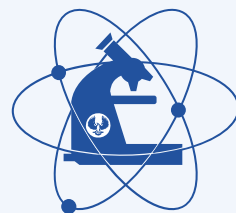


Case studies in biochemistry

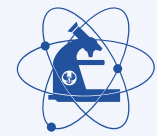
Penelope Coates



SA PATHOLOGY

66 year old woman, serial tests

	April	May		
Albumin	38	39	g/L	(34-48)
Globulin	30	28	g/L	(26-41)
Protein	68	67	g/L	(65-85)
Tot.Bili	5	10	g/L	(6-24)
GGT	14	107	U/L	(0-60)
ALP	88	134	U/L	(30-110)
ALT	23	25	U/L	(0-55)
AST	24	21	U/L	(0-45)



SA PATHOLOGY

71 year old woman, monitoring on warfarin

Sodium	129	mmol/l	(137-145)
Potassium	10.4	mmol/l	(3.5-4.9)
Chloride	91	mmol/l	(100-109)
Bicarb	24	mmol/l	(22-32)
Glucose	1.8	mmol/l	(3.8-5.5)
Urea	9.0	mmol/l	(2.7-8.0)
Creatinine	104	umol/l	(50-120)
Phosphate	3.02	mmol/l	(0.65-1.45)



SA PATHOLOGY

71 year old woman, monitoring on warfarin

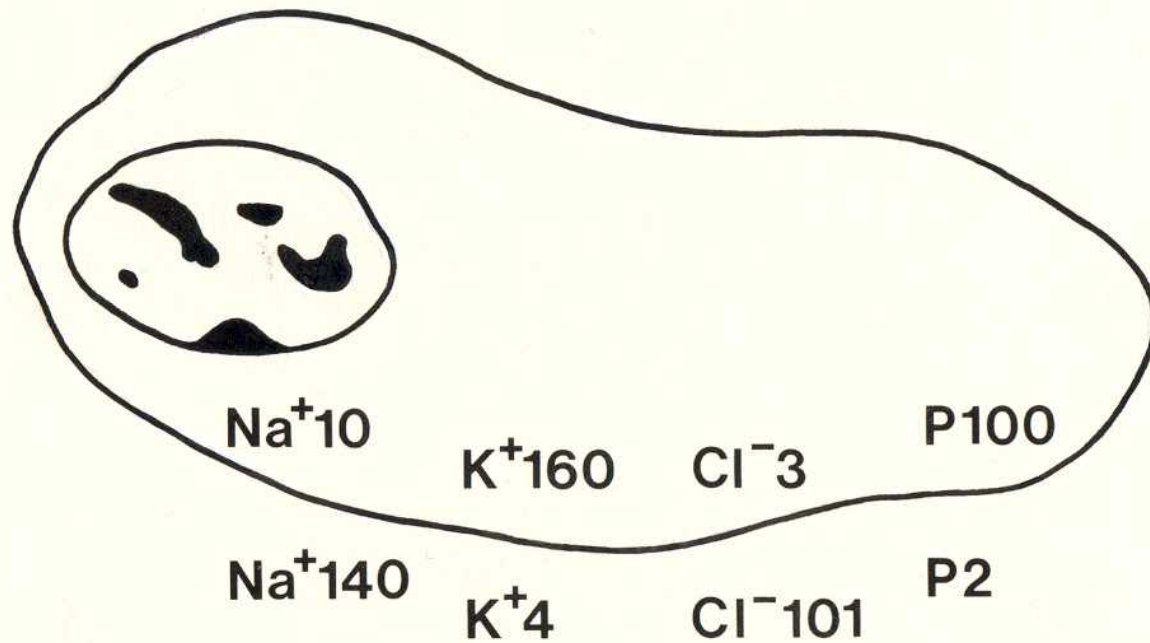
Sodium	129	mmol/l	(137-145)
Potassium	10.4	mmol/l	(3.5-4.9)
Chloride	91	mmol/l	(100-109)
Bicarb	24	mmol/l	(22-32)
Glucose	1.8	mmol/l	(3.8-5.5)
Urea	9.0	mmol/l	(2.7-8.0)
Creatinine	104	umol/l	(50-120)
Phosphate	3.02	mmol/l	(0.65-1.45)

