Medical Conferences

World Congress Notes 2004
•CRPS

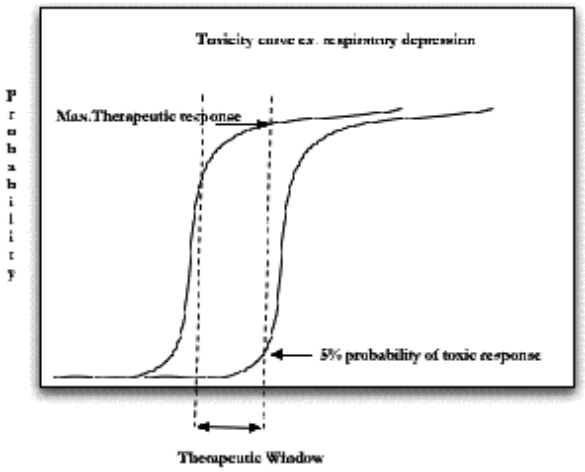
Preop stress best indicator of CRPS development
3 out of 4 get better naturally
rate 5.4/100 000
treatment goal to speed up natural recovery rate
Treatment
1) Activity-most important, if not used, it wont get better
2)Physical Treatment
-Tricyclics work best but side effects a problem
NNT=3
NNH=4 (1 in 20 have serious effects)
-Anti depressants
NNT=3
-Opiates
Morphine safe but efficacy not sure (1 in 2500 addicte) safer then NSAID
-IV sympathectomy-controversial-guanethidine displaces Nor from vesicles, the Nor may have an important role.
-Capsaicin-controversial
-TENS-can work in 30%
(NB Valproate only prophyl. Treatment shown to work in migraine NNT 1.6)
-Amputation-doesn't work

All patients post opo get hyperalgesia and allodynia
Diabetic Neuropathy-pain is in beginning only, disappears at end stage.

CRPS-only 20-25% have sympathetically mediated pain.

• Pharmacokinetics
Propofol-
MAC Awake- <3 mcg/ml=80 mcg/kg of propofol

Variability of pharmacokinetic models = 30% (i.e., concentration will be +/- 20% of what you dial in)



Ceiling effect of opiates (ex. 3mg/kg fenta) can reduce need for (ex. Isoflurane to 0.3%=MAC Awake) to stop movtement at skin incision. I.e., minimum need of Isoflurane for hypnosis.

Fentanyl infusion, short acting for 1 hr only.

Concentration of propofol (mcg/ml)

4	hypnosis
3	awake (if used alone)
2	anesth. If low dose opiate added
0.5	anesth if high dose opioid added

<0.5 anti emetic/anti pruritic

MAC Awake for volatiles = 0.4 MAC (ex. Isoflurane = 0.5 %)

Propofol maintenance for GA 100-200 mcg.kg/min (=420-840 mg/ hr for 70 kg)

Desflurane ->Carbon Monoxide esp if dessicated soda lime (enfl/isofl too but des 50X)
Sevoflurane an ether
Non arrhyth. Can use adrenaline
2-3 % metabolised
1 MAC hr -> 22 micromole/l Fluoride (>50 is nephrotoxic)
Compound A is nephrotoxic in rats
1l/min has no renal effect

gamma GST=prox. Renal tubule marker of damage
theta GST= distal. Renal tubule marker of damage

Sevo vs propofol = 3X more PONV
Sevo vs Isoflurane = patient satisfaction same, discharge time same
Sevo vs halothane = 30 X more expensive, only 50% of blinded anesth. Could tel difference

NB. OR efficiency is 30% of hospital costs.

• 1st RCT in 1060
1st metaanalysis in 1975

Drug trials
Phase I establish safety
Phase II establish efficacy
Phase III Compare to standard treatment
Phase IV Report advers effects on large population

Cohort = observational study

False negative=beta error
False positive=positive=alpha error

Phase IIb study=proof of concept

Meta analysis will be proved wrong 35% of time

Retrospective analysis good at hypothesis generation only

• Corticoids are anti COX2
European “POINT” study, 11000 patients on NSAIDS, 1 % risk of hemorr. (age/ duration/ dose).

• ACLS 2000

Lignocaine replaces by amiodarone

• Inotropes
Dopamine is an inoconstrictor (include. Coronary) retards return of stunned myocardium)
Dobutamine is an inodilator. Best for coming off CPB

• Local Anesthetics

pipecholxylidines

methyl=mepivacaine
butyl = bupivacaine = racemic mixture
propyl=propivacaine -> L form = ropivacaine

• Allergy
Many rashes are not harbingers for severe reactions. Therefore don’t follow these up unless other symptoms/signs
No family tendancy.

Adrenaline must be given early to stop mediator release.

Methylene blue 1.5 mg/kg bolus -> 120 mg in G5% worked when adrenaline and steroids didn't. It inhibits NO release. Allergy ->NO -> cardiac depression. (heart empty too.)
Low dose Vasopressin may work. It reverses endothel changes. A good next line treatment after Adrenaline. Start with a couple of units and increase logarithmically. Not a 40 U bolus. This is for pulseless VF only.

If morphine allergy (unlikely) use fentanyl since no cross reactivity. Morphine potent skin histamine releaser but rare systemically.

X-Ray contrast reaction not allergic.

Steroids given pre Treatment don't work unless given as HUGE dose.

• Alveolar recruitment
once opened, Vt contributes only 30% to volume increase
Add pO2 + pCO2 if > 300 mmHg ->< 10% shunt = all airways opened
When titrating PEEP, use high FIO2 to exxagerate tendency to coolapse (ex. At 21% less collapse, but airways not opened).

• PONV Tramer

Omit N2O	NNT=5	
Odansetron	8mg	NNT=5 (best dose for prevention)
	16 mg	NNT=5
	4	NNT=10

1 mg efficient in 40%

• Licker
ACEI
-works rapidly on circulatory ACE
-works slowly on endothelial ACE
-Thins muscle layer of vessel wall (ie, a growth factor)
- Indications:
    vent dysfunction post MI
    diabetic nephropathy
    mitral valve incompetence
-risk of renal failure if renal artery stenosis > 50% (seen in 15-20% of vascular patients)
-treat if decreased BP with 2.5 micrograms angiotensin II or 1 mg terlipressin (or ornipressin)
-chronic ACEI + drop in BP at induction of anesthesia, not a problem in 3 studies

Preop:
Stop if:
    HTA/renal failure (48 hrs before)
Continue if :
    CCF

NB In USA, most continue

• Bupivacaine
Slows propagation wave of depolarization in heart -> increase QRS -> re-entry

NB. Re-entry
If you have 2 conduction paths of differing speeds (ie a fast and slow conduction pathway). By the time the slow path meets the fast path, nothing happens because the fast path is in its absolute refractory period. If something (ex. a drug) slows down the SLOW path, this time the slow signal reaches the fast path when it no longer is in its refactory period and it can conduct retrograde -> re-entry.

In overdose, CV and CNS overlap, therefore no alert

• Anesthetics act on the A portion of the GABA receptor. I.e., not non specific
MAC is response to movement-takes place at the spinal cord
If you anesthetize just the brain, you need 2X MAC
Volatile at high dose can inhibit pain transmission in the spinal cord

Clinical sign -> analgesia
BIS ->consciousness

• Colloid vs Crystalloids

-1l G5% ->72 ml stays intravascular
-1l R/L% ->214 ml stays intravascular
-1l Albumin% ->650 ml stays intravascular

-Crystalloids have a plasma effect lasting 30 min
-10% drop in Hb = 5% increase in plasma volume

-Epidural alone ->decrease in Hb (Holte Anesthesiology 2001)
-In humans (unlike animals)-spleen NOT a source of volume.
-Plasma is 80% water

-COP not related to Albumin but Total Protein

• Fleisher
- Most post op MI are NOT due to high grade stenosis (ELLIS,J.A.C., 1997)
    -plaque rupture
    -supply/demand

-Preop test those with moderate risk (not high nor low) (i.e., 1-2 risk factors)

-Peripheral vascular surgery as risky as Aortic surgery
-Moderate risk=ortho, carotid, prostate

Fleisher suggests we test only those with limited activity (< 2 flights - risk doubles) plus symptoms should be tested
-Coriat-fresh preop PTCA wont change risk. Better to be aggressive postop. Esp. monitor Troponins aggressively.

"CASS"- little evidence that preop CABG/PTCA effect on mortality (except for 3 vessel disease)

-Kaluza after PTCA plus stent wait at least >28 days

-Consider: if you send for a preop test -> probably will get a PTCA (which doesn't help re. Periop MI) but may paradoxically INCREASE risk re. Thrombosis of stent by stopping anti-thrombotics.

• Periop Beta blockers

-Mangano's study flawed. Many on placebo were in fact on preop beta blockers that were stopped (also they had more IHD)

-Beta blocker not titrated to HR effect is not protective. Since decreased HR ->decreased shear stress ->decrease plaque rupture
-?may be best to start postop (most dangerous period is extubation and following 24 hrs)

-Consider clonidine patch
-Statins ->stabilize plaque but need to take at least 7 days. Polderman found it protected even if already beta blocked.

-Overall best probably:
    -beta blockers
    -aspirine
    -statins

• Allergies - Moss

Occurs in 1/5000 - 1/20,000 (may be decreasing because of LMA -> less use of NMB)
Criteria for anaphylaxis:
    -characteristic clinical signs
    -increased tryptase and histamine
    -RIA test
    -Skin test

Causes:
-NMB=60%
-Latex=15%
both of these are also seen in very young and very old

66% -increased IgE=anaphylaxis
33% - non immune mediated =chemically mediated= anaphylactoid (but symptoms similar, therefore need specialized investigations). Histamoine a big player here.

1) Immunol. Reaction:
-latex
-chymopapain
-sux

-rocuronium (other NMB too)

2) Chemically mediated: (mainly histamine. Anti H1+H2 useful prevention here -abolished effects of morphine/vanco - plus give drug SLOWLY since metabolism of histamine v. rapid)
-vancomycin (if pre treated with anti H1+H2, can give 1 gm over 10 min rather then 1 hr)
-protamine
-atracurium/mivacurium (NB. Cis atracurium devoid of histamine release, but like all NMB can cause immunol. Reaction)
-morphine (NB. Most opioid reactions are histamine release not immunol.(2%). Skin test difficult to interpret.)

75% of deaths are due to pulmonary manifestations, we are getting better at treating CV.

Propofol can cause selective release of mast cells in lungs -> v. deadly pulmonary problems

77% upon inducion
16% during maintenance
(NB. If late onset, think latex -
esp gyne. Passes from uterus -> blood
or tourniquet release -> A/B or latex)

Initial symptoms:
-No pulse
-decreased ETCO2
-urticaria
-dyspnoea
-cough, wheeze, stridor

-preceeding “Sense of Doom”
-32% with cardiac arrest only
-Mortality 5-6%
-tachycardia and oedema can last several hours

watch for:
-recurrence
-increased severity in pregnant and beta blocked

70% females
atopy and food allergies seen in 20-30% of Latex allergies (nuts, avocado, papaya).
Contact dermatitis can be risk factor for latex (IgE)
H1 and H2 block CV but not cutaneous manifest. - NOT first line drugs

Mediators:
-leukotienes are important (negative inotropes)
-Tryptase
    -co-released with histamine
    -v. big protein in mast cells
    -v. robust 1/2 life (just take it and put it on shelf)
    -Pos. Pred. Value = 92%
    -Neg. Pred. Value = 65% (therefore important medico-legally)
    -Cut off of 25
    -causes bronchoconstriction. A mediator not just a marker.

