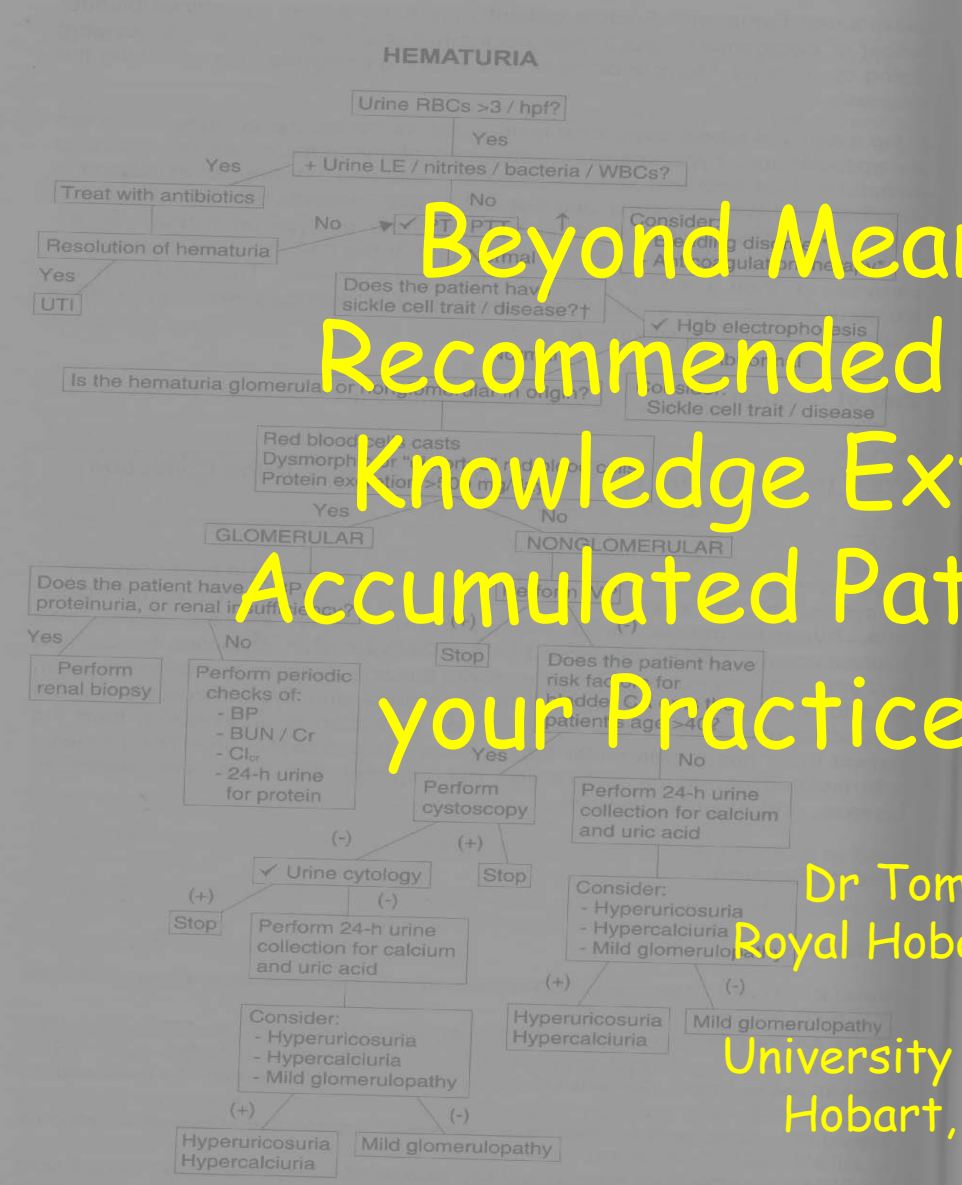
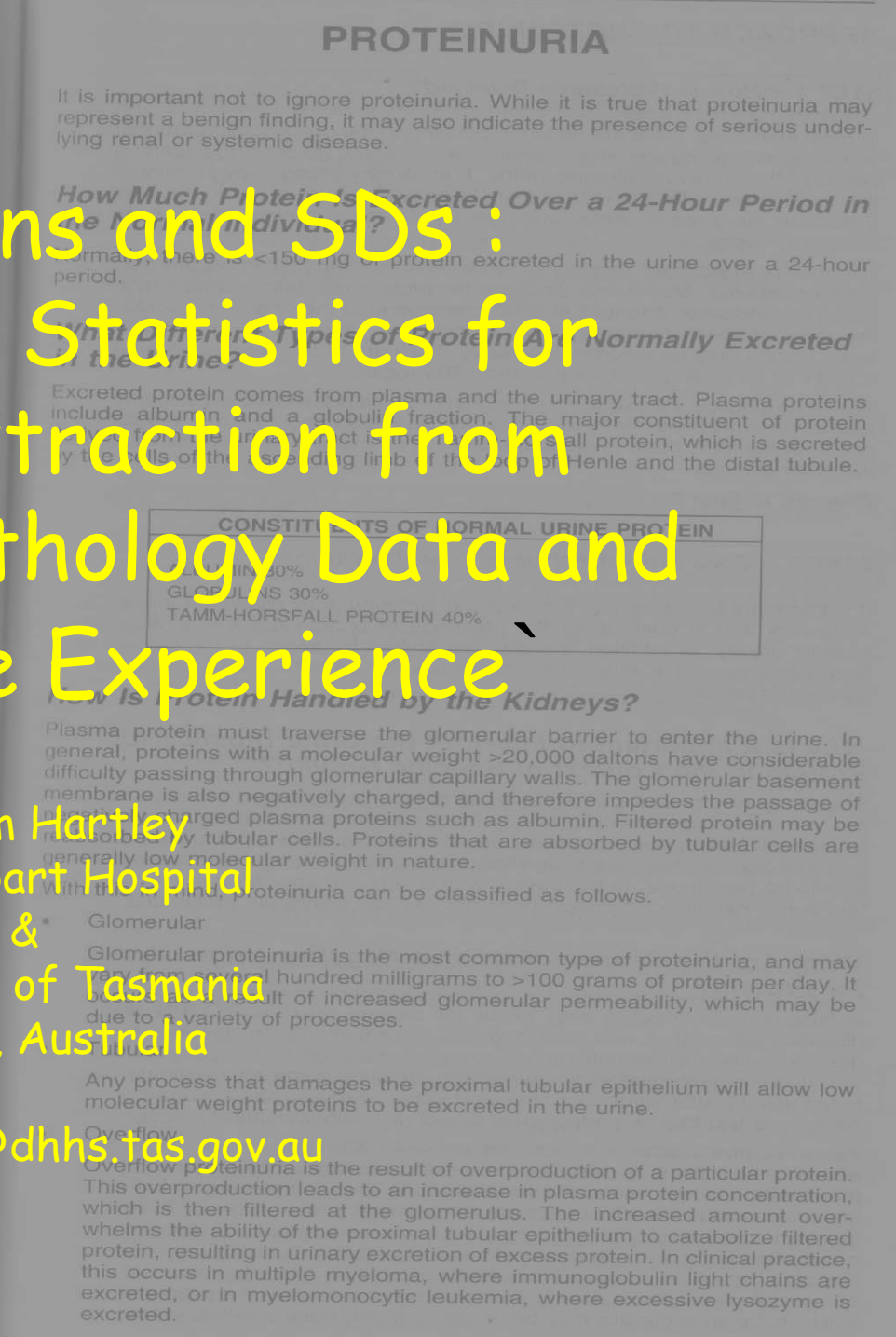
Beyond Means and SDs : Recommended Statistics for Knowledge Extraction from Accumulated Pathology Data and your Practice Experience

Dr Tom Hartley
Royal Hobart Hospital
&
University of Tasmania
Hobart, Australia

tom.hartley@dhhs.tas.gov.au

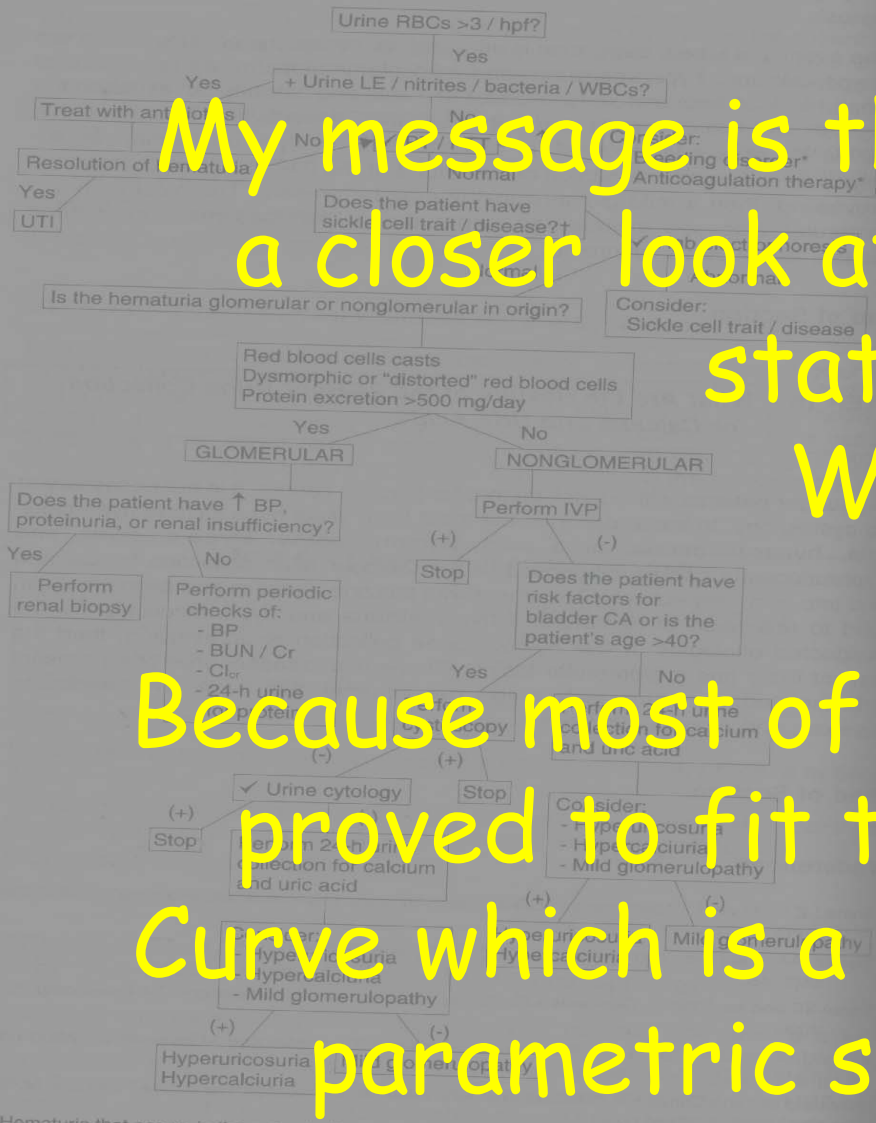




My message is that we should take a closer look at non-parametric statistics.

Why ?

Because most of our data cannot be proved to fit the Normal Error Curve which is a prerequisite for all parametric statistical tests



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.

†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

PROTEINURIA

It is important not to ignore proteinuria. While it is true that proteinuria may represent a benign finding, it may also indicate the presence of serious underlying renal or systemic disease.

How Much Protein Is Normally Excreted Over a 24-Hour Period in the Urine?

Normally, there is <150 mg of protein excreted in the urine over a 24-hour period.

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins include albumin and a globulin fraction. The major constituent of protein derived from the urinary tract is the Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 30%
GLOBULINS 30%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

[illegible] proteins are [illegible] to enter the urine. In general, proteins with a molecular weight >[illegible] Daltons have considerable difficulty passing through glomerular capillary walls. The glomerular basement membrane is also negatively charged, and therefore impedes the passage of negatively charged plasma proteins such as albumin. Filtered protein may be reabsorbed by [illegible]. Proteins that [illegible] by tubular cells are generally low molecular weight in nature.

With this in mind, proteinuria can be classified as follows.

- Glomerular

  [illegible] proteinuria is the most common type of proteinuria, and may vary from subclinical [illegible] to >[illegible] grams of protein per day. It occurs as a result of increased glomerular permeability, which may be due to a variety of processes.

  [illegible]

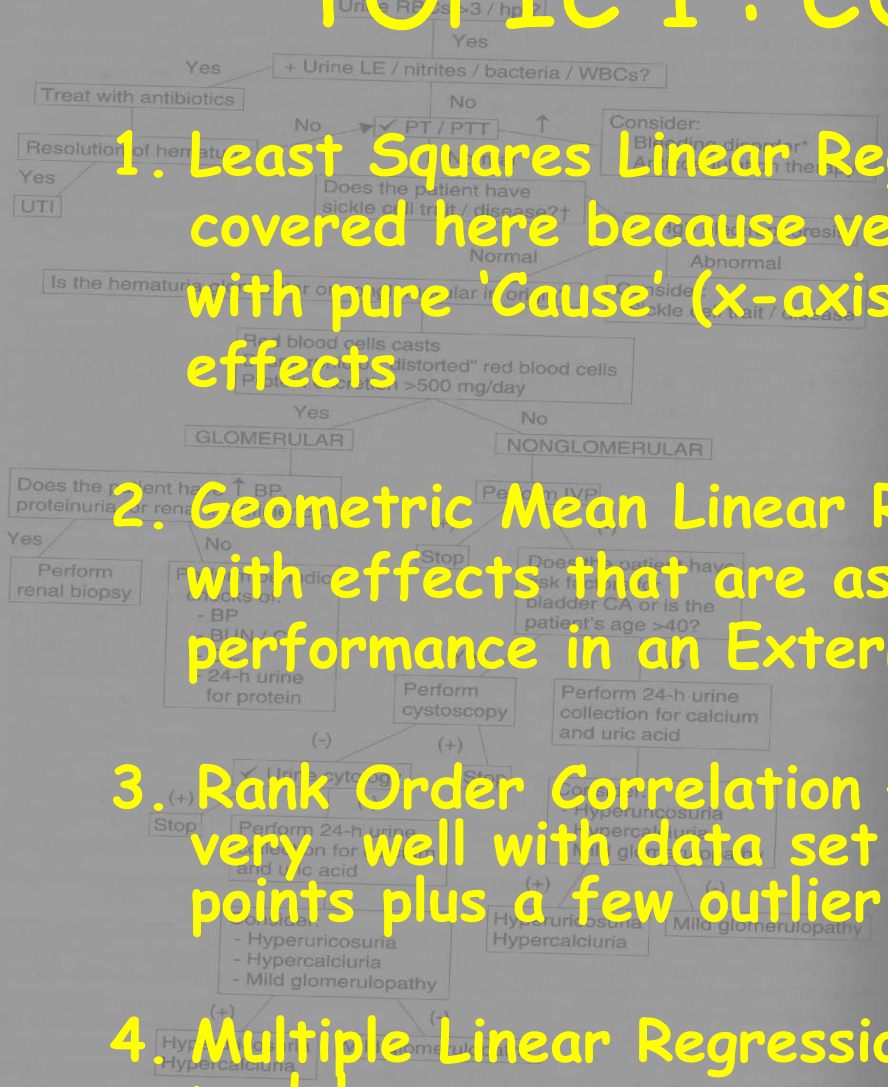
  [illegible] damages the [illegible] tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

- Overflow

  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

TOPIC 1 : CORRELATION

1. Least Squares Linear Regression – not covered here because very often we are not dealing with pure 'Cause' (x-axis) and 'Effect' (y-axis) effects
2. Geometric Mean Linear Regression – deals very well with effects that are associated eg comparative performance in an External QAP program
3. Rank Order Correlation – (a Non-parametric test) deals very well with data set where there is a cluster of points plus a few outlier points.
4. Multiple Linear Regression – deals with multiparameter models



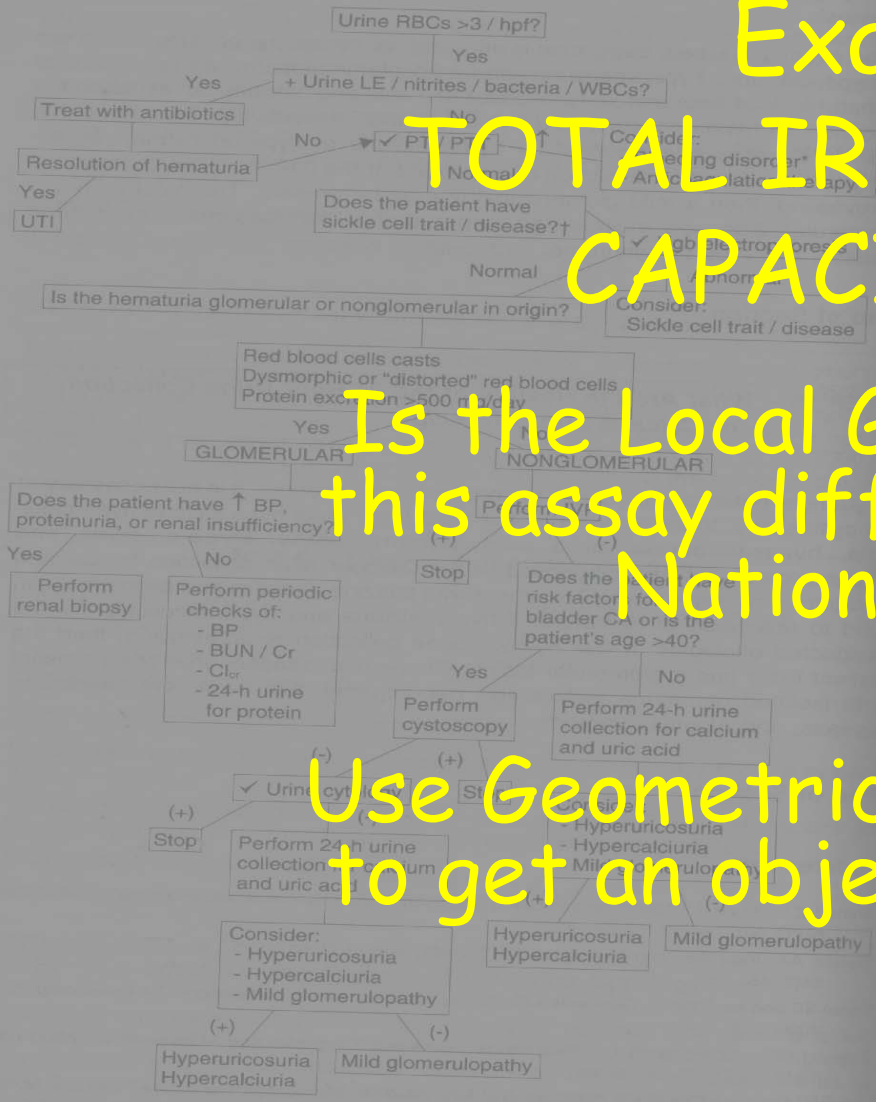
*Hematuria that occurs in the absence of an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.
†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

Example 1
TOTAL IRON BINDING CAPACITY EQAP

Is the Local Group performing this assay differently from the National Group ?