Max. temperature on 28.1.09 = 45.7C



SA PATHOLOGY

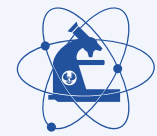
Electrolyte distribution in the cell



SA PATHOLOGY

61 year old man, inpatient, post op

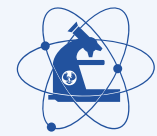
Sodium	121	mmol/l	(137-145)
Potassium	3.8	mmol/l	(3.5-4.9)
Chloride	90	mmol/l	(100-109)
Bicarb	23	mmol/l	(22-32)
Glucose	42.5	mmol/l	(3.8-5.5)
Urea	4.1	mmol/l	(2.7-8.0)
Creatinine	69	umol/l	(50-120)



SA PATHOLOGY

61 year old man, inpatient, post op

		Prev. day		
Sodium	121	134	mmol/l	(137-145)
Potassium	3.8	4.4	mmol/l	(3.5-4.9)
Chloride	90	97	mmol/l	(100-109)
Bicarb	23	27	mmol/l	(22-32)
Glucose	42.5	8.4	mmol/l	(3.8-5.5)
Urea	4.1	6.8	mmol/l	(2.7-8.0)
Creatinine	69	77	umol/l	(50-120)



SA PATHOLOGY

36 year old man

Sodium	116	mmol/l	(137-145)
Potassium	4.5	mmol/l	(3.1-4.2)
Chloride	82	mmol/l	(100-109)
Bicarb	23	mmol/l	(22-32)
Anion gap	16	mmol/l	(7-17)
Glucose	57.1	mmol/l	(3.8-5.5)
Urea	9.5	mmol/l	(2.7-8.0)
Creatinine	101	umol/l	(50-120)



36 year old man, type II DM

Sodium	116	mmol/l	(137-145)
Potassium	4.5	mmol/l	(3.1-4.2)
Chloride	82	mmol/l	(100-109)
Bicarb	23	mmol/l	(22-32)
Anion gap	16	mmol/l	(7-17)
Glucose	57.1	mmol/l	(3.8-5.5)
Urea	9.5	mmol/l	(2.7-8.0)
Creatinine	101	umol/l	(50-120)

A useful formula: True plasma Na = measured Na + glucose/4

e.g. in this pt: Na = 116 + (57/4) \cong 130 mmol/l



SA PATHOLOGY

73 year old man, pale ? anaemic

Sodium	141	mmol/l	(137-145)	Albumin	46	g/L	(34-48)
Potassium	10.3	mmol/l	(3.5-4.9)	Tot.Bili	7	g/L	(6-24)
Chloride	94	mmol/l	(100-109)	Protein	76	g/L	(65-85)
Bicarb	28	mmol/l	(22-32)	GGT	27	U/L	(0-60)
Anion gap	29.3	mmol/l	(7-17)	ALP	1	U/L	(30-110)
Glucose	8.0	mmol/l	(3.8-5.5)	ALT	13	U/L	(0-55)
Urea	7.8	mmol/l	(2.7-8.0)	AST	17	U/L	(0-45)
Creatinine	90	umol/l	(50-120)	LD	238	U/L	(110-230)
Phosphate	0.95	mmol/l	(0.65-1.45)				
Calcium	0.56	mmol/l	(2.10-2.55)				

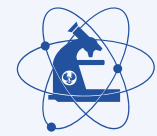


SA PATHOLOGY

A 43 year old man with HT

History

- Hypertension 5 years
- not controlled on ramipril + hydrochlorothiazide
- Type II diabetes 2 years
- Diet control
- Recent increase in urine output, nocturia x2

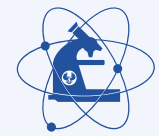


SA PATHOLOGY

A 43 year old man with hypertension (2)

Examination

- Height 175 cm, weight 89 kg, BMI 29
- Blood pressure 150/90
- Clinically normovolaemic
- No clinical diabetes complications

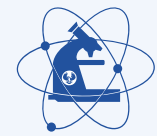


SA PATHOLOGY

43 year old man with HT

Biochemistry

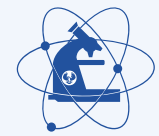
Sodium	140	mmol/l	(137-145)
Potassium	2.6	mmol/l	(3.1-4.9)
Chloride	100	mmol/l	(100-109)
Bicarb	32	mmol/l	(22-32)
Glucose	12.2	mmol/l	(3.8-5.5)
Urea	1.8	mmol/l	(2.7-8.0)
Creatinine	45	mmol/l	(50-120)



SA PATHOLOGY

Questions

- What diagnoses should we consider?
- What further investigations should we recommend?
- What should be done before any further investigations?

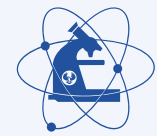


SA PATHOLOGY

Medications changed to oral potassium supplement and prazosin for 3 weeks

Questions

- 1. Why was this done?
- 2. Is any other patient preparation necessary?



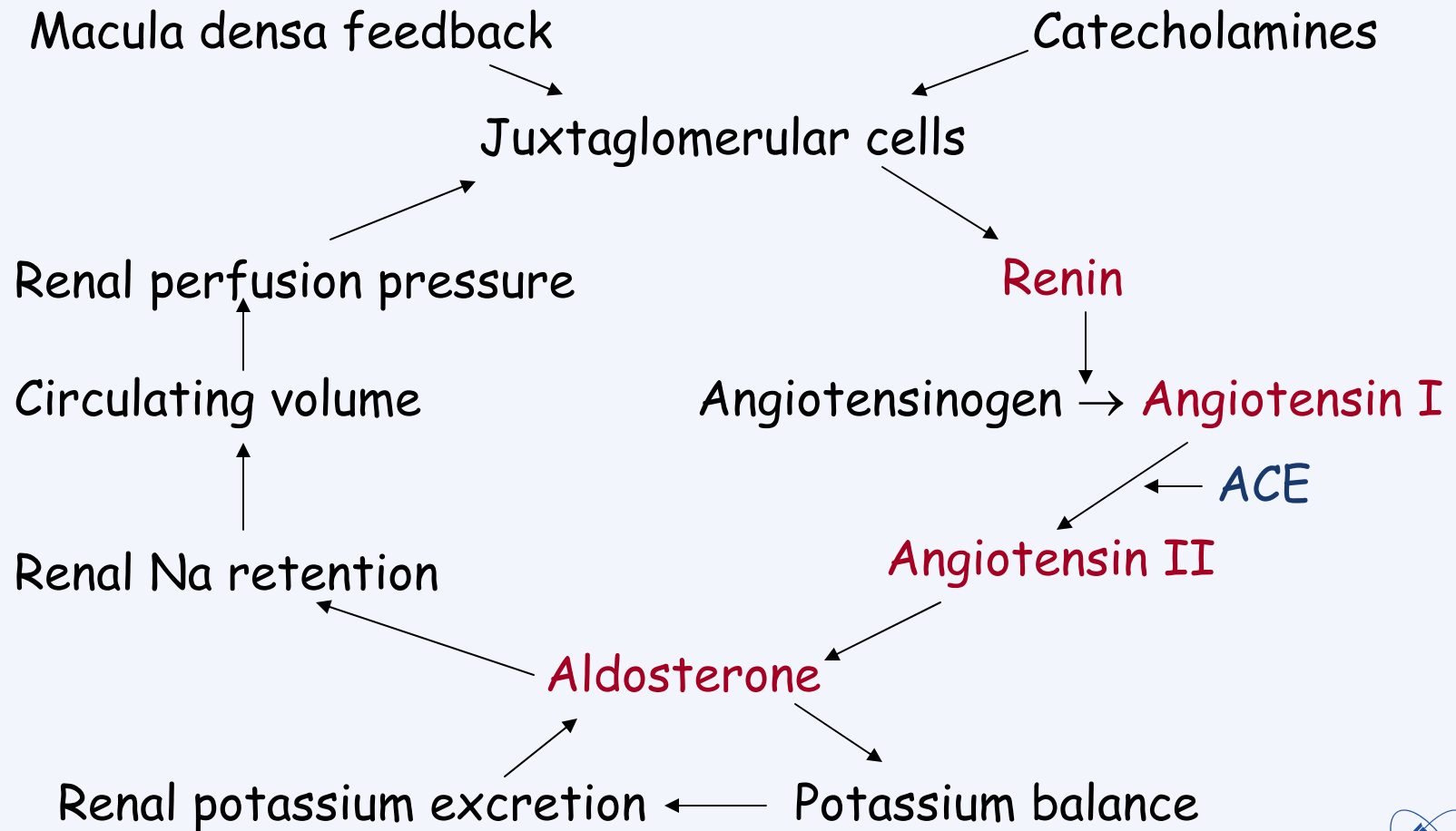
SA PATHOLOGY

Primary aldosteronism

- 5-13% of patients with hypertension (need not be hypokalaemic)
 - Note: suppressed renin alone in 25% of patients with essential hypertension
- All patients with HT and low K should be screened
 - 50% of these patients have hyperaldosteronism
- Aldosterone:renin ratio widely accepted as screening test