Anti IgE may be new treatment in some

• Malcolm Fisher - Diagnosis of Allergies

Test during reaction:
-Histamine
-Mast Cell Tryptase
-serum Complement(increase not necessarily assoc. with adverse effects, therefore not. V. helpful)
-Urinary methyl Histamine (need urinary catheter)
-Specific IgE (increases for 10 min - when you will be most busy)
-Total IgE (useless)

Do tryptase at 1 hr when it rises, peaks between 2-3 hrs, can do it when patient better.
Increases in some non immunol. reactions, i.e., increase in tryptase does not mean IgE mediated.
Can be done even on dead patient!

Anaphyl.=ECHO=”empty, contracting heart”

Troponin increases during reaction. Also Hct can increase (hemoconcentration)

After reaction:
-History
-Local anesth. - v.v.v. rare (if in dental chair ask where they woke up, if not ICU, not allergy)

Skin Tests:
-v. valuable (intradermal)
-only good for IgE mediated reaction
-4-6 weeks post reaction
-Prick vs. I/dermal don't know which best
-screening not useful (too many false positives)

Prick better in:
-latex
-kids
-convenience
-cost

Local Anesthetics:
-do a progressive challenge
-up to 1/100th dilution.
-in all patients you can find at least 1 L.A. that is safe

Positive skin test lasts 4-30 yrs ("a disease for life")

RAST tests-experimental

Can be allergic Dexamethasone

• Steele

For Iliac bone graft
-paravertebral block at T11-L1
(at top of spinous process 2 1/2 cm from midline)

• Strichartz
v. little L.A. penetrates nerve, most -> blood

PNS
-chronaxy=duration of currents pulse
-Nerve action potential=all or nothing
-usually painful, even if you reduce 0.3mSec to 0.1 mSec

Urmey showed 30% had paresthesia but no motor response to PNS

-within a fascicule, the sensory and motor nerves are bundled seperately, i.e., you can put needle in a nerve but only get 1 modality (sensory or motor) . Therefore one can insert a needle intraneurally without pain using a PNS.
-<0.5 mA may be too low-you can be in fascicle at this level.

-When paraesthesia ellicited, in only a minority was a fascicle impaled.

-After tourniquet ->nerve ischemic. No response to PNS for 10-20 minutes. Therefore care in postop blocks.
-Sciatic nerve - Peroneal N. lateral / Tibial N. medial

PNS:
-If increase amplitude or duration ->greater charge -may stimulate muscle directly
-Use higher frequency (2 Hz) ->faster response (shorter and easier)
-Connect needle to anode - not cathode +)

• Neuropathic pain
-activation of Na channels (No Pgs -> COX inhibitors don't work)
therefore use Na channel blockers

Brussels Notes 2004

• Loss of aeration when supine

-lung collapses under own weight
-diaphragm rises up -> compresses by increased intra abdo pressure
-enlarged heart compresses lower lobes

- when you look at CT you don't see lung tissue, but aeration

-You can have 30% oedema of lung with a normal CT

-Prone position-blood flow not due to gravity. In prone, most flow still to dorsal (i.e., non dependent) regions. Prone tends to uniformise flow
More homogenous lung vol cf. to supine ->increase FRC (=PEEP 12) -> more uniform V/Q
Air now goes more posterior (previously dependent region)

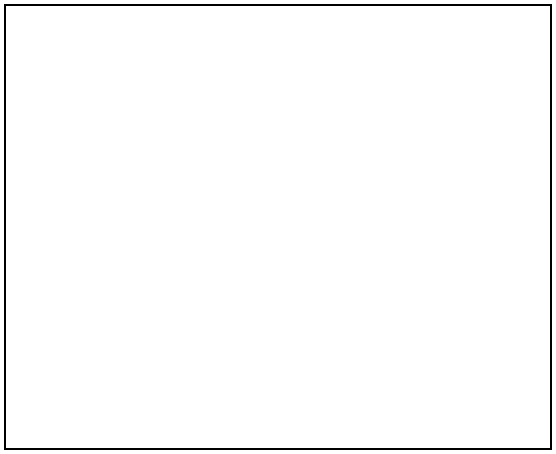
May be that prone makes chest wall stiffer ->decreased compliance ->more ventilation goes to the posterior regions which become relatively more compliant.

In ARDS, 50-75% are prone responders
No effect on mortality

P/F <300 = ALI mortality = 30%
<200 = ARDS mortality = 60%

(Hubmaier)
Gradients in lung due to stresses created by different shapes between chest wall and lung

NB.
Compliance = resistance to change in volume
Shear force = resistance to change in shape (ex. Liquid has very little shear force since it can change shape easily, but v. little compliance, lung is the opposite



Therefore in prone position ther may be a better fit between lung and chest wall causing less stress forces ->decreased gradient and better V/Q

• Abdo sepsis (Ramsey)

If using diagnostic CT, must use contrast IV, enhances image of abcess.

After bowel anastomosis, no macroscopic leakage for first few days.

Laparotomy is immunosuppressive, therefore don't do it lightly.
If no improvement after first laparotomy, 91% mortality
2nd laparotomy-91% die
3rd laparotomy -100% die
(i.e., you get 1 chance to get it right…excepion is pancreatitis)
NB.
Upper GI leak has a higher mortality because you cant exteriorize the problem (duodenum difficult to mobilize) (cf. lower GI)

NB. Venous measurement of lactate as good as arterial.

Acalculous cholecystitis
<2% - we ressusc better (i.e., like stress bleed)

Diagnosis= ECHO -> >4mm wall thickness, sloughed mucosa

• Preop optimization

3 Million operations / yr in UK vs 8.4 Million in France

Wilsons study of optimizing fractured neck of femur.
Aim is to achieve a DO2 600 ml/min/m2
1) Fluid load to PCWP = 14 (achieve goal in 40%, but must keep giving as DO2 will drop off if fluids stopped)
2) Dopexamine 0.125 microgram/kg/min (i.e., a very low dose

reduced mortality by 2/3rds (NNT = 6)

Sinclairs study

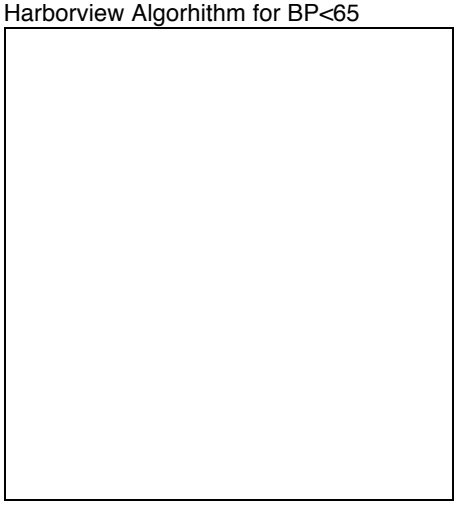
Used esoph doppler to optimize SV
Gave a mean of 750 ml colloid

Control group dropped SV by 6 ml during surgery with subsequent decreased C.O. (undetected)
Treatment group SV was up 13 ml (C.O. up by 1 l.

I.e., occult hypovolemia common.

Angiotensin II - AFFERENT ARTERIOLAR VASOCONSTRICTOR/MESANGIAL CONSTRICTION -> DECREASED GFRa compensatory effect -> decreased solute load to nephron -> metabolic load.

Harborview Algorhithm for BP<65



• VAP (Chastre)

tracheobronchitis shows no increase in mortality
routine cultures- studies show no benefit. Therefore don't use. (pos pred. Value 7.5%)
i.e., the m/o's you isolate are rarely those that cause the VAP.

Inevitable colonization of ICU patients with high grade m/os
These do not need treating
Rouine surveillance not helpful.

Diagnosis (if ventilated > 3 days) (early VAP<96 hrs>late VAP)

	Cut off
ETA	10^6
PSB	10^3
BAL	10^4 (>5% intracell. M/o's)

Only 50% of clinical VAP had m/o's
3% per day of mech. Ventil patients get VAP
98% correl. Bet proximal quantitative tracheal cultures and BAL
In prolonged ventil. - not on A/B - semi quantitative prox. Aspirates > 10^6 is good.

Wrong A/B increases mortality by 50%

Recent A/B muddle results of BAL, long term A/B for other infections does little.

Fagon's approach:

-Clinical suspicion
-B/scope before A/B
-direct exam - treat or not
-quantitative culture-alter initial treatment or stop

Fagan doesn't use invasive diagnostic tech. For diagnosing VAP if recent introd. Of A/B or recent (<3 day) change in A/B.

• US ICUs
50% are in hospitals < 300 beds. They don't publish, therefore are research results applicable?
Soweto Baragwanath hospital..biggest in S. hemisphere. 35000 deliveries / yr!!

• NorAdr -> decreaes lactate, increases pHi intestinal, increases CO when vol repleted by alpha1 receptors in heart(+ inotropy)

Adr -> increases C.O. and BP but increases lactate

Alpha agonist pro inflamm.
Beta agonist anti inflamm.

• Enteral feeds
all benefits seen in trauma patients (i.e., young) ..maybe good bowel function is an indicator of good prognosis, i.e., EN is only an indicator not the cause of better prognosis.

Abdo distension is a very important sign and a contra-indication
Aim for 20-25 Kcal/kg/day (non protein Cal)
No longer 2000 Kcal/day - now around 1200 Kcal/day)

EN start at 30 ml/hr - 4 hr do aspirates
If >120 ml ->prokinetics
If < 120 ml -> 60 ml/hr
Aim for 800 ->1000 ->1200ml/day

• Everest
PO2=43
PCO2=8 ->PO2=35
If PCO2=40 ->PO2=3

• Hawthorne effect = if you stop looking at something it will recur.

• Percut tracheo

at rings 1-2 or 2-3

• CPR

D	Defib
C	Compression
B	Breath + airway
A	Adrenaline

• Lung fluid dynamics
Pmv=7
Ppv=-2
Reflection coeff. = 0.7 (rel high cf. to other tissues)
Lung has rel high extravascul. Protein content (is about 50% protective foer a given increase Pmv cf. to other tissues…i.e., increased Pmv -> H20 leaves and dilutes the extravascul. Colloid).

• Ppeak and Pplateau recruit, PEEP keeps open
keep plateau pressure <35

Gattinoni:
-feels when you get an increase in pCO2 = sign of overdistension

recruitement measure 3 things:
1) increase paO2

2)increase paCO2
3) difference between plateau pressure and PEEP

in overdistension ->increase dead space ->apneic oxygenation ->increase pO2 ->increase paCO2

when recruited ->increase paO2 and decreased paCO2

increase PEEP, measure Pplateau, the difference between the 2 should stay the same, when it increase, you have over-recruitement

If auto PEEP of say +20, patient must generate - 20 to generate flow. If add PEEP, now patient only has to generate -1 (rationale for using PEEP in COPD/asthma).

Normal resp. compliance is 100 ml/cm H2O, if 20 cm H2O, only 20% of lung available.

• In case of pneumonia, esp if < 5 days onset, 1200 mg of ciprofloxacin - as good as or better then Imipenem +/- aminoglycoside (1X/day).

For pseudomonas = beta lactamine and quinolone

• Bion
Crohn's disease get increase gut permeability but no MOF-as do their healthy relatives.
Best measure is microalbiminuria of endothelial (including gut) damage.