Use Geometric Mean Regression to get an objective assessment

HEMATURIA



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.

†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

PROTEINURIA

It is important not to ignore proteinuria. While it is true that proteinuria may represent a benign finding, it may also indicate the presence of serious underlying renal or systemic disease.

How Much Protein Is Excreted Over a 24-Hour Period in the Normal Individual?

Normally, there is <150 mg of protein excreted in the urine over a 24-hour period.

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins include albumin and a globulin fraction. The major constituent of protein derived from the urinary tract is the Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 3%
GLOBULINS 20%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

Plasma protein must traverse the glomerular barrier to enter the urine. In general, proteins with a molecular weight >20,000 daltons have considerable difficulty passing through glomerular capillary walls. The glomerular basement membrane is also negatively charged, and therefore impedes the passage of [illegible] Filtered protein may be [illegible] Proteins that are absorbed by tubular cells are generally low molecular weight in nature.

[illegible] in the proteinuria [illegible] as follows.

- Glomerular

  Glomerular proteinuria is the most common type of proteinuria, and may vary from several hundred milligrams to >100 grams of protein per day. It occurs as a result of increased glomerular permeability, which may be due to a variety of processes.

- Tubular

  Any process that damages the proximal tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

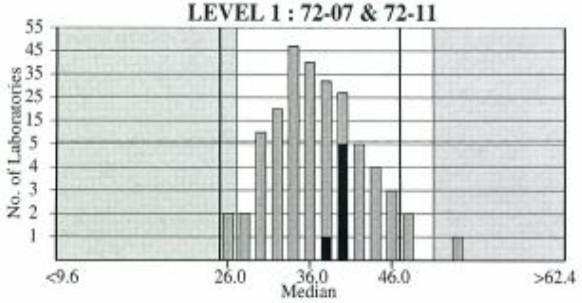
- Overflow

  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

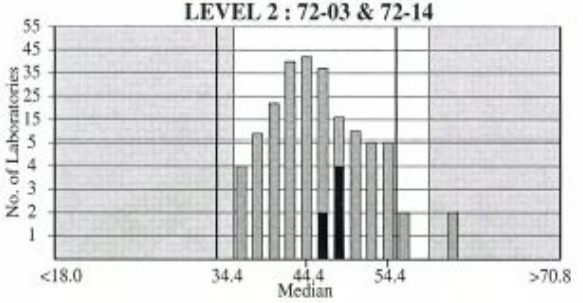
Prepared by:
RCPA-AACB Chemical Pathology QAP Group

TOTAL IRON BINDING CAPACITY (µmol/L) : Tasmania Subgroup Report for Cycle 72 - All Specimens

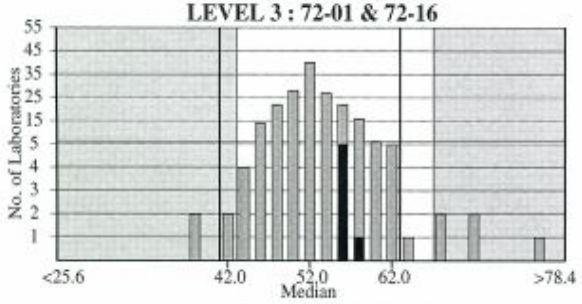
LEVEL 1 : 72-07 & 72-11



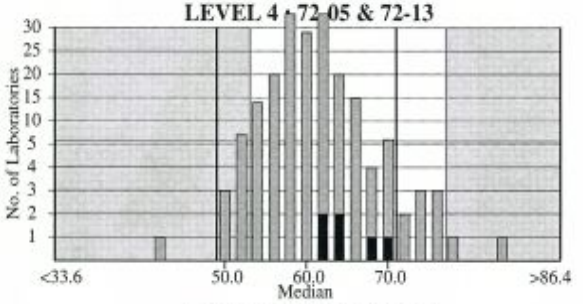
LEVEL 2 : 72-03 & 72-14



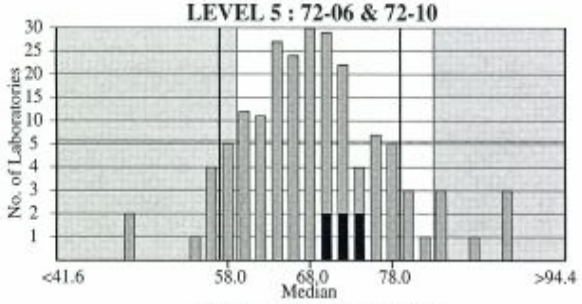
LEVEL 3 : 72-01 & 72-16



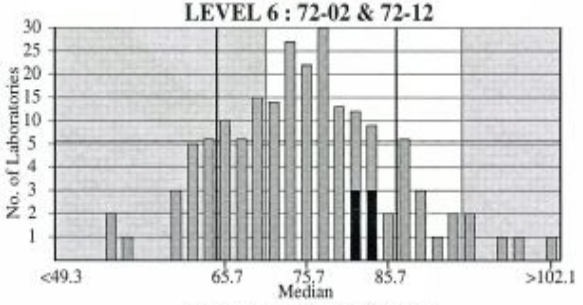
LEVEL 4 : 72-05 & 72-13



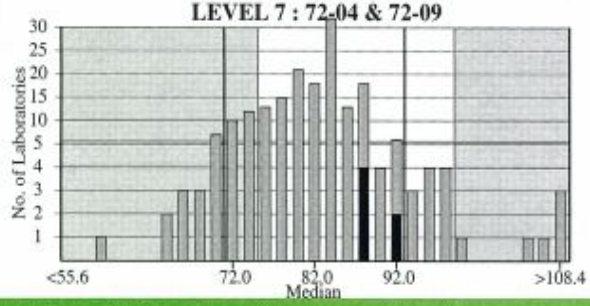
LEVEL 5 : 72-06 & 72-10



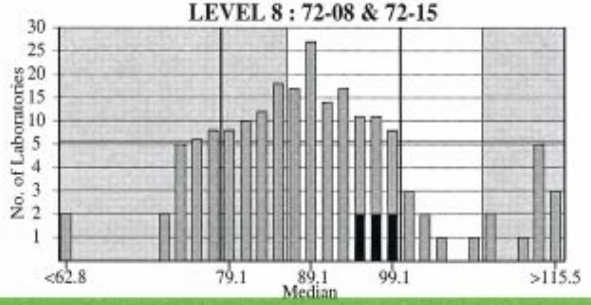
LEVEL 6 : 72-02 & 72-12



LEVEL 7 : 72-04 & 72-09

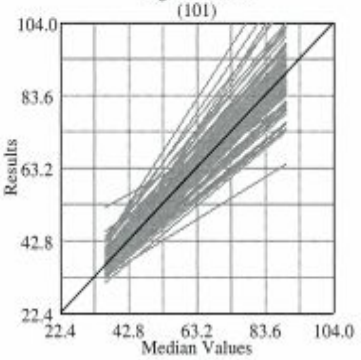


LEVEL 8 : 72-08 & 72-15



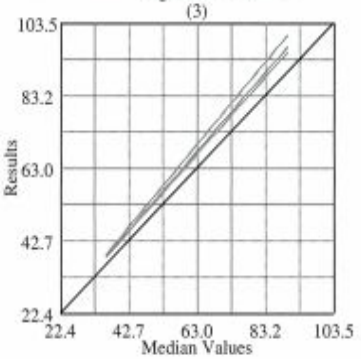
All Results

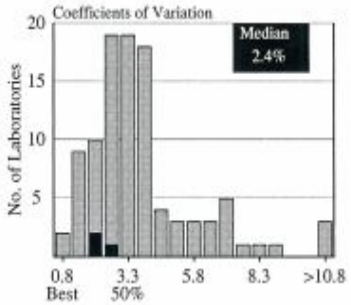
Regression Lines
(101)

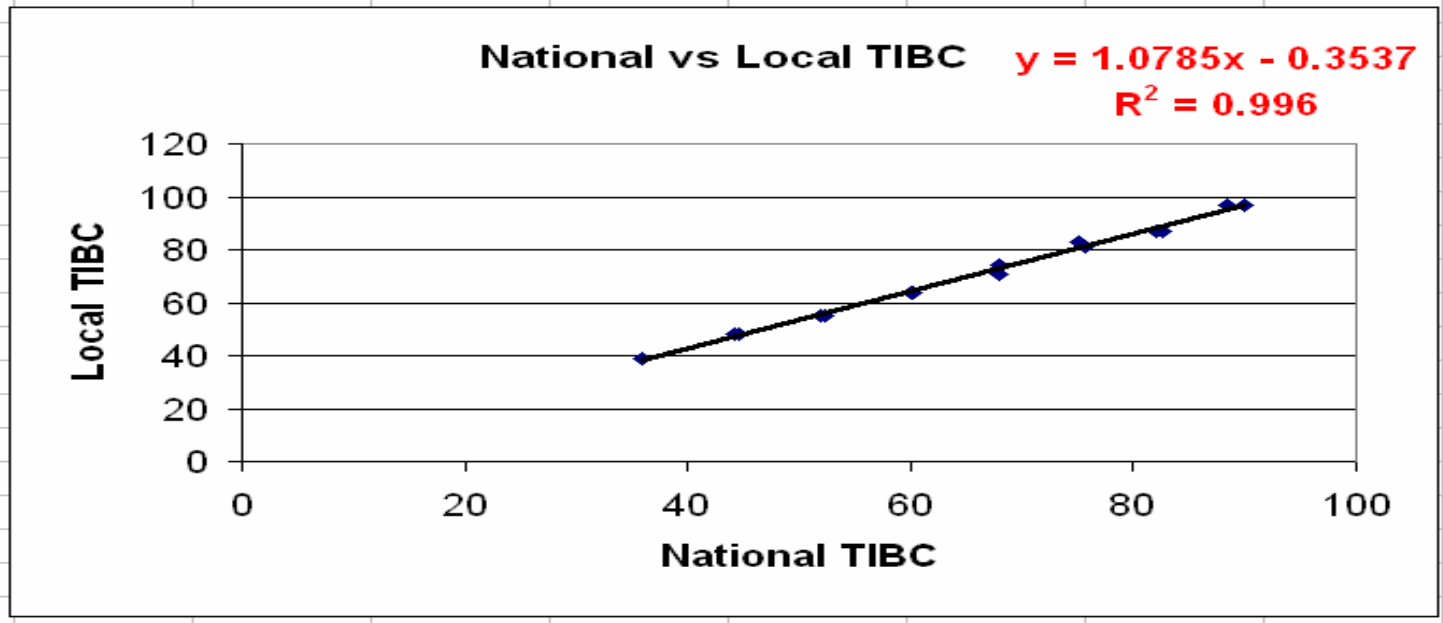


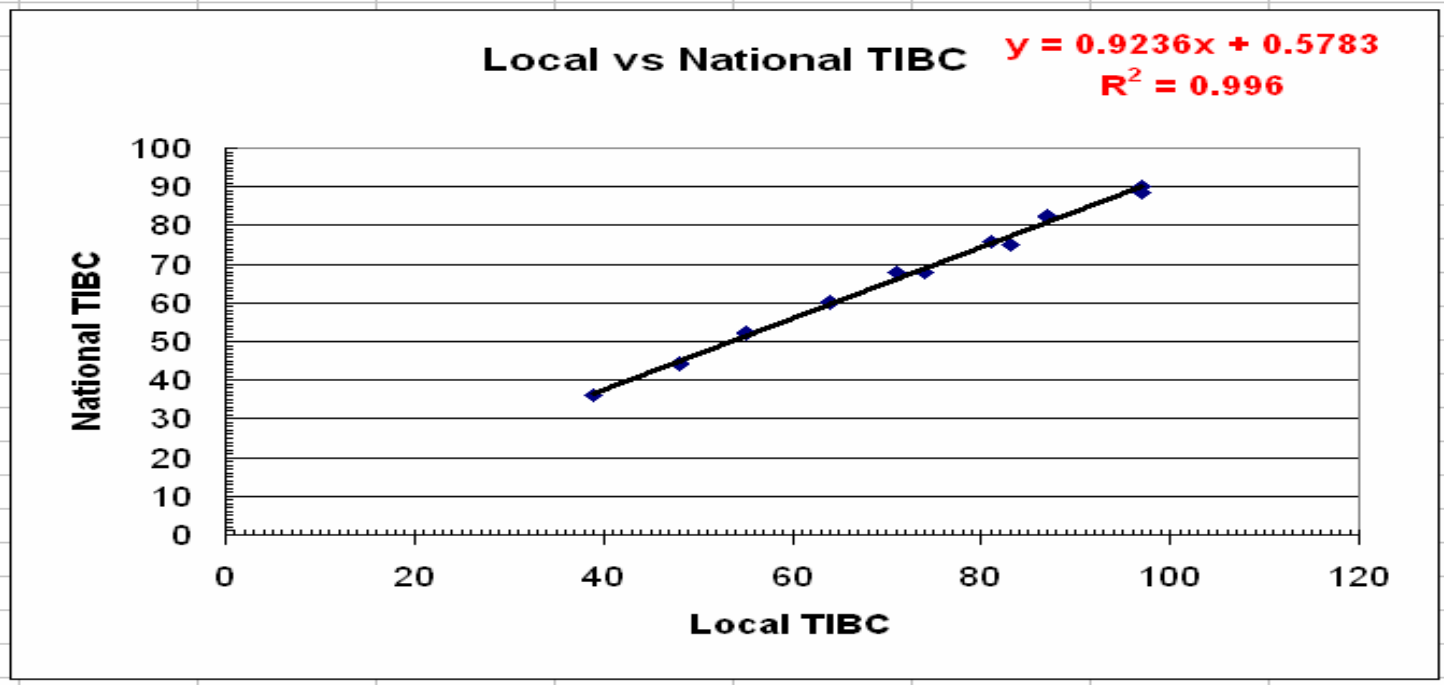
Tasmania Subgroup

Regression Lines
(3)









Y on x and x on y regressions both suggest either a + 8% or a -8% systematic bias depending upon your point of view, local or National.