Role of aldosterone in BP control

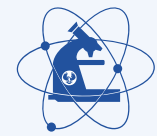


SA PATHOLOGY

A young diabetic man

- 28 year old man, type I DM diagnosed 1999
 - 1 episode DKA 2001, nil since
 - No complications
- Fit and active, labourer, surfs most days
- Main concern is nocturnal hypoglycaemia: wants to change from NPH to glargine

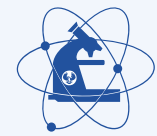
- 184 cm; 86 kg; BMI 25; BP 124/80
- No clinical evidence of complications



SA PATHOLOGY

Results

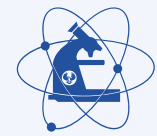
Fasting glucose	7.0	mmol/L	3.8-5.5)
Cholesterol	6.2	mmol/L	(<5.5)
Haemoglobin	173	g/L	(135-175)
P.C.V.	0.53	L/L	(0.40-0.50)
Platelets	203	x10 ⁹ /L	(150-400)
White cell count	4.67	x10 ⁹ /L	(4.00-11.0)
HbA1c	4.6	%	



SA PATHOLOGY

Results

Fasting glucose	7.0	mmol/L	3.8-5.5)
Cholesterol	6.2	mmol/L	(<5.5)
Haemoglobin	173	g/L	(135-175)
P.C.V.	0.53	L/L	(0.40-0.50)
Platelets	203	x10 ⁹ /L	(150-400)
White cell count	4.67	x10 ⁹ /L	(4.00-11.0)
HbA1c (HPLC)	4.6	%	
Repeat HbA1c (Boronate affinity)	6.9	%	



SA PATHOLOGY

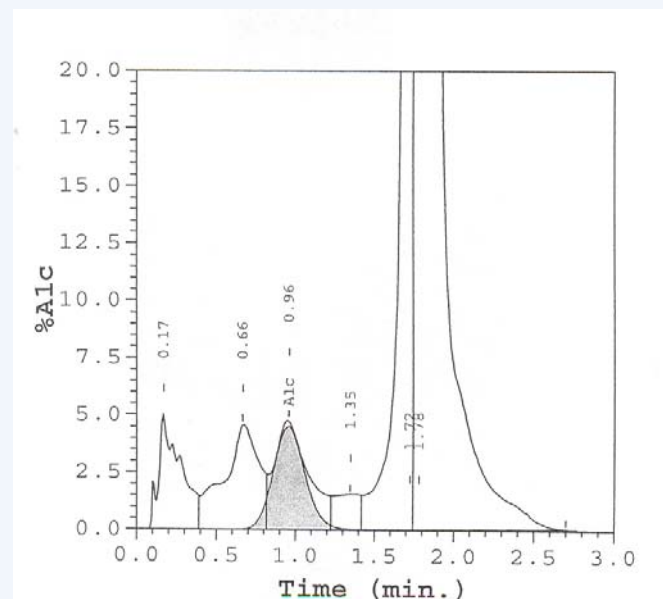
The patient: continued

Review chromatogram:

- Unknown Hb peak

Sequence β globin gene

- “The patient is heterozygous for the haemoglobin variant Hb J-Calabria in the beta- globin gene”
- Single base substitution G>A at codon 64 (glycine>aspartic acid)

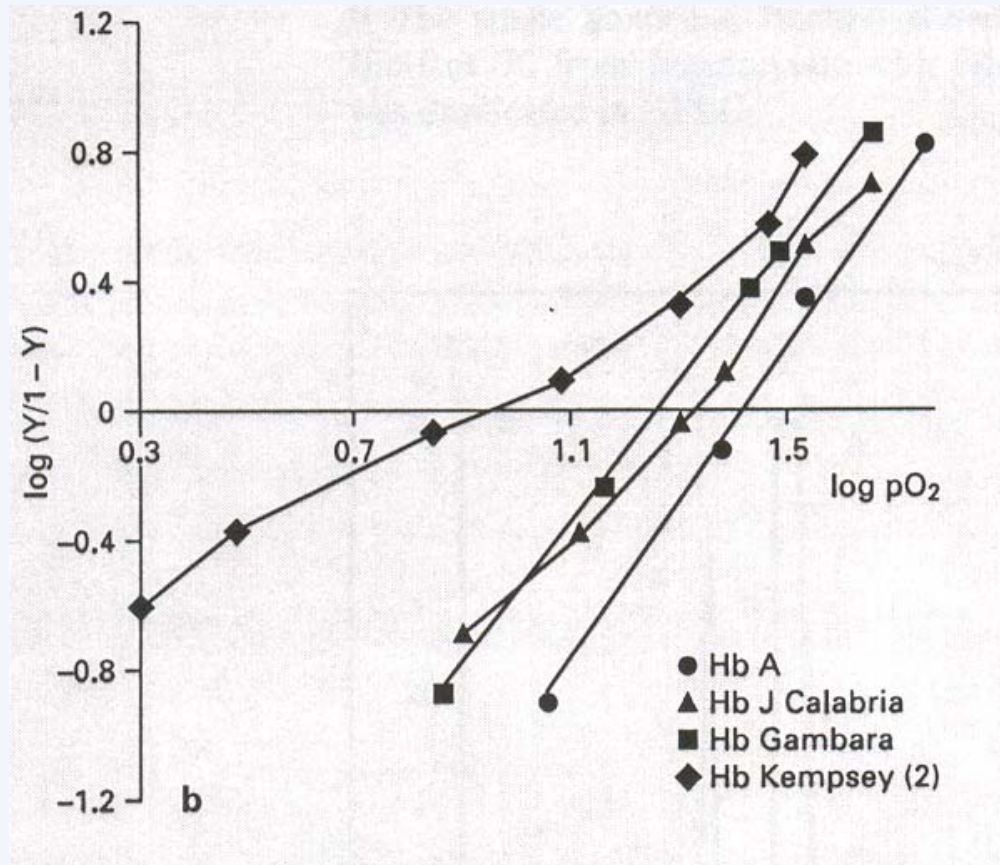


Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
Ala	---	2.4	0.17	84149
LAlc/CHb	---	2.9	0.66	102157
Alc	4.8	---	0.96	109894
Unknown	---	0.8	1.35	30193
Unknown	---	23.5	1.72	836471
Ao	---	67.3	1.78	2398505
Total Area:				3561370



SA PATHOLOGY

Hb J Calabria: oxygen affinity



David et al. Acta Haematol 2002;108:132

SA PATHOLOGY

Thirst in a young man

History

- Nocturia ++, drinks 13L daily, cold water at night
- No family history
- Otherwise well

Examination

- Height 177 cm, weight 80 kg, BMI 26
- Blood pressure 122/80
- Normally hydrated
- No abnormal findings



