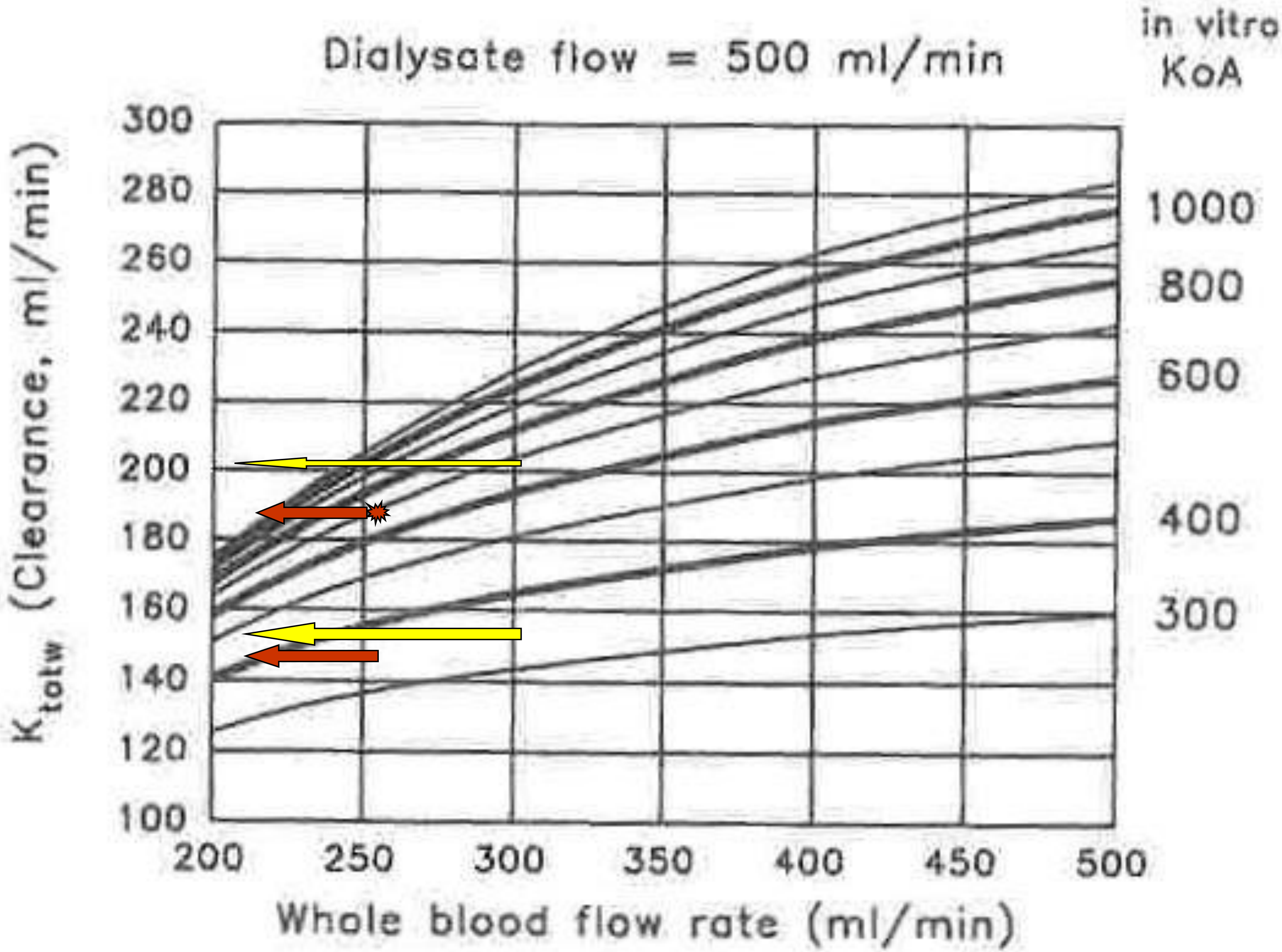
K0A values of 500–800

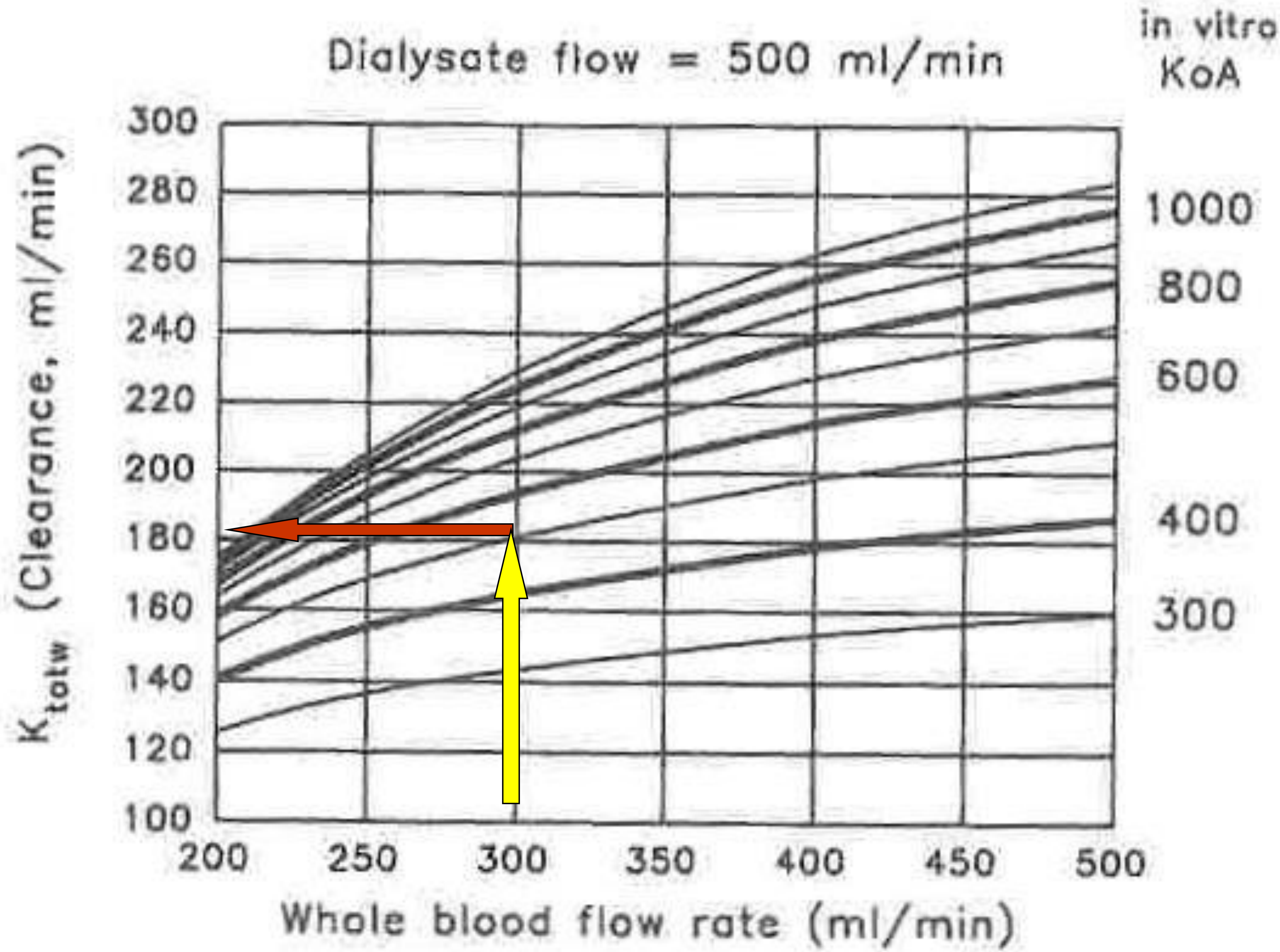
- F6 = 578
- F7 = 677
- F8 = 726
- F60 = 736
- PS10 = 637
- Ps13 = 746
- PES13 = 629
- PES16 = 757

"high-efficiency"dialysis

K0A values >800

- PS16 = 1064
- PS160 =1145
- PES160 =1167
- PS18 =1292
- PES18 =1123
- PS180 = 1265
- PES180 = 1321
- F80 = 911
- F70 = 839


Dialysate flow = 500 ml/min
in vitro
KoA
1000
800
600
400
300
K_{totw} (Clearance, ml/min)
300
280
260
240
220
200
180
160
140
120
100
200
250
300
350
400
450
500
Whole blood flow rate (ml/min)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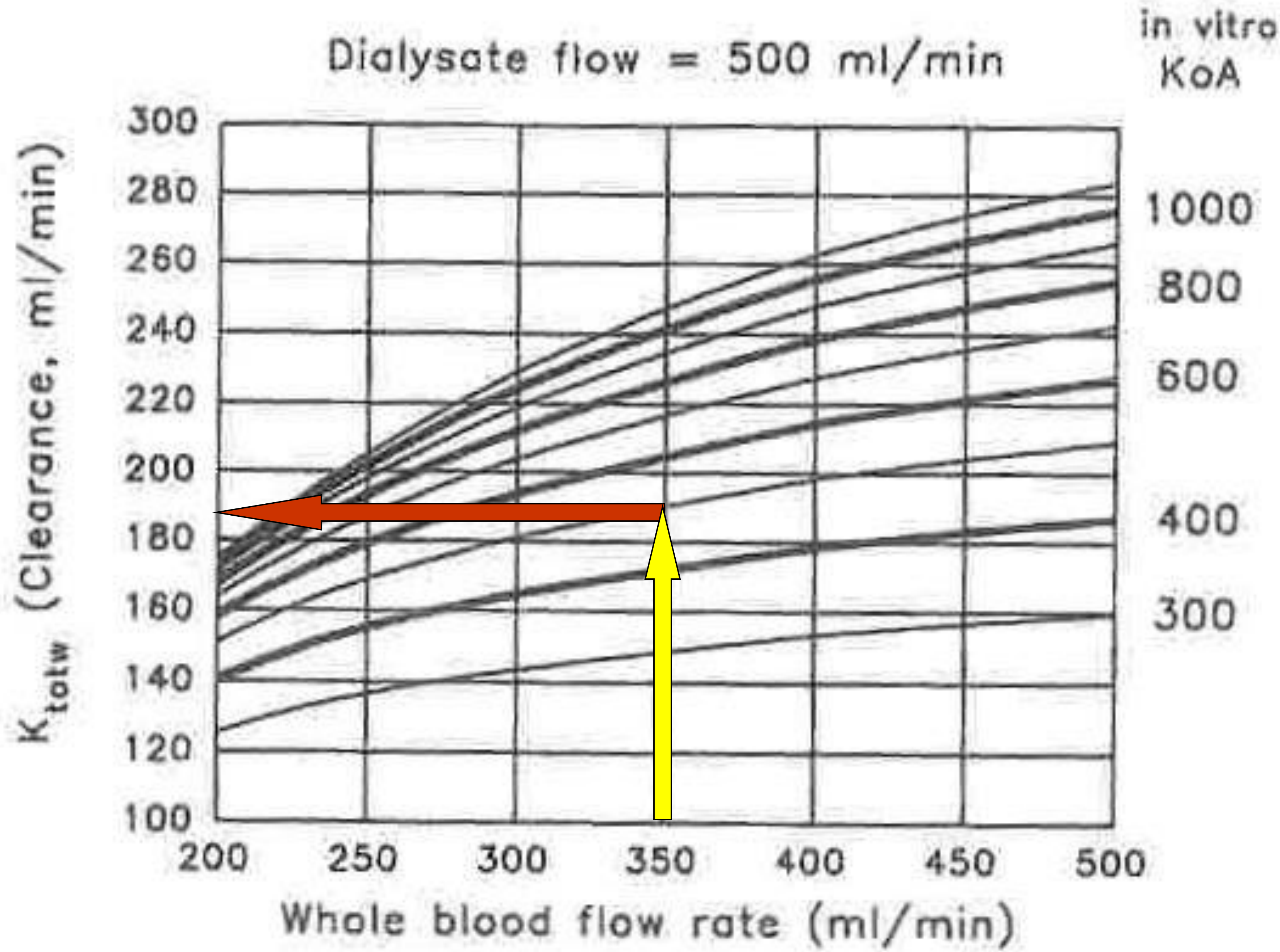
Whole blood flow rate (ml/min)



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in vitro KoA
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800
600
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K_{totw} (Clearance, ml/min)
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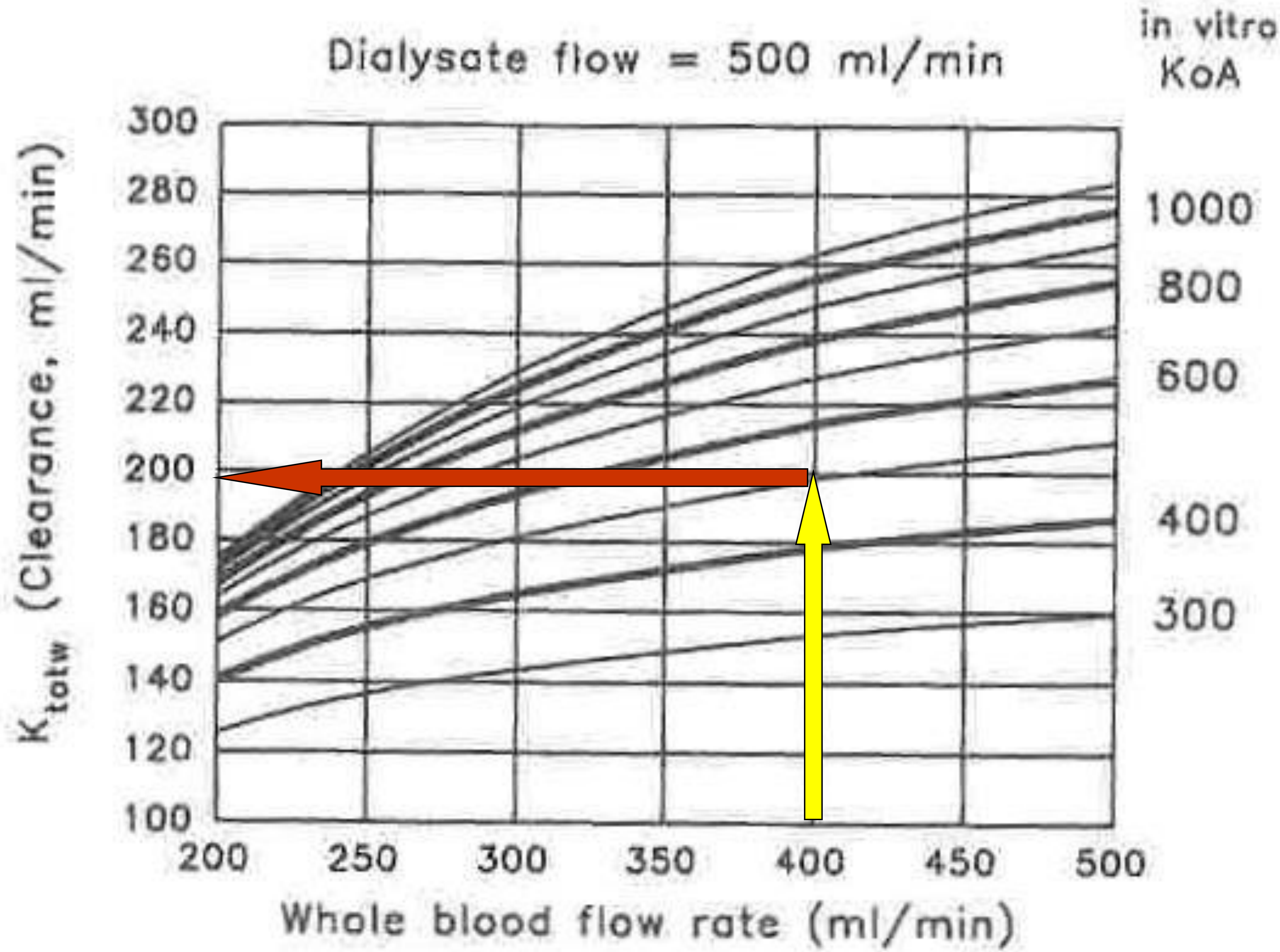
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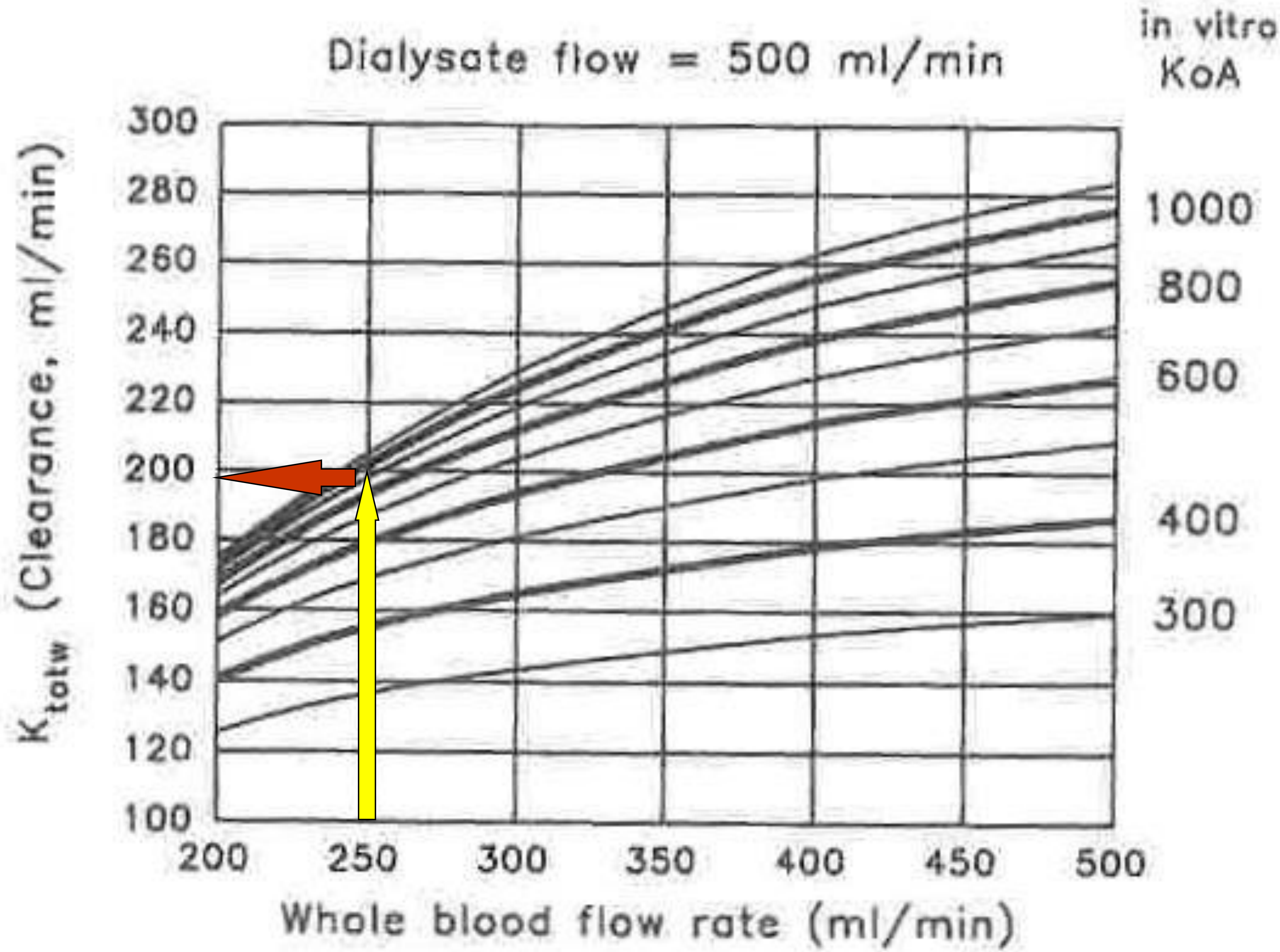
Whole blood flow rate (ml/min)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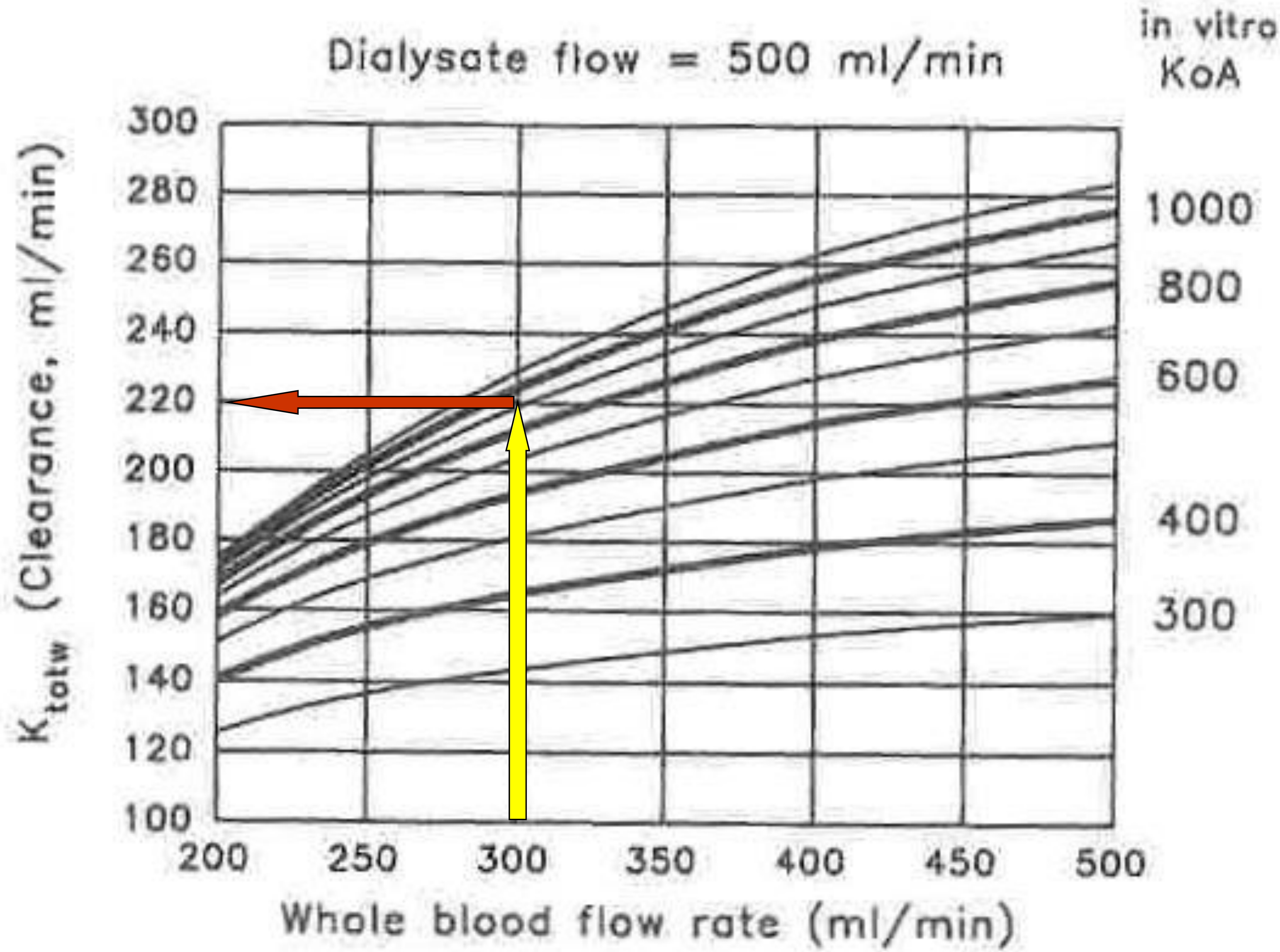
Whole blood flow rate (ml/min)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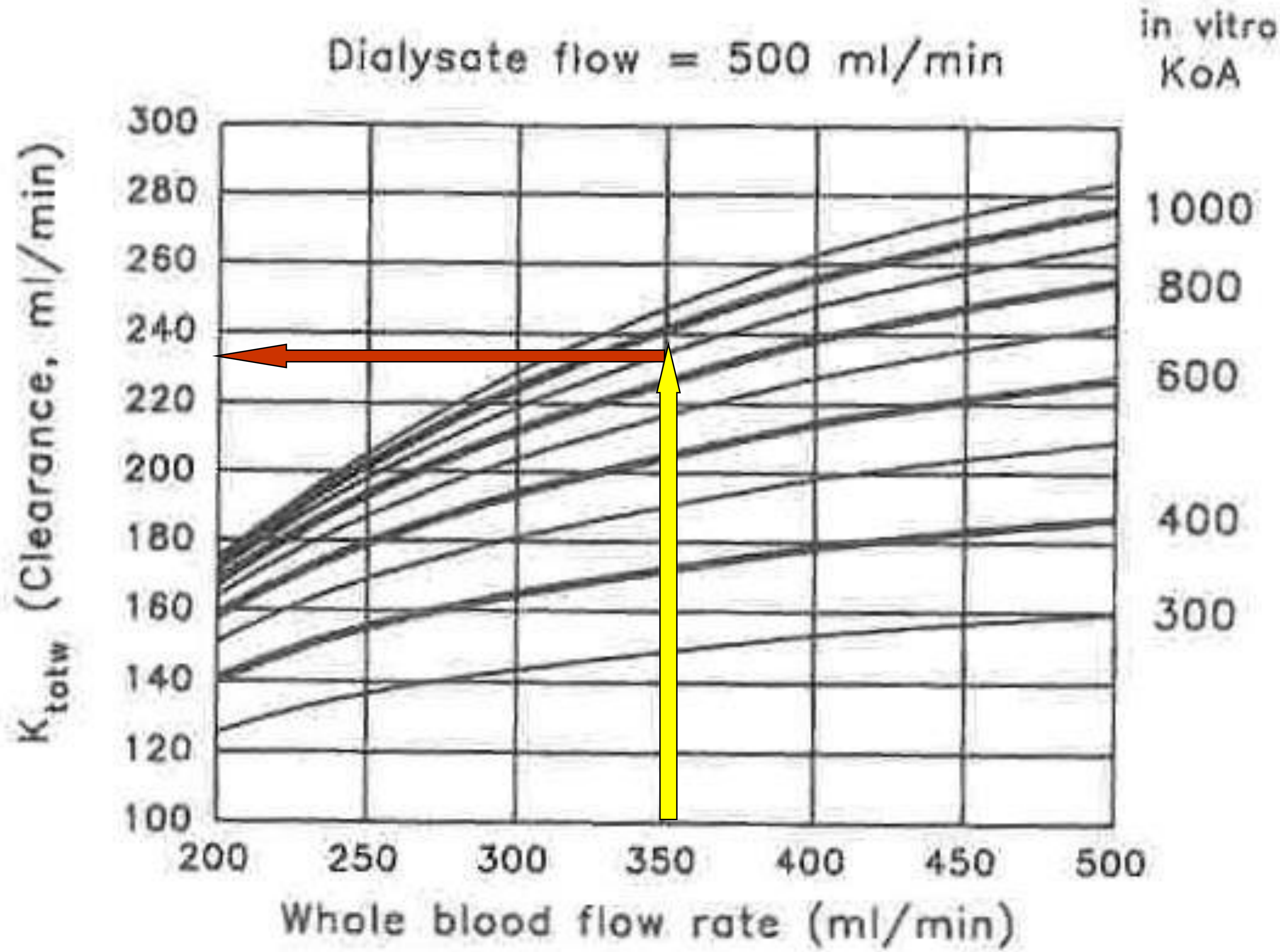
500
Whole blood flow rate (ml/min)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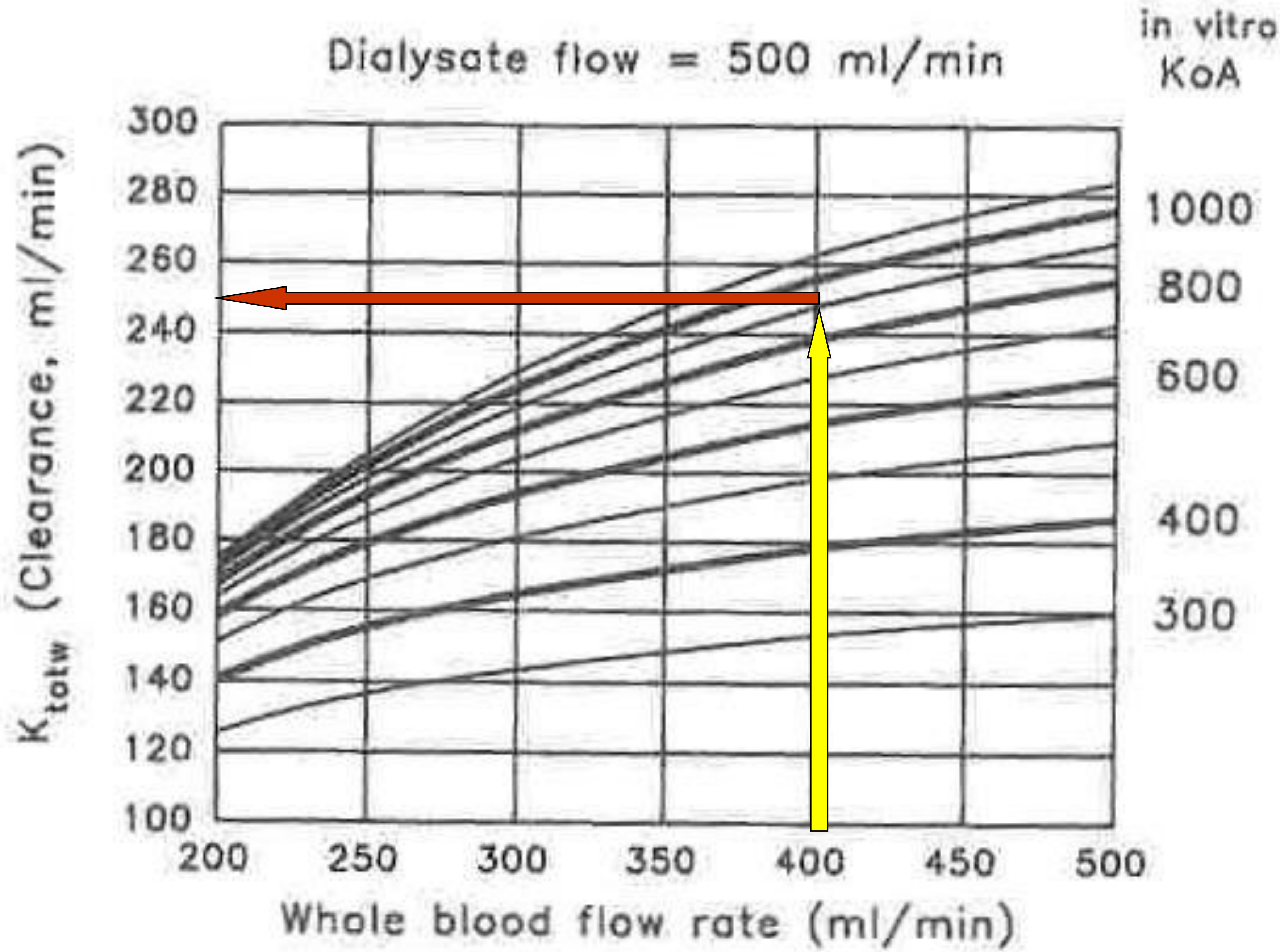
400
450
500
Whole blood flow rate (ml/min)



Dialysate flow = 500 ml/min
in vitro
KoA
1000
800
600
400
300
300
280
260
240
220
200
180
160
140
120
100
K_{totw} (Clearance, ml/min)
200
250
300
350
400
450
500
Whole blood flow rate (ml/min)

KUF

Permeability dialyzer to water

Volume in ml of liquid taken from the patient over time Is taken to per mm Hg pressure is called KUF.

↑ TMP	←	Water permeability less	← KUF ↓
↓ TMP	←	Water permeability more	← KUF ↑

Definitions of flux, Permeability, and efficiency

Flux

- Measure of ultrafiltration capacity
- Low and high flux are based on the ultrafiltration coefficient(Kuf)
  Low flux; Kuf <10 ml/h/mmHg
  High flux; Kuf >20 ml/h/mmHg

Permeability

- Measure of the clearance of the middle molecular weight molecule (eg, β2-microglobolin)
- General correlation between flux and Permeability
  Low Permeability; β2-microglobolin clearance<10ml/h/mmHg
  High Permeability; β2-microglobolin clearance>20ml/h/mmHg

Efficiency

- Measure of urea clearance
- Low and high efficiency are based on the urea KoA value
  Low efficiency; KoA <500 ml/min
  High efficiency; KoA >800 ml/min

Classification of High-Performance Dialysis

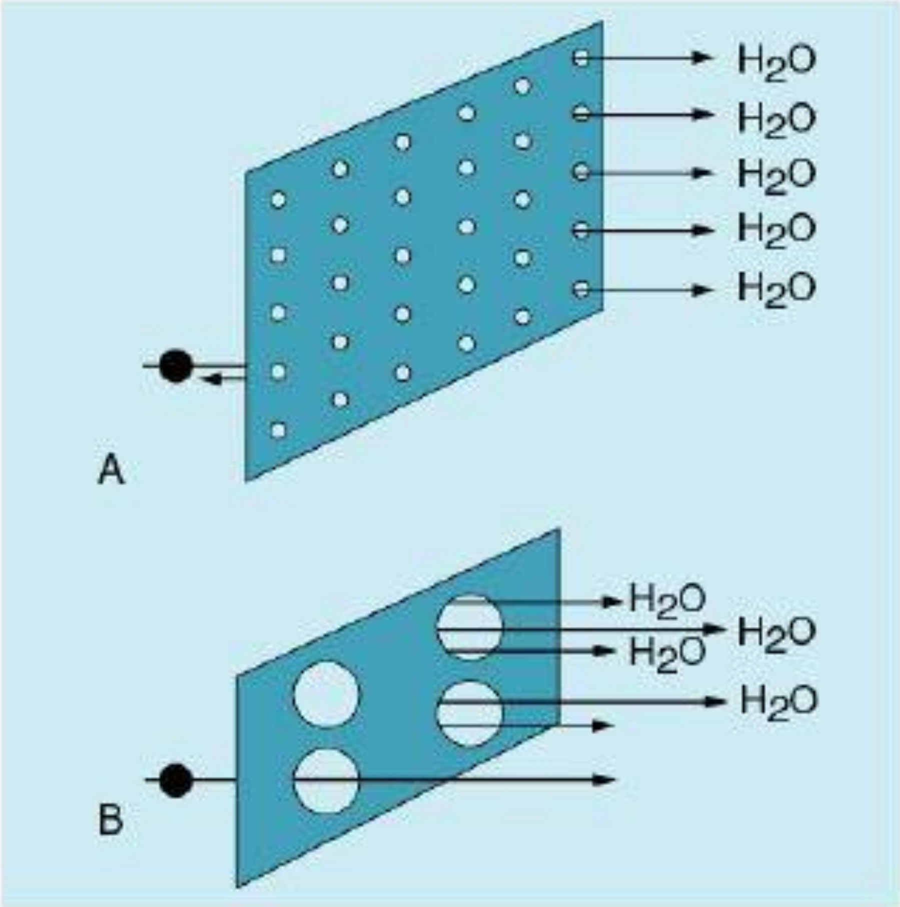
- High-Efficiency Low-flux hemodialysis
- High-Efficiency High-flux hemodialysis
- Low-Efficiency High-flux hemodialysis

Differences between High and Low-Efficiency Hemodialysis

	High Efficiency, ml/min	Low Efficiency, ml/min
Dialyzer KoA	≥800	<500
Blood flow	≥350	<350
Dialysate flow	≥500	<500
Bicarbonate dialysate	Necessary	optimal

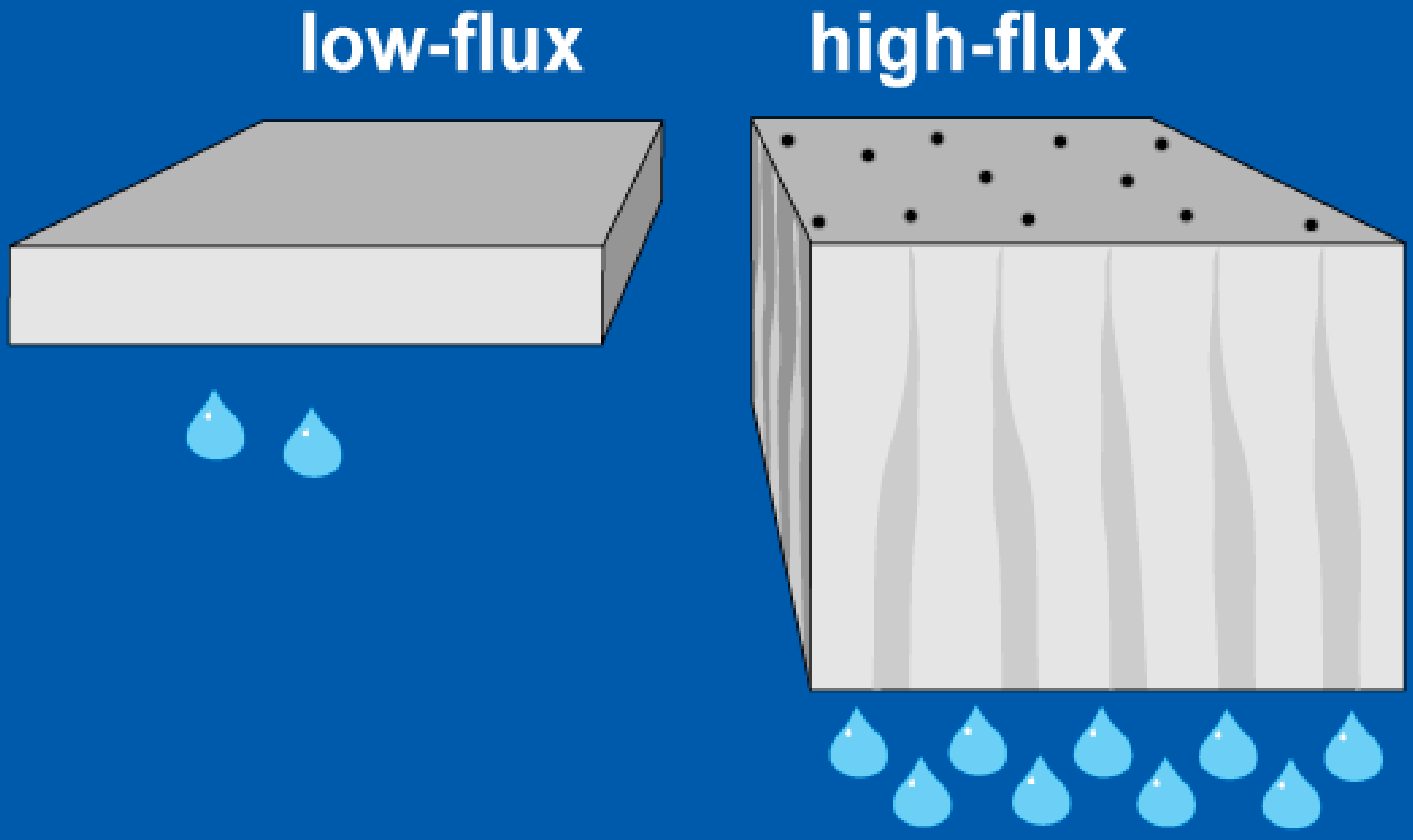
Ko- mass transfer coefficient; A- surface area

Membrane Flux and Pore Size 1

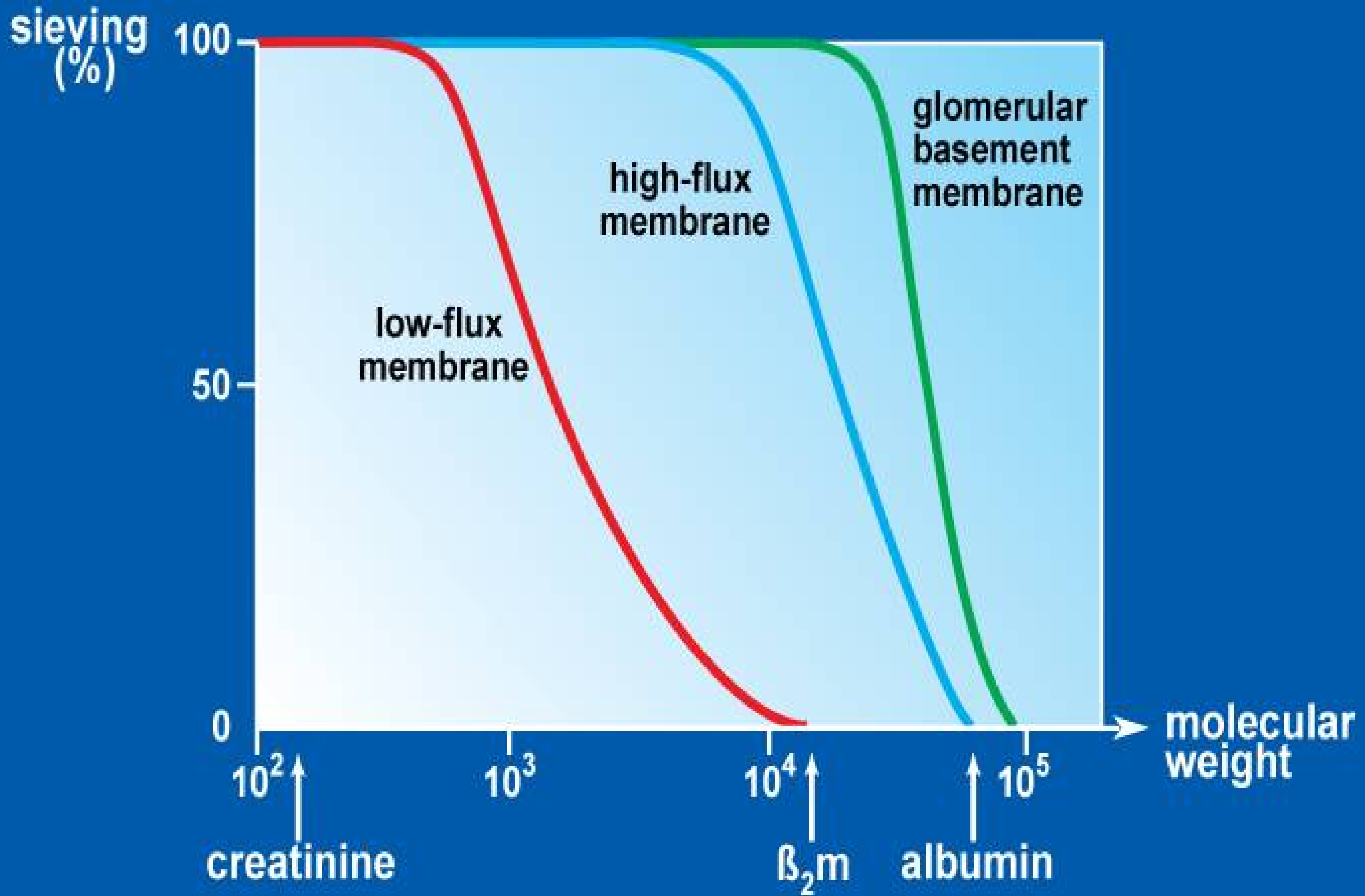


Sivasankaran Ambalavanan, Gary Rabetoy & Alfred K. Cheung; www.kidneyatlas.org

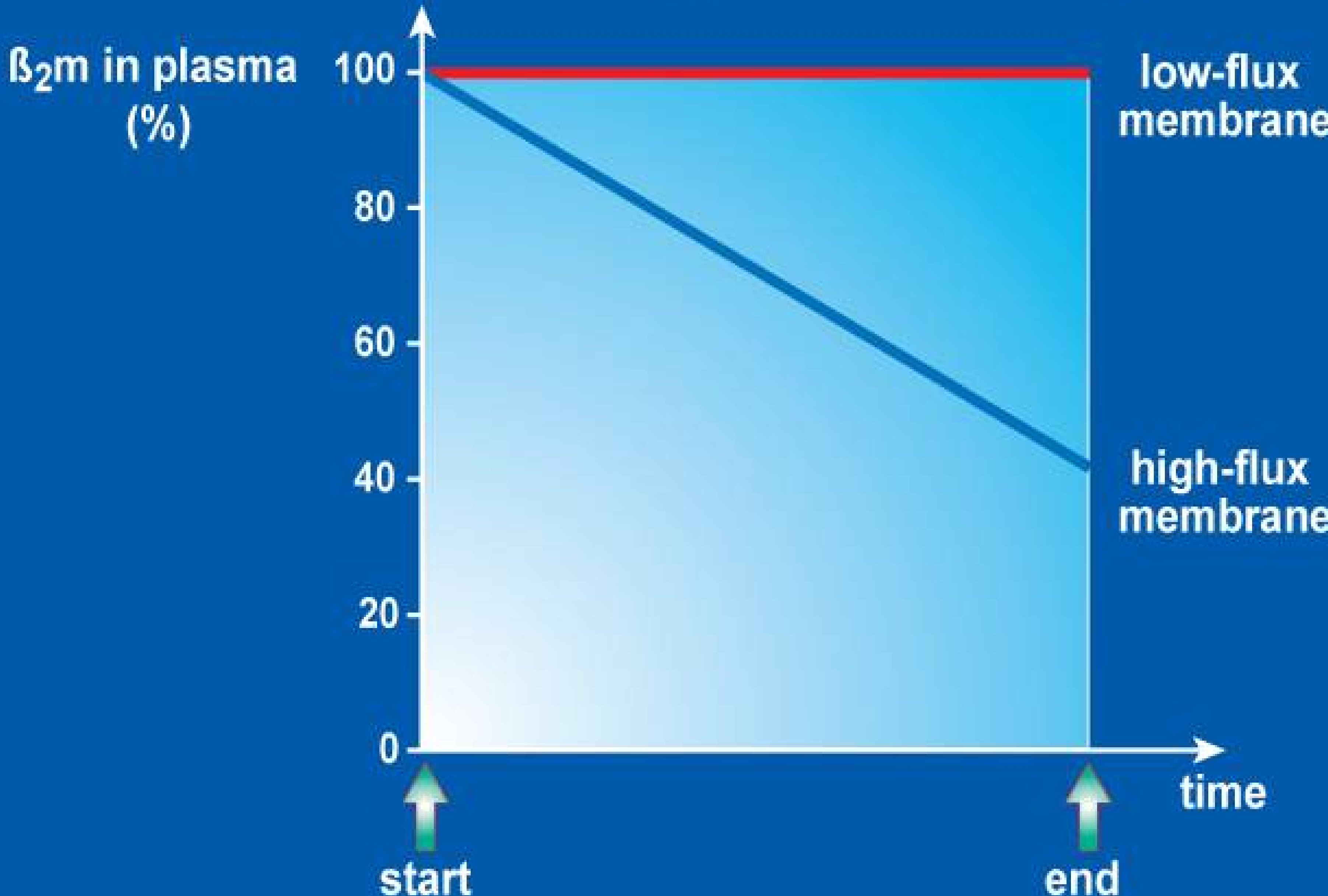
Membrane Structure



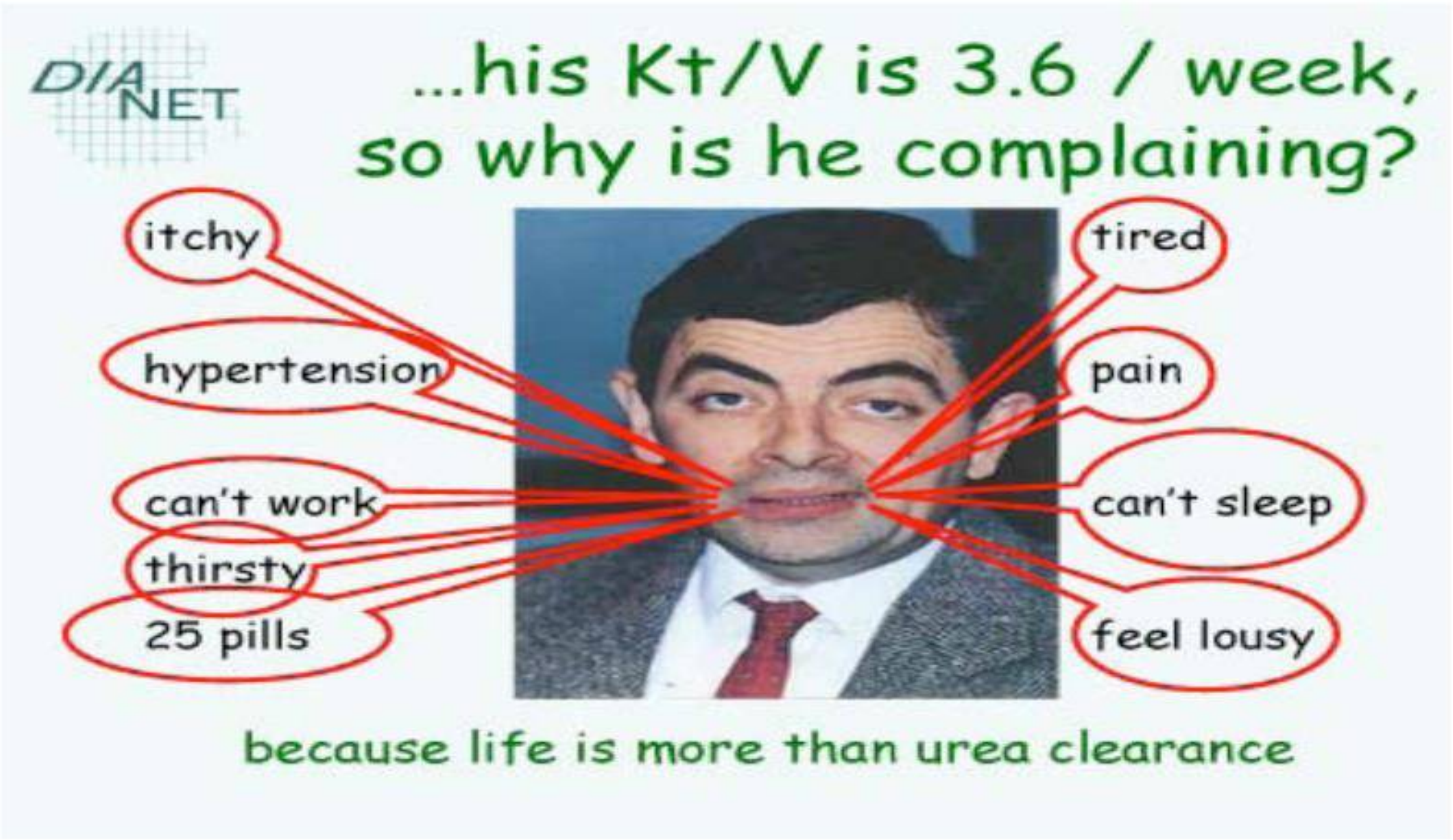
Membrane Permeability



Removal of $ß_2m$ during HD



Adequate dialysis vs Optimal dialysis



Uremic Toxin: Middle Molecule with biological potential

- Adrenomedullin
- AGE
- Angiogenin
- AOPP
- Atrial natriuretic peptide
- Cholecystokin
- Clara cell protein
- Complement factor D
- Cystatin C
- Cytokines
- Delta sleep inducing protein
- Endothelin
- β-Endorphin
- Ghrelin
- Glomerulopressin
- GIP I
- GIP II
- Leptin
- β-Lipotropin
- Macrophage-colony-stimulating factor
- Methionine-enkephalin
- **ß$_2$-Microglobulin**
- Neuropeptide Y
- Orexin A
- Retinol binding protein

Clinical Performance Measures in Hemodialysis 2015

- 1.sp Kt/V >1.4
- 2.Alb>3.5 g/dl
- 3. Hb> 10 and <12 g/dl
- 4. Ph> 2.5 and <5.5 mg /dl
- 5. Ferritin> 200 and<800 ng/ml
- 6. Ca*Ph < 55
- 7.iPTH > 150 and <600 pg/ml
- 8.Predialysis MAP< 105 mmhg
- 9.Interdialytic weight gain<4% dry weight
- 10.Weekly treatment> 720 min
- 11. Prevalence of AVF> 90%

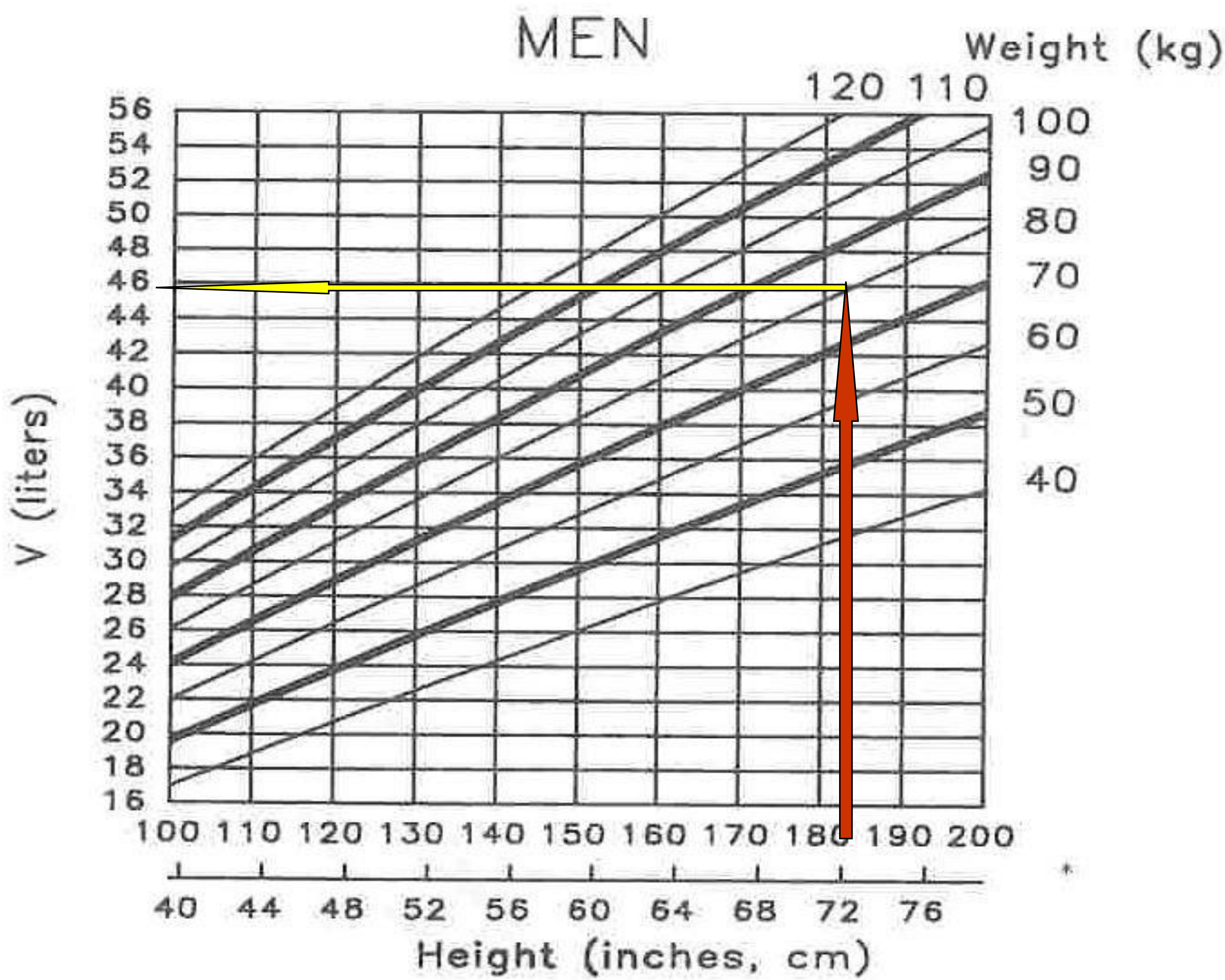
One example:

For a male patient with 183 cm height & 80 kg weight

our needs include:

- Calculate V:

Based on the mentioned chart, volume of distribution of urea in this patient is: 46 liters or 46,000 ml


MEN
Weight (kg)
120 110
100
90
80
70
60
50
40
56
54
52
50
48
46
44
42
40
38
36
34
32
30
28
26
24
22
20
18
16
V (liters)
100 110 120 130 140 150 160 170 180 190 200
40 44 48 52 56 60 64 68 72 76
Height (inches, cm)

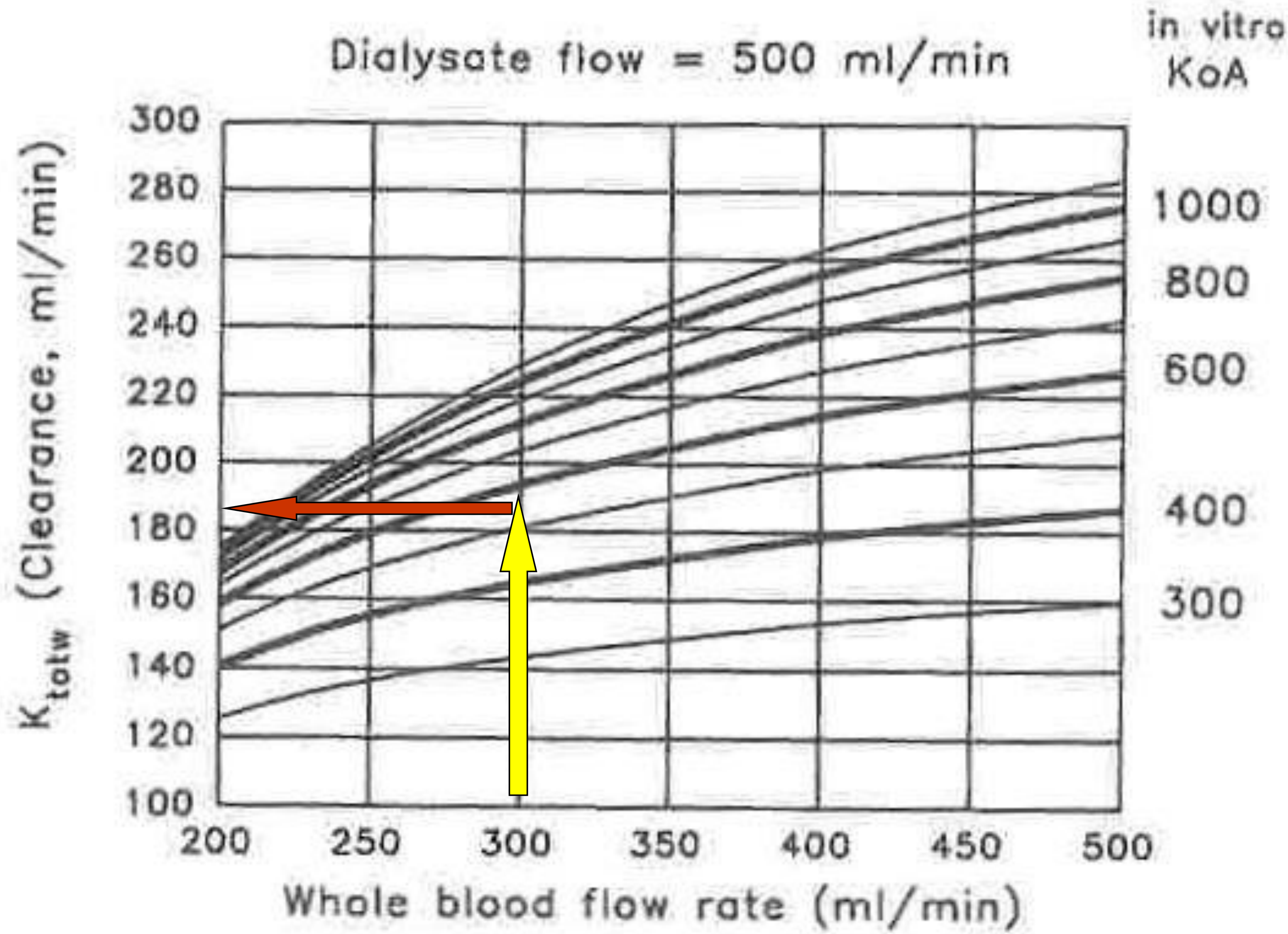
One example:

A male 183 cm Weight 80 kg to the dialysis program we need for this patient is:

- Calculate V:

-Calculate clearance (K)

If you want to use a filter with the KOA=500 and blood flow rate=300ml/min BFR, the filter circumstances would be 180ml/min according to KoA chart



Dialysate flow = 500 ml/min
in vitro
KoA
1000
800
600
400
300
K_{totw} (Clearance, ml/min)
300
280
260
240
220
200
180
160
140
120
100
200
250
300
350
400
450
500
Whole blood flow rate (ml/min)

One example:

$KT/V = 1.3$

$180T/46000 = 1.3$

$T = 1.3 \times 46000/180 = 332\ min$

$T = 5.5\ h$

One example:

- **If the same patient, if we use a filter with KoA=600. the filter clearance would be 195ml/min according to KoA chart .**
- **The time required to reach KT/V = 1.3 about 300 minutes or 5 hours would be equivalent**

مثال کاربردی:

بیمار آقایی با 70kg با 180cm قد است.

-زمان (T) ، 4 ساعت

-K.T/V هدف 1/3

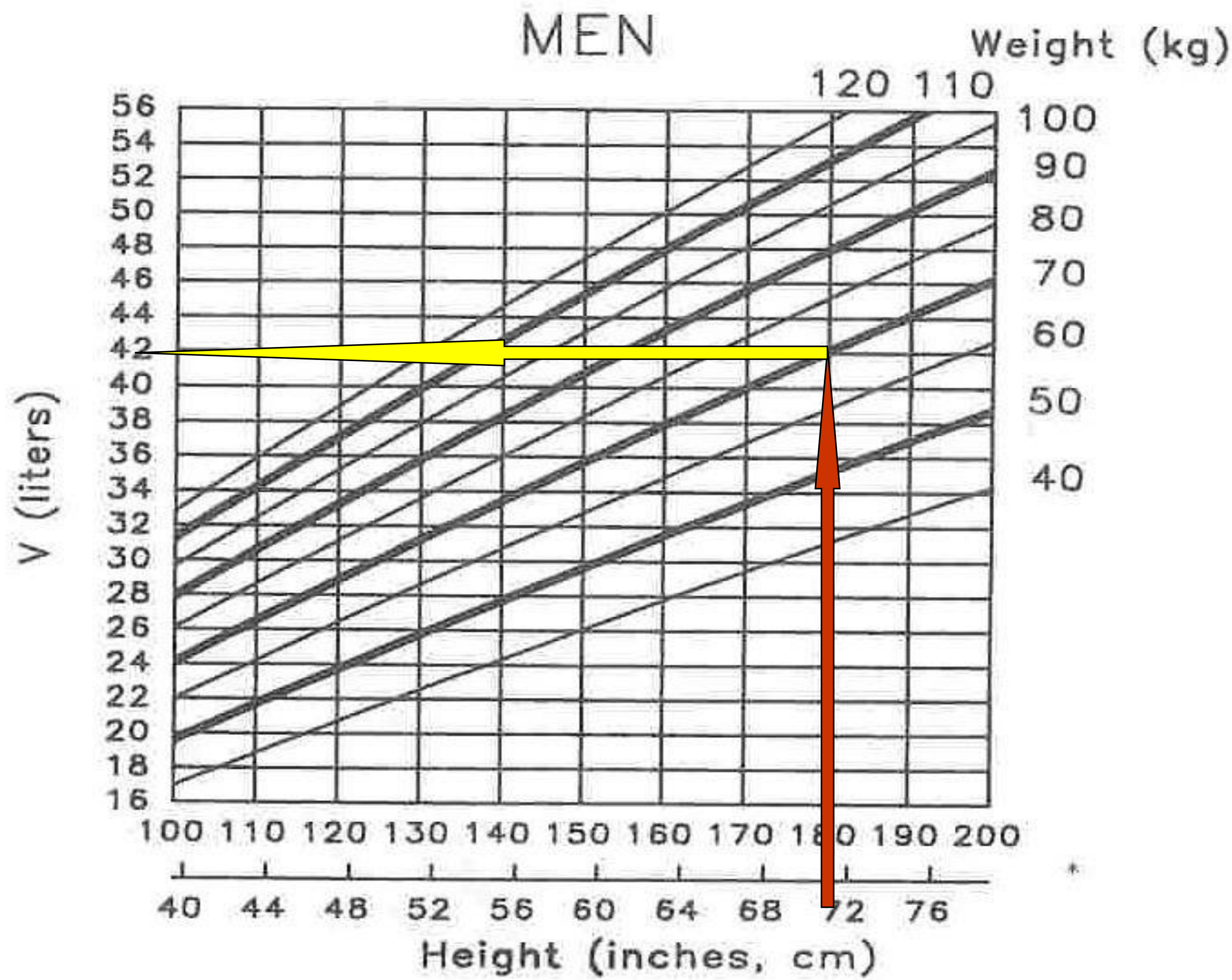
سوال:

۱-حجم توزیع اوره چند لیتر است؟

۲-کلیرانس را محاسبه کنید؟

۳-اگر سرعت جریان خون پمپ این بیمار حین دیالیز ۳۵۰ سی سی در دقیقه باشد KOA صافی چند است؟

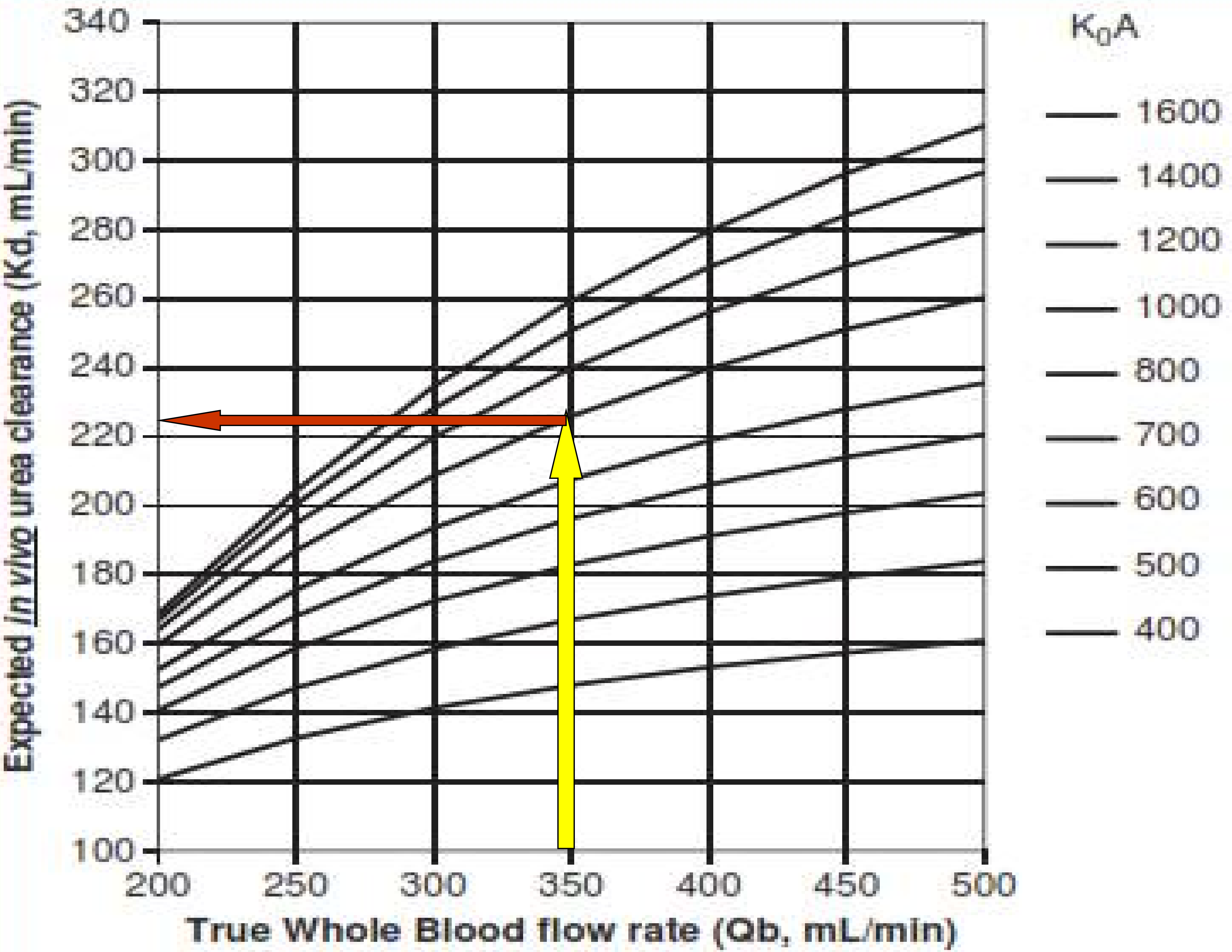
۴-با استفاده از جدول نوع صافی را معین کنید.


MEN
Weight (kg)
120 110
100
90
80
70
60
50
40
56
54
52
50
48
46
44
42
40
38
36
34
32
30
28
26
24
22
20
18
16
V (liters)
100 110 120 130 140 150 160 170 180 190 200
40 44 48 52 56 60 64 68 72 76
Height (inches, cm)

۱ – محاسبه حجم (**V**)، در این فرد ۴۲ لیتر یا۴۲۰۰۰ میلی لیتر

۲–محاسبه کلیرانس

- (K . 240) / 42000= 1/3
- K= (1/3 . 42000) / 240
- K= 227(cc/min)



K0A
1600
1400
1200
1000
800
700
600
500
400
Expected in vivo urea clearance (Kd, mL/min)
340
320
300
280
260
240
220
200
180
160
140
120
100
200
250
300
350
400
450
500
True Whole Blood flow rate (Qb, mL/min)

Dialyzer classification by efficiency

"low-efficiency" dialysis

K0A urea values

<500

- **F4= 365**
- **F5 = 475**
- **PES10 = 518**

" moderate-efficiency " dialyzers

K0A values of 500–800

- **F6 = 578**
- **F7 = 677**
- **F8 = 726**
- **F60 = 736**
- **PS10 = 637**
- **Ps13 = 746**
- **PES13 = 629**
- **PES16 = 757**

"high-efficiency"dialysis

K0A values >800

- PS16 = 1064
- PS160 =1145
- PES160 =1167
- PS18 =1292
- PES18 =1123
- PS180 = 1265
- PES180 = 1321
- F80 = 911
- F70 = 839

CONCLUSION

High-Efficiency Dialysis

- Higher clearance of small solutes, such as urea, compared with conventional dialysis without increase in treatment time
- Better control of chimistery
- Potentially reduced morbidity
- Potentially higher patient survival rates

High-Flux Dialysis

- Delayed onset and risk of dialysis-related amyloidosis because of enhanced β2-microglobolin clearance

- Increased patient survival resulting from higher clearance of middle molecular weight molecules

- Reduced morbidity and hospital admissions
- Improved lipid profile
- Higher clearance of aluminum
- Improved nutritional status
- Reduced risk of infection
- preserved residual renal function

THANKS FOR ATTENTION