Geometric Mean (GM) Regression Formulae

The slope is easily calculated from the two equations we have already got :

$$\text{GM Slope} = \text{SquareRoot}\left(\text{Slope}_{y \text{ on } x} \;/\; \text{Slope}_{x \text{ on } y}\right)$$

$$= \text{SquareRoot}\,(1.0785/0.9236) = 1.081$$

Alternatively GM Slope = SDy / SDx

GM Intercept = Mean of y data – GM Slope * Mean of the x data

$$= 68.0625 - 1.0806 * 63.4375$$

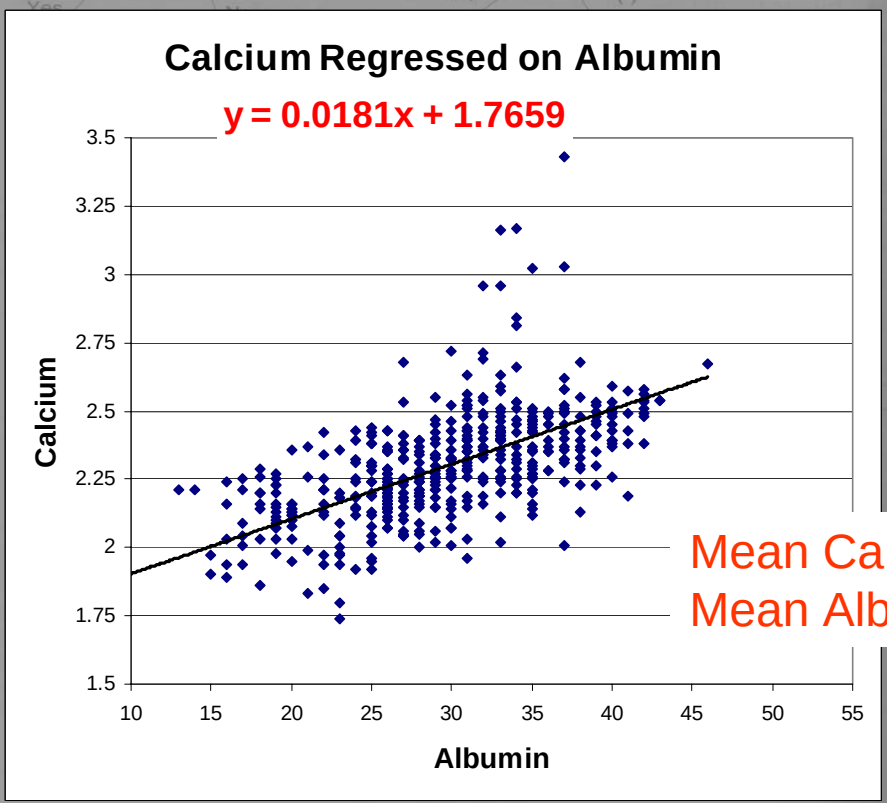
$$= -0.4881$$

Geometric Mean Regression : Local = 1.081 * National - 0.4881

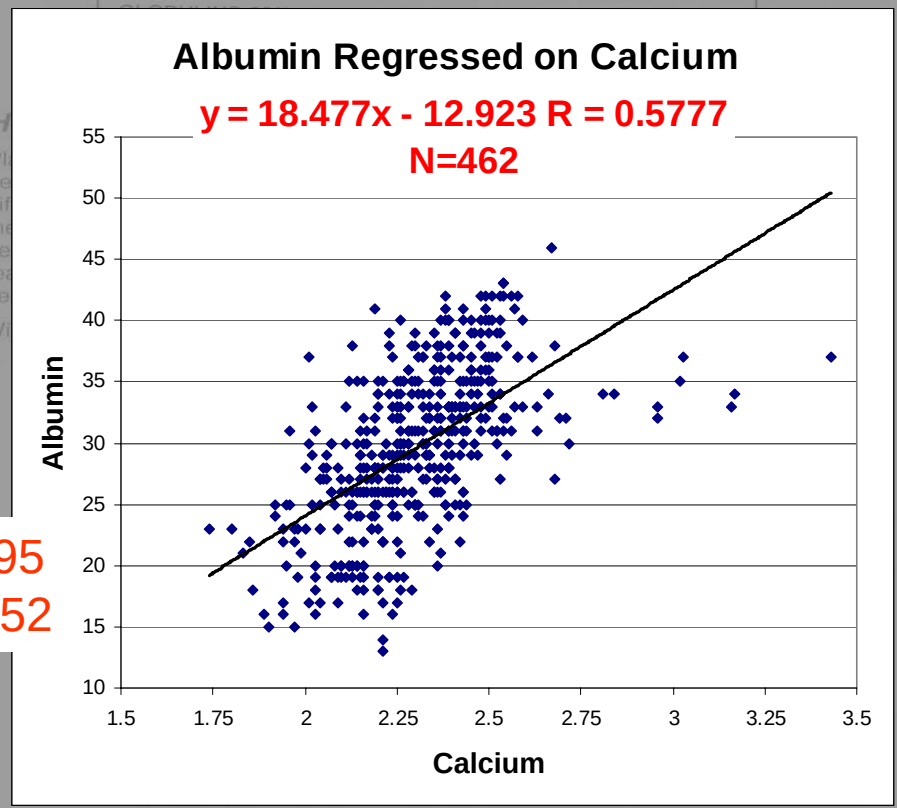
The geometric mean regression analysis suggests that the consensus agreement should be that the local labs are reading 8% higher than the National labs.

Example 2
Albumin versus Calcium - a physiological relationship

Objective is to describe the functional relationship between the two parameters. The objective is not to predict one from the other. Recommendation is that you use Geometric Mean Regression



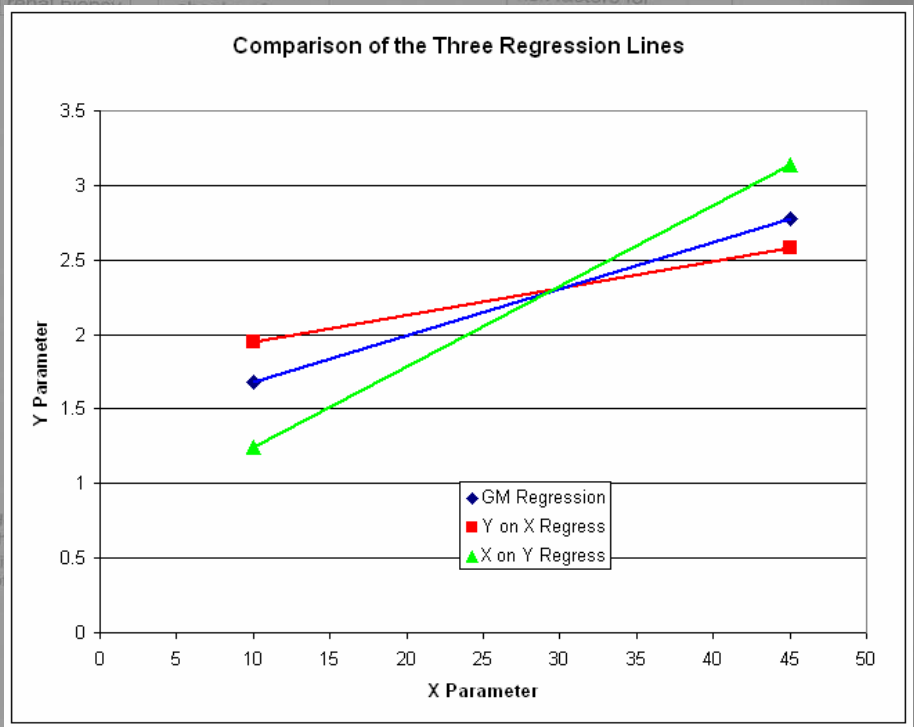
Mean Ca = 2.295
Mean Alb = 29.52

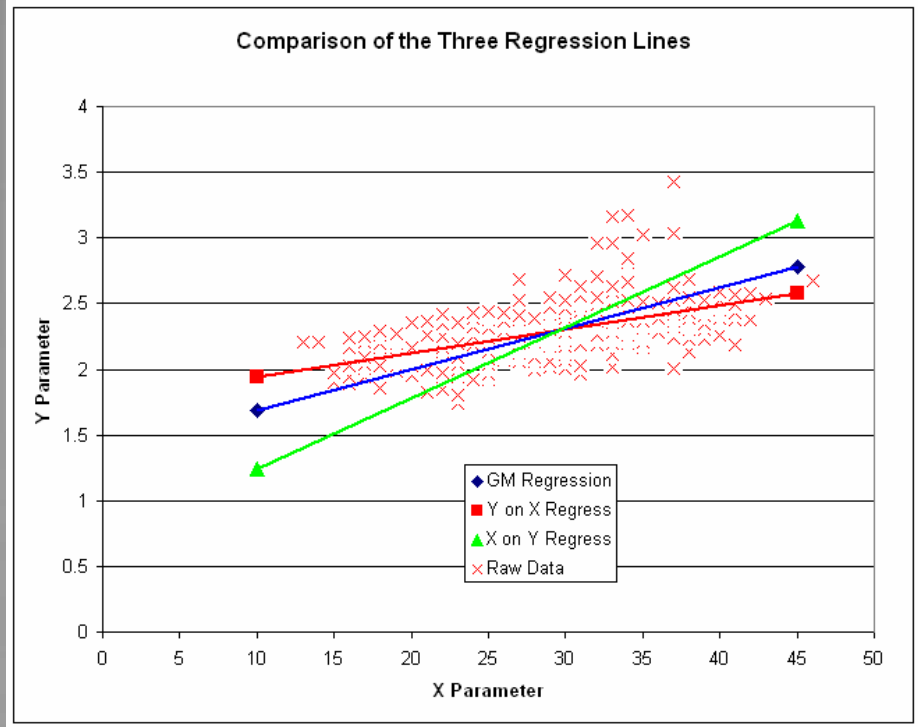


Albumin versus Calcium – a physiological relationship

GM Regression Equation

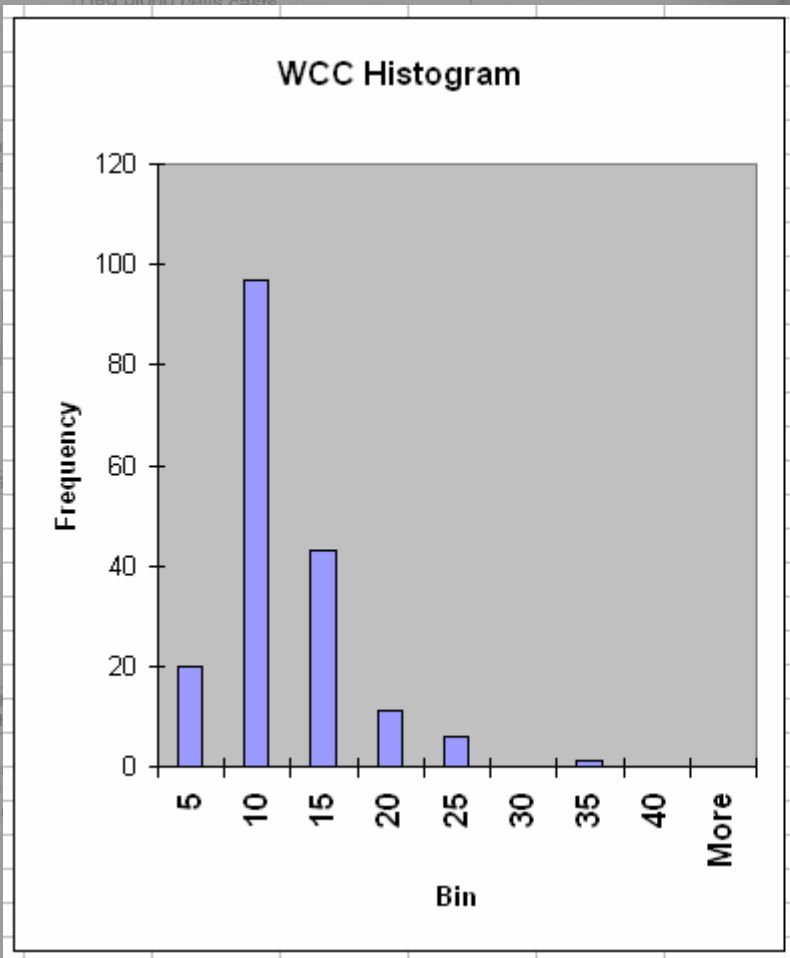
Calcium = 0.03130 * Alb + 1.37

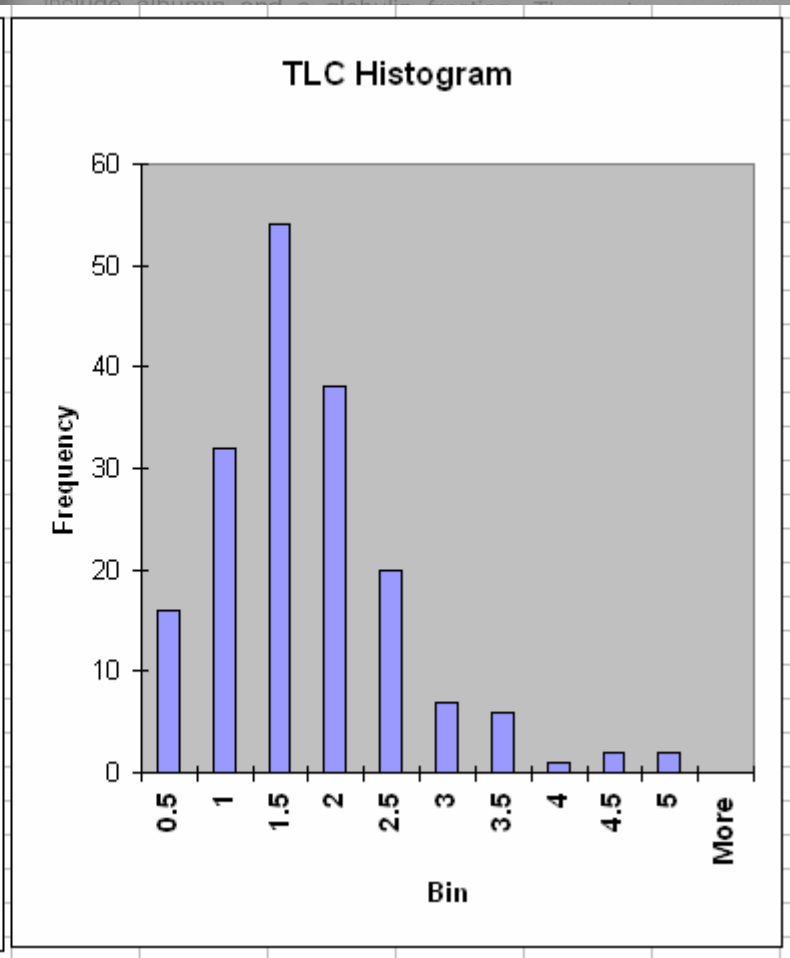




Example 3
Rank Order Correlation

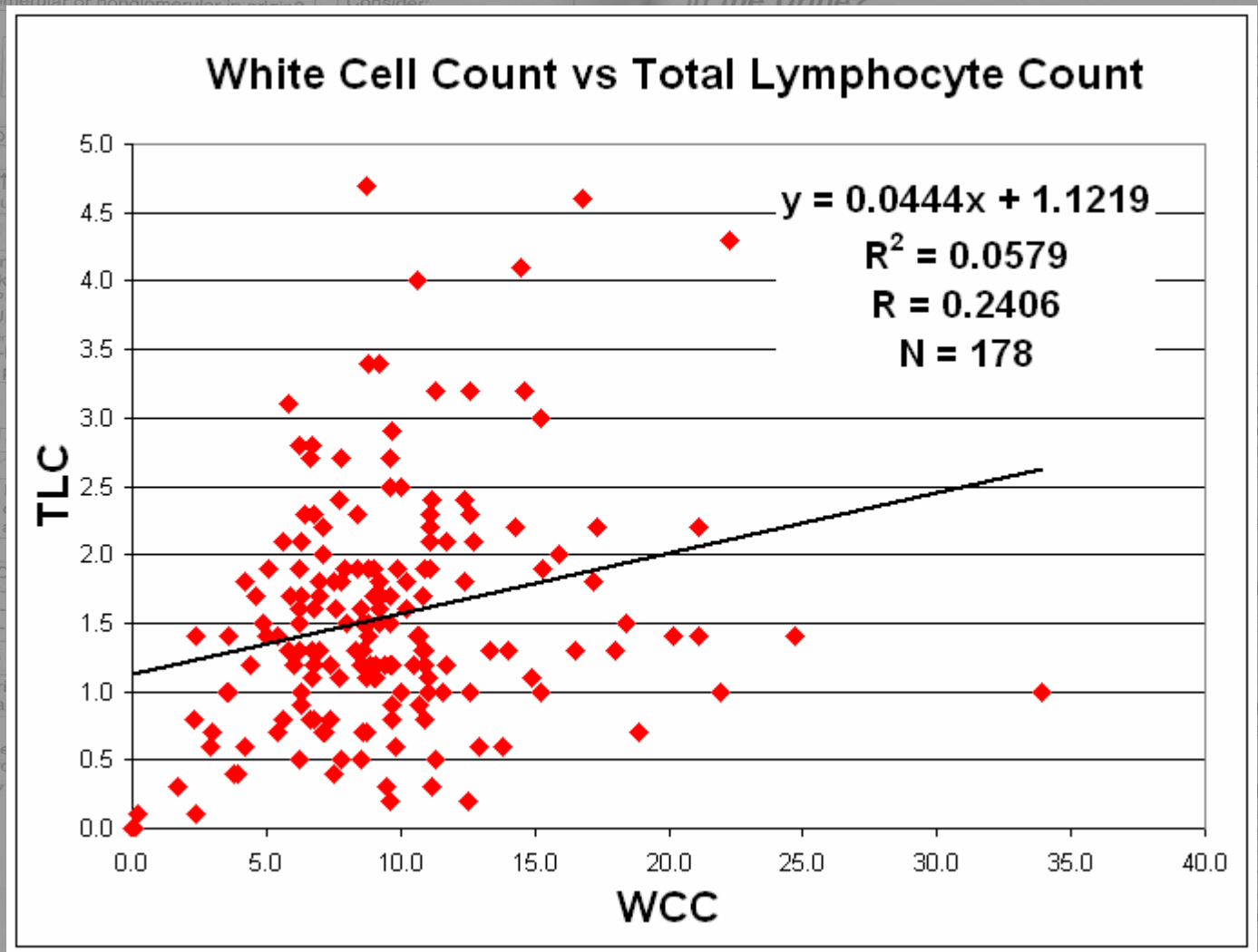
WCC versus TLC : no real physiological relationship but tend to parallel each other and have skewed histograms





Example 3
Rank Order Correlation

WCC versus TLC : no real physiological relationship but tend to parallel each other and have skewed histograms



Rank Order Correlation : WCC vs TLC

VassarStats: Web Site for Statistical Computation

- Utilities
- Clinical Research Calculators
- Probabilities
- Distributions
- Frequency Data
- Proportions
- Ordinal Data
- Correlation & Regression
- t-Tests & Procedures
- ANOVA
- ANCOVA
- Miscellanea
- HOME

After data have been entered, click one or the other of the «Calculate» buttons according t
you are starting out with ranks or raw data. If you wish to perform another analysis with a
set of data: click the «Reset» button if the value of n for the new set of data is exactly 17
Reload or Refresh button of your browser if the value of n is greater or smaller than 178.

http://faculty.vassar.edu/lowry/VassarStats.html

Data Entry

	Ranks for		Raw Data for	
pairs	X	Y	X	Y
1	1	1.5	0.03	0
2	2	1.5	0.1	0
3	3	3.5	0.2	0.1
4	4	8	1.7	0.3
5	5	32	2.3	0.8
6	6.5	89.5	2.4	1.4
7	6.5	3.5	2.4	0.1
8	8	19	2.9	0.6
9	9	25	3	0.7
10	10	43.5	3.5	1
11	11.5	89.5	3.6	1.4
12	11.5	43.5	3.6	1
13	13	11	3.8	0.4
14	14	11	3.9	0.4

Data Import

```
0.03    0
0.1     0
0.2     0.1
1.7     0.3
2.3     0.8
2.4     1.4
2.4     0.1
2.9     0.6
3       0.7
3.5     1
3.6     1.4
3.6     1
3.8     0.4
3.9     0.4
```

Import Raw Data

Rank Order Correlation : WCC vs TLC

n	r_s	t	df
178	0.2123	2.88	176

P		
	one-tailed	0.002236
	two-tailed	0.004471

N = 178 r = 0.2406

Reset Calculate

t	df
3.289	176

Probability

directional	0.000608
non-directional	0.001216

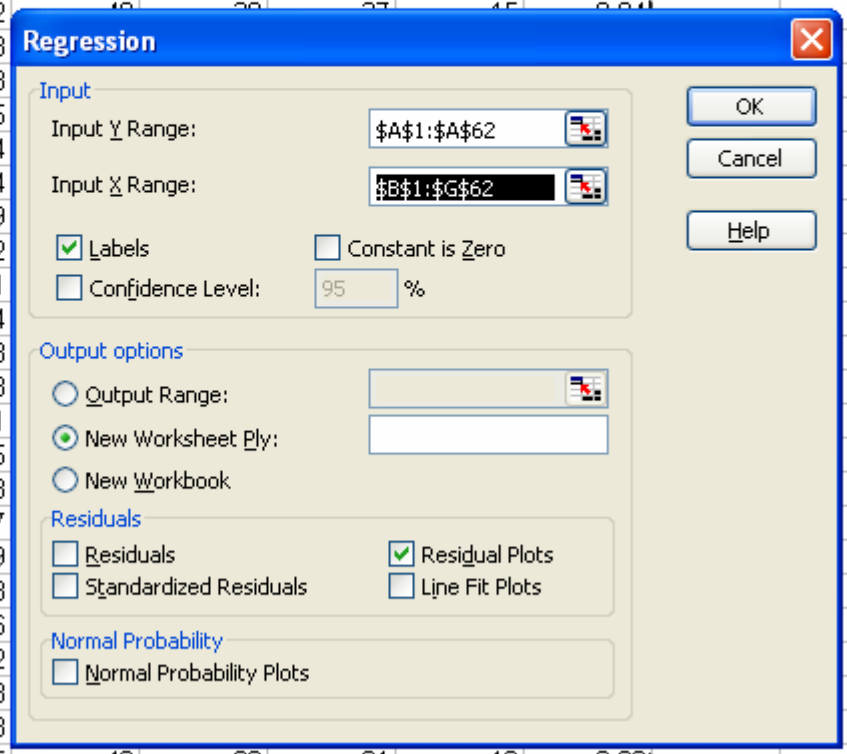
37 times

Example 4

MULTIPLE LINEAR REGRESSION

Use this for multiparameter modelling eg Ionised Ca

	A	B	C	D	E	F	G	H	I
1	Ca2+	Tca	Alb	Glob	Bic	AG	Phos		
2	1.29	2.58	44	46	31	14	1.33		
3	1.38	2.71	45	24	29	11	1.1		
4	1.33	2.71	44	27	32	12	1.11		
5	1.33	2.53	37	31	15	19	1.46		
6	1.34	2.73	42	27	31	15	1.12		
7	1.3	2.6	42	45	29	11	1.61		
8	1.21	2.42							
9	1.36	2.63							
10	1.23	2.43							
11	1.26	2.45							
12	1.28	2.34							
13	1.22	2.54							
14	1.22	2.39							
15	1.22	2.42							
16	1.42	2.81							
17	1.21	2.24							
18	1.19	2.33							
19	1.24	2.58							
20	1.2	2.41							
21	1.22	2.35							
22	1.18	2.3							
23	1.47	2.77							
24	1.25	2.29							
25	1.18	2.3							
26	1.22	2.36							
27	1.27	2.52							
28	1.29	2.58							
29	1.23	2.3							
30	1.2	2.35	43	28	31	13	0.98		
31	1.22	2.34	42	31	29	12	1.09		



MULTIPLE LINEAR REGRESSION

	A	B	C	D	E
1	**SUMMARY OUTPUT**				
2					
3	***Regression Statistics***				
4	**Multiple R**	**0.9687**			
5	**R Square**	**0.9383**			
6	**Adjusted R Square**	**0.9315**			
7	**Standard Error**	**0.0188**			
8	**Observations**	**61**			
9					
10	**ANOVA**				
11		***df***	***SS***	***MS***	***F***
12	**Regression**	**6**	**0.291137098**	**0.04852285**	**136.9104006**
13	**Residual**	**54**	**0.019138311**	**0.000354413**	
14	**Total**	**60**	**0.31027541**		
15					
16		***Coefficients***	***Standard Error***	***t Stat***	***P-value***
17	**Intercept**	**0.72856**	**0.05172**	**14.1**	**0.0000**
18	**Tca**	**0.42451**	**0.01715**	**24.7**	**0.0000**
19	**Alb**	**-0.00565**	**0.00093**	**-6.1**	**0.0000**
20	**Glob**	**-0.00174**	**0.00055**	**-3.2**	**0.0025**
21	**Bic**	**-0.00445**	**0.00075**	**-6.0**	**0.0000**
22	**AG**	**-0.00528**	**0.00111**	**-4.7**	**0.0000**
23	**Phos**	**-0.02662**	**0.01235**	**-2.2**	**0.0357**
24					

Ionised Ca = 0.425 TCa + 0.728 – 0.00565 Alb – 0.00174 Glob – 0.00445 Bic – 0.00528 AG – 0.027 Phos

TOPIC 2 : BAYESIAN NETWORK ANALYSIS

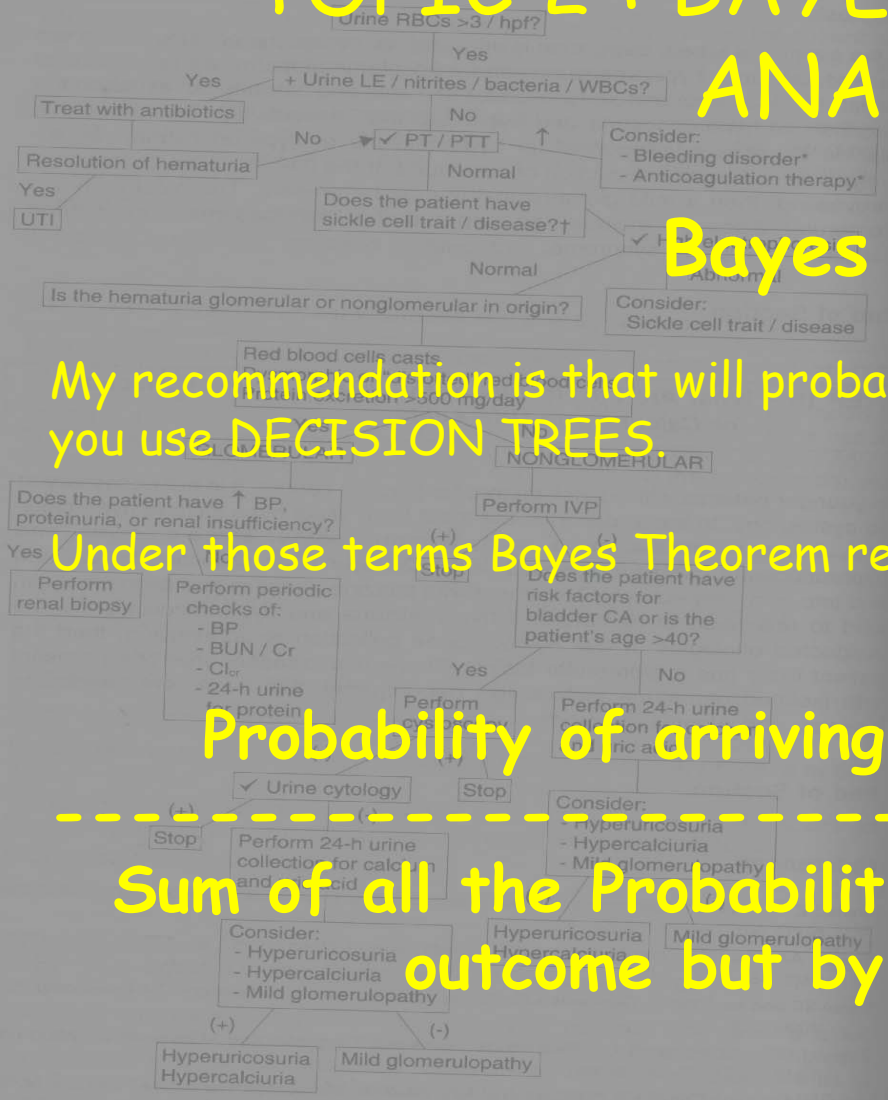
Bayes Theorem

My recommendation is that will probably find Bayes Theorem easier to apply if you use DECISION TREES.

Under those terms Bayes Theorem reads as :

Probability of arriving at your Target Outcome

Sum of all the Probabilities of arriving at the SAME outcome but by all possible routes



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.

†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

How Much Protein Is Excreted Over a 24-Hour Period in the Normal Individual?

Normally, there is <150 mg of protein excreted in the urine over a 24-hour period.

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins include albumin and α-globulin fraction. The major constituent of protein [illegible] is Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 30%
GLOBULINS 30%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

Plasma protein must traverse the glomerular barrier to enter the urine. In general, proteins with a molecular weight [illegible] have considerable difficulty passing through the glomerular capillary wall. The glomerular basement membrane is also negatively charged, and therefore impedes the passage of negatively charged plasma proteins such as albumin. Filtered protein may be reabsorbed by tubular cells. Proteins that are absorbed by tubular cells are generally low molecular weight in nature.

With this in mind, proteinuria can be classified as follows.

- Glomerular

  Glomerular proteinuria is the most common type of proteinuria, and may [illegible] >100 grams of protein per day. It [illegible] of increased glomerular permeability, which may be due to a variety of processes.

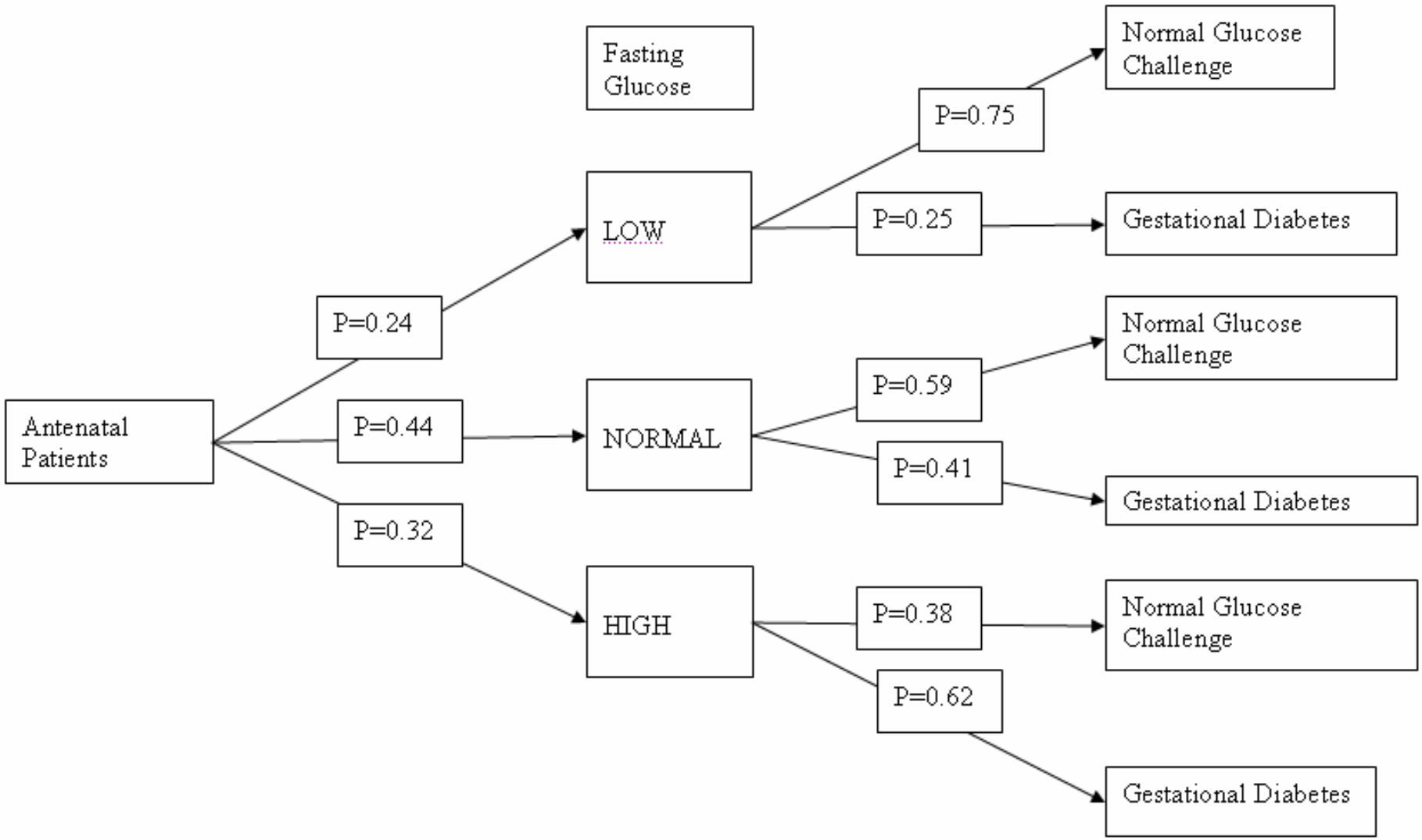
- Tubular

  Any process that damages the proximal tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

- Overflow

  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

Decision Tree Based Upon a Fasting Glucose Reference Study

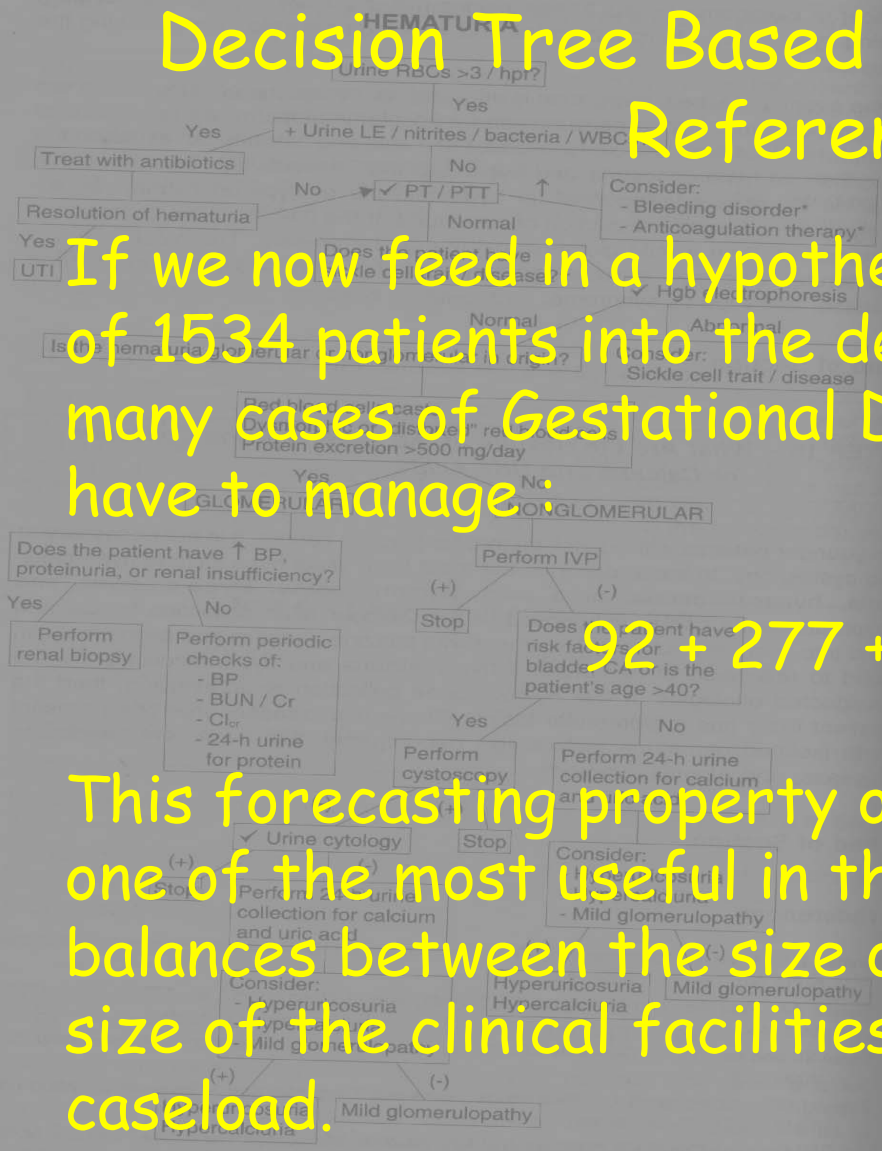


Decision Tree Based Upon a Fasting Glucose Reference Study

If we now feed in a hypothetical Antenatal Clinic Size of 1534 patients into the decision tree we can see how many cases of Gestational Diabetes they are going to have to manage:

92 + 277 + 304 = 673.

This forecasting property of our analyses is perhaps one of the most useful in these times of critical balances between the size of clinical caseloads and the size of the clinical facilities available to service that caseload.



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.
†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

PROTEINURIA

It is important not to ignore proteinuria. While it is true that proteinuria may represent a benign finding, it may also indicate the presence of serious underlying renal or systemic disease.

How Much Protein Is Excreted Over a 24-Hour Period in the Normal Individual?

Normally, there is <150 mg of protein excreted in the urine over a 24-hour period.

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins [illegible] the glomerular capsule. The major constituent of protein [illegible] the urinary tract is Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 30%
GLOBULINS 30%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

Plasma protein must traverse the glomerular barrier to enter the urine. In general, proteins with a molecular weight >20,000 daltons have considerable difficulty [illegible] the glomerular basement membrane, which is negatively charged and therefore impedes the passage of negatively charged plasma proteins such as albumin. Filtered protein may be reabsorbed by tubular cells. Proteins that are absorbed by tubular cells are generally degraded [illegible]

With this in mind, proteinuria can be classified as follows.

- Glomerular

  Glomerular proteinuria is the most common type of proteinuria, and may vary from several hundred milligrams to >10 grams of protein per day. It is usually the result of increased glomerular permeability, which may be due to a variety of processes.

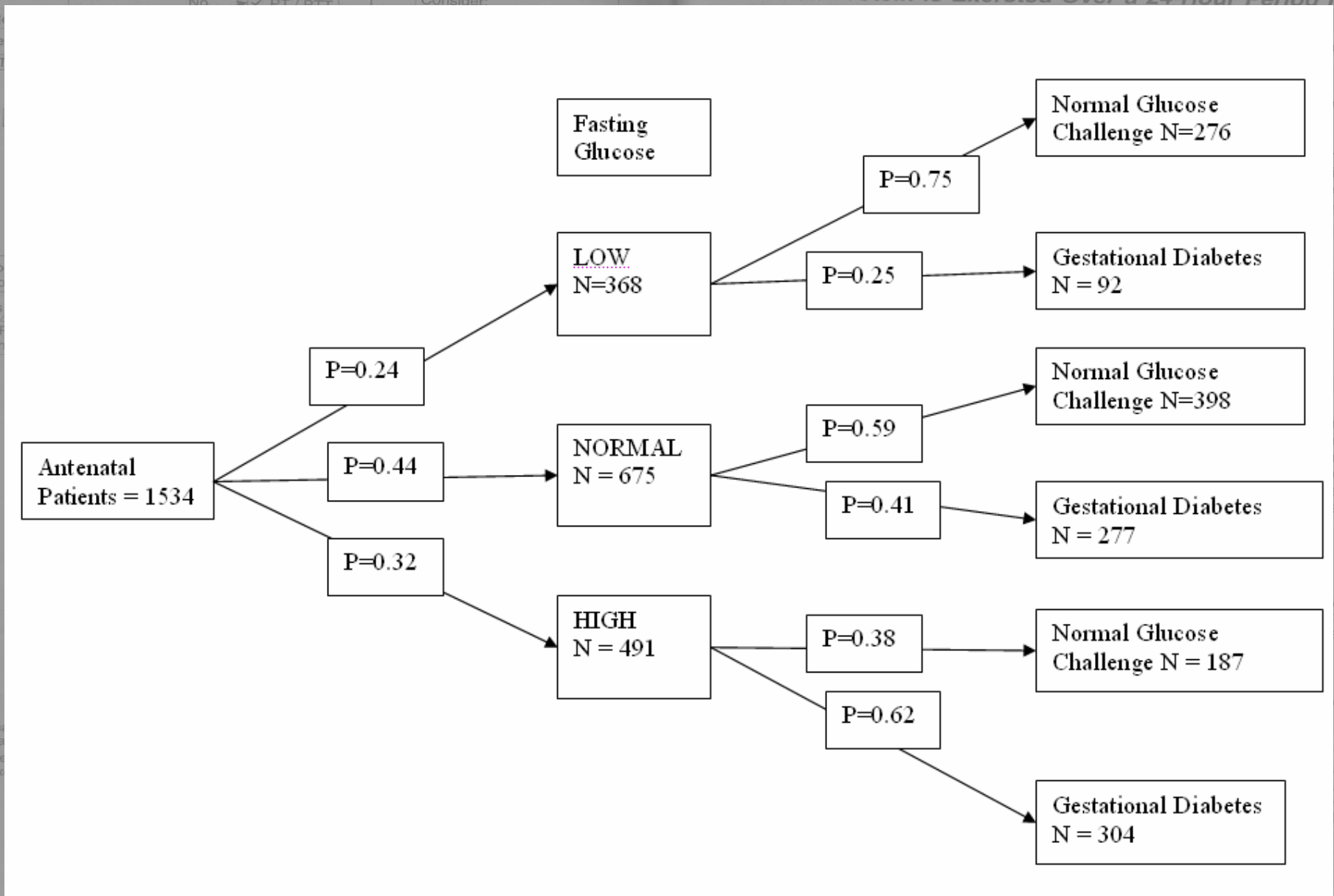
- Tubular

  Any process that damages the proximal tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

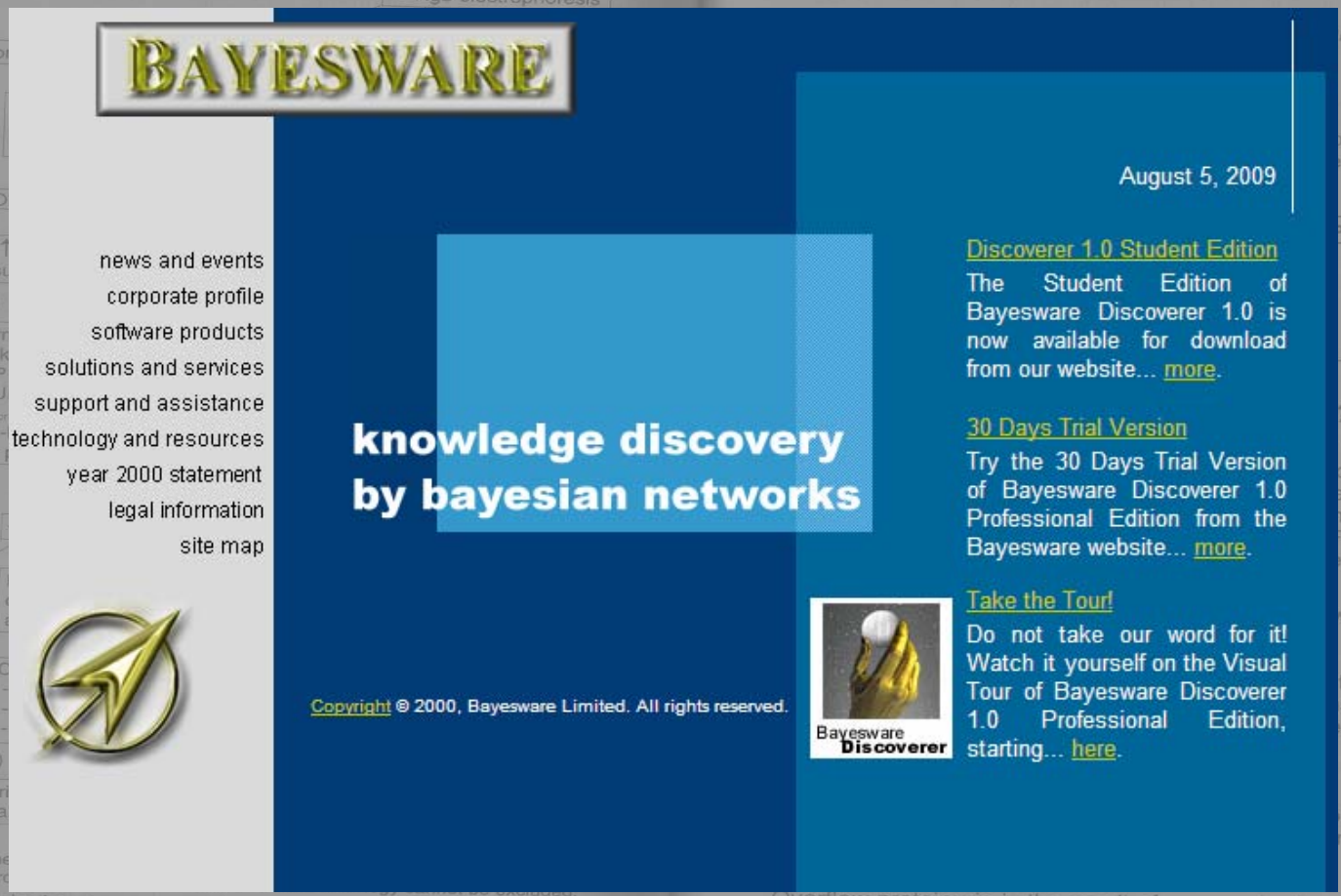
- Overflow

  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

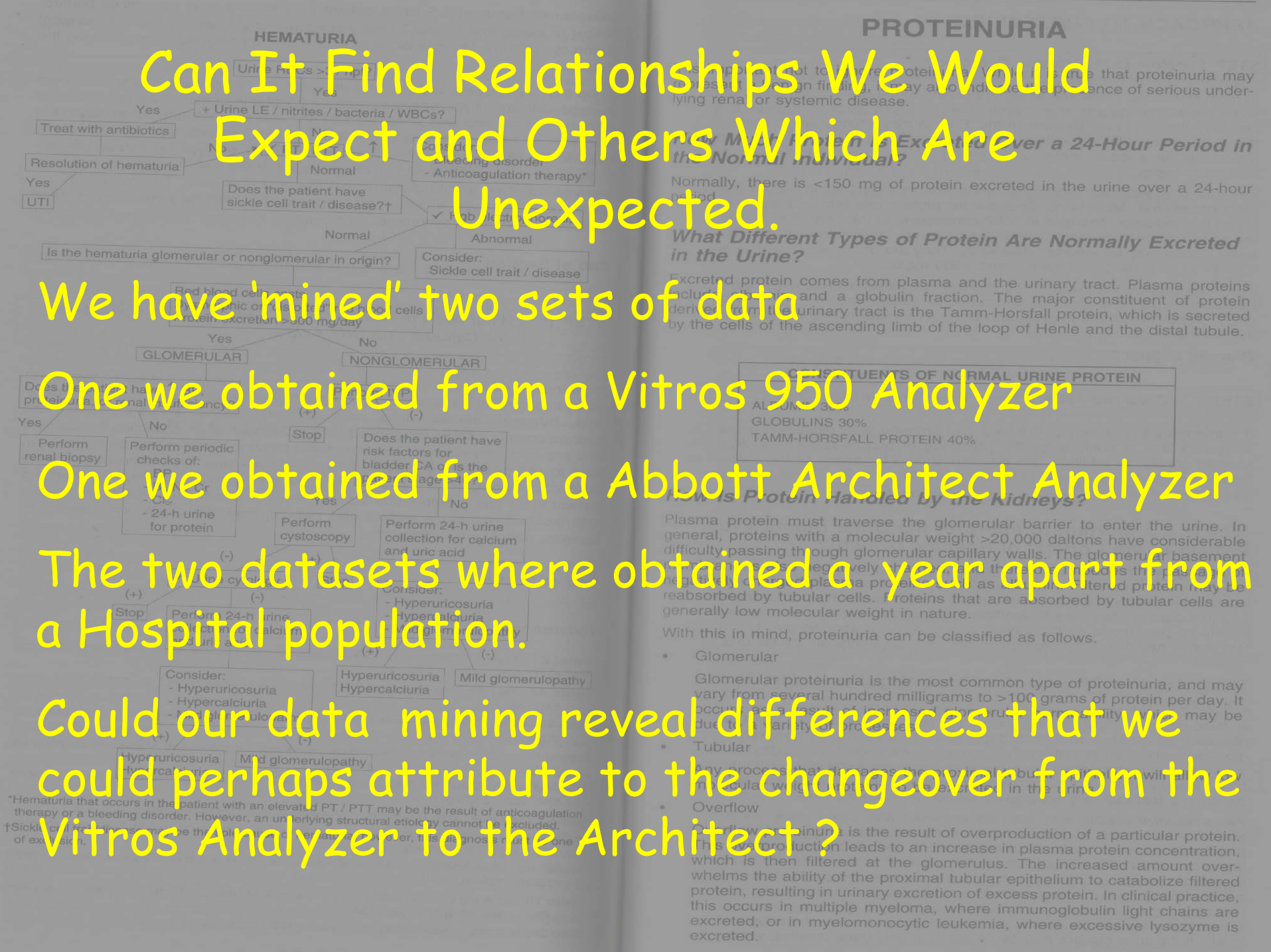
Decision Tree Based Upon a Fasting Glucose Reference Study



What Happens When We Search for A Decision Tree in Laboratory Data ?



www.bayesware.com


HEMATURIA
PROTEINURIA
Can It Find Relationships We Would Expect and Others Which Are Unexpected.
We have 'mined' two sets of data
One we obtained from a Vitros 950 Analyzer
One we obtained from a Abbott Architect Analyzer
The two datasets where obtained a year apart from a Hospital population.
Could our data mining reveal differences that we could perhaps attribute to the changeover from the Vitros Analyzer to the Architect ?

The Electrolytes Dataset

N = 286 Vitros results + 349 Architect results = 635

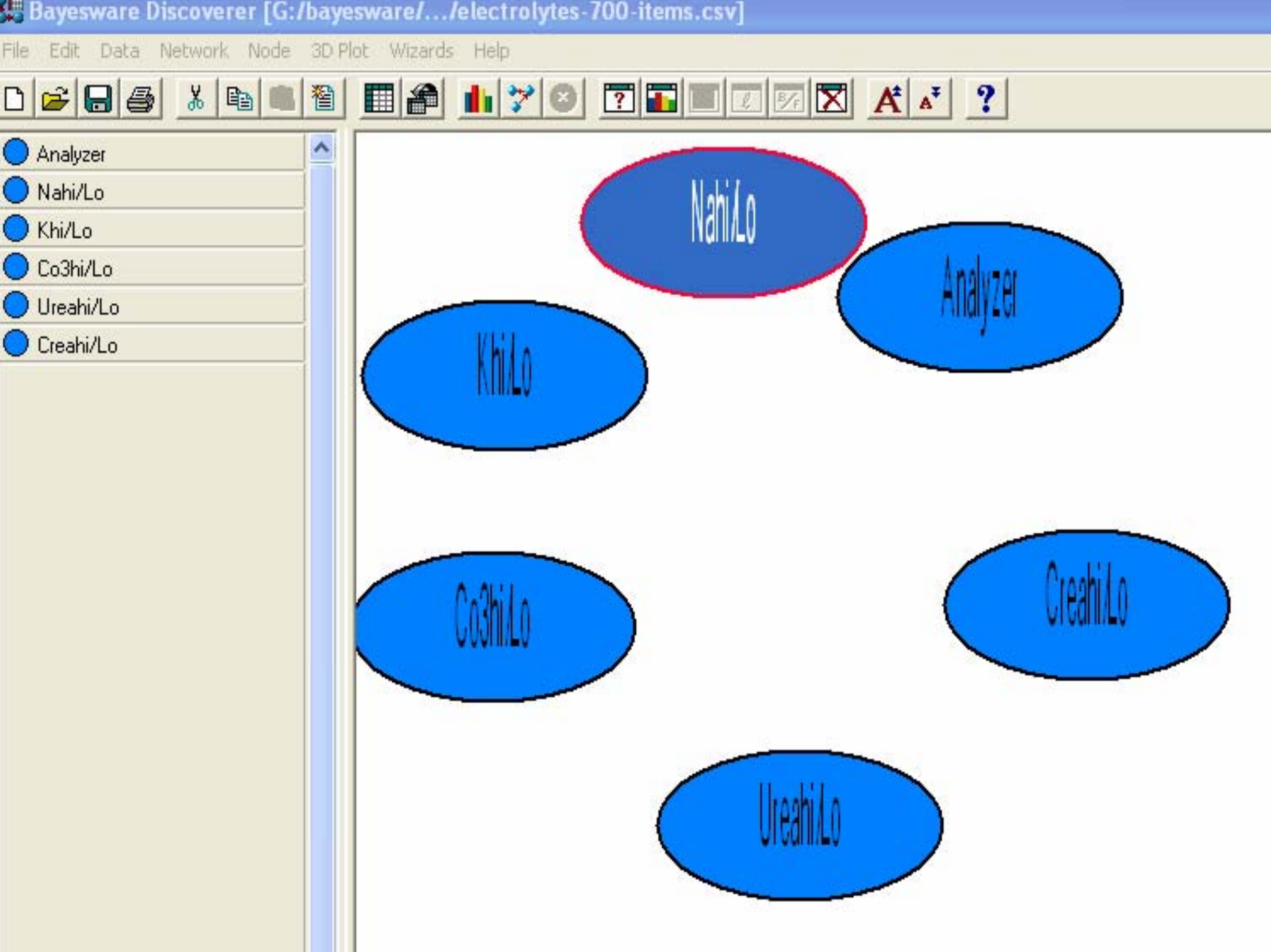
Results were scored as L,N or H according to the ref ranges in use at the time.

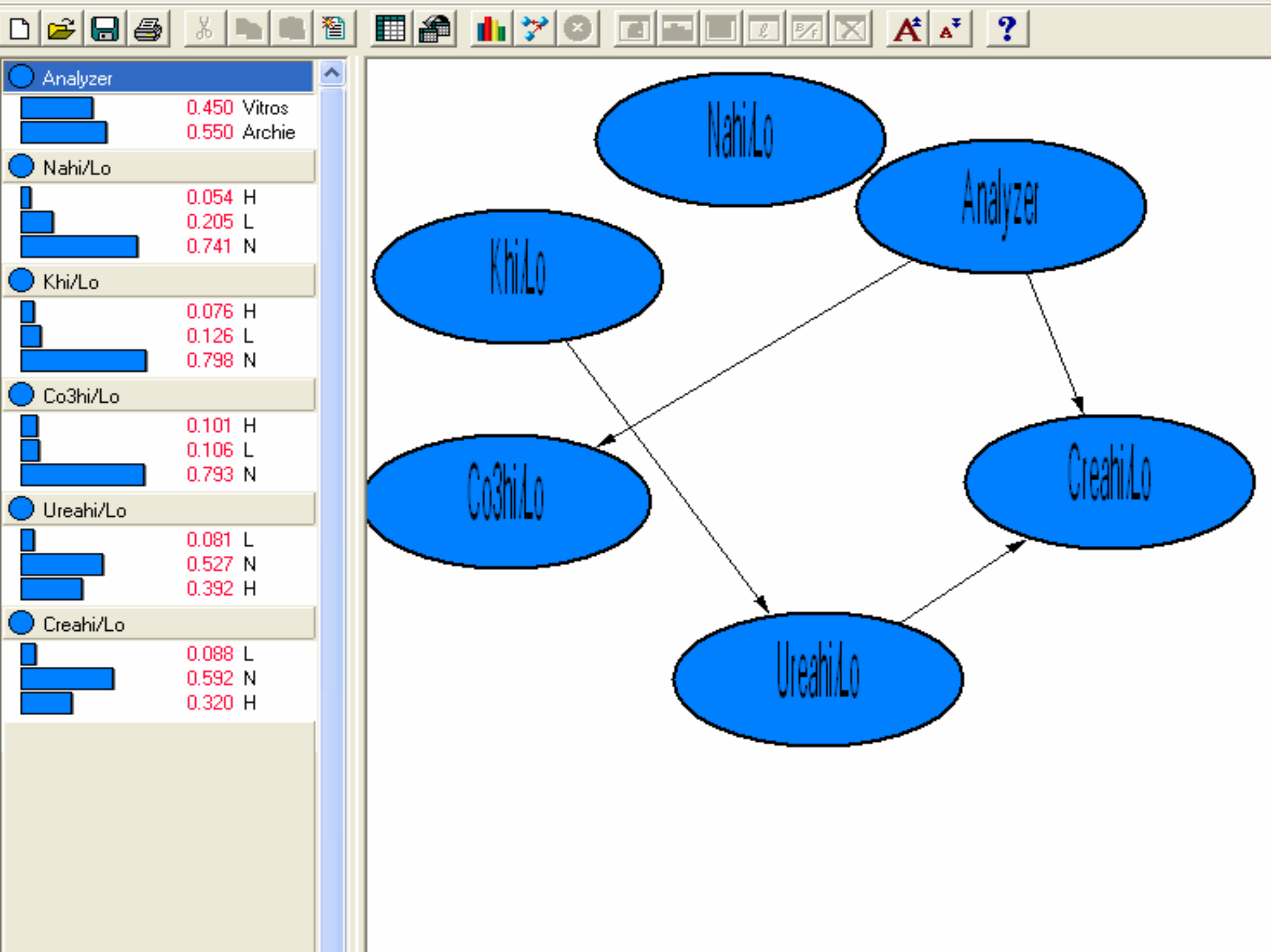
Raw Data

	A	B	C	D	E	F
342	142	4	23	8.7	74	Vitros
343	141	4.4	50	9.8	74	Vitros
344	141	5	42	13.3	74	Vitros
345	137	4.5	26	3	75	Vitros
346	140	3.9	26	3.5	75	Vitros
347	142	4	25	3.9	75	Vitros
348	140	3.8	30	4.3	75	Vitros
349	142	4	30	4.3	75	Vitros
350	139	4.1	25	2	36	Archie
351	142	4.1	24	3	43	Archie
352	132	3.6	30	4.8	43	Archie
353	145	4.4	26	4.9	43	Archie
354	139	3.2	20	1.1	44	Archie
355	140	3.3	23	3.4	44	Archie
356	142	3.8	22	3.9	44	Archie
357	136	3.5	27	3.9	46	Archie
358	133	4.6	20	5.2	47	Archie
359	142	3.9	22	2.6	48	Archie

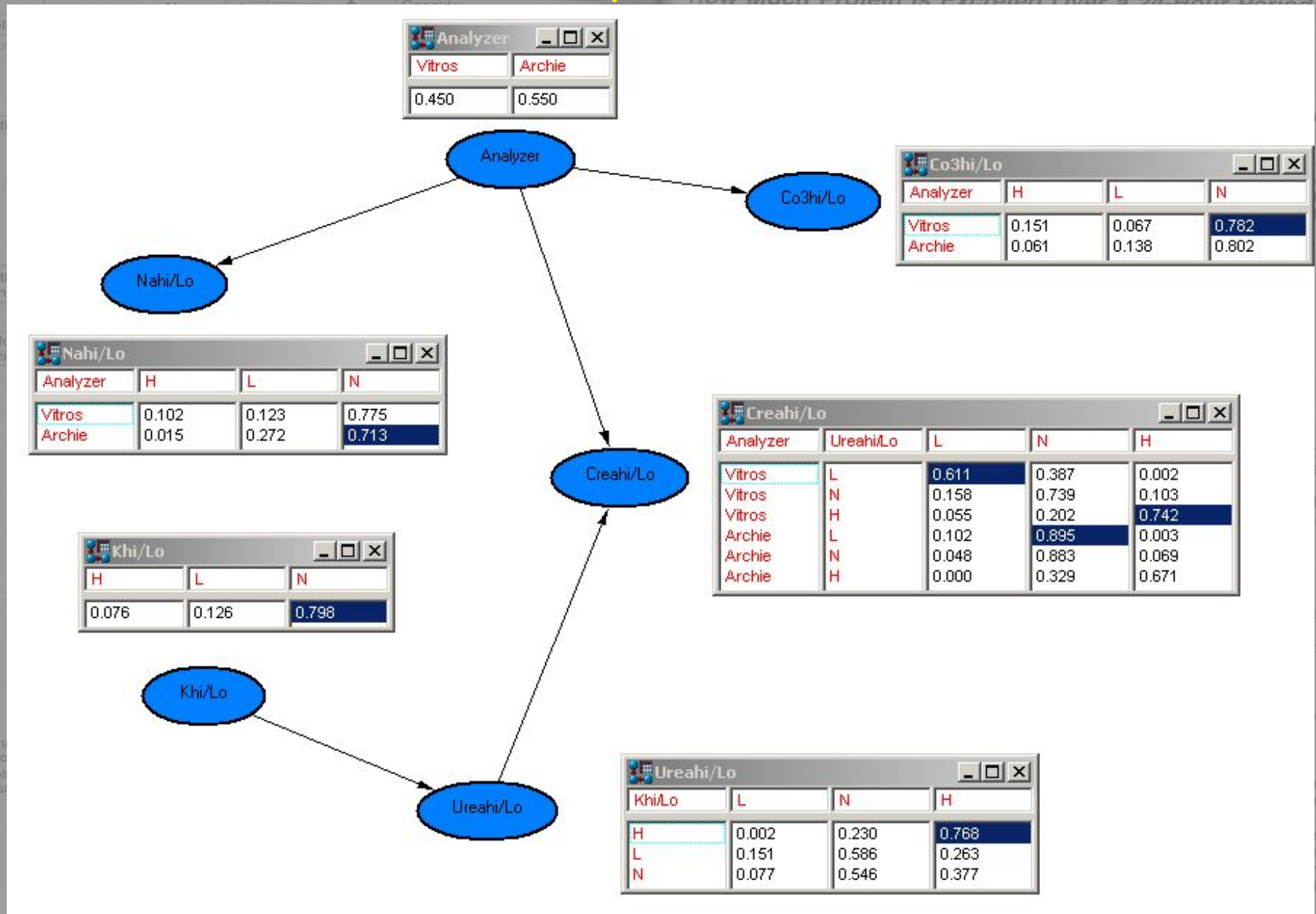
Transformed Data

	A	B	C	D	E	F
1	Analyzer	NaHi/Lo	KHi/Lo	CO3Hi/Lo	UreaHi/Lo	CreaHi/Lo
2	Vitros	H	H	L	H	H
3	Archie	H	H	L	H	H
4	Vitros	H	H	N	H	H
5	Vitros	H	H	N	H	H
6	Vitros	H	L	H	H	L
7	Vitros	H	L	H	H	L
8	Vitros	H	L	H	N	N
9	Vitros	H	L	L	N	H
10	Vitros	H	L	N	L	N
11	Vitros	H	L	N	H	N
12	Vitros	H	L	N	H	H
13	Vitros	H	L	N	H	H
14	Vitros	H	L	N	N	H
15	Archie	H	L	N	N	N
16	Vitros	H	N	H	H	L
17	Vitros	H	N	H	N	N
18	Vitros	H	N	H	N	N
19	Vitros	H	N	H	H	H
20	Vitros	H	N	L	H	H
21	Archie	H	N	L	N	N
22	Vitros	H	N	N	N	L
23	Vitros	H	N	N	N	L
24	Vitros	H	N	N	H	L
25	Vitros	H	N	N	L	N
26	Vitros	H	N	N	N	N
27	Vitros	H	N	N	H	N

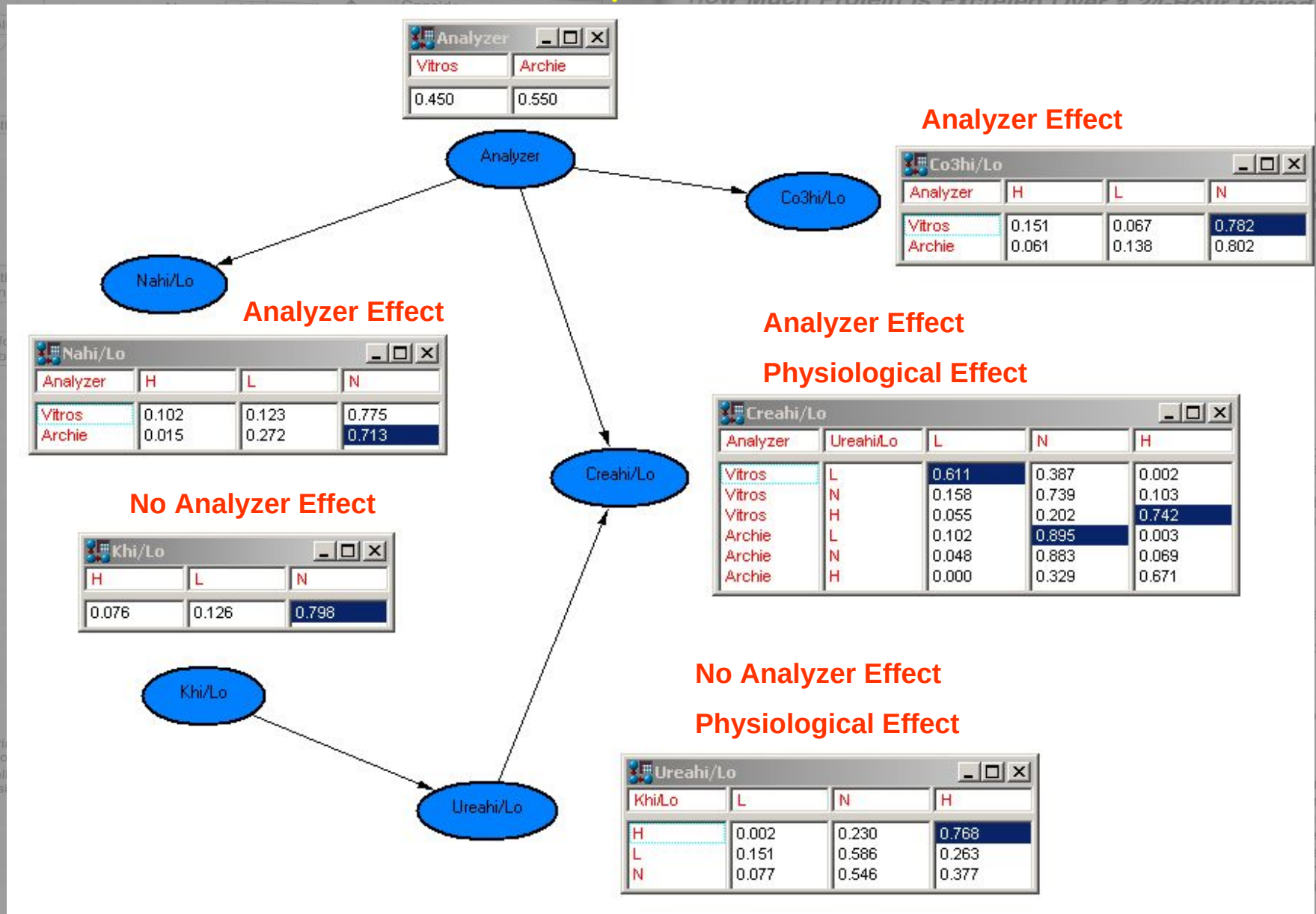

Bayesware Discoverer [G:/bayesware/.../electrolytes-700-items.csv]
File Edit Data Network Node 3D Plot Wizards Help
Analyzer
Nahi/Lo
Khi/Lo
Co3hi/Lo
Ureahi/Lo
Creahi/Lo
NahiLo
Analyzer
KhiLo
Co3hiLo
CreahiLo
UreahiLo


Analyzer
0.450 Vitros
0.550 Archie
Nahi/Lo
0.054 H
0.205 L
0.741 N
Khi/Lo
0.076 H
0.126 L
0.798 N
Co3hi/Lo
0.101 H
0.106 L
0.793 N
Ureahi/Lo
0.081 L
0.527 N
0.392 H
Creahi/Lo
0.088 L
0.592 N
0.320 H
Nahi/Lo
Analyzer
Khi/Lo
Co3hi/Lo
Creahi/Lo
Ureahi/Lo

Electrolytes Network : Na, K, HCO3, Urea, Creat

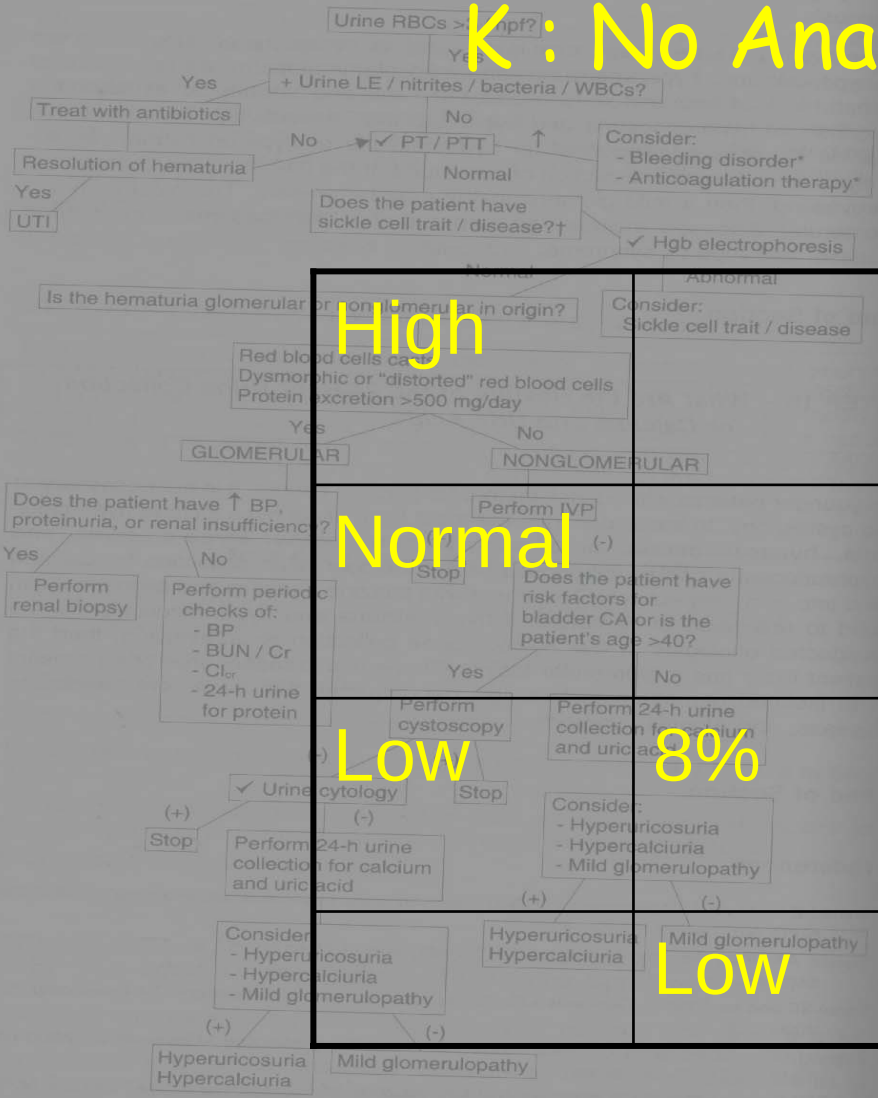


Electrolytes Network : Na, K, HCO3, Urea, Creat



K : No Analyzer Effect

High			13%
Normal		80%	
Low	8%		
	Low	Normal	High



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.
†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

PROTEINURIA

It is important not to ignore proteinuria. While it is true that proteinuria may represent a benign finding, it may also indicate the presence of serious underlying renal or systemic disease.

How Much Protein Is Excreted Over a 24-Hour Period in the Normal Individual?

Normally, there is <150 mg of protein excreted in the urine over a 24-hour period.

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins include albumin and a globulin fraction. The major constituent of protein derived from the urinary tract is the Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 30%
GLOBULINS 30%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

Plasma protein must traverse the glomerular barrier to enter the urine. In general, proteins with a molecular weight >20,000 daltons have considerable difficulty passing through glomerular capillary walls. The glomerular basement membrane is also negatively charged, and therefore impedes the passage of negatively charged plasma proteins such as albumin. Filtered protein may be reabsorbed by tubular cells. Proteins that are absorbed by tubular cells are generally low molecular weight in nature.

With this in mind, proteinuria can be classified as follows.

- Glomerular

  Glomerular proteinuria is the most common type of proteinuria, and may [illegible] hundreds of milligrams to >100 grams of protein per day. It [illegible] as a result of increased glomerular permeability, which may be due to a variety of processes.

- Tubular

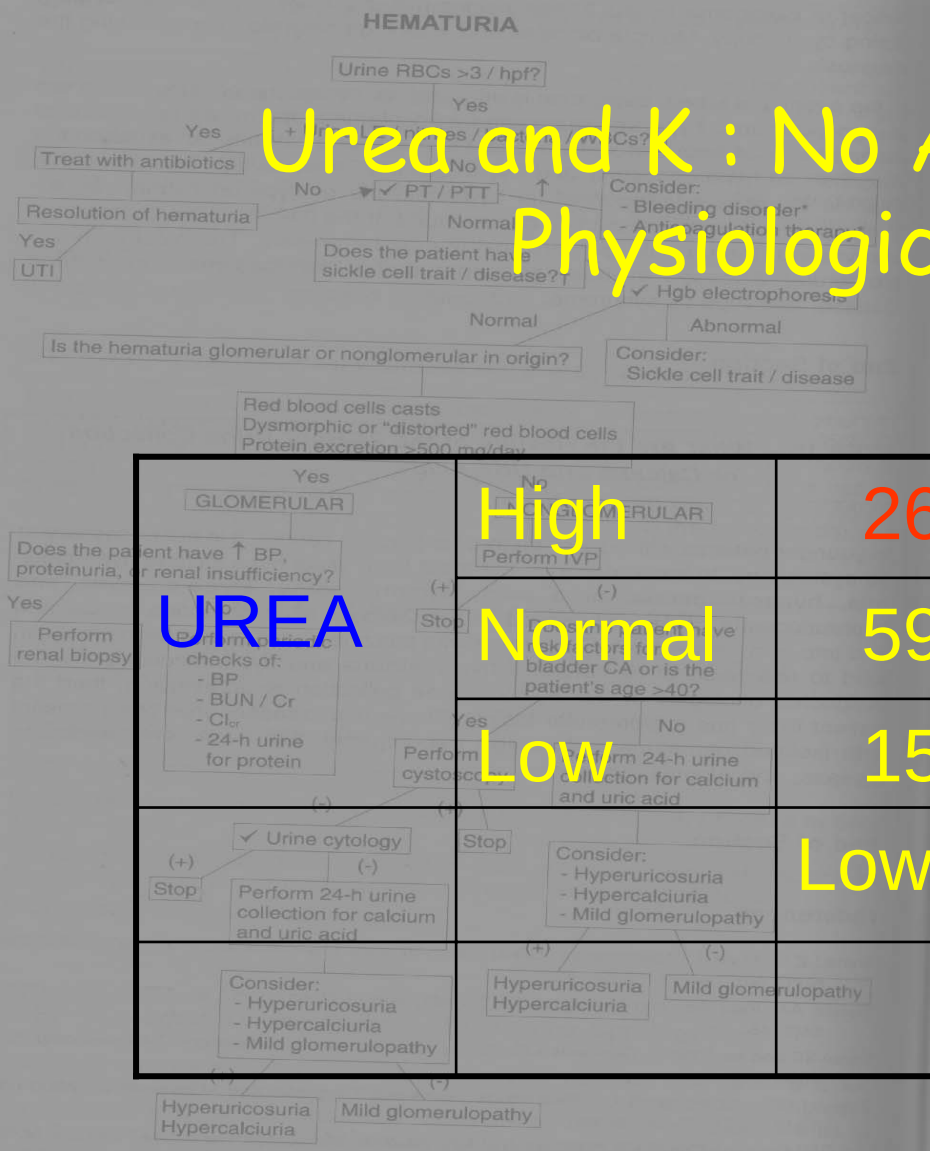
  Any process that damages the proximal tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

- Overflow

  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

Urea and K : No Analyzer Effect
Physiological Effect

UREA	High	26%	38%	77%
	Normal	59%	55%	23%
	Low	15%	8%	0%
		Low	Normal	High
		POTASSIUM		



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.
†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

PROTEINURIA

It is important not to ignore proteinuria. While it is true that proteinuria may represent a benign finding, it may also indicate the presence of serious underlying renal or systemic disease.

How Much Protein Is Excreted Over a 24-Hour Period in the Normal Individual?

Normal physiologic handling of protein excreted in the urine over a 24-hour period

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins include albumin and a globulin fraction. The major constituent of protein derived from the urinary tract is the Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 30%
GLOBULINS 30%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

Plasma protein must traverse the glomerular capillaries to enter the urine. In general, proteins with a molecular weight >20,000 daltons have considerable difficulty passing through glomerular capillary walls. The glomerular basement membrane is also negatively charged, and therefore impedes the passage of negatively charged plasma proteins such as albumin. Filtered protein may be reabsorbed by tubular cells, whereas proteins that are synthesized by tubular cells are generally low molecular weight in nature.

With this in mind, proteinuria can be classified as follows.

- Glomerular

  Glomerular proteinuria is the most common type of proteinuria and may vary from subnephrotic amounts to >100 grams of protein per day. It occurs as a result of increased glomerular permeability, which may be due to a variety of processes.

- Tubular

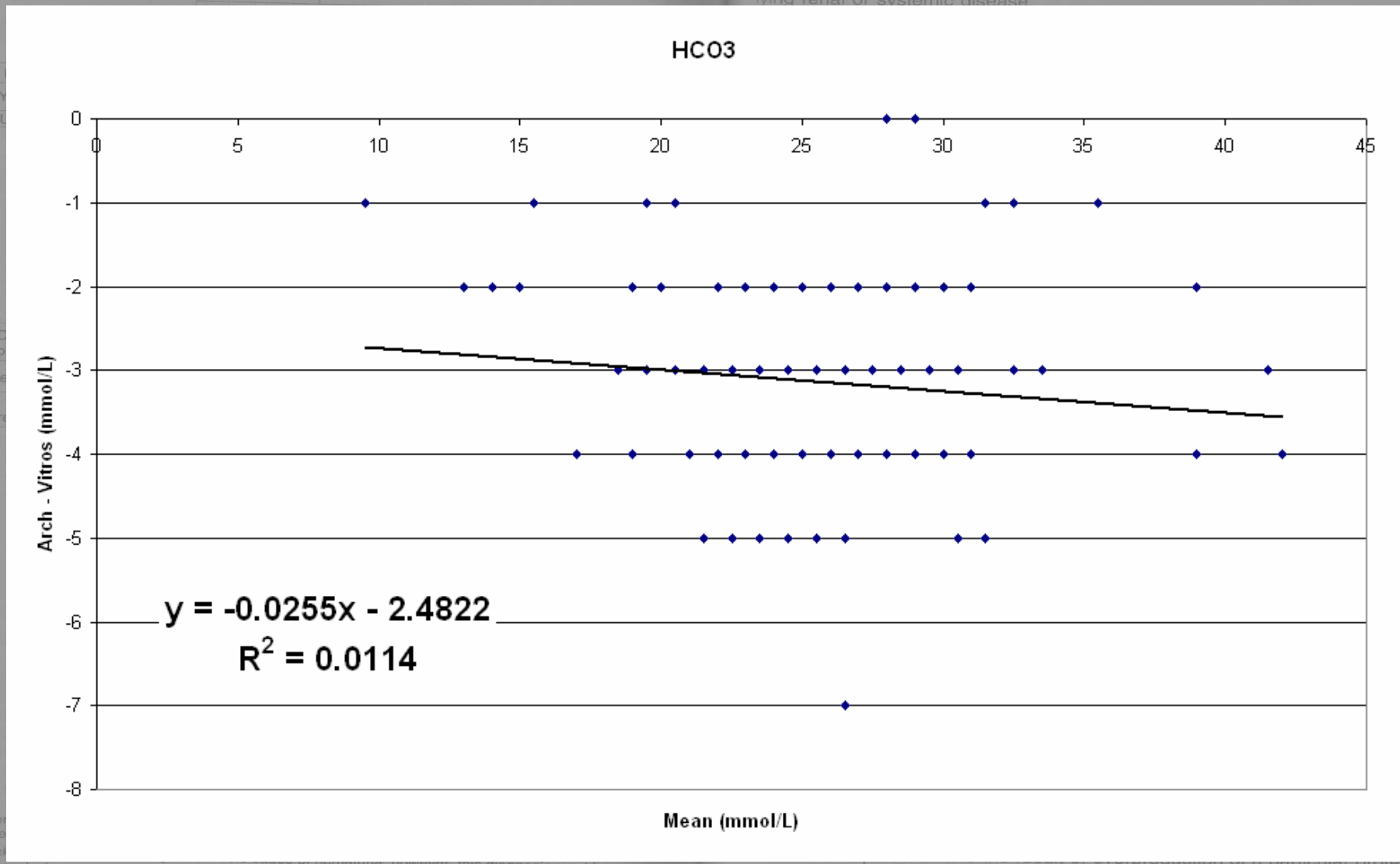
  Any process that damages the proximal tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

- Overflow

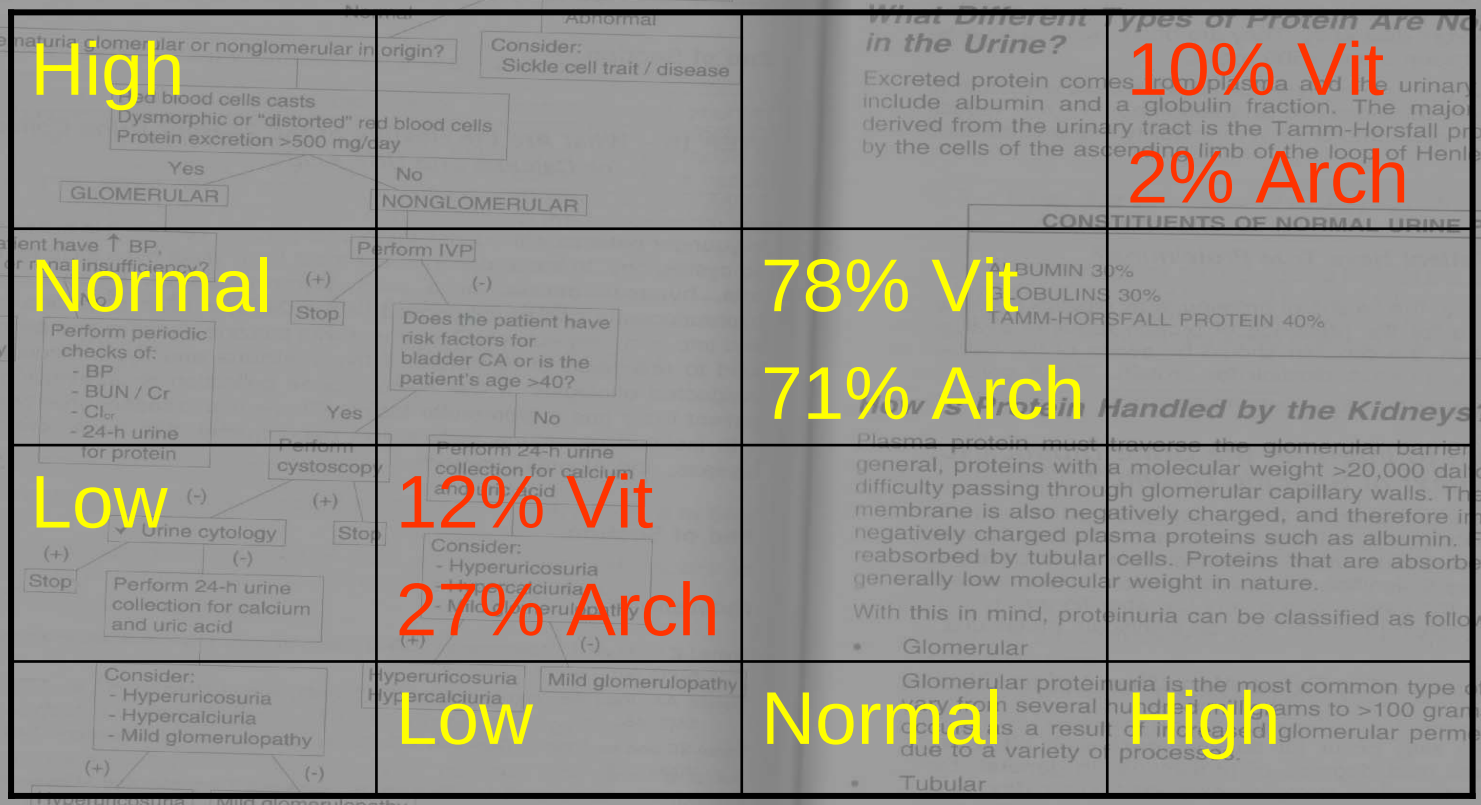
  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

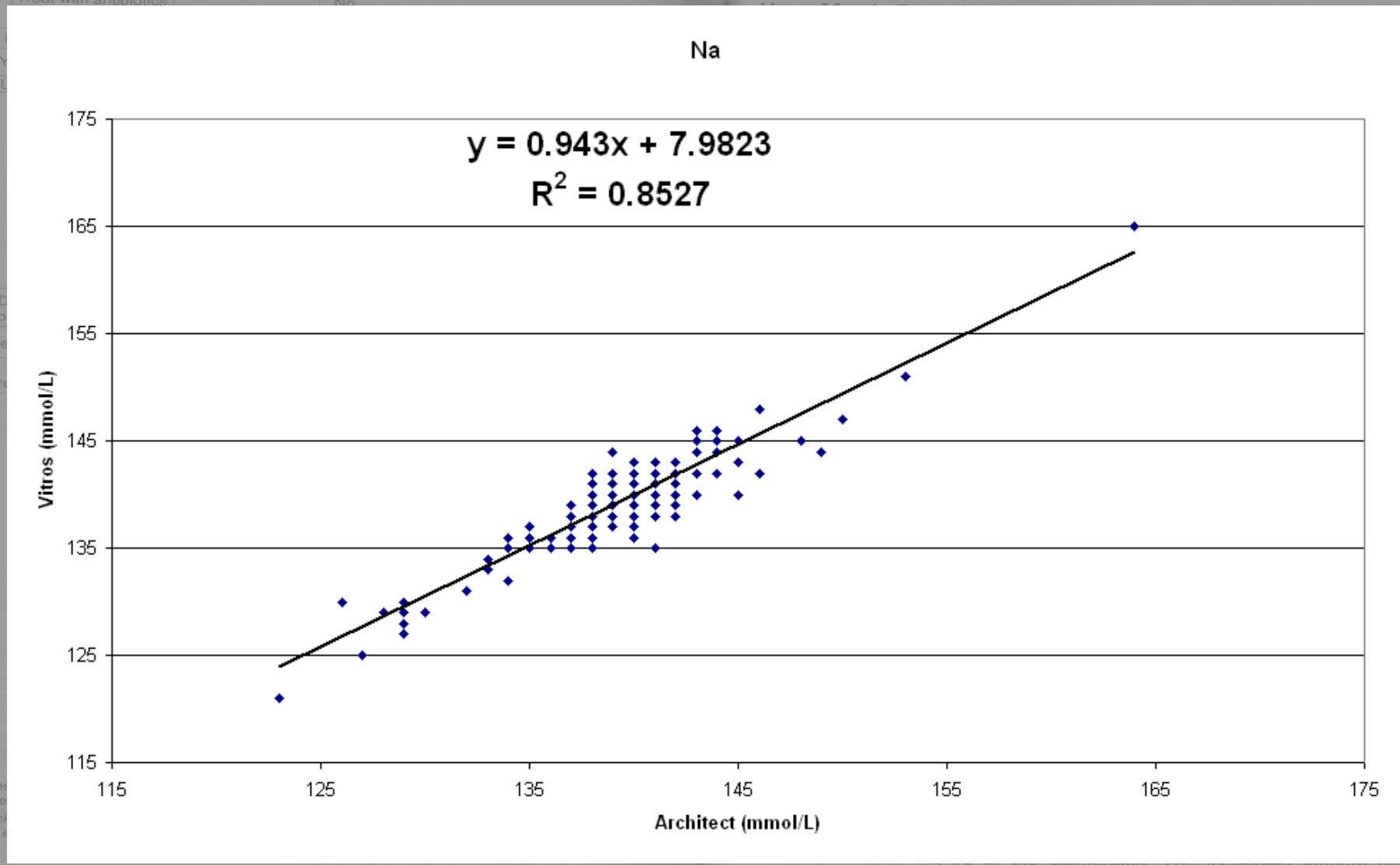
Bicarbonate : Analyzer Effect

High			10% Vit 6% Arch
Normal		78% Vit 80% Arch	
Low	7% Vit 14% Arch		
	Low	Normal	High


HCO3
Arch - Vitros (mmol/L)
Mean (mmol/L)
y = -0.0255x - 2.4822
R2 = 0.0114
0
-1
-2
-3
-4
-5
-6
-7
-8
0
5
10
15
20
25
30
35
40
45

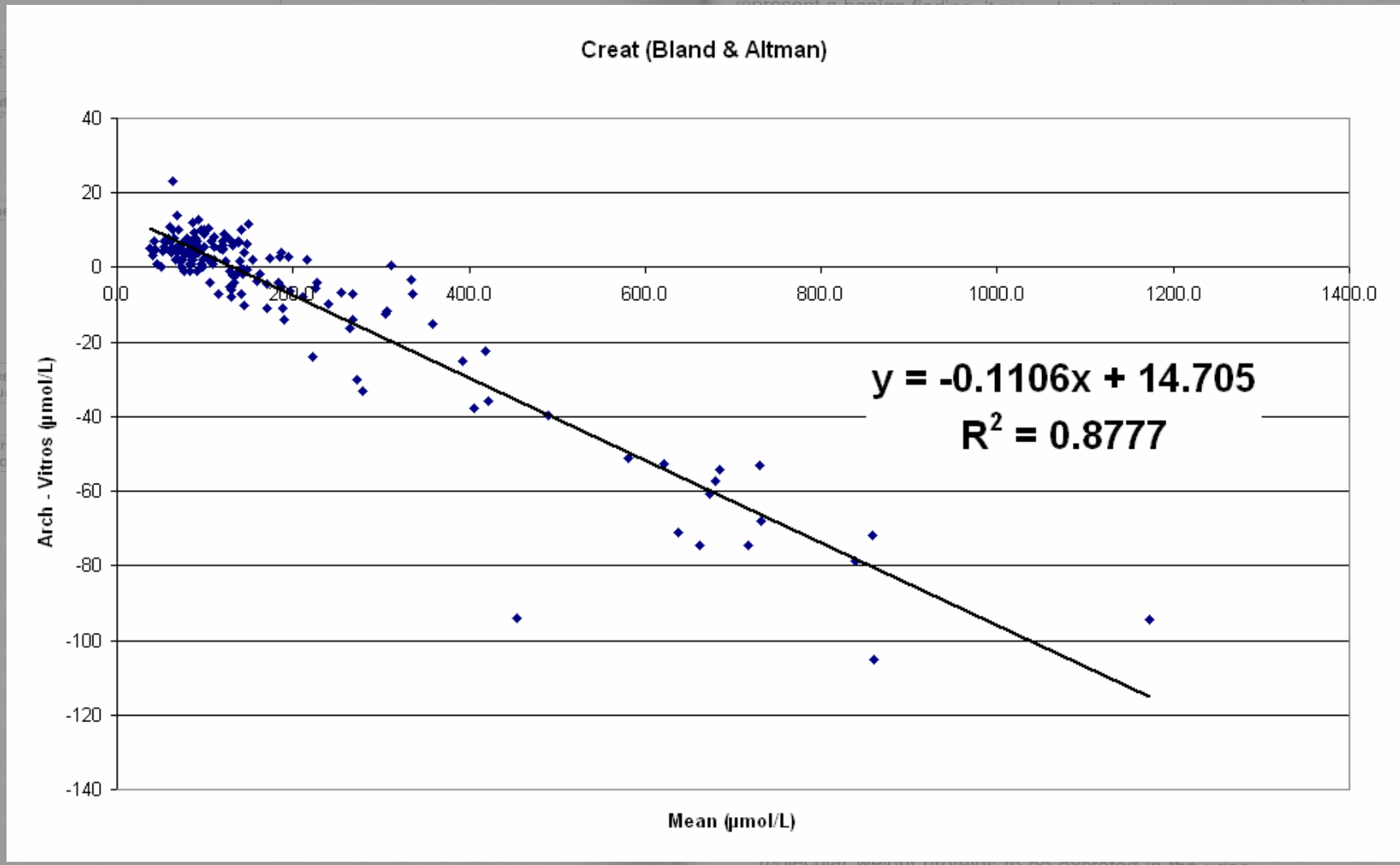
Sodium : Analyzer Effect

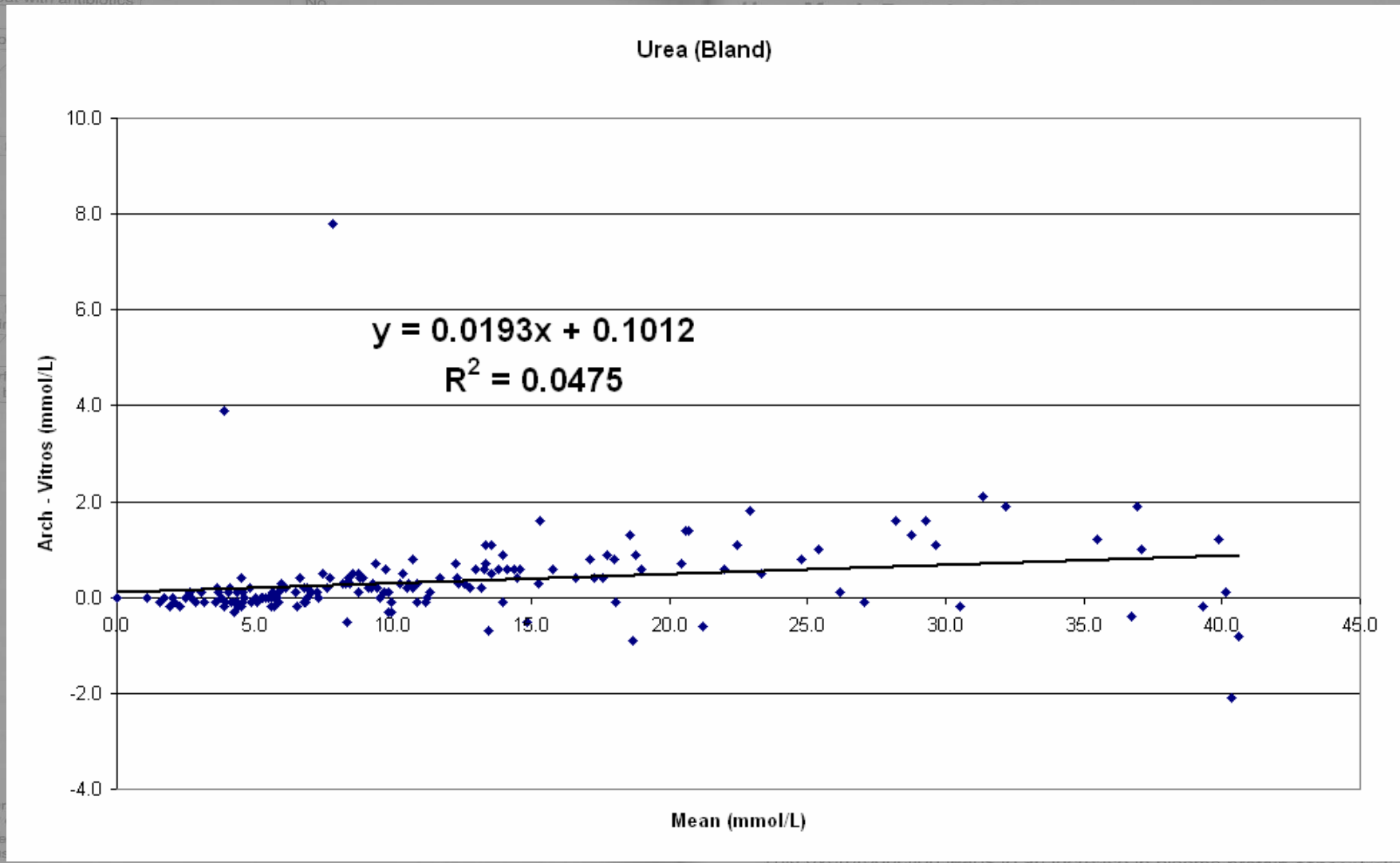


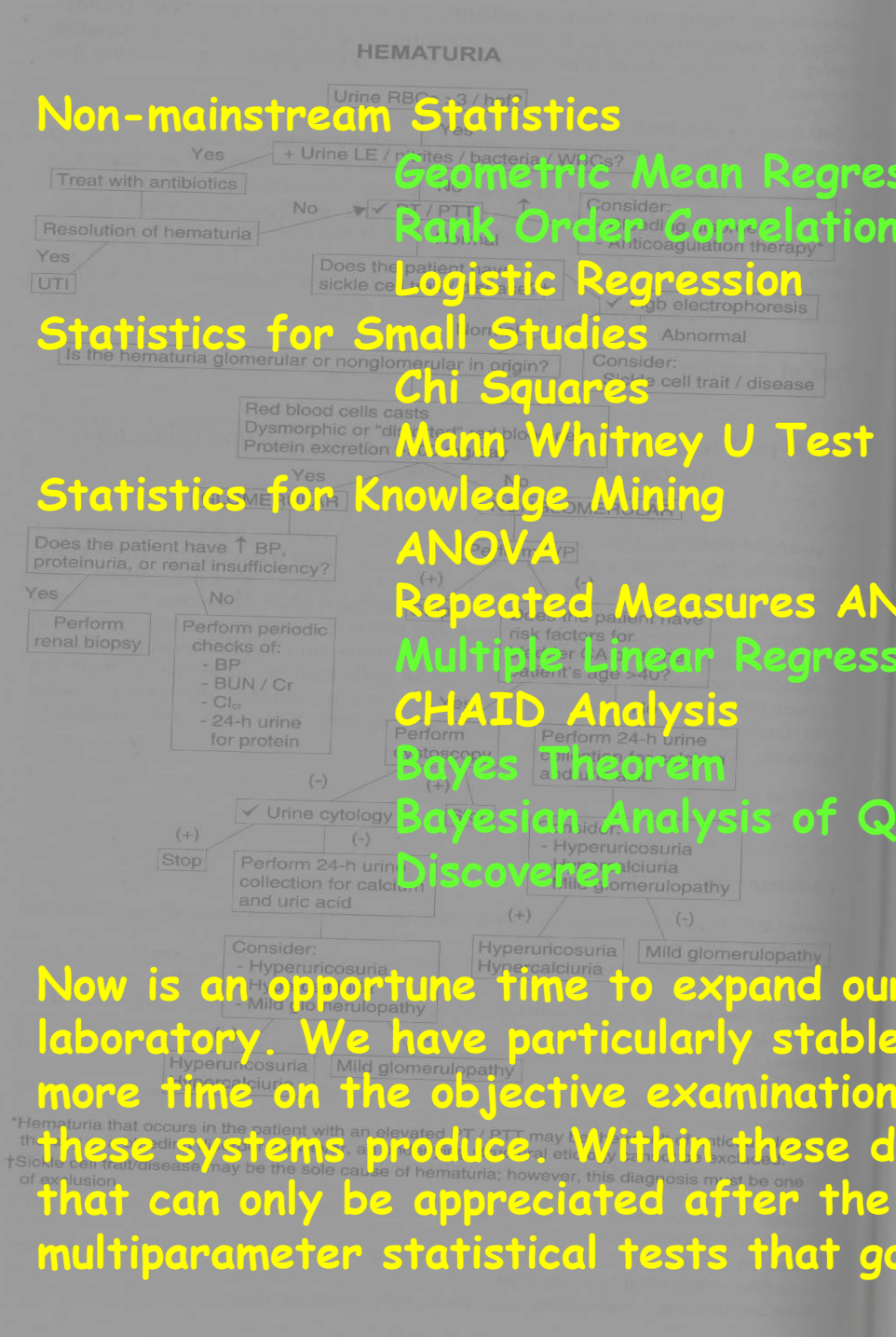

Na
y = 0.943x + 7.9823
R2 = 0.8527
Vitros (mmol/L)
Architect (mmol/L)
115
125
135
145
155
165
175

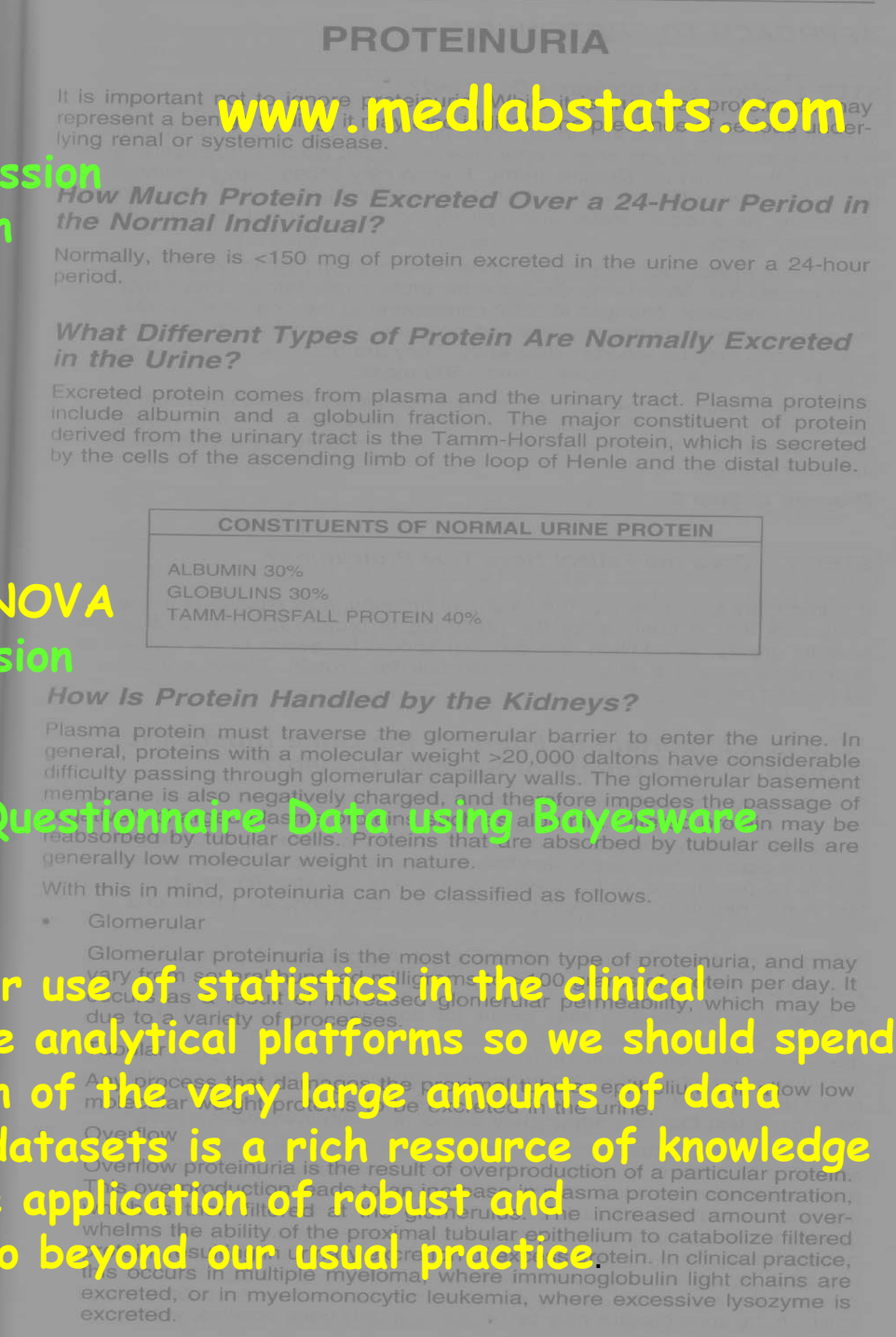
Urea and Creat : Analyzer Effect and Physiological Effect

CREAT \ UREA	Low	Normal	High
High	0% Vit 0% Arch	10% Vit 7% Arch	74% Vit 67% Arch
Normal	39% Vit 90% Arch	74% Vit 88% Arch	20% Vit 33% Arch
Low	61% Vit 10% Arch	16% Vit 5% Arch	6% Vit 0% Arch


Creat (Bland & Altman)
Arch - Vitros (µmol/L)
Mean (µmol/L)
y = -0.1106x + 14.705
R2 = 0.8777
40
20
0
-20
-40
-60
-80
-100
-120
-140
0.0
200.0
400.0
600.0
800.0
1000.0
1200.0
1400.0


Urea (Bland)
y = 0.0193x + 0.1012
R2 = 0.0475
Arch - Vitros (mmol/L)
Mean (mmol/L)
10.0
8.0
6.0
4.0
2.0
0.0
-2.0
-4.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
45.0





Non-mainstream Statistics www.medlabstats.com

Geometric Mean Regression
Rank Order Correlation
Logistic Regression

Statistics for Small Studies

Chi Squares
Mann Whitney U Test

Statistics for Knowledge Mining

ANOVA
Repeated Measures ANOVA
Multiple Linear Regression
CHAID Analysis
Bayes Theorem
Bayesian Analysis of Questionnaire Data using Bayesware Discoverer

Now is an opportune time to expand our use of statistics in the clinical laboratory. We have particularly stable analytical platforms so we should spend more time on the objective examination of the very large amounts of data these systems produce. Within these datasets is a rich resource of knowledge that can only be appreciated after the application of robust and multiparameter statistical tests that go beyond our usual practice.