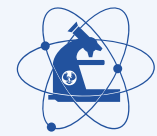
SA PATHOLOGY

33 year old man, thirsty and polyuric

Sodium	146	mmol/l	(137-145)
Potassium	4.2	mmol/l	(3.5-4.9)
Chloride	105	mmol/l	(100-109)
Bicarb	33	mmol/l	(22-32)
Glucose	5.1	mmol/l	(3.8-5.5)
Urea	4.4	mmol/l	(2.7-8.0)
Creatinine	106	umol/l	(50-120)
Osmolarity	296	mmol/l	(265-285)

Spot urine specimen

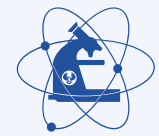
Osmolality 93 mosmol/kg



SA PATHOLOGY

Questions

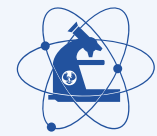
- What condition(s) should we consider in this man?
- How should this be investigated?



SA PATHOLOGY

Water deprivation test

Time	S.osmo (mosmol/kg)	U.osmo
07:40	301	
10:15	290	91
11:15		75
12:15		86
13:15		100
14:15		123
15:15		147
16:20	306	204
17:10		383
17:14		535
20:05		548
23:15		600



SA PATHOLOGY

Previously healthy 76- year old man

Sodium	142 mmol/L	(137 – 145)
Potassium	4.3 mmol/L	(3.5 – 4.9)
Chloride	106 mmol/L	(100-109)
Bicarbonate	31 mmol/L	(22 – 32)
Glucose	4.2 mmol/L	(3.8-5.5)
Urea	13.5 mmol/L	(2.7-8.0)
Creatinine	0.235 mmol/L	(0.05– 0.12)
Phosphate	0.93 mmol/L	(0.65-1.45)
Calcium	3.16 mmol/L	(2.10-2.55)
Albumin	37 g/L	(34-48)
GGT	20 U/L	(0-60)
ALP	59 U/L	(30-110)
ALT	23 U/L	(0-55)
LD	258 U/L	(110-230)



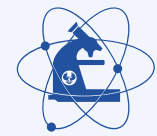
SA PATHOLOGY

Previous results

	6.02	4.05		
Na	142	142	mmol/L	(137 – 145)
K	4.1	4.3	mmol/L	(3.5 – 4.9)
Cl	106	106	mmol/L	(100-109)
Bic	23	31	mmol/L	(22 – 32)
Gluc	4.7	4.2	mmol/L	(3.8-5.5)
Urea	6.6	13.5	mmol/L	(2.7-8.0)
Cr	0.120	0.235	mmol/L	(0.05– 0.12)
P04	0.96	0.93	mmol/L	(0.65-1.45)
Ca	2.49	3.16	mmol/L	(2.10-2.55)
Calc. GFR	55	25	ml/min/ 1.73m ²	(>60)

Further investigations

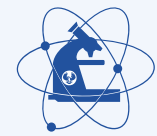
PTH	0.5 pmol/L	(0.8-5.5)
Hb	105 g/L	(135-175)
Platelets	170 x 10 ⁹ /L	(150-400)
WCC	5.23 x 10 ⁹ /L	(4.00-11.0)
ESR	44 mm	(0-15)



SA PATHOLOGY

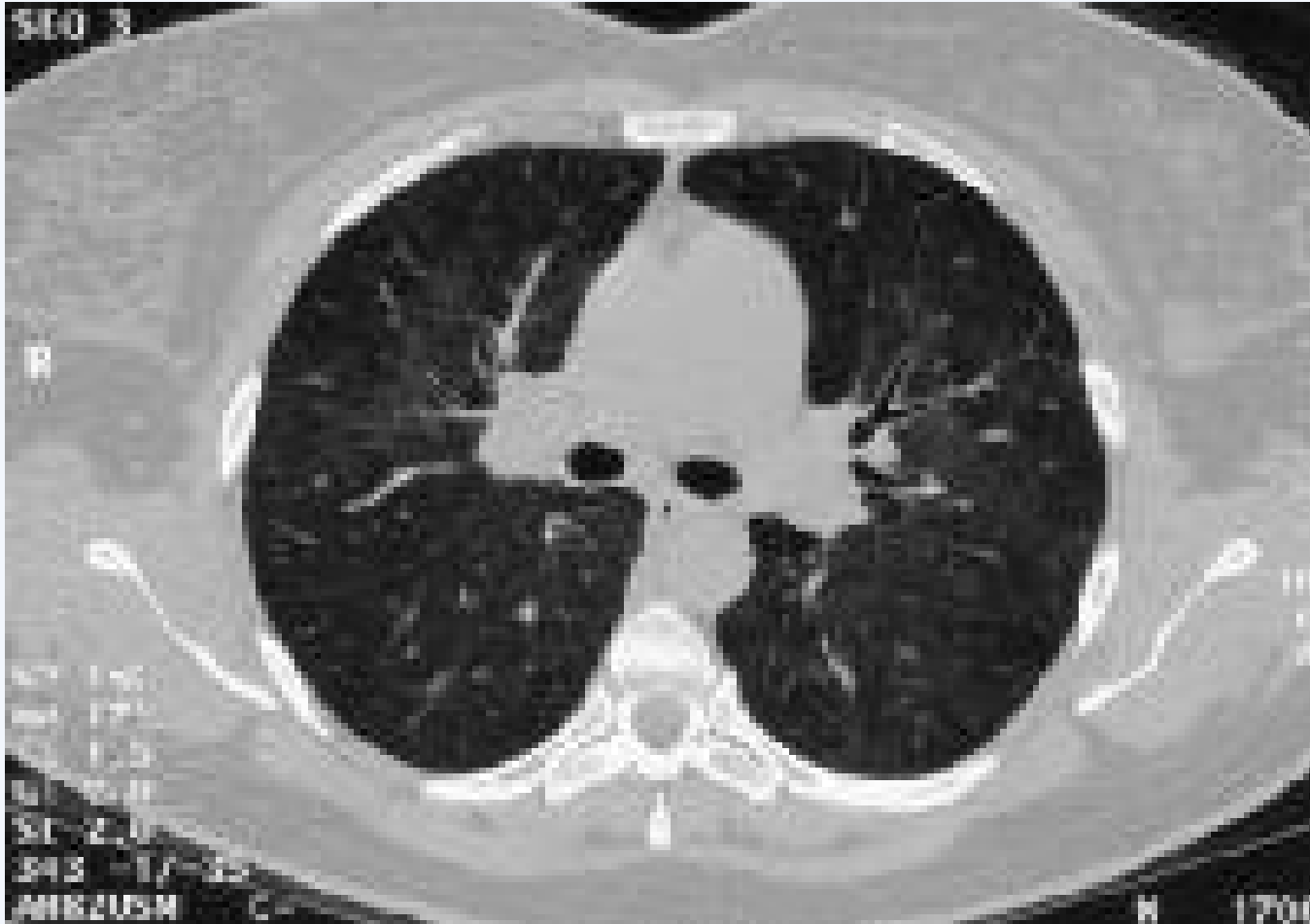
Further investigations (2)

25-OH vit D	91 nmol/L	(60-160)
1,25 vit D	154 pmol/L	(50-160)
Ca⁴⁵ absorption	1.00	(>0.6)
PSA	2.0 ug/L	(0-6)
BJP	Not detected	
EPG	Normal	
ACE	35 U/L	(41-139)
24 h ur Ca	17.8 mmol	(2.5-7.5)
24h ur PO4	60 mmol	(13-55)



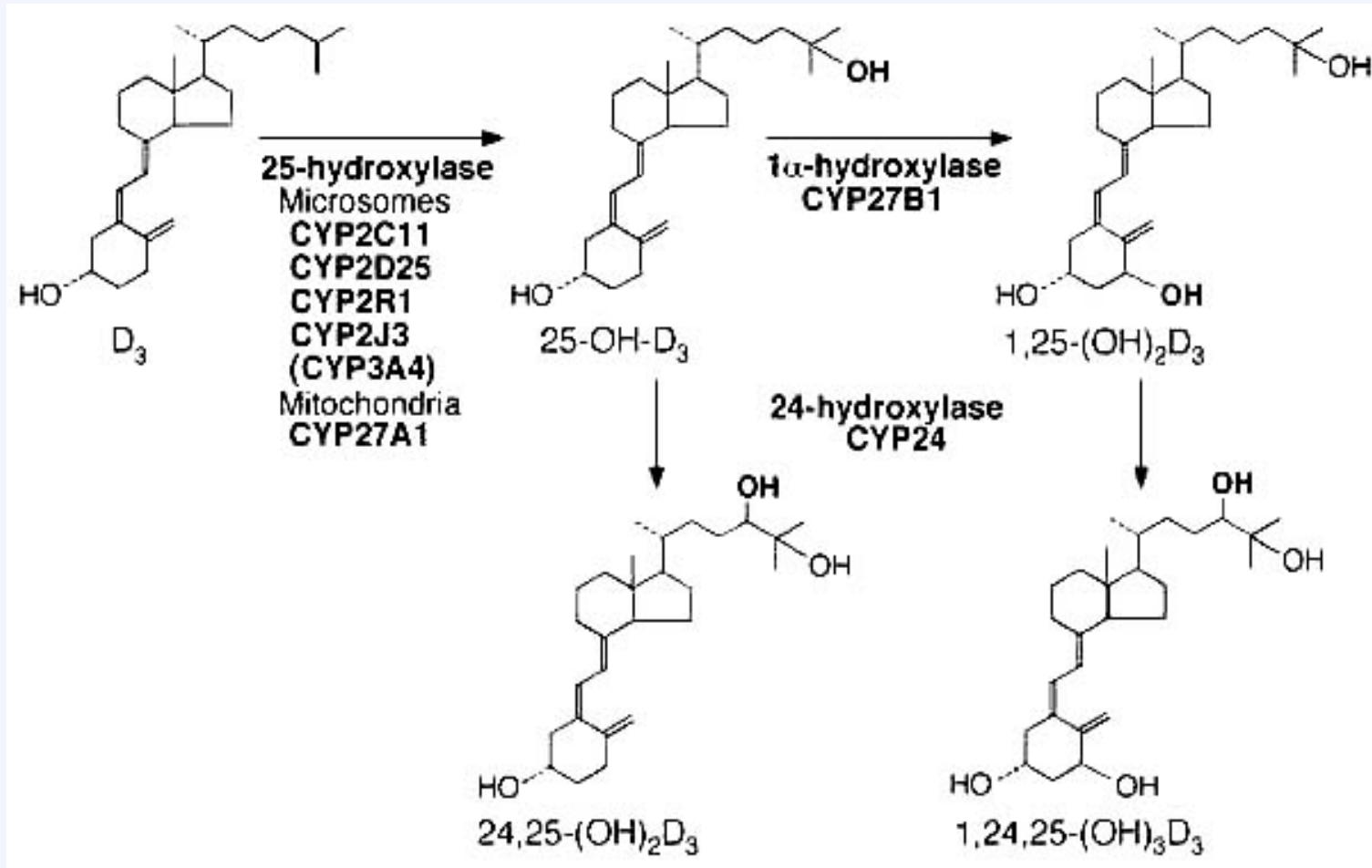
SA PATHOLOGY

Further investigations (CT chest)



SA PATHOLOGY

Vitamin D metabolism



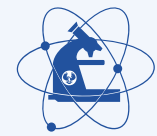
SA PATHOLOGY

Hypercalcaemia in granuloma is due to local production of $1,25(\text{OH})_2\text{D}$

- Hypercalcaemia previously described in an anephric patient
- In vitro conversion of calcidiol to calcitriol by macrophages ? via γ -IFN
 - ? Role of calcitriol as immunomodulator
- Increased mRNA for $1-\alpha$ hydroxylase
- Resistance to normal feedback



- Sarcoidosis
 - Noncaseating granuloma
 - 1 or more of: hilar adenopathy, pulmonary infiltrates, skin/eye lesions
 - Genetic susceptibility (racial differences in incidence, HLA-assoc.)
 - Lifetime risk 0.85% in Caucasians
 - Hypercalciuria 30-50%, hypercalcaemia 2-63%, ? worse in sun



SA PATHOLOGY