The Kidney in Aging

The changes that occur in the kidney with aging is OF THE MOST DRAMATIC OF ANY ORGAN SYSTEM.

Age related charges in kidney structure and function

- At age 2 GFR at adult level. Reamins at 140 ml/min/1.73 msq until age 40
- Then declines by on average 8 ml/min/msq per decade

This age related decline is accelerated by:

1. Systemic hypertension
2. Diabetes
3. Lead exposure
4. Smoking
5. Atherosclerotic vascular disease
6. Male gender

Important!

- The reduction in creatinine clearance is accompanied by reduced daily urinary creatinine excretion due to reduced muscle mass.
- That means the relationship between s-creat and CrCl changes
- S-Creat remains stable but GFR declines
- That means your GFR can be significantly reduced but the s-creat remains normal

eGFR

- Cockcroft-Gault formula takes age into consideration
- MDRD formula was validated in subjects between 18-70 years.
- Best method in elderly still controversial

Proteinuria

- Microalbuminuria and overt proteinuria increases with advanced age in absence of diabetes, hypertension or elevated sCr.

Renal blood flow

- Renal blood flow declines by 10% per decade after age 40
- Most profound in renal cortex
- Redistribution from cortex to medulla

Renal mass

- Renal mass increase from 50g at birth, to 400g at age 40.
- Then declines to < 300g at age 90
- This correlates with the reduction in BSA
- This loss in mass is cortical and medulla is mostly spared

Glomerular number

- Glomerular number decrease
- Size change controversial
- Shape changes with decreased lobulation
- GBM undergoes folding and thickening, then condenses into hyaline material with glomerular tuft collapse

- Degeneration of cortical glomeruli results in atrophy of efferent and afferent arterioles with global sclerosis

- In JXM, glomerular tuft sclerosis leads to formation of direct channels between afferent and efferent arterioles - aglomerular arterioles

Sclerosed glomeruli

- Increases with age but at variable rate
- < 5% age 40, up to 30% age 80

Reasons for reduction in GFR:
1. Reduced glomerular lobulation - reduce surface area for filtration
2. Increased glomerular sclerosis - also reduce surface area
3. Increase in Tubulointerstitial fibrosis
4. CVS hemodynamic changes: hpt. Reduced cardiac output
5. Increased cellular oxidative stress cause ET cell dysfunction

Glomerulosclerosis/ proteinuria

Atherosclerosis

Hypertension

Impaired Angiogenesis

Aging

Vascular/cardiac Hypertrophy

Antioxidant capacity

NO

Prostacyclin

Glucose

ET-1

AT11

Superoxide anion

Oxidative stress

Age related alterations in fluid and electrolyte homeostasis

- No age- specific changes
- Aged however more prone to disturbed urea and creatinine and electrolyte abnormalities when ill
- Aged kidney can maintain normal levels in health but fail to compensate during illness.

Disorders of SODIUM balance

- The normal aged kidney can adjust appropriately in low/high s-Na states but response time is impaired
- Renal response to dietary Na restriction is blunted due to blunted reabsorption in ascending limb of loop of Henle.
- Proximal Na handling intact

Elderly patient therefore more prone to sodium wasting and hyponatremia

Renal response to sodium load

- Sluggish
- Reduced natriuresis
- Augmented response to AT11 with greater fall in renal perfusion, impaired natriuresis and augmented kaliuresis.
- Altered response to all vasoactive mediators

Hyponatremia

- Most common electrolyte disorder in elderly
- 1/4 of all hospitalized patients

Causes of hyponatremia in elderly:
1. Decreased ability to excrete free water
2. Water intoxication in setting of diuretic therapy
3. Over secretion of AVP
4. Hypervolemic hyponatremia due to CCF
5. Antidepressants, NSAIDS etc.