• Cohen:
neutropenic fever
- empiric A/B = betalactamine+quinolone+/- aminoglycoside
-rarely do anaerobes cause problems
-if suspect, treat fungi early (>2 day ->increase mortality), therefore Amphotericin B -only one covering candida and aspergillosis but toxic (decreases GFR)

KT impregnated with minocyclin and riamycin -> decreased coloniz., decreased infection, lasts 21 days.

• Resp. drive and resp. rate are different parameters
-sedation may decrease resp. drive but not rate, therefore to monitor morphine, resp rate is not a good parameter.

• Fractured neck of femur has a 15-20% mortality in UK

• Hubmayer:
-inverse rel. between RR and Vt is irrespective of CO2-i.e., its mechanical drive (H-Breuer reflex) not chemical driven.
-longer inspiratory time -> delay in neural output leading to next inspiration.

• Hyponatremia:-chronic -> solute (K+, A.A.) exported from cell -> bringing water with it (cell dehydrated), if rapid correction (i.e., extracellula osmolality is higher then i/cellular -> further dehydration(-> demylinating syndrome). Therefore increase 10 mMol/day

-acute response -> cells swell
chronic -> cells shrink
-rapid correction -> shrink

Ex. If dehydrated and then drink tap water -> decrease serum Na. Treat with Saline -> increase BP ->decrease ADH (NB. Body protects volume first , osmolality second) -> kidney will excrete electrolyte free water, once vol. problem solved.

-If great increase in serum Na-add DDAVP (or aqueous pitressin) cant give 1/2 N saline- normal kidney will excrete free water readily.

• Pulmonary embolism

1) Diagnosis:

D Dimer < 500 mcg - high neg. predictive value

Suspicion of PE:
a) ECHO - massive PE (look for dilated RV/septal shift)
suspected ->thrombolysis
non diagnostic ->V/Q/spiral CT
other diagnosis

ECHO-moderate/mild PE
a) D Dimer-
<500 = excluded
>500 -> compression U/S
+ Treat
- confirm V/Q
+ Treat
+/- angio
-

above algorhithm avoids angio 80% of time

2) Treatment
-NorAdr
-Heparin (decrease dose if periop) -5-10.000 U bolus -> 15,000-40,000U/day
-recanalis: thrmbolysis/catheter/embolectomy
(NB thrombolysis is relatively C/I if surgery < 10 days - risk of bleeding may be less then we thought - 1 million units of urokinase as a bolus)
- Warfarin
start day 1
PT 1.5-2.5
Overlap with heparin 4-5 days
-LMWH
OK if non life threatening PE
-Thrombolysis
followed by heparin
only if h/dynamically unstable (up to 14 days post PE)
IV=pul. Angio
Urokinase = 4400 bolus, 4400/kh/hr for 12 hr
Filter- not recommended -> high rate of recurrent DVT

If warfarin reversal needed rapidly -> 15 ml plasma/kg
Risk of bleed (major) on oral anticoagulants = 1 bleed / year
LMWH-OK even in massive (>50%PE)

At 2 hrs - 70% who will die are already dead
Platelets release serotonin ->pulmonary vasoconstriction ->RV isch.and dysfunction ->septal shift ->decrease C.O. -> decrease BP ->decrease RV perfusion

Treatment

• Myocardial Infarct

(NB. TIMI 3 flow = complete reperfusion at 90 min

Chest pain:
-ECG diagnostic in 50%
-non Q wave MI- similar mortality to Q wave MI
- unstable angina
-3% will die
-6% will have non fatal MI
-90% - OK
- heparin infusion stabilises the plaque

-Troponin- unlike CPK, it picks ups minimal myocardial damage
-"T" better at predicting risk cf. to "I" (easier to measure and more robust)
-max. sensitivity at 12 hrs
If increased ST segment -> Troponin - = do well with thrombolysis
+ = less likely to reperfuse (ie missed time window before rise in Troponin)
-mortality much more tightly correlated with weather troponin + or - cf. to whether anterior or inferior M.I.

• Hillman
Drain all hemothoraces
Operate if > 300 ml/hr for 4 hr
Or
1500 ml/day

percut tracheo at 1-3 tracheal ring = mid pt. Between S/S notch and cricoid

• Ronco

clearance inversely porportional to Mol. Wt.
Cytokines are about 80,000 Daltons (glomelular threshold is 50,000 Daltons)

• Gattinoni
1 proton ->CO_2 + NH_4^+ (a bicarbonate generator)
• Pulsus paradoxus
Spont ventil. ->increase VR -> septal shift -> decreased C.O.

• Dreyfus
low pressure ventilation with high volume (used neg. pressure chamber) -> lung injury (i.e., vol is important)

consider TPP when talking of ventil. Pressures esp chest wall/abdo. Normally = 2 cm H_2O but can be between 10-15 cm H_2O
ACCP recommends:
Vt 5-8 ml/kg
Low plateau pressure <35
Lowest FiO_2
PEEP trial

We normally sigh 10 x/hr
With IPPV-occ. Recruitment maneuvre (increase PAW to 40-60) improves aeration on CT. Constant Vt -> decreased compliance over time.

• Eisenberg
Thrombolytics take 1 hr to work in MI
PTCA-level I only if < 1 hr door to dilation
Once coronary artery patent, you leave behind a very procoagulant platelet rich thrombus.
Give heparin, aspirin BEFORE fibrinolytic since it -> increase free thrombosis ->increase clotting

ACCP:
MI in 1st 24 hrs
-No prophyl. Anti-arrhythmics
-Aspirine (160-320 mg chewed)
-Beta blockers (IV 5 mg metoprolol, 5 mg atenolol -NB 13 benefit for 1000 treated, cf. thrombolysis where 18/1000)
-ACEI (ex. Captopril 6.25 mg ->2 hrs later -> 12.5 mg ->25 mg BD) (esp if CCF/decreased Ej.F/big ant. MI)
-GTN (+/-)

(?Heparine (esp if unstable angina))

MI
Increased ST and Trop. Negative ->=thrombolysis (if <12hrs)
Increased ST and Trop. Positive ->=PTCA

• Aminoglycosides and quinolones kill in a concentration dep. Fashion
Beta lactamines kill in a time dep. fashion (therefore long lasting best ex. Ceftriaxone)

Site penetration:
Lung
Good-quinolones, macrolides
Poor-beta lactamines, aminoglycosides
Aztreonam is the only beta lactamine that can be used in a pencilline allergic patient-exclusively gram - activity
Cipro:
400 mg IV X 3 or 750 mg X2 if P.O.

• Q10 ratio = ratio of reaction rate measured at 10 degree apart
$CMRO_2$=2

• Cardiac Arrest
68% are aystolic/EMD ->6% survive
32% are VF/pulseless VT ->42% survive
50-80% of Cardiac arrest patients will have premonitary signs

bi-phasic defib. -> use lower energy (about 150 J)

• Thrombophilia
5% of unexplained DVTs ->malignancy (therefore CXR)
Lupus anticoagulant-warfarin doesn't work
-LMWH may be better then oral anticoagulants (esp in malignant disease)

• Mervyn's LVF tutorial
Lasix just dries them out therefore decreasing VR and C.O.
Reason they are breathless is the decrease C.O. -> decrease SvO2
In pulmonary oedema give 4 puffs of GTN spray
Heart failure may be chronic inflammatory state
Main metabolic substrate of heart is FFA
Carvedilol=beta blocker and vasodilator

Treatment LVF
-GTN-but tolerance after 24 hrs
-ACEI (or AngioII blockers)
-+/- diuretics

-CPAP ->decreases WOB
-Inotropes
-phosphodiesterase inhibitors=felt better, died quicker
-levosimedon-increases Ca sensitivity
-GIK-decreases FFA (ie. Anti inflammatory)
25% Glucose + 50 UI Insulin + 80 mMol KCL @ 1.5 ml/kg/hr

• VAP Diagnosis
Pneumococcus
Urinary antigen
Blood (delay)
Best treatment beta lactamine + macrolide

Legionella
Urinary antigen
MRSA
Sputum

Get A/B in early > 4-8 hrs -> increased mortality

• Do CT before LP in meningitis only if lethargic, coma, focal sign, papilloedema. Treat within 30 minutes.

4% herniated after LP (Rennichi, BMJ, 1993; 301,953)
Therefore use small needle and drain just what you need
10 mg dexamethasone only if PRIOR to A/B then 6mg-6 hrly for 4 days -> 52% decrease in mortality

empiric treatment in adults:
Age:
< 50 =3rd generation cephalo (ex. ceftriaxone)
> 50 = ceftriaxone+ampicillin+vancomycin (for peni resistant pneumococc.)

Meningococc. Meningitis-rel normal CSF early on. Give Act Prot C if not C/I
•Enteral nutrition - Mythen

Prokinetic erythromycin = 200 mg 3X/day

cont feed vs intermittent=no evidence
diarrhea=live yoghurt, exclude clostridium

All studies showing benefit were in surgical/trauma patients I.e., relatively well patients
Analogous to periop optimization (evidence good) vs. ICU optimization (no proof)

Immunonutrients do not decrease mortality
NOBS=feeding induced non occlusive bowel necrosis Syn. (=nec. Enterocolitis in kids)…a steal phenomenon

Gut function test-put NG tube -> give pentagastrin if poorly -> no decrease in pH
If well -> decrease pH

Look for residuals, tenderness, distension=early sign of GI dysfunction

Feed stomach-give 1000 kCal glucose IV peripherally and start feed gently (ex. 30 ml/hr) go up looking for early signs of dysfunction

Mythen doesn't use prokinetics

• Trumpet player generates > 150 cm H2O - no trauma (it's the TPP that counts) i.e., it's the stretch of the lungs that counts. Pressure with no stretch doesn't matter.

Also collapse ->re-expansion is damaging

Overdistension can release cytokines and translocation of m/os, endotoxin -> systemic effect

• Coagulation
endothel. Very active -> glycosaminoglycans (=SAGS), NO, Pgs
VIIa circulaing is only 1%
40% of patients receiving 1 unit platelets will develop antibodies.

• DDAVP
indications:
vW
mild hemophilia

• Plasminogen ->lysine analogues (ex. epsicap, tranexamic acid) ->Plasmin ->aprotinin (protease inhibitor) ->fibrin -> FDPs

• Bleeding ulcer
mortality unchanged 5-10% (30% rebleed)
High risk lesion (Forrest type)
Treatment
Endoscopy
Stops 90%--but 30% re-bleeed

Histamine antagonists - no use
Omeprazole-start after endoscopy (2X 40 mg /day IV)
NNT=6

Antibiotics if varices (decreased death by 10%)
Best may be slero and drugs

Therefore early vasoactive therapy ->endoscopy ->if fails ->TIPS

• Armys approach to bleeding

-gauze and pressure (purified shrimp shell = “Chiltosan” in hemostatic dressing)
-tourniquet-“Spanish Windless”-v.effective-release occassionally if bleed starts re apply

VIIa-acts if hypothermic but not if acidotic, therefore correct with bicarb
If non compressible hematoma, resuss. To palpable radial pulse/conscious but no more
Keep systolic BP 85-90 (unless head injury)
Patients are hemophiliacs when they are 33 degrees centigrade
Fresh whole blood if possible (5-10% in Iraq)

Quick clot increase temperature to 70 degrees-may burn

Don’t forget acidosis encourages bleeding

Give :
FFP-5-10 ml/kg
Cryo - 1-2 U/10 kh
Platelets - 1-2 U/10 kg

Before factor VIIa (may need 3-4 doses)

VIIa: -90 microgram/kg
-$0.81/microgram
-decrease PT
-TEG- all parameters improve
-v. effective in reversing warfarin
-v. effective in lupus anticoagul.
-T 1/2 is 90 min
-seems v. safe

• I/cerebral hemorr
no treatment
only 20% survive well (40% die, 40% disabled)
prognosis rel. to vol of blood
40% have significant increase in blood after 1st CT-ie ongoing
bleeding probably multifocal, peripheral to hematoma

• Burns in kids -> give beta blockers, decreased net muscle loss

• Critical care polyneuropathy-myopathy

70% of sepsis patients have CCPM
CCPN ->decrease reflexes
CCPM -> preserved reflexes (increase CK=necrosis)

•

Brussels Notes 2005

• CV Normal Values

Value	Normal value
Cardiac Index	2.5-4.2 L/min/m2
SVR	700-1600 dynes/sec/m2 (= (80*MAP-CVP)/CO)
PVR	20-130 dynes/sec/m2 (= (80*PAM-PCWP)/CO)
Stroke Vol Index	40-60mL/beat/m2
LVSWI	45-60 g/m./m2 (=MAP-PCWP)*SVI/0.0136)
RVSWI	5-10 g/m./m2 (=PAM-CVP)*SVI/0.0136)

SPV = Normal value <10 mmHg
? Up = Normal value <5 mmHg
? Down = Normal value <5 mmHg

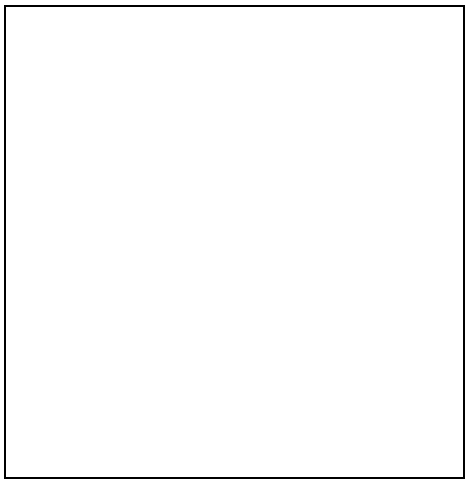
PPV = Normal value <13%
SVV = Normal value <10%
Arterial Pulse Contour Analyses

Systolic pressure variation is defined as the difference between the maximal and minimal values of systolic arterial pressure recorded over a respiratory cycle.
SPV = ?Up + ?Down Normal value <10 mmHg
Sometimes calculated as a fraction by the equation: SPV = SBP max – SBP min/(SBP max + SBP min/2)
? Up = SBP max – Apnoeic baseline Normal value <5 mmHg
(Represents the augmentation of systolic pressure due to the increase in LVEDV and the decrease in LV afterload during inspiration.)
? Down = Apnoeic baseline – SBP min Normal value <5 mmHg
(Represents the fall in LVEDV and the increase in Left Ventricular afterload during early expiration.)
Pulse pressure variation is the maximal difference in pulse pressure seen over a respiratory cycle, where pulse pressure equals systolic blood pressure minus diastolic blood
pressure.
PPV = [(SBP – DBP)max – (SBP – DBP)min]/[(SBP – DBP)max + (SBP – DBP)min/2]
= PP max – PP min/(PP max + PP min/2) Normal value <13%
Stroke volume variation is the percentage of change between the maximal and minimal stoke volumes divided by the average of the minimum and maximum over a floating
period of 10 seconds.
SVV = SV max – SV min/(SV max + SV min/2) Normal value <10%

DO2 = CI X Hb X SaO2 X 13.9
= 3 X 12 X 0.96 X 13.9 = 500 ml/min/M2

VO2 = CI X Hb X SaO2-SvO2 (=extraction ratio) X 13.9
= 3 X 12 X (0.96-0.72) X 13.9 = 125 ml/min/M2

Algorhythm for hypotension:
for BP<65



• Pulse contour analysis
-PICCO needs dicrotic notch
-LIDCO measures MAP,therefore no dicrotic notch necessary
-NB compliance rel. stable unlike resistance

-APCO (McGee) -algorhithm requires only a peripheral “a” line(+demo data ex. age, sex, ht, wt)
-In hypovolemia ->increase diastolic BP ->smaller pulse pressure.
-Thermodilution is not a great “gold standard” 5-25% error

• Pinsky
- If you give fluid in hypotension without monitor ->increase in BP in only 50%
-Starling measured RAP and C.O.
- In sponttaneous breathing-if CVP decreases on inspiration, they are preload responsive.

• Max. data one can integrate at one moment is 7 +/- 2

• Kellum
“Need Cash for Alcohol Research”
Pro. Vs. Anti inflamm. Phenotype -> genetic predisposition. Difference in mortality is X5 (i.e., pro inflamm. Phenotype ->increaset TNF ->less death from sepsis but more auto immune disease). If increase IL-10=anti inflamm. Phenotype -> increase death from sepsis.

-ARDS mortality
DD allele- 50% die
ID allele- 25% die
II allele-10% die

• Mythen
crystalloid vs colloid
R/Lactate -> increase N+V, pain, double vision, wt. Gain

• Dorman
Pre op stress test losing favor (you don’t want to know if they have IHD, but if they will have a CV event)
-low Posit. Pred. Value
-Little proof that pre op CV risk assessment improves outcome
preop angio ->revascul. ->increase mortality (Darwinian selection)
No proof drug eluting stents reduce periop mortality
Goldman moved from risk assessment (no improvement) to risk management:
-Beta blockers
-Clonidine (if beta blockers C/I)
-statins (beware hepatic toxicity)
-aspirin
-decrease stress (regional vs GA-no proof)
-GTN/Ca blockers (no use)

• Ince
In kidney, decreased microvascular pO2 in cortex before medulla (ie redistribution shock)

S.D.F. = “Sidestream Dark Field Imaging” (Sub-lingual)

Terlipressin-increases BP and UO but decreases S/L microcirculation (also increased core toe temperature gradient) -> death
-Toe temperature still a good monitor

Tongue is close to heart (carotid artery feeds-central venous circulation).
S.A.H.-hyperventilation -> severe microvascular vasoconstr. And sluggish flow

-2 theories of Sepsis
-microvascular
-cytopathic hypoxia

Septic shock = "MMDS" (Microcirculatory and Mitochondrial Distress Syndrome)

If you just fluid ressusc. Muosa is better perfused, serosa stays hypoxic. Add iNOS inhibitor -> both recover.

Assess:
-Cap refill time
N = 4-5 sec in adults / <= 2 sec in kids (a 6 sec cut off ->AUC of 0.8)

- Skin temperature

Give fluids and 100 microgms of GTN (best by infusion 2-4 mg/hr)

SDF vs OPS -> SDF light comes from the side, less reflective with deeper penetration, better image, can see WBCs

S/Lingual CO2-good monitor

Occult increased lactate-longer it takes to recover, worse the prognosis (cf. marathon runner)

• Fluid responsiveness

passive (45 degree) leg raise- for 7 min good test
-Pulse oximeter signal variation works too.
-delta up not v. large cf. to delta down
T/Thoracic ECHO can measure IVC diameter, predicts CVP

• Gattinoni
Fresh water turtle / hibernating frog= oxyconformers
- metabolic shutdown (by 95%)
- decrease protein turnover (increase 1/2 life)

increase lactate/increase base def. ->vol ->either h/dyn failure (increase VO2/ decrease lactate) OR dobutamine -> either Pump failure (increase VO2 /decrease lactate) OR mitochondrial failure

• Teboul
For PPV/SVV need Vt =>8ml/kg (if less, will not reduce preload)
In ICU about 50% are vol. responsive

P. pressure = K X S. Vol/Art. Compliance (doesn't change rapidly over short term)
Therefore PP proportional to S. Vol

Change in PPV = PP max - PP min /(PP max + PP min)/2

PPV- 12% threshold between responders and non responders

• Michard
Fluid responsiveness

I/Thor blood vol. = 800-1000 ml/M2

Neither PCWP nor ECHO derived diastolic area help (ie, you don't know where you are on the Starling curve)

• Cirrhosis
Portal hypertension =>20 mmHg
Terlipressin or NorAdr + IV Albumin are good vs ARF (Hepato-renal syndrome)

Give A/B (ceftriaxone)-even if not septic

VIIa good vs esophageal bleed (repeat 2 hrly)
TEG good monitor

Drug Treatment for Esophageal Varices:
-Terlipressin 2 mg (for 5 days) or Ornipressin
OR
-Somatostatin 500 micrograms/hr (analog Octreotide)

- Resuss (HCT 25-do not overfill -> increased Portal pressure
-Endoscopy (max. 2 tries) -always intubated
-TIPS or Surgical shunt

(NB. Vasopressin + GTN -> cardiac problems-therefore only if no Terlipressin)

• Albumin + frusemide ->increased UO, better oxygenation, increased CO,increased wt. loss
Albumin+ A/B in Spont. Bact. Peritonitis-improves renal function and mortality
Ascites-Albumin improves response rate to diuretics and decreases recurrence of ascites (cf. to other colloids)

• Acute liver failure
-Terlipressin-dilates brain vessels (V2 receptor) cf. to periphery
-most die due to cerebral oedema

Treatment:
Keep Se. Na 150-155 (Mannitol/hypertonic saline)
Short term hyperventilation
Short term barbs
Propofol

(No longer use lactulose/neomycin)

still 20-30% die
aim:
ICP <20
CPP > 50

• Status Epilepticus
-Give either :
If Early
lorazepam (0.1 mg/kg) OR
midazolam (0.2 mg/kg) OR
Propofol (3-5 mg/kg -> 1 mg/kg/hr) beware propofol infusion syndrome -> death OR
Pentothal (1-3 mg/kg -> infusion)

If Late
Ketamine (1-5 mg/kg ->1-5 mg/kg/hr)

Occ. Lignocaine

• CPR
Delayed Neurol. Death-hours to days later
Treat:
-hypothermia (32-34 degrees) decreases death rate from 55% ->42% - keep cold for 12-24 hrs
- NNT =6

-Normoglycemia
-No reflow -> heparin / rt-PA
-BARBS (only useful in pre-arrest)

• DDAVP/Aprotinin
-In Ortho. Surgery ->less blood loss but not a major impact

Surgical bleed = “hypoprolenemia”

• Amato
PEEP + 12 optimal usually
Dep zones difficult to recruit

• PP Hemorrhage

PPH - causes of death

Abruptio-19%
Rupture-16%
Atony-15%
Previa -7%

Aim for fibrinogen > 150
Platelets > 100,000
Factor VIIa 90 mg/kg (1-2 shots)

• Lung zones on CT-gas/tissue (patient supine) effect of PEEP
Upper ->overdistended
Middle ->recruitable (see P flex)
Lower -> PEEP has no effect

• Rehur
-Normovol. Hemodilution
5% Albumin vs 6% HES
-both give 90% vol effect
-if just vol load (ie add but don't withdraw blood) only get 40% vol. effect in both
HES will increase troponin I but only if already increased (not if normal)
X match- succinyl linked gelatin and high mol. Wt (450) HES influences (not low mol. Wt HES)

•Morgan

Strong Ion Difference
a) H_2O
pH = 6.8 at 37 degrees (at 25 degrees = 7.0)
H^+ = 140 nM
H_2O = "X" M - i.e., lots more H_2O molecules, cf. to H^+

b) NaCl - pH = 6.8 at 37 degrees
Na=100
Cl= 100

c)Strong Ions ="remain ionized irrespective of pH

Na = 140
Cl = 100
Therefore SID = 40

This 40 is made up with weak ions:
-CO_2 ->HCO_3^- = 24
Albumin =A tot(weak anion) = 16

Stewarts law
SID
Increase =metabolic alkalosis
Decrease= metabolic acidosis
A Tot
Increase =metabolic acidosis
Decrease= metabolic alkalosis

Base excess=SID excess
A^- + Bicarb = buffer base

Giving $NaHCO_3$ corrects negative BE. It's the Na (strong cation) that corrects it, not the bicarb.

Renal effect of acid-base is wrong, lots of Na (Moles!) vs K (mMoles), no Na-K exchange
nor Na-H exchange. Ammonium controls Cl not H^+, it gets rid of Cl while saving Na thereby altering SID.

Hyperchloremic metabolic acidosis-poor name. Its not the absolute value of chloride, it's the difference between Na and Cl (get effect if you infuse water)
Ex. If in 1 l solute you have : Na=140 and Cl=100 ->SID = 40
Dilute with 1 l H_2O
Na = 70 and Cl = 50 -> SID = 20

• Derek Angus
-Dialysis-cost ineffective
73% die by 6 months
$200,000 / QALY-if proposed as a new treatment, it would be refused

Rule of thumb: to be cost effective ->20% survival by 6 months
Xigris=$100,000/QALY

• Plasma has 2 volumes
-circulating and non-circulating
-i.e., volume enmeshed in endothelial glycocalyx (analagous to Briscoes Cone Effect)
Therefore do not use change in Hct t measure vol-eg. Albumin penetrates the glycocalyx, HES does not -> different vol of distribution.

• Coral Reef Shark adapts to decrease O2 (when tide goes out and it gets trapped in lagoon) by using more glucose and less O2 for same work
i.e., substrate shift - same as pre-conditioning

•High O2 ->vasoconstricts (+radical formation) reversed by Vit C .
285 Million yrs ago atmosphere composed of 35%O2 -> giant insects but O2 increases inflammatory response.

Rats acclimatize to 100% O2, do not die quickly-form acute phase proteins (ie, anti-oxidants-Superoxide dismutase)-otherwise they die within 2 days

Vit E (alpha-tocopherol) good free radical scavenger ->decreases lymph flow by 8X if inhaled after inhalation injury but increased mortality in general population

•Lactic acidosis
RBC produce lactate from glucose -> liver ->glucose = Cori Cycle
-Pyruvate is the substrate from oxidative phosphorylation
- Pyruvate (produced from glucose ->hexokinase ->Glucose 6 P AND Lactate as well as alanine)
-Kidney also converts lactate -> glucose

-Marathon runner at end of race has a pH=7.05 and Lactate 11 mM

•PvO2 vs PcvO2
-normally - kidney and gut extract little O2 cf. to brain. Therefore lower body has higher PvO2

-v. heterogeneous
-heart SvO2 =37
-kidney SvO2 =92

usually a 5% difference (ex. SvO2 70% = ScvO2 65%)

-Chronic CCF patients live with a SvO2 of 50% but have no reserve, even though well supported)

DO2 = CI X Hb X SaO2 X 13.9
= 3 X 12 X 0.96 X 13.9 = 500 ml/min/M2

VO2 = CI X Hb X SaO2-SvO2 (=extraction ratio) X 13.9
= 3 X 12 X (0.96-0.72) X 13.9 = 125 ml/min/M2

• In vW
Minirin works the 2nd time (12-24 hrs after), occ. 3rd time (never more)
-avoid hypotonic fluid (fluid restrict)-it has an ADH effect
-use for aspirin/liver/kidney dysfunction, needs at least 20-30,000 platelets

• ASH
JAMA 9/3/05
Publishing Cardiac surgeons results:
-> No change in referals
->No change in quality

i.e., little practical impact

• Van Den Berghe

-tight glucose control -> less polyneuropathy
-its glucose that is toxic (not insulin that is beneficial)
-most glucose goes to muscle (not liver) (to protect other organs)
-if glucose increases ->increased transport
->insulin dependant
->insulin independent

->increased pyruvate ->mitochondria ->increased oxid. Phosphoryl. -> increased toxic oxidative. Radicals ->increased iNOS activity ->increased pernitrites (v. toxic)

Glucose Transport Enzymes:

Glut 2
In hepatocytes
Glycemia dependant
Passive
Glucose toxicity

Vs.

Glut 4
In Muscle
Insulin dependant
(therefore glycemia indep.)
glucose protecetd

-Lipids-increase TG s ->increase death (glucose control ->decreased TG s)
Increased LDL/HDL -> decreased death (tight glucose control -> increased LDL/HDL
This may be the key factor

•Fludrocrtisone (=aldosterone)
700 X mineralo. Activity cf. to cortislo
-No cortisol in the unstressed patient is not a problem

• Marshall
doesn't feel that early A/B (empirical)therapy is proven (i.e., if not given early -> increased mortality). He waits for germ.

"Almost all n/comial infections come from patient"

• Hebert
Hb = 5 in 60% of healthy volunteers ST-T changes seen

In IHD harm if Hct > 33%

In Jehovahs Witness retrospective study

Mortality increased with dercreasing Hb only if IHD not in healthy patients

• Ince

most blood transfusions use 10-19 day old blood (ie, wide variation)
In rats if > 28 days old -> no recovery of microvascular pO2 in gut/kidney
If fresh blood ->recovery (difference in elongability measured by LORCA)

Preservatives: SAG-M / CPD-A / CPD = not an issue

But even old blood is a good colloid- as judged by ability to open up microcircul. Cf. to other colloids

-H/dilution (Hct 15) recruits microcircul

Old RBCs lose O2 storage capacity, we don't know why. Not ADP nor deformability

• Weiskopf
Are RBCs efficacious?
-RBCs never demonstrated to be efficiacious
-> 14 Days old -> no 2,3 DPG - Hb p50=11 mmHg
Therefore No O2 offloaded - in theory

-32 volunteers made anemic to Hb =5
-VO2 stayed the same
-No increase in lactate
-No critical level demonstrated
Now if you Beta block ->DO2 drops from plateau with dropping Hb (equivalent to O2 diss. Curve - i.e., you drop on to the steep part of grpah0 at Hb 6

-now look at cognitive function (use DSST)-down to Hb 5 -> altered
return to Hb 7 -> DSST returns to normal

If at Hb 5 plus added O2 -> DSST reverts to normal

Repeat above but treat with :
a) fresh blood (NB p50=26)

b) 21-28 day old blood (NB p50=15)

DSST restored better with older blood (but neither were leuko reduced)

• Hypothermia

34 degrees-tachycardia
32 degrees-shivering stops
30 degrees-tachy arrhyth.
28 degrees-At Fib ->V Fib

NB in hypothermic arrth. - lignocaine/atropine do NOT work

-one person survived at 9 degrees

-Coag and ABG studies affected by temp.therefore correct.

Hct rises 2% for every 1 degree drop in temp.

Treat:
-if below 30-32 degrees
-CPB
-Immerse in warm water
-h/dialysis

rewarm- if neurol. Damage suspected keep at 32-34 degrees

• Nicardipine little increase in HR-pure arteial dilator
Esmolol B1 blocker

Brussels 2006

• Van Den Berghe
Increased glucose -> excess iNO? Mitochondrial damage

• Ringer Lactate – 280 mOsm (slightly hypo osmolal) ; NaCl (308)
Ringer accidentally used tap water instead of distilled in frog heart preparation, and noticed an increase in contractility (found to contain Ca++)
Hartmann in US, improved on this

Fresh Whole Blood	Component therapy
-500 ml blood in 70 ml anticoag	1 unit (335 ml, 55% Hct)
	1 plt concentrate (50 ml, 5.5 x 109)
	1 unit FFP (275 ml, 80% coag factor activity
Final product 570 ml	Final product 660 ml
Hct = 33-43%	Hct= 29%
130-350 K plts/ml	88,000 plts/mL
86% coag factor	65% coagulation factors

• Gattinoni
use PEEP only on recruitable lung. Ex. Go from 5->15 cm H2O, if improvement in 2 out of 3 (pO2, pCO2, or compliance) then there is recruitable lung.
Normal lung wt. 1 kg. some % of lung will always be unrecruitable in disease (=consolidated lung).

• Dellinger
Aim for mixed venous sat 65% (= superior vena caval sta 70%)

1601 – first proof of treatment of scurvy with citrus fruit
?1747 – Lind rediscovers treatment on Capt Cooks expedition
248 yrs later British board of trade adapts treatment

(Newtons first law of medicine…Docs at rest stay at rest unless acted upon by an outside force)

mortality if 6 hr surviving sepsis guideline bundles achieved = 29% (if not 50%)

• Mervyn
Pro/Con S/Sepsis
SDD – 7% absolute risk reduction

GI prophylaxis – little proof for ranitidine/sucralfate
PPH much more effective in bleeding patients but increase 22% mortality (beware of first impressions).

Steroids 8% decrease in mortality if given fludrocortisone as well as hydrocortisone.
Bundles neither tested nor validated.

Steroids use for max. 7 days. Can increase viral infections.

• Pesenti

	Normal	ALI	
Lung wt 1 kg		>2.5 kg	
FRC	2.5 l	.5 L	
Min Vent<7l/min	>15 L		
MinV /FRC	<3	>30	(i.e., 10X increased stress)

"baby lung"is small not stiff. Compliance is a measure of how much good lung is left.
Chest wall has its own compliance, uses up 50% of energy to move lung (this includes diaphragm and abdo contents).

Resistance = difference between peak airway pressure – plateau pressure/flow
Normal <5
ARDS 15 cm/H2O/L
COPD 26

Expiratory time = resistance X compliance
With low Vt and increased resp rate ? short exp. Time? auto PEEP

• Menon

No classI RCT documenting better outcome in NeuroICU.
Following mild injury, 30% will not return to old job.

• Pinsky
Muller manouver inspire vs closed glottis. Good way to increase VR.

Inf MI is really a rt Vent MI
Replace Rt Vent with dacron, you do OK
Remove tricuspid valve (ex. SBE in drug addicts, you do OK cf. mitral).
Spont. Vent?decreased CVP, increased PressRtAt, increase Svol
Little correl. Bet RVEDV and SV (because preload is wall stress prior to contraction. RV filling is below its unstressed vol.)
increase RVEDV?decreased eject fract.
increase LVEDV?increased Ej fract

70% of RV contraction comes from the R wall being pulled by the L vent. Therefore a strong L vent makes Rt Vent better.
Only 2 things to help Rt vent 1) increase coronary artery flow 2) improve L vent contraction

Rt Vent Ej Fract. Normal 45% (cf L vent 55%)
Constant variation of RV input (50% quiet breath, vs 400% Mueller Man.) but LV output constant.
Asthma? v. negative i/thoracic pressure. Equivalent to adding a very large afterload on RV

• BNP as marker of CCF
<100 pcg/ml CCF unlikely (Neg Pred Value >90%)
>500 (PPV <90%) (also increased in ARF and septic shock, PE)

Most useful: if < 100 to rule out

CXR pedicule – vertical from L s/clav-to horizontal from R main stem bronchus
Normal 48 mm (if > 70 mm abnormal)

• Atalectasis

Immediate onset during G.A. responsible for venous admixture/shunt
P/F ratio normal 400-500

• PE

helical CT Pos Pred value 86%
multislice CT may give false positive. New scanner 16 slices with 9 sec breathold for a 1 mm slice.

• Monty

after 90 min 1 L NaCl only 20% remains.

Replace deficit 2-3 ml/kg/hr with R/L
Expand plasma with colloid.

Difficult to cf. colloid to crystalloid. You cant get to goal…with crystalloid, it leaks out before endpt. Reached.

Central venous sat place at junction of SVC and Rt At. Gradient bet central venous and mixed venous, changes are similar but gradient varies from patient to patient.

Aim for Svol Index >=35 if not ? dopexamine.

• SAMU in France they take 1-1 ½ hr longer then other countries.
2-5% of trauma have C-spine injury (up to 14% unstable) (3-25% of C spine injury occur after insult)

Best tech to intubate C-spine injury:
Rapid sequence with manual in line (remove front of collar, use cricoid, and tracheal introducer)
Forget steroids

In head injury keep BP between 120-150 systolic

Penetrating trauma
If unstable = lost more then 2 l of blood (chest or abdo)

If hollow viscus injury you can wait, it will be seen in 12-24 hrs.

• Obesity
more obese then starving in world
(actual wt. – ideal wt.) X 0.25 = adjusted B wt.

beware of malabsorption if prior bariatric surgery

CT scan table holds max. 160 kg max.
Axilla a good site for line placement.

• End of life
Grief:
-denial
-anger
-depression
-acceptance

bioethic principles:
-autonomy
-beneficience
-non-malificience
-redistributive justice

• Fourniers gangrene
starts as cellulitis

fasciitis
type I – abdo/fournier – polymicrobial
type II – extremities – staph/strep pyogenes

CT/MRI good diagnostic tools

Surgical emergency, cut til bleeding encountered

Antibiotics for 3 weeks

Always add clindamycin (even if resistant) since reduces production of super antigen responsible for toxic shock syndrome.

Disporportionate pain
Underlying disease
Grey, odor, necrosis, sinus or ulcer
Do early gram stain

MRSA
Community acquired (more virulent) diff. from nosocomial
Treatment Linezolid (good oral bioavailability but toxic if > 7 days, expensive)

• 80% of septic shock patients are deficient in fludrocortisone
hydrocort. Deficiency doesn't predict mineralocort. Def.

In surv/sepsis bundle ACTH test optional
< 7 days
<300mg / day
not in severe sepsis only septic shock
only if BP < 90 and non responsive to fluids/vasopressors

In ARDS
Methylpred improves: P/F, Pplat, LOS in ITU
But no decrease mortality at 60 days.

After 40 days, more methylpred treated patients went back to mech. Ventil cf to plaacebo. i.e, early beneficial later deleterious.
? masked early signs of infection
? N-M effects

fibroproliferation starts on day 1 – not later as prev thought, therefore? Start early ? shorter course.

CINM (Crit Illness Neuro Myopathy)
Rel to :
Duration of IPPV
Prolonged SIRS
Hyperglyc
??NM blockers (controversial)

• CPR Ewe

Out of hospital survivors +1% (medical futility)
3 phases:
1) electrical phase – shock-defibrill the answer, lasts 4-5 min
2) circulatory phase – cardiac massage here, defibrill harmful (low energy stores in myocardium)
3) Metabolic phase

Role is to prolong the electrical phase by perfusing the heart (coronary artery flow)

Less then 1/5 lay people will start CPR for fear of mouth to mouth.

Most import. Factor in survivalis coronary perfusion pressure. Without CPP the V F gets finer and finer until asystole (i.e., uses up energy).

Consider rather cardio cerebral resusc. Every breath? cerebral perfusion plummets.
Chest compression CPR as good or better outcome as CPR with breath (in pigs/clinical).

Guidelines changed from 2:15 ? 30:2 with no good evidence.
Lay people took 16 seconds to give 2 breaths (v. long interruption max. 12 breath/min)
In reality < 50% of CPR in compression time (aim for 80-100/min)

V Fib
3 min CPR before defib. (as you are usually beyond the electrical phase)
but if seen (ex. In hospital) defib immediately
Everytime you stop to breath, massive decrease in BP/CPP, then starts at a lower pressure (takes time to build up)

Energy – biphasic 150-200 J ? 150-360J

Amiodarone 300 mg

70 % could use thrombolysis (MI/PE)
hypothermia NNT = 6 (when initail rhythm VF)
32-34 degrees for 12-24 hrs

• Pepe

3 R's of education: repetition, reiteration, redundancy

VF – overtime heart uses up energy so v. diff. to defibrill.
Defib detremental to isch. Heart

observed that in practice paramedics ventilations were 37/min
only compressed about 40/min.
I.e., not enough comression time.
Don't stop to feel pulse
During IPPV, coronary perfusion drops, slow breaths to 6/min

20% of C.arrest will not be cardiac
use single shock, not 3 stacked shocks

Passive leg raising (45 degrees) good fluid challenge.
50% non responders (Axler)

• RSVT (respiratory systolic variation test)
give increasingly large VT and measure lowest systolic pressure, slope will help to differentiate from delta up (i.e., a decreasing slope equals fluid responsiveness).

Probably fluid responsive:
SPV>10
SVV>10
PPV>13

• Pinsky
SIGap best predictor of mortality after trauma (better then lactate)

• PPV – "reverse Pulsus paradoxus" first described in NEJM 1973

Pitfalls:
-RV dysfunction?IIV?increase RV afterload?decrease Svol

correlation of PPV/SVV/SPV to Svol is 0.9

SVV/SPV may lose value if high vascular compliance (ex. Young)

• CvO2 sat during GA may be near 80
separate high and low CvO2sat then do lactate and separate into high/low (<2, >2)

In Rivers study ScvO2 on entry was v. low (48)

O2 extraction = 1 – SvO2

"Life should be kept as simple as possible…but not simpler" Albert Einstein

ScvO2 vs Smixed venO2 – values differ (ex. 5-10%) changes are tracked usually.

S/L capnometry N=45 mmHg (delta S/L – arterial normal =5)

• Pepe

To motivate people – do like Lawrence of Arabia "there is gold in Aqaba"

• Blast Injury
primary – Air emboli in pul vessels
solid organs rarely damaged
open vs closed vs bus (worst because of bouncing blast wave)
secondary – ballistic (shrapnel)

tertiary – blast wind (overpressure)

Flames
Toxic effect
Hepatis B from implanted bone of an infected suicide bomber

• Maki

Soviets secretly made tons of weaponized (dispersable) anthrax
Made resistant to penicillin/tetracycline, therefore use fluoroquinolones (wasn't invented at time of Soviet production)

Negative pressure room for v. contagious patient

• Mythen

NCEPOD – 2.8 M ops/yr
20,000 deaths
67% emergent/urgent
87% >60 yrs old
84% >= ASA III

Cepod 1990 – none of the recommendations implemented in CEPOD 2000

3% mortality with non elective surgery (within 30 days)

Next yr individual surgeons will be named (not risk adjusted)

ICNARC
If elective surgery admission 10% died
If emergency 30% died.

POMSurvey – a binary descriptor – GI problems accounted for 55% of increased length of stay (irrespective of site of surgery)

Triage tool – CardioPulEx test (see Older Chest 99)
Mortality dropped from 15?6 %
By admitting all to ICU
Anaerobic Threshold used as a triage tool, so all didn't have to go to ICU

If > 11 ml/min/kg – 99% survival
If < 11 ml/min/kg + ECG evidence of myo. Isch. 58% died

Therefore triage:
< 11 ? ICU 4% died
>11 + Myo Isch ? HDU – 1.7% died
>11 no myo isch ? ward – 0% died

•
DO2 = CO * Hb * Sat *(13.5/BSA)

CO = HR * SV

SV = Ej Fract. * EDVol

• **PE**

ECHO

"D" sign i.e., LV assumes a D shape
LV septal shift

If RV dysfunction ? thrombolysis + heparin
No mortality if no RVDys
i.e., even if no h/dyn instability, Rvdysf a prognostic factor
But shock best predictor of mortality (30 – 40%)
Risk of dying during a/coag is low – greatest risk is not diagnosing

h/dyn resolves by 7 days

thrombolysis ? i/cranial hemorr in 1-3.0% (otherwise we would lyse more often)
rTPA 60 mg bolus then 40 mg over 2 hrs

• Pul Oedema

	Alv oedema protein/plasma protein	PCWP
Hydrostat. Oedema	<0.65	>18
Permeability Oed.	>0.65	<18

BNP - in differentiating ALI from Pul Oedema
<= 250 specificity – 90%
sensitivity 40%

• Asthma in kids

s/c adrenaline 1/1000 (1 mg/ml)

dose 0.01ml/kg (max. 0.3 ml)
terbutaline
10 mcg/kg load? 0.5 – 4 mcg/kg/min (max 10 mcg/kg/min)

steroids
methylpred 2 mg/kg load?1 mg/kg Q6 IV

Mg sulfate 50-70 mg/kg load ? 10-20 mg/kg/hr
(NNT = 3)

• **Poor mans R/Lactate**
1 L of water + 1 teaspoon salt / 4 teaspoons sugar +/- baking soda / KCL

must get fluid in early (most fluid loss in first 8 hrs)

• Anaphylaxis

Adrenaline
Give at first **IM** (0.5 mg every 5 min or until IV drugs diluted) – best in outer thigh

Next IV dilute to 1/100,000 ? 5-15 mcg/min
Beta effect ? increase cAMP?decrease mediator release
Alpha effect ? decrease cAMP?increase mediator release

If on Beta blocker increased severity (increase mediator release)
? **Glucagon** 1 -5 mg + infusion 5 – 15 mcg/min (expect N+V)

• Internet
1840 first binary code Morse code – 1.4 V (as today)

• Hubmayer

Normal lung reaches max. stretch at 35 cm H20 – i.e., structural limit

Most resistance is the ETT.
Sq. wave pressure? decelerating flow (as the alveola fills, the back pressure decelerates flow)

pC02 = VC02/Ve * (1-Vd/Vt) - measures the efficiency of the lung as a C02 eliminator

Hypercapnia well supported at any level if h/dyn stable

To improve oxygenation:
- increase CO !
- PEEP – best early when inducible (atalectasis) , not so good later (fibrosis/consolidation)

Any level of PEEP OK if keep Pplateau below 30

You never stop recruiting, but overdistend other alveoli
Therefore get balance right

If normal person took every breath to inspir. Capacity, you would damage your lungs by running out of surfactant. Use predicted body wt, not actual wt for Vt.

For a given Pplateau, the higher Vt has a higher mortality then lower Vt

• Ince
RBC's secrete NO + ATP ? if hypoxic? vasodil. (i.e., regulate vascular diameter)
Cause shunting at microcircul. Level

Pulsatility changes the production of NO (i.e., pulsatility is a physiolo signal)

• **AC ventil settings**
Inspir Flow – 60 l/min
Tpause – 0.2 sec
Back up rate – 15/min
PEEP – 5-10

• Morgan ABGs
HCO3/BE – derived values

1) oxygenation –

A-a gradient = pA02 – pa02
pA02 = pi02 – paC02/0.8

but - pA02 is a myth, there is a spectrum, like a 3 compartment model in p/kinetics

A-a gradient varies	with age:	Delta 7 (young) Delta 14 (old)
	with Fi02 –	**air 7-14** **100% O2 31-56**

Causes of raised A-a gradient:
V/Q mismatch
Shunt (extreme variant of V/Q)
Zdiffusion defect (rare)

Good rules:
Breath air Pa02 = 102-age/3
Breath100% O2 = 500 * Fi02

2) Acid base
Forget bicarb

SBE says to get your pCO2/pH curve back to normal, you have to correct the SID with Na(HCO3) if neg, or (H)Cl if positive.

paCO2 = last 2 digits after pH +/- 5
ex. pH 7.15 – should hyperventil to pC02 15 (+/-5)
.55. 55

Albumin affects anion gap
Osmolal gap for ethylene glycol poisoning

• SID (Denis Edwards – handout)

Henderson-Hasselbach does not provide diagnostic information.
Anion Gap = (Na+ + K+) – (Cl- + HCO3-)
there is an apparent excess of cations, the AG in healthy patients is largely due to albumin (normal AG 10-12 mMol/L)

Stewart emphasized 3 components:
-pCO2, strong ions, weak anions

SID= (Na+ + K+ + Ca++ + Mg++) – (Cl- + lactate-)
Normal value is 40 mMol/L

SID = (HCO3-) + (Alb-) + (Pi-)

• **Notes from ASA 2006 Chicago**

• Blood-Gas barrier - West

Type IV collagen = air-blood barrier = 0.05 micron (thin to allow diffusion, but rel strong)
Thoroughbred horses – bred to run, period. All bleed into lungs when they run

During race:
Mean PAP = 70
LAP = 70 (because of increased C.O.)
MAP = 240
RAP = 40
PcapPress = 100 mmHg

Breaks pul caps causes bleeding in all horses.

Cyclists – after sprint uphill of 4 km (i.e., highly trained athlete, at maximal effort)
HR 177
Do a BAL and you find increased RBCs, proteins (not seen in controls).

i.e., something happens to theintegrity of the blood-gas barrier in top class athletes.
At 80% of max. level (VO2 max), no changes in BAL, only seen in maximum exercise. Therefore the barrier keeps its integrity except under v. high stress in elite athletes.

Pathophysiology
The dilemma of the blood-gas barrier, it must be thin (0.2 micron) to allow passive diffusion, but must be v. strong to preserve its integrity.

Therefore a conflict between thin and strong. Strength comes from type IV collagen.

"stress failure". Ex. In neurogenic pulmonary oedema, there is an increase in pul. Cap pressure (sympathetic storm) causing a breakdown of endothelium causing a leak of protein rich oedema.
Stress failure leads to a disruption of the barrier, causing exposure of electrically active basement membrane, causing activation of platelets, leukcytes, alveolar macrophages, causing a release of cytokines. i.e., a biochemical cascade.

In Goodpasture's syndrome, abnormal type IV collagen causes bleeding (same in kidney, i.e., glomerulus).

HAPE – (stress failure) – increase PAP but normal pul venous pressure, therefore not LVF. High permeability oedema with protein and RBCs (Hacket showed with BAL).
Assoc. with exercise, no evidence of inflammation (therefore it is a mechanical "stress failure").
Hypoxic pul vasoconstriction is uneven, therefore some caps protected, some not.
Protein is higher in HAPE then ARDS! Key to treatment is a decrease of the PAP.

Lung overinflation (leads to an increase alveolar stress leading to stress failure), causing increase in capillary permeability. It is high lung volume, not pressure that is the problem, damaging capillary endothelium and alveolar epithelium.
NB. Laplace's Law
Tension=Pressure/Radius (in sphere, it is P/R; in a cylinder, it is 2 x P/R)
i.e., if the pressure stays the same, as radius increases, the tension increases.

Look at a scanning electron micrograph. In stress you see "breaks". At high lung volumes, you see massive amount of endothel/epithel breaks.

In mitral stenosis, thickening of basement membrane as a compensatory mechanism, i.e., re-modelling.

Pain mechanisms – Eisenach

Many women in early labor get contractions similar to painless Braxton-Hicks contractions but now feel severe pain…why?
Progesterone blocks the estrogen receptors at cervical level. The day before labor (for reasons not understood) progesterone levels fall, leading to unopposed estrogen activity. This in turn leads to an inflammatory state (i.e., PGE2, cytokines. Etc,.) in cervix causing ripening and increasing pain sensitivity (opioids do not work well in early labor).

Do nerve blocks prevent chronic pain? One study used long lasting nerve blocks (liposomal bupivacaine) which only stopped hypersensitivity the duration of the block. Do not forget, the local anesthetic only stops electrical activity, NOT the transmission of substances from the periphery to the spinal cord (where glial cells become active and secrete PG's).

The pharmaceutical industry tried to block capsaicin receptor (peripheral receptor and achieved no pain relief but a good anti emetic (some reckon a good peripheral analgesic is worth around 4.5 billion dollars).

There is a good correlation between area of hypersensitivity and risk of developing chronic pain.

Remifentanil (or high dose opioid) causes an increase in hypersensitivity.

COX inhibitors good at preventing centrally administered opioid tolerance (ex. Spinally administered morphine in chr pain) (where the increase in PGE is the probable cause.

Wisdom tooth extration, is a common experimental pain model. Ibuprofen is v. effective but this effect occurs before measurable peripheral PGs.

Kehlet showed that best predictor of chronic pain postop is severe acute postop pain. But is it the cause…we don't know.

Brussels 2007

• Patients managed by critical care specialist during entire stay (cf. to no critical care doc) had a 28% INCREASE in mortality (increase SMR) . This used Project Impact data. Based on 101,000 patients. If data is massaged, at best it shows that there is no difference in mortality. NB. All prior studies had selection bias.

? Once protocols, run by well motivated nurses gave same result as ICU with dedicated doc.

V. surprising result but good methodology. ? Imapct on Leapfrog recommendations.

Looked at closed ICU's (more like European model, with the same result…this was 5% of the entire database)

- Mitch Fink

• Fluid responsiveness
Pearse looked at CVP vs Str. Vol. (guess what the result was)

Low dose dopexamine in GI surgery – unpublished meta-analysis shows important impact on mortality (may vasodilate at microcirculatory level – GTN may be as good).

Improve oxygenation all along the 02 chain (i.e., Lung (CPAP) ?Heart (fluid/inotropes?micro-circulation (GTN/dopexamine? mitochondria (NO inhibitor)

-R. Pearse

• Periop Ischemia

Most is ST depression / Non Q wave

Aspirin may decrease inflammation and stabilize plaques

Great periop risk
Pul Hypertension-(esp if RV Syst > 35)
Low Albumin
COPD
S.A.S.

New Polderman study shows we should aim for HR 50-60 (Circulation 2006)

Perop Intensive Inspiratory training for 1 month may decrease respiratory complications (pneumonia 7% vs 16%). But worked only in those whose strength improved, i.e., only those that got stronger benefited (Hulzebos, JAMA 2006, Preop Intensive Inspiratory training)

For Sternotomy patients..Chlorhexidine (0.12%) oral rinse/nasal gel, started 1-2 days pre op? decreased nosocomial infection and MRSA (Segers, JAMA 2006)

Don't forget preop tooth care ? decrease postop problems

- Wiener Kronish

• If use ARDSNet table for PEEP/Fi02 for best PEEP, the only factor that influenced outcome, was Vt (6 vs 12), not PEEP.

Some use Pflex +2 cm H20 PEEP, but may be best using a decrimental approach (i.e., work from the top of the PV curve)

Gattinoni used 4 parameters to determine lung recruitment (change in compliance, increased PaC02 (over distended lung), increased P02, increased delta (PEEP – Pplateau)).

• ABG Tutorial

2 sections:
-oxygenation
-acid base

1)Oxygenation
Pa02 (air)= 102-age/3
Pa02 (suppl. 02)= 500 X FI02 (ex. FI02 = 0.5, expect 250 mm Hg)

A-a gradient = PI02 – (PaC02-RQ) gives a simplified answer (based on Rileys 3 compartment model…is a ball park figure)
If normal and hypoxic, then cause is hypoventilation
If raised and hypoxic, then cause is V/Q imbalance

Rule of thumb, PaC02 = last 2 digits of pH (ex. in met acidosis, pH of 7.15 should give a pC02 of around 15)
Also
pH never completely corrected in metabolic acidosis by resp component

2) Acid base

Ask 3 questions
-PC02 (high, normal, low)
-pH (high, normal, low)
-Rel. of PC02 to pH –if it doesn't fit, then something else going on. (9 possible scenarios (ex. pH/PC02 = normal; pH/PC02 = high/low; Low/high, etc.)

Remember use only the 2 measured variables (pH and PC02), the BE, etc are calculated.

Ethylene glycol? glycollate (confuses point of care machine to think its lactate), in fact glycolate is only differentiated from lactate by CH3.

If pregnant, after 10 weeks, you should hyperventilate (about 27 mm Hg) also get an increase WBCs.

-Morgan

• 2 Million patients a year undergo high risk surgery in UK
-Bennett

• TNF
discovered by cancer researchers. The supernatant of macrophages, that kill cancer cells (causes not necrosis but apoptosis)

Kinase = an enzyme that adds a P04 to a protein, causing a conformational change which allows it to interact with other proteins (i.e., phosphorylation).

Phosphatase removes the P04.

Polymorphism – one example of an altered base pair that can increase the risk of death when exposed to TNF. It is carried by 20% of the population.

Caspase- initiates apoptosis. Viruses activate genes that inhibit caspases, so the host cell doesn't die.

• VAP
sit up > 30 degrees
measure intra abdo pressure-worry if it > 15 cm H20 (esp > 20-25)

Most air swallowed during talking, therefore intubated patients have decreased bowel sounds.

• Percut Tracheostomy

between ring 2-3 or 3-4
But German autopsy study showed from below C5 to ABOVE the cricoid.

Make small vertical incision.
Some ENT surgeons say the percut method causes more long term stenosis (esp if tracheal ring fracture).

Kits cost $350-$400

•Dissect Aortic Aneurysm

Investigation of choice is contrast enhanced CT
A- proximal – surgical management
B- Distal – usually medically managed (syst BP 100-110)

Treatment is to decrease Dp/Dt max (i.e., normalize BP, + beta blockers + decrease pulse pressure .

The turkey is the animal model for DAA. They put reserpine in food to stop it.

• Meninigitis

bacteria if present take 2-3 days to identify

Some use procalcitonin to aid in distinguish viral from bacterial

• Smoke inhalation
mortality has decreased 50% in last 20 yrs

criteria based on bronchoscopy, look for increased blood flow (like a stuffy nose with a cold) and Cast formation

Beware of secondary pulmonary oedema after 5 days (a permeability oedema, parenchyma involved due to WBCs adhereing, Kerly b lines, pneumonia,etc)

1st phase - immediate
decrease p02/FI02 due to casts (fibrin, neutrophils), hyperaemia
Involves the upper airway initially, not the parenchyma

Initial treatment – in first hours
-remove casts via bronchoscopy

-aerosolized :
heparin (+/- Rh ATIII) (for fibrin casts)
N Acetyl Cysteine

In burns, fluid resusc with R/L. Titrate to U.O.

-Herndon from Shreiners, Texas

• Porphyrias
Makes grass green and urine red

Partial defect in heme enzyme

AIP is commonest

All acute porphyrias are hepatic porphyrias. (cutaneous are chronic)

Acute attack

Females mainly
Neurol. Dysfunction – risk of life (mainly motor)
Skin – sunlight induced (porphyrins accumulate under skin)
Often assoc. with gynecol or obstetric problems
Severe abdominal pain (100%)
No abdo signs
Red urine after light exposure 9after 30-45 minutes)
Mental symptoms

Avoid
lipophilic drugs
fasting
infection
stress
alcohol

Diagnosis
Look for urinary ALA and PBG (always seen in acute attack) in urine, faeces, blood
Don't ask for porphyrins – doesn't help in acute attack

Management
Remove trigger
Opiates for pain
Chlorpromazine
High carbohydrates
HemeArginate infusion for 3 days (works in 99%)

• TeGenero – phase 1 study that went tits up

caused an uncontrooled, undifferentiated T cell response with immune activation and cytokine release.

Treated with methylprednisolone and Il 2 receptor antagonist (daclizumab) plus 4L/hr HVVH filtration
SurvSepsis guidelines

4/ 6 got better in 48 hrs, 2 /6 took weeks.
v. high TNF (also IL 6, 8, 10 increased)

-Ganesh

• APC improves micro circulation (probably less WBC adherence)

micro-circulation goes from 100 microns (arterioles to caps to venuoles) to 100 microns.
Measure
global capillary perfusion. (homogenous or not)
capillary density (more important for tissue then overall flow)

Bulk of the 02 exchange occurs on the arteriolar side, but inflammation occurs with WBC adhesion on the venuole side. Also see WBCs translocating into the tissues.

“cryptic shock” = microcirculatory shock despite OK systemic hemodynamics.

• Glycocalyx (1-2 micron thick)
on inner surface of vessel

If damaged, leukocyte adhesion, platelet adhesion, loss of sheer stress

Can destroy with heparinase

Glycocalyx is a barrier to colloid extravasation

Albumin (unlike HES or dextran) infiltrate the Glycocalyx and is superior in creating a colloid osmotic force (i.e., it plugs the Glycocalyx). If in sepsis, the Glycocalyx is destroyed, the albumin will not work as an colloid osmotic force.

TNF can damage the Glycocalyx.

-Rehn

• Treatment of micro-circulation

Saline is pro-inflammatory when looking at micro-circulation (unlike R/Lactate), you can see rolling of WBCs in venuoles, but RBCs scoot by.

You may need a fluid that decreases inflammation, i.e., decreases WBC stickyness on venuoule side.

Consider that HES is at present in saline not R/L.

Ethyl pyruvate reduces WBC stickyness.

Vasopressin and Noradr in septic shock, improved BP but not micro-circulation.

L-arginine (an NO donor) *plus* Noradr or vasopressin improves micro-circulation. NB. L-arginine alone does not improve micro-circulation, i.e., you must restore systemic BP (which alone does not guarantee an improved micro-circulation), in fact L-arginine as a vasodilator will decrease systemic BP.

This is a new exciting approach, i.e., a vasopressor and a vasodilator (at micro-circulation level). Could use GTN as an NO donor.

First give adequate fluid
Then get BP up with vasopressor
Then give GTN for the micro-circulation

Aim for a warm toe and a healthy tongue.

Distributive shock
Dobutamine can help micro-circulation
APC can help micro-circulation by decreasing WBC obstruction.

2 aspects-
1) correct shunting between and within organs (correct inflammation, coagulation, etc)

2) open micro-circulation – don’t reduce viscosity too much.

Not monitored by systemic variables

All like using steroids (hydrocortisone-mechanism isn’t known), which normalises hemodynamics, recruits microvessels, increases microcapillary density. Occurs within 1 hour and lasts 24 hrs.

• Normal lung has no m/os in periop lung on biopsy.

In patients ventilated for . 4 days, found using micro arrays (measure all m/os known to Man) found diverse colony of oral and stomach m/os – inclu. Helico Bacter.), i.e., a large diversity at first.

Antibiotics (for any reason, inclu. For non-lung reasons) – selects a single m/o, causing less diversity. Diversity is a good sign (the other m/os keep the pathogenic m/os in check). Know the % of pathogens in the community. I.e., start with a large community, but antibiotics cause one (pathogenic m/o) to rule the roost. The above is a problem with empiric antibiotics. We over treat 60%.

-Wiener Kronish

• Pulmonary aspiration

radio isotopes showed 90% of supine, ventilated patients, showed aspiration.

Others using pepsin (comes only from stomach) also showed a 90% incidence.

These are the most important risk factor for pneumonia.
Cont. sub glottic suction, in animal models, shows decreased VAP but damaged tracheal mucosa (from suction).

"LoTrach" cuff (designed by P. Young). No leak, uses low vol, low pressure cuff. Very effective.

-Mark Blunt

• Recent publication (Osman, CCM, 2007) shows that in septic patients, filling pressures do not predict fluid responsiveness, therefore SurvSepsis guidelines based on filling pressures should be changed.

Stroke Vol changes on IPPV = 10 – 20 ml (i.e., small in absolute terms)

delta Pulse pressure = Ppmax-Ppmin/PPmean

Berkenstadt A/A, 2001 showed SVV vs CVP very poor correlation.

• Rel. of SV to Ppressure

PP rises as you go distal (ie, increase reflectance)

If you double CO, you don't double pressure-ie, determined by arterial elastance (this is a law of physics, if it weren't for elastance, doubling the flow would double the pressure)

Reciprocal changes in SV and BP = changes in vaso motor tone

I.e., if you remove pressure "braking the output" you get an increase in CO. I.e., on one hand if you decrease BP you decrease afterload, you get an increase in outflow from the heart. On the otherhand, if you increase afterload you increase BP.
A bit similar to the equipoise in the Venous return curve.

Look at the response over 5 breaths.

SV and PP are linked due to ventricular-arterial coupling and vasomotor tone.

Can use delta PP to measure CI. Can use to measure ongoing bleeding, i.e., will continually remain fluid responsive.

34 papers show that PPV and SVV works! Stop already!

Spont breath leads to an increased rt vent preload leads to decrease LV preload (and St Vol). = ventricular interdependance with spont ventil.

PPV leads to decrease in rt Ventil S vol, leads to decrease LV St Vol (i.e., in series). I.e., minimal ventricular interdependance wit IPPV.

Use 10 ml/kg IPPV. And 5 breaths to calculate PPV or SVV.

Pittsburgh Protocol

Hemodynamically Stable ?
Yes
No – Preload responsive?
Yes/No
Is hypotensive and reduced motor tone?
Yes-Vol and vasopressor
No – (50% of patients) volume only

Yes – vasopressors alone (ex. spinal shock)

No- a heart problem (ex.PE) . do ECHO – add inotrope.

Reassess

-Pinsky

• Excessive fluid balance is an independent predictor of mortality in sepsis. Therefore care with fluid overload (? Sicker patients 3rd space more?)

50% of patients are responders to fluid challenge.

Predicting responsiveness:

1) Preload reserve
CVP/PAOP useless

Assessment of preload are not predictive of responsiveness, i.e., doesn't tell you if you are on the steep or flat part of the Starling curve.

2) a)Syst pressure variation
b) Ppresuure variation = K Svol/arterial compliance (which doesn't change over short term)

PPV better correlates with SVV (but SPV still pretty good).

One can also measure:
Delta Aortic blood flow with oesophageal doppler, IVC flow with ECHO/doppler, even delta pulse oximetry (using same threshold as PPV, i.e., 12%)

Must use a Vt of >= 7ml/kg

-Teboul

•Raising the legs as fluid challenge.

>45 degree.

Measures Aortic blood flow using esoph doppler. Even works with patients breath spontaneously.

Produces effects in 1 minute (attenuated later). Need real time CO monitor. No change in HR seen, in either responders nor non responders.

French can-can is NOT passive leg raising!

-Monnet

• 40% of patients with a CVP of <6 did not respond to fluid (Magder).

• Definition of ARDS from ARDSNet is flawed ;
P/FI02 <300 = ALI
P/FI02 <200 = ARDS

Regardless of PEEP or FI02

I.e., they didn't take mechanical properties into account. Ex. some patients had Pplateau from 60 to 10!

CXR seen by experts…50% disagreed (looking for 4 quadrant infiltrates).
Non hydrostatic oedema, but many intensivists measure PCWP wrongly. Many ARDS patients had PCWP > 18.

-Marini

• Reason why ARDS studies often negative. Once identified to enter trial (based on P/F ratios), we apply standard ventil settings. If you look at patients response after 24 hrs of differing ventil settings, the groups separate out :

	P/FI02	Mortality
-ARDS	<200	60%
-ALI	<300	30%
-Acute resp failure	>300	6%

Therefore you start with what appears as an homogenous group, but because it is not based on lung pathology, it seperates out later (heterogenous pathology).

We have a poor definition of ARDS

NB. No good biomarkers of alveolar-blood vessel disruption.

-Kacmarek

• Updated Survivng Sepsis Guidelines

Not industry funded
New sponsoring organizations
Changed methodology
- Quality of evidence
  - A=high
  - B=single RCT
  - C=historical
  - D=expert opinion (need 70% to agree in a vote to get strong recommendation!)
- Strength of recommendation
  - 1=Do it
  - 2=Suggest

Ex.
Early antibiotics = 1C
Dopa or NorAdr (not Adr, leads to splanchnic vasoconstriction)
Vasopressin-not finalized
SAFE= no difference between saline and Albumin re. mortality
CVP 8-12 / Scv02 > 70% = 1B (Rivers study…but see Osman CCM 2007, refutes the relevance of CVP)
Early is best (Rivers), Late isn't much better then never, i.e., once onset of MOF, then resuscitate, no difference in mortality seen…seen in 6 studies).
ACP=2B

You may want to restrict fluid…later!
Steroids
- a) unresponsive to fluid/vasopressors
- b) Corticus=non refractory septic shock , i.e., did respond to resusc. "no benefit in non responders (??to synacthen??). Earlier reversal of shock with steroids but not more patients reversed.

PDSA cycle (plan, do, study, act)

-Dellinger

• Surviving Sepsis Guidelines in Kids

Big 5 (re-examine) :
EGDT (early goal directed therapy)
Low Vt
Tight glucose control
Steroids
APC

Push 20 ml/kg until 60 ml/kg (no difference between crystalloid and colloid in kids)
Cap refill < 2 sec
Diuresis > 1ml/kg/hr
(BP not reliable)

If cathechol resist shock, give steroids (also if no response to ACTH)
APC did not work in kids…no indication
Tight glucose control – avoid hypoglycemia! At all costs
Majority of recommendations are level 2 (i.e., suggestions)

Most important factor is to recognize a sick kid then volume resiscitate!

• Rivers based his study on Boulos paper (transfused serum from septic shock patients, caused mitochondrial hypoxia).

NB. At 24 hrs, both groups get same amount of fluid, etc,. only timing is different.

Look at inflammatory mediators;
(IL 8, Caspase 3, TNF)
If early resusc.-all go down
If later – it was high and there was a 2ndary rebound increase (i.e., the 2nd hit theory).

Timing of resusc dtermines the inflammatory mediator profile and outcome.

Also lactate clearance determines later course of MOF and death. Uncorrected global tissue hypoxia potentially delivers a 2nd hit or amplified expression of biomarkers hours after initial presentation.

NB. Even early resusc group had a 30% mortality!

Early resusc with bundles, 21 studies with 3000 patients. NNT 4-5 patients
Before, mortality 41% . After – 28%.

-Rivers

• S/Lingual microcirculation

Looked at s/l capnometry (easier then SDF or OPS)
Septic patients very perturbed despite Pcv02 > 70 (i.e., well resuscitated)

Good correlation between S/l capno and lactate

pCo2 gