THE HEMODIALYSIS PRESCRIPTION: TREATMENT ADEQUACY

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NASHVILLE, TENNESSEE
THE DIALYSIS CYCLE
# DESIGN OF THE NATIONAL COOPERATIVE DIALYSIS STUDY

## TABLE 7  CONTROL ACHIEVED ACCORDING TO STUDY GROUP

<table>
<thead>
<tr>
<th>Group and Factor Analyzed</th>
<th>Duration of Dialysis (Hr:Min)</th>
<th>Midweek Predialysis BUN (mg/dl) Mean ± S.E.M.</th>
<th>Time-Averaged BUN (mg/dl) Mean ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4:29 ± 0:03</td>
<td>71.2 ± 1.4</td>
<td>51.3 ± 1.1</td>
</tr>
<tr>
<td>II</td>
<td>4:31 ± 0:03</td>
<td>104.9 ± 1.7</td>
<td>87.7 ± 1.4</td>
</tr>
<tr>
<td>III</td>
<td>3:19 ± 0:03</td>
<td>73.1 ± 1.4</td>
<td>54.1 ± 1.1</td>
</tr>
<tr>
<td>IV</td>
<td>3:14 ± 0:03</td>
<td>109.1 ± 1.5</td>
<td>89.6 ± 1.2</td>
</tr>
<tr>
<td>TIME*</td>
<td>P &lt; 0.0001</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>BUN*</td>
<td>P &gt; 0.1</td>
<td>P &lt; 0.0001</td>
<td>P &lt; 0.0001</td>
</tr>
<tr>
<td>Interaction*</td>
<td>P &gt; 0.1</td>
<td>P &gt; 0.1</td>
<td>P &gt; 0.1</td>
</tr>
</tbody>
</table>

* The probabilities indicate the significance of differences between means for the variable with respect to the experimental factor.  *(Reproduced with permission from Lowrie EG, Laird NM, Parker TF, Sargent JA, The effect of the hemodialysis prescription on patient morbidity, N Engl J Med 1981; 305:1176–1181.)*
REVISED NCDS RESULTS EXPRESSED AS Kt/V

MORBIDITY, NOT MORTALITY
COMPARATIVE MORTALITY RATES

Five year RRT survival for U.S. vs. Japan (by age)
IMPLICATION OF US DIALYSIS MORTALITY RATE
IMPLICATION OF US DIALYSIS MORTALITY RATE

Expected Remaining Lifetime: ESRD, Cancer (3 types) & General Population
Age 40 and 59, 1988

<table>
<thead>
<tr>
<th>Age 40</th>
<th>General Pop.</th>
<th>Prostate Cancer Pop.</th>
<th>ESRD Pop.</th>
<th>Colon Cancer Pop.</th>
<th>Lung Cancer Pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.4</td>
<td>9.3</td>
<td>4.5</td>
<td>1.3</td>
<td>4.9</td>
<td>4.3</td>
</tr>
</tbody>
</table>

Exp. Remaining Lifetime (Years)

<table>
<thead>
<tr>
<th>Age 59</th>
<th>General Pop.</th>
<th>Prostate Cancer Pop.</th>
<th>ESRD Pop.</th>
<th>Colon Cancer Pop.</th>
<th>Lung Cancer Pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.4</td>
<td>18.0</td>
<td></td>
<td></td>
<td>4.9</td>
<td>4.3</td>
</tr>
</tbody>
</table>

N.A. (Not Available)
## Table 6. Survival in a Dialysis Unit With Kt/V of 1.67

<table>
<thead>
<tr>
<th>Initial Age</th>
<th>No. of Patients</th>
<th>Survival 5-Year</th>
<th>Survival 10-Year</th>
<th>Survival 15-Year</th>
<th>Survival 20-Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>112</td>
<td>93%</td>
<td>88%</td>
<td>80%</td>
<td>71%</td>
</tr>
<tr>
<td>35-44</td>
<td>84</td>
<td>92%</td>
<td>81%</td>
<td>63%</td>
<td>39%</td>
</tr>
<tr>
<td>45-54</td>
<td>111</td>
<td>88%</td>
<td>76%</td>
<td>53%</td>
<td>—</td>
</tr>
<tr>
<td>55-64</td>
<td>98</td>
<td>83%</td>
<td>60%</td>
<td>21%</td>
<td>—</td>
</tr>
<tr>
<td>&gt;64</td>
<td>40</td>
<td>69%</td>
<td>64%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>All patients</td>
<td>445</td>
<td>87%</td>
<td>75%</td>
<td>55%</td>
<td>43%</td>
</tr>
</tbody>
</table>

Data from Laurent et al.\textsuperscript{71}
Kt/V AND MORTALITY

Hakim et al, JASN, May 1994

<table>
<thead>
<tr>
<th>#</th>
<th>YEAR</th>
<th>Kt/V + SD</th>
<th>MR</th>
<th>SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1988</td>
<td>.82 + .32</td>
<td>22.8%</td>
<td>1.03</td>
</tr>
<tr>
<td>2</td>
<td>1989</td>
<td>.96 + .28</td>
<td>17.8%</td>
<td>.70</td>
</tr>
<tr>
<td>3</td>
<td>1990</td>
<td>1.01 + .40</td>
<td>15.7%</td>
<td>.79</td>
</tr>
<tr>
<td>4</td>
<td>1991</td>
<td>1.18 + .41</td>
<td>9.1%</td>
<td>.61</td>
</tr>
</tbody>
</table>
## Kt/V & RISK OF MORTALITY

<table>
<thead>
<tr>
<th>KT/V</th>
<th>no DM</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 &lt; 1.2</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1.2 &lt; 1.4</td>
<td>0.64</td>
<td>0.70</td>
</tr>
<tr>
<td>≥ 1.4</td>
<td>0.67</td>
<td>0.60</td>
</tr>
</tbody>
</table>

n = 1082

n = 691
Kt/V & MORTALITY: MINNESOTA EXPERIENCE

**Cox Regression Analysis**

<table>
<thead>
<tr>
<th></th>
<th>Kt/V</th>
<th>Relative Risk</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiabetic</td>
<td>$\uparrow 0.1$</td>
<td>0.95</td>
<td>0.012</td>
</tr>
<tr>
<td>N=1082</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>$\uparrow 0.1$</td>
<td>0.93</td>
<td>0.004</td>
</tr>
<tr>
<td>N=691</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Collins, et al. AJKD 23:272, 1994
CHANGING TRENDS IN THERAPY

Delivered Kt/V and URR for HD Patients*
Prevalent > 1 year, 1991 and 1994

URR (%)  
CMA 1990/91  
DMMS 1993/94  
59.8  63.2  1.11  1.21

Kt/V (Daugirdas)

* only for thrice weekly HD
CHANGING TRENDS IN THERAPY
CHANGING TRENDS IN THERAPY


Mean Blood Flow Rate (ml/min)

- **CMA 1990/91**
- **DMMS 1993/94**

<table>
<thead>
<tr>
<th>Dialzer Membrane</th>
<th>1991</th>
<th>1994</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmodified Cellulose</td>
<td>295</td>
<td>324</td>
</tr>
<tr>
<td>Modified Cellulose</td>
<td>328</td>
<td>343</td>
</tr>
<tr>
<td>Synthetic</td>
<td>369</td>
<td>373</td>
</tr>
</tbody>
</table>
CHANGING TRENDS IN THERAPY

Mean Treatment Time for Hemodialysis Patients*, 1991 and 1994

- CMA Study (1991): 195.1 minutes
- DMMS - Wave 1 (1994): 194.9 minutes

* Only patients on 3 times/week schedule
Mortality by Delivered Kt/V, 1990-93

Linear RR = 0.93 / Δ 0.1 Kt/V
(p = <0.01)

Patients > 1 year
Bicarbonate only
Stratified by region
Adj. for comorbid

USRDS Case Mix Adequacy Study, 1990/91, n = 2,410
MEMBRANE FLUX: A POTENTIAL CONFOUNDING VARIABLE

- CHANGES IN Kt/V WERE IN PART ACCOMPLISHED BY USE OF HFM
- POTENTIAL BENEFITS OF HFM
  - IMPROVED PROTEIN CATABOLIC RATE
  - IMPROVED TG METABOLISM
  - IMPROVED EPO RESPONSE
  - IMPROVED BETA$_2$-MICROGLOBULIN REMOVAL
- HOWEVER, BECAUSE OF LOW T$_D$, THE FULL EFFECT OF HFM IS NOT EVIDENT. REMOVAL OF HIGH MW SUBSTANCES ARE ALSO TIME DEPENDENT.
INFLUENCE OF DOSE AND DIALYZER CHOICE ON NUTRITION

GOAL: HEMO-Kt/V > 1.2
PD-Kt/V > 2.1 (week)
# Adequacy and Nutritional Status

**NUTRITIONAL PARAMETERS AND YEARLY AVERAGE KT/V**

<table>
<thead>
<tr>
<th>N</th>
<th>Yearly Average Kt/V</th>
<th>Albumin</th>
<th>Transferrin</th>
<th>PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>&lt; 0.86</td>
<td>3.5</td>
<td>220</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 0.3</td>
<td>± 34</td>
<td>± 0.19</td>
</tr>
<tr>
<td>16</td>
<td>&gt; 1.21</td>
<td>3.9*</td>
<td>257*</td>
<td>1.00*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 0.2</td>
<td>± 64</td>
<td>± 0.19</td>
</tr>
</tbody>
</table>

* P < 0.05
ADEQUACY AND ALBUMIN LEVEL
HEMODIALYSIS TIME: THE UNRESOLVED PARAMETER

- $K_D$ IS A MERE TECHNICAL ISSUE
- MINIMUM $T_D$ HAS ITS BASIS ROOTED IN PHYSIOLOGY
- SHORT TIME MAKES HEMODIALYSIS UNFORGIVING:

<table>
<thead>
<tr>
<th>Prescribed $Kt/V$</th>
<th>Calculated $Kt/V$</th>
<th>Delivered $Kt/V$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.56 ± 0.28</td>
<td>1.50 ± 0.28</td>
<td>1.37 ± 0.23</td>
</tr>
</tbody>
</table>

- EXCEPT FOR TASSIN, NO MODERN STUDIES HAS EXAMINED LONG (>5 HOURS) TIME AND OUTCOME
## THE NCDS POPULATION

<table>
<thead>
<tr>
<th>Table 5. NCDS Inclusion/Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, 18-70 years (mean, 49.0 ± 12.7)</td>
</tr>
<tr>
<td>(US 1988 mean, 57 years)</td>
</tr>
<tr>
<td>(US 1988 median, 60 years)</td>
</tr>
<tr>
<td>Average time on dialysis, 4.2 ± 2.3 years</td>
</tr>
<tr>
<td>No diabetes</td>
</tr>
<tr>
<td>(1988 US acceptance rate, 30%)</td>
</tr>
<tr>
<td>No malignancy</td>
</tr>
<tr>
<td>No significant cardiovascular disease</td>
</tr>
<tr>
<td>No hospitalization for past 6 months</td>
</tr>
<tr>
<td>Te range, 2.5-5.5 hours during study</td>
</tr>
<tr>
<td>(mean before participation, 4.3 hours)</td>
</tr>
<tr>
<td>Cooperative</td>
</tr>
<tr>
<td>Compliant</td>
</tr>
</tbody>
</table>
FACTORS RELATED TO DIALYSIS ADEQUACY

- **HEMODIALYSIS RELATED FACTORS**
  - DOSE
    - LOW MW SOLUTES
    - HIGH MW SOLUTES
    - DIALYSIS TIME
  - MEMBRANE
    - FLUX
    - BIOCOMPATIBILITY
    - REUSE

- **PATIENT RELATED FACTORS**
  - NUTRITION
  - ACIDOSIS
  - CA x P
  - BLOOD PRESSURE
  - LIPIDS
  - CARDIOVASCULAR MORBIDITY
  - INFLAMMATION
ALTERNATIVES FOR THE HEMO STUDY

HEMO STUDY

**Choice**
- Dialysis Dose
- Dialysis Time
- Biocompatibility
- Flux
- Nutrition

**Controversy**
- We know the answer
- Does not reflect U.S. practice
- Confounded by reuse techniques
- Definition
- Prohibitive cost

Remember: Limited Funds Dictates 2 x 2 Design
THE HEMODIALYSIS (HEMO) STUDY

AN NIH-NIDDK SPONSORED RANDOMIZED, MULTI-CENTER CLINICAL TRIAL
THE CHOICE: OBJECTIVES OF THE HEMO STUDY

In patients undergoing 3x/week maintenance hemodialysis, to determine whether higher dose, or high-flux membrane affect mortality (primary outcome), or morbidity (secondary outcome)
DOUBLE POOL KINETICS
THE RATE EQUATION

Rate equation

\[ \frac{eKt}{V} = spKt/V - 0.6\frac{(K/V)}{V} + 0.03 \]

\((K/V \text{ in hours}^{-1})\)
RATE EQUATION AS A FUNCTION OF TIME

\[ eKt/V = spKt/V - 0.6K/V + 0.03 \]

\[ = spKt/V(1 - 0.6/T_d) + 0.03 \]

Predictions of the Rate Equation

\[ Kt/V \]

\[ T_d \]

(time on dialysis in hours)
RELATIONSHIP OF $K_t/V_{SP}$ TO $K_t/V_{DP}$ AND AS A FUNCTION OF REBOUND
THE DIALYSIS CYCLE
Standard dose
\[\text{eKt/V} = 1.05\]
\[\text{spKt/V} \approx 1.25\]
\[\text{URR} \approx 65\%\]

High dose
\[\text{eKt/V} = 1.45\]
\[\text{spKt/V} \approx 1.65\]
\[\text{URR} \approx 75\%\]
Flux

Low-flux dialyzers: $\beta_2$M clearance < 10 ml/min

High-flux dialyzers: $\beta_2$M clearance > 20 ml/min
Time to Death by Kt/V Group

Adjusted RR for High Kt/V: 0.96 (0.84 - 1.09), p = 0.52
Time to Death by Flux Group

Adjusted RR for High Flux:
0.92 (0.81 - 1.06), p = 0.24
Interactions of Treatments with Baseline Characteristics

Did treatment effects differ between subgroups for seven pre-specified baseline factors?

- Age
- Years of dialysis
- Gender
- Comorbidity
- Race
- Albumin
- Diabetes
### Predictors of Mortality by Cox Regression

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Relative Risk</th>
<th>95% Confidence</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose</td>
<td>0.96</td>
<td>(0.84, 1.09)</td>
<td>0.52</td>
</tr>
<tr>
<td>High flux</td>
<td>0.92</td>
<td>(0.81, 1.06)</td>
<td>0.24</td>
</tr>
<tr>
<td>Age (per 10 yrs increase)</td>
<td>1.44</td>
<td>(1.35, 1.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.86</td>
<td>(0.74, 0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>Race (African American)</td>
<td>0.76</td>
<td>(0.65, 0.89)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.24</td>
<td>(1.06, 1.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Years of dialysis</td>
<td>1.04</td>
<td>(1.02, 1.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline serum albumin (per 0.5 g/dL increment)</td>
<td>0.51</td>
<td>(0.43, 0.62)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Model also includes 2 other sig. variables: ICED, albumin x time

Analysis stratified by clinical center
Time to Death by Kt/V Group
Females (484 Deaths)

Adjusted RR for High Kt/V: 0.81 (0.67 - 0.97), p = 0.02
Time to Death by Flux Group
Duration of Dialysis > 3.7 Years (298 Deaths)

Adjusted RR for High Flux: 0.68 (0.53 - 0.86), p = 0.001
HEMO STUDY SUMMARY

1) THE HIGHER DOSE OF HEMODIALYSIS THRICE WEEKLY DID NOT:
   IMPROVE SURVIVAL,
   REDUCE HOSPITALIZATIONS, OR
   MAINTAIN SERUM ALBUMIN

2) USE OF A HIGH FLUX MEMBRANE DID NOT:
   IMPROVE SURVIVAL,
   REDUCE HOSPITALIZATIONS, OR
   MAINTAIN SERUM ALBUMIN
3) HOWEVER, EFFECTS MAY VARY AMONG CERTAIN SUBSETS OF PATIENTS:

A) IN WOMEN, THE HIGHER DOSE OF DIALYSIS MAY BE ASSOCIATED WITH INCREASED SURVIVAL

B) IN PATIENTS WITH > 3.7 YEARS ON DIALYSIS, USE OF A HIGH FLUX MEMBRANE MAY BE ASSOCIATED WITH INCREASED SURVIVAL

C) THE RESULTS ON THESE SUBSETS SHOULD BE INTERPRETED CAUTIOUSLY AND BE FURTHER INVESTIGATED
ARE WE CONFOUNDING DETERMINATION OF ADEQUACY BY THE USE OF Kt/V?

Kt/V
Kt = AMOUNT OF DIALYSIS, A GOOD THING
V = VOLUME~WEIGHT~MUSCLE MASS, A GOOD THING

A GOOD THING/A GOOD THING
UREA VOLUME AND SURVIVAL

OPTIMAL Kt = 45L
THEREFORE: P = 45/L

P IS THE POINT OF INFLECTION TO 0 SLOPE

RELATIVE RISK OF DEATH
MINEFIELDS AVOIDED BY THE HEMO STUDY

- DESPITE ITS LENGTH, WE AVOIDED BEING ECLIPSED BY CHANGES IN COMMUNITY PRACTICE PATTERNS
  - $T_D$, $Q_B$, $Q_D$ SIMILAR TO USRDS
  - MEMBRANES SIMILAR
  - STANDARD LEVEL $Kt/V$ DELIVERED WAS BETTER OR EQUAL TO COMMUNITY PRACTICE THROUGHOUT THE STUDY. THE COMMUNITY RECOMMENDATIONS EXCEEDED HEMO STANDARD $Kt/V$ FOR ONLY A SHORT TIME
- DOSE AND FLUX GOALS ACHIEVED
- MORTALITY NOT OVERESTIMATED
- ADEQUATELY POWERED
- WHAT WAS PILOTED IS WHAT WAS STUDIED
WHY THE HEMO STUDY WAS NEEDED

• RAPIDLY GROWING ESRD POPULATION
  – 10 %/YEAR GROWTH RATE, COSTING $BILLIONS
  – WORSENING COMORBIDITY
  – MAJORITY TREATED BY HEMODIALYSIS

• US ANNUAL GROSS MORTALITY OF 21-23%

• OBSERVATIONAL AND CORRELATIONAL STUDIES DEMONSTRATING IMPROVED SURVIVAL FOLLOWING TREATMENT CHANGES
  – HIGHER DOSE AS MEASURED BY $Kt/V OR URR
  – BIOCOMPATIBLE MEMBRANES
  – REMOVAL OF HIGH MW SUBSTANCES (FLUX)
What situations require clinical guidelines to be updated?

- Changes in evidence on the existing benefits and harms of interventions
- Changes in outcomes considered important
- Changes in available interventions
- Changes in evidence that current practice is optimal
- Changes in values placed on outcomes
- Changes in resources available for health care

BMJ 2001;323:155-157
PLACES TO GO NEXT

- Changing a number?
- Changing an approach:
  - Cardiovascular Risk Reduction
  - Control of Co-morbid Conditions
  - Solute Removal: beyond small solutes
  - Volume Control
  - Nutrition
  - Anemia Correction
  - Bone Disease

ADAPTED FROM MUJAIS; ADEMEX STUDY
LARGE MOLECULE REBOUND

![Graph showing solute concentration over time for intracellular, extracellular, and single pool models.](image)
MEMBRANE FLUX: A POTENTIAL CONFOUNDING VARIABLE

- Changes in Kt/V were in part accomplished by use of HFM

- Potential benefits of HFM
  - Improved protein catabolic rate
  - Improved TG metabolism
  - Improved EPO response
  - Improved beta2-microglobulin removal

- However, because of low T_D, the full effect of HFM is not evident: removal of high MW substances are also time dependent—longer times are necessary to show benefits of HFM
HEMODIALYSIS TIME: THE UNRESOLVED PARAMETER

• $K_D$ IS A MERE TECHNICAL ISSUE
• MINIMUM $T_D$ HAS ITS BASIS ROOTED IN PHYSIOLOGY
• SHORT TIME MAKES HEMODIALYSIS UNFORGIVING:

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<tr>
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<td>1.50 ± 0.28</td>
<td>1.37 ± 0.23</td>
</tr>
</tbody>
</table>

• EXCEPT FOR TASSIN, NO MODERN STUDIES HAS EXAMINED LONG (>5 HOURS) TIME AND OUTCOME
POTENTIAL PARAMETERS TO CONSIDER WITH NOCTURNAL AND DAILY HD

IS IT INCREASED TIME OR INCREASED QUANTITY?
FACTORS THAT MAY INFLUENCE MORBIDITY AND SURVIVAL ON HEMODIALYSIS

- MEMBRANES: SYNTHETIC, FLUX
- DIALYSATE: SODIUM, BICARBONATE
- PHOSPHATE, Ca x P, Ca
- EPO
- DIALYSIS KINETICS
- DIALYSIS TIME
- NUTRITION

ALTERNATE DIALYSIS SCHEDULES
ISSUES TO BE CONSIDERED

- DEFINITIONS OF THE MODALITIES
- INDIVIDUAL STUDIES OF EACH OF THE MODALITIES
- DAILY HEMODIALYSIS vs NOCTURNAL HEMODIALYSIS
ALTERNATIVES TO STANDARD HEMODIALYSIS TREATMENTS

• SLOW LONG-DURATION HEMODIALYSIS
  – THRICE WEEKLY; BIOINCOMPATIBLE MEMBRANE; 6-8 HOURS; \( Q_B = 200-220 \text{ mL/min}; Kt/V > 1.8 \)

• SHORT DURATION DAILY DIALYSIS
  – 5-6 TIMES EACH WEEK; HIGH FLUX BIOCOMPATIBLE MEMBRANE; 1.5-2.5 HOURS; \( Q_B > 400 \text{ mL/min}; Kt/V < 0.2-0.8 \)

• NOCTURNAL HEMODIALYSIS
  – 5-7 TIMES EACH WEEK; BIOCOMPATIBLE MEMBRANE; 6-8 HOURS; \( Q_B = 250-300 \text{ mL/min}; K = 0.9-1.2 \)
Elevated Serum Phosphorus Increases Mortality Risk


\[ P=0.03 \quad \text{**}P<0.0001 \quad (n=6407) \]

US PTS 39% > 6.5

<table>
<thead>
<tr>
<th>Serum Phosphorus Quintile (mg/dL)</th>
<th>Relative Mortality Risk (RR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1-4.5</td>
<td>1.00</td>
</tr>
<tr>
<td>4.6-5.5</td>
<td>1.00</td>
</tr>
<tr>
<td>5.6-6.5</td>
<td>1.02</td>
</tr>
<tr>
<td>6.6-7.8</td>
<td>1.18*</td>
</tr>
<tr>
<td>7.9-16.9</td>
<td>1.39**</td>
</tr>
</tbody>
</table>
NOCTURNAL HD AND PHOSPHATE CONTROL

PHOSPHATE REMOVAL mmol

<table>
<thead>
<tr>
<th>P REMOVAL/SESSION</th>
<th>P REMOVAL/WEEK</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONVENTIONAL</td>
<td>NOCTURNAL</td>
</tr>
</tbody>
</table>

KI 1998; 53:1399-1404
DIETARY PHOSPHATE INTAKE: CONVENTIONAL vs NOCTURNAL HD

KI 1998; 53:1399-1404
CONVENTIONAL HD vs NOCTURNAL HD: PHOSPHATE CONTROL

• PHOSPHATE LEVELS
  – 2.1 mmol/L (~6 mg/dL) DECREASED TO 1.3 mmol/L (~3.9 mg/dL) WITH THE START OF NOCTURNAL HD

• BY THE 4th MONTH OF NOCTURNAL HD, NONE OF THE PATIENTS WERE USING PHOSPHATE BINDERS

KI 1998; 53:1399-1404
NOCTURNAL vs DAILY SHORT HEMODIALYSIS

• NOCTURNAL HD
  – LONG TREATMENTS
  – PHOSPHATE CONTROL IMPROVED
  – BLOOD PRESSURE CONTROL IMPROVED
  – ALBUMIN IMPROVED
  – HOME THERAPY

• DAILY SHORT HD
  – SHORT TREATMENTS
  – PHOSPHATE CONTROL NOT IMPROVED
  – BLOOD PRESSURE CONTROL IMPROVED
  – ALBUMIN IMPROVED
  – HOME OR IN-CENTER THERAPY
PRINCIPLE BEHIND THE USE OF STANDARD Kt/V

• UREA IS REMOVED IN A MORE EFFICIENT MANNER AT THE SAME WEEKLY KT/V AS YOU INCREASE DIALYSIS FREQUENCY.

• REMOVAL OF LESS DIFFUSIBLE SOLUTES IS EVEN MORE EFFICIENT AT THE SAME WEEKLY KT/V.
STATUS OF DAILY DIALYSIS

- NO PROSPECTIVE STUDIES OF INCIDENT PATIENTS
- PATIENT SELECTION IS NOT RANDOM
- PATIENTS NUMBER IN THE 100’S
- NO STANDARDIZATION OF REGIMENS
- NO OUTCOME STUDIES
- NOCTURNAL vs DAILY
- ACCESS FUNCTION NOT COMPROMISED
THE DIALYSIS CYCLE

- Influence of Dialysis
- Influence of Diet/Nutritional Status
- Area Under Curve
  \[ TAC \] /TIME
As you increase the frequency, on the x axis here, and maintain the same time average BUN, the need for dialysis diminishes, the dose of dialysis expressed on a weekly basis is less.
RATIONALE FOR USING THE STANDARD Kt/V

- Predicts the currently accepted minimum standard for continuous urea clearance.
- Predicts the approximate level of native kidney urea clearance requiring dialysis intervention.

DEPNER
STANDARD Kt/V

Standard Kt/V = \frac{\text{continuous removal rate}}{\text{average peak concentration}}

In a steady state, removal is equal to generation (G).

Standard Kt/V = \frac{G}{\text{average peak concentration}}

FOR A CONTINUOUS THERAPY, PEAK=MEAN
CONTINUOUS VS INTERMITTENT THERAPY

intermittant

continuous
STANDARD WEEKLY Kt/V MODEL

- CAPD
- IHD
- SDHD
- NHHD

Dialyses per week

stdKt/V weekly

spkt/V each dialysis
## RELATIONSHIP BETWEEN WEEKLY AND STANDARD Kt/V

<table>
<thead>
<tr>
<th>MODALITY</th>
<th>WEEKLY Kt/V</th>
<th>STANDARD Kt/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHORT DAILY DIALYSIS</td>
<td>3.5-4.5</td>
<td>2.7-3.2</td>
</tr>
<tr>
<td>NOCTURNAL HEMODIALYSIS</td>
<td>5.0-6.0</td>
<td>3.7-4.2</td>
</tr>
</tbody>
</table>

LEYPOLDT, SEMINAR DIAL, 2004
SUMMARY AND CONCLUSIONS

• MULTIPLE LINES OF EVIDENCE SUGGEST DAILY TREATMENTS IMPROVE:
  – ADEQUACY
  – BLOOD PRESSURE CONTROL
  – HOSPITALIZATION RATE
  – NUTRITION

• TRIALS OF THE MODALITIES ARE REQUIRED

• NOCTURNAL HD NEEDS TO BE INCLUDED IN SUCH TRIALS
  – LACSON AND DIAZ BUXO: NHD FIRST, DHD SUBSEQUENTLY
  \textit{AM J KIDNEY DISEASE} \textbf{2001; 38}:225-230
STANDARD Kt/V: A CONTINUOUS CLEARANCE EQUIVALENT

DEPNER
PLACES TO GO NEXT

TIME!!

DAILY/NOCTURNAL TREATMENT REGIMENS
THE REAL KEY TREATMENT VARIABLE

MD_x_t

COMORBIDITY

AFTER DR. C RONCO
THE EYE OF GOD