Hypernatremia:

- Especially frail + institutionalized
- Failure to recognize thirst

Potassium balance:

- Reduced total body potassium - 20%
- Due to: reduced muscle mass, altered cell membranes, nutritional deficiency, inability of kidney to conserve potassium

Hypokalemia

- 11% of elderly at OPD
- Diuretic therapy

Hyperkalemia

- Not common
- But more prone to high K+ due to NSAIDS, K-supplements and TMX-S, ACE-inh, ARB, Spirinolactone

Acid-base

- Decrease in s-bicarb with age
- Reduced ability to excrete acid load to to reduced nephron number

Ca+, PO4+ and Mg+

- S-Ca, PO4, i-Ca, Mg and PTH remain normal
- Tendency to slightly higher PTH

Ca+ metabolism is significantly impaired:

- Reduced intestinal Ca absorption
- Reduced renal 1alpha-hydroxylase activity
- Reduced 1,25(OH)2VitD3 activity
- Reduced intestinal adaptation to dietary Ca-restriction

Low Vit-D levels common in frail elderly:

- Lack of sun exposure
- Dietary deficiency
- Impaired conversion to calcitriol
- Changes in GH and ILGF-1
- Renal Ca absorption remains unchanged

Phosphate:

- Reduced renal tubular reabsorption of PO4
- Decreased intestinal PO4 absorption
- Impaired renal adaptation to dietary PO4 restriction
- Little effect in serum levels
- Mg levels do not change

Kidney disease in elderly:

- Little threat to well-being
- 50% of normal is adequate to sustain good renal health
- Acquired kidney disease can accelerate natural decline in GFR
- Incidence of primary kidney disease same as for young - spectrum of disease differ

- Nephrotic syndrome: membranous, proliferative and RPGN, FSGS
- Substantial proportion of minimal change
- Nephritic syndrome: RPGN
- Secondary kidney disease increases with age: hpt, DM, CCF etc
- Vasculitis and deposition disease: amyloid, light chain deposit, fibrillary GN

AKI in elderly:

- Enhanced susceptibility to AKI secondary to: septic shock, volume depletion, nephrotoxins, obstructive causes.

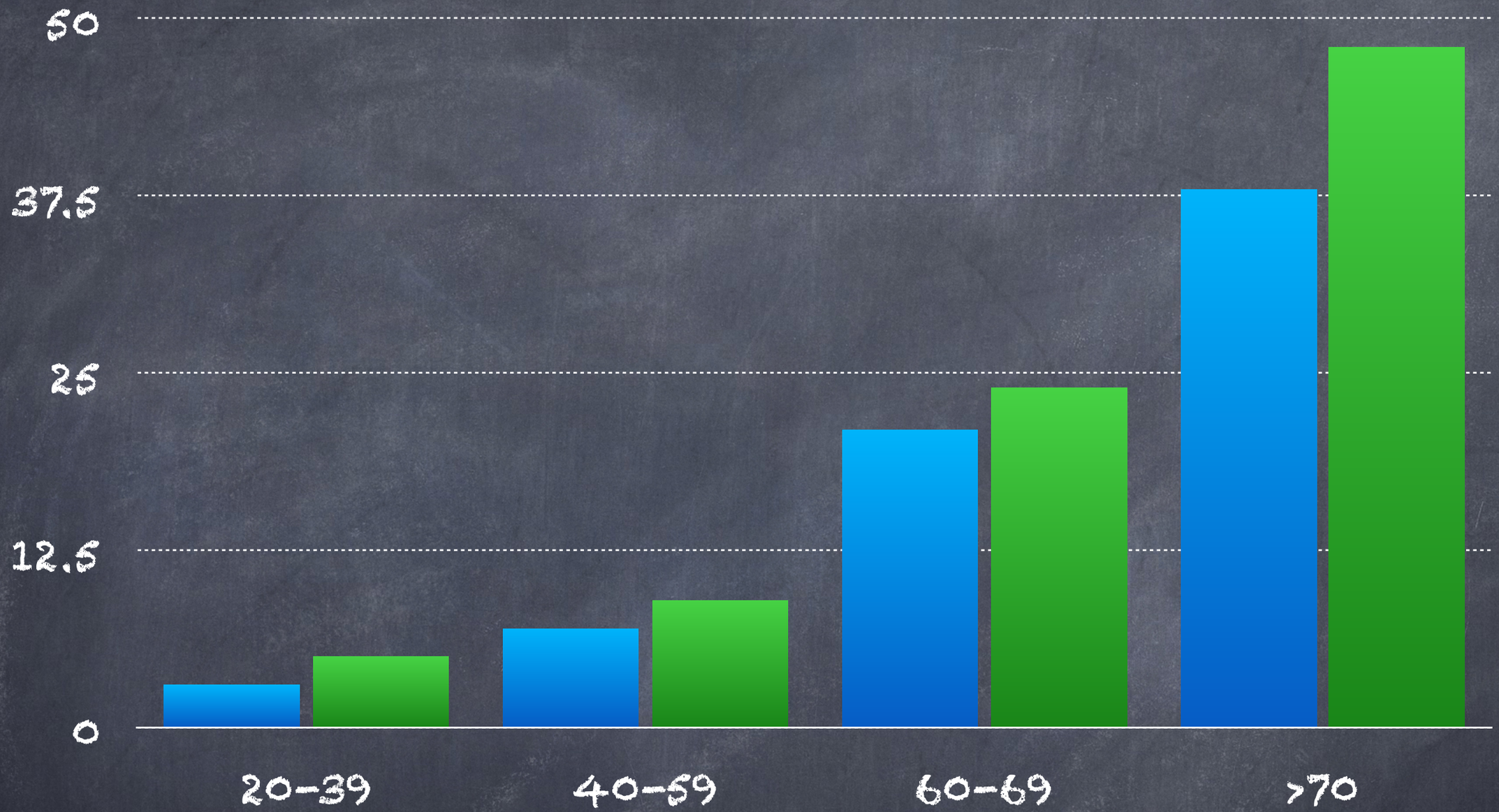
- Nephrotoxic causes more common than shock associated AKI: amino-glycosides, NSAIDS, ACE-inhibitors

- Elderly more prone to pre-renal failure: reduced sodium intake, diuretic use, salt wasting (predisposed to dehydration)
- More prone to contrast induced nephropathy due to volume depleted state
- More prone to complications and toxicity of drugs and procedures

DIAGNOSIS	% OF BIOPSY
Pauci-immune GN	31.2
AIN	18.6
ATN + nephrotic	7.5
Atheroemboli	7.1
ATN necrosis alone	6.7
Light chain cast	5.9
Post-infectious GN	5.5
Anti-GBM GN	4.0
IgAN H-S + purpura	3.6
Non-diagnostic	9.9

CKD in elderly

- Prevalence highest in older age groups
- More elderly with ESRD enter dialysis every year esp after age 75
- In addition to direct burden of CKD ESRD at 75 increases risk of death 3 fold



Prevalence of CKD by age group between 1998-1994 and 1999-2004

- Elderly less likely to be transplanted
- Significant impact on health budget
- More likely to die of CVS disease than progress to ESRD: CKD 52% risk of death in 1 year compared to 26% without CKD

- Aggressive management of risk factors and CVS disease

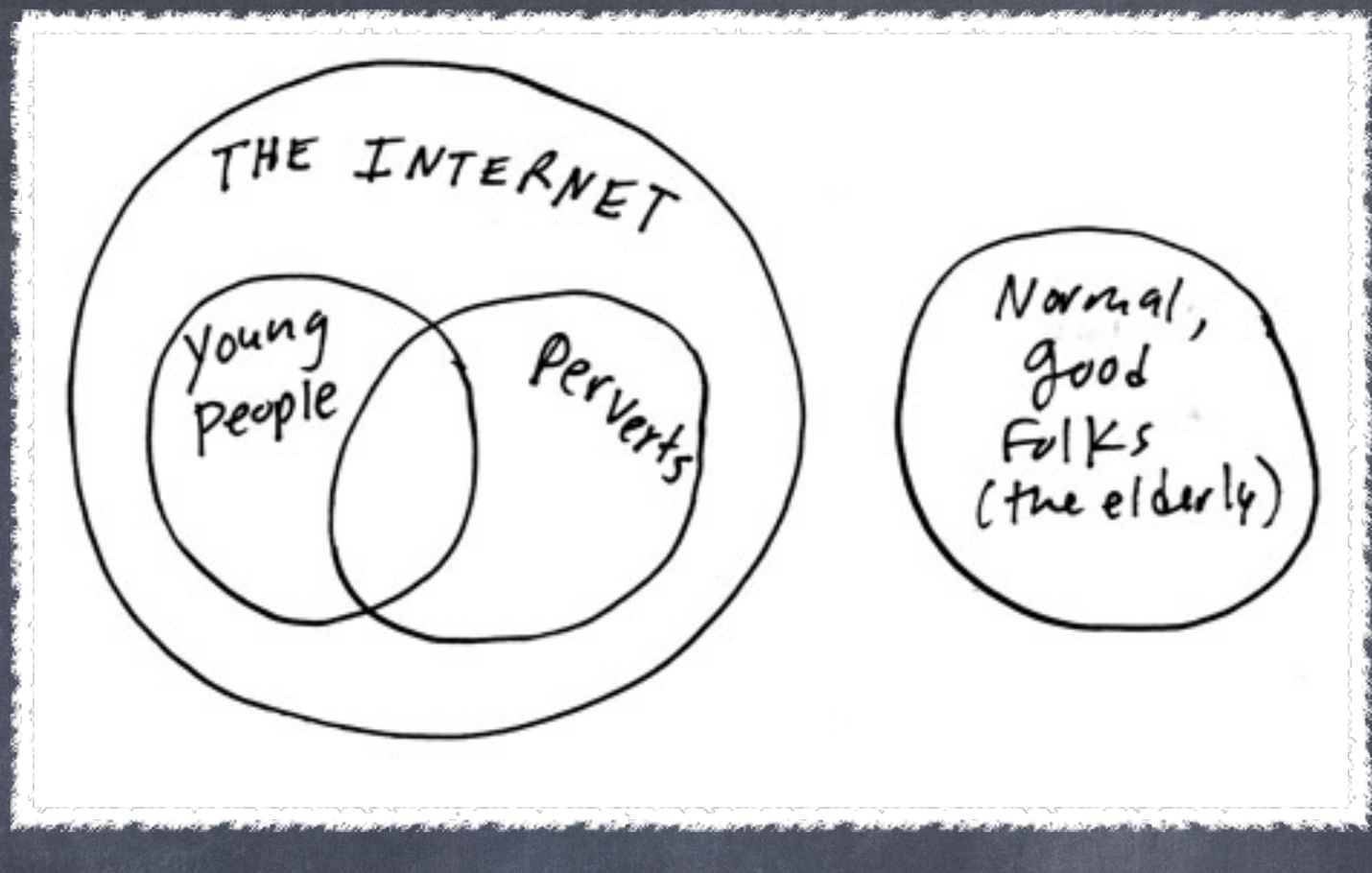
Hypertension in the elderly

Older patients have unique needs and co-morbid conditions that make selection of appropriate medication important

Minimize side effects

Minimize cost

Poor compliance



The elderly are more prone to side effects of treatment and this has to be kept in mind

JNC VII

- Proper technique for measuring blood pressure
- Provide written and verbal feedback

Why treat Hpt

- Decreased stroke 35-40%
- decreased MI 20-25%
- decreased CCF 50%

Goal

- < 140/90
- < 130/80 in diabetes or renal disease
- < 160 systolic for ISH
- Over 50 yrs - control of systolic more important

Treatment

- Lifestyle modifications 4-6 months
- If BP 20mmHg above systolic goal or diastolic 10mmHg above diastolic - start with drug therapy initially
- Initial drug - Thiazide diuretic (diuretic, ACE/ARB, long acting CCB)

Thiazides

- 6.25 - 50mg
- Remember hypoK+, HypoNa+, hyperuricemia, hyperglycemia
- Low dose and replace K+ helps to prevent hyperglycemia
- Renal failure, pancreatitis
- Monitor s-K+ and creatinine once or twice per year
- Chlorthalidone superior to HCTZ

2nd line Rx based on co-morbidity

Medication	Co-morbidity	Avoid with
Thiazide	1st line for all	Gout, hypoNa+
CCB	CAD, DM	Heart Block
ACE	CAD, post MI, CHF, DM, CRF	Angioedema
ARB	CHF, DM, CRF	Angioedema
Beta Blocker	CAD, post MI, CHF, DM	Asthma, heart block
Aldosterone antagonist	CHF, post MI	Hyperkalemia

START LOW and GO SLO but GO

This will help avoid side effects and ensure compliance

Most will eventually require standard doses

One month follow-up intervals till goal reached then 3-6 monthly

ISH

- Enough data to justify systolic BP > 160
- Between 140 and 159 depends on co-morbidity
- Related to large vessel stiffness
- Diastolic related in increased small vessel resistance

Oldest of old:

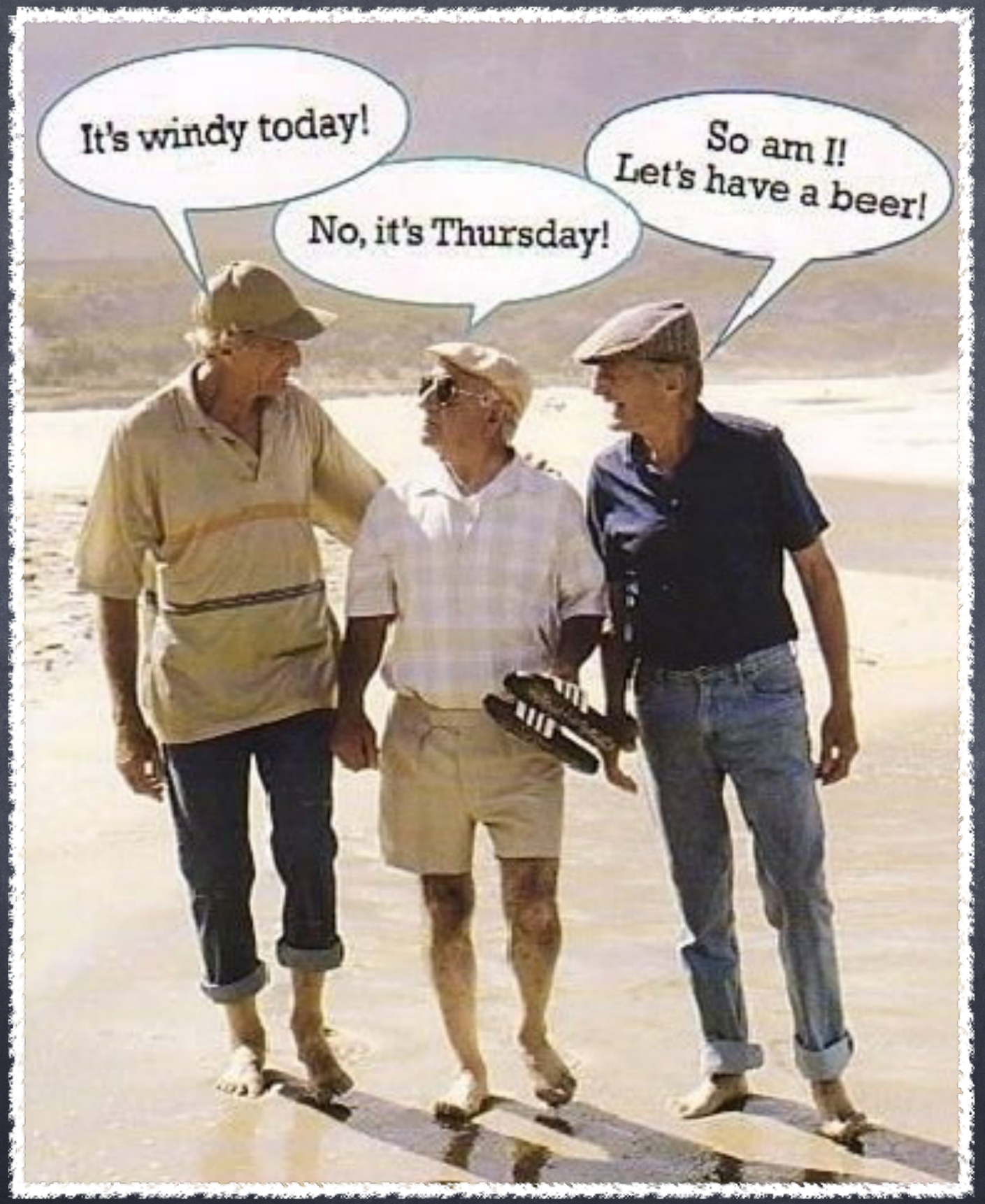
- HYVET trial
- Patients > 80 with systolic > 160
- Target < 150/80
- Indapamide +\- perindopril
- 21% reduction in mortality - mainly stroke
- 64% reduction in CCF
- Few adverse events

Widened pulse pressure:

- Independent risk for CV events
- 10mmHg increase causes 24% increase in stroke and 32% in CHF
- THE LOWER THE DIASTOLIC, THE HIGHER THE RISK
- Diuretics lower pulse pressure
- Beta-blockers increase pulse pressure

Finally !

- Minimize polypharmacy
- Simple treatment plan
- Inexpensive drugs
- Educate and empower patients
- Team approach - pharmacist, nurse


It's windy today!
No, it's Thursday!
So am I!
Let's have a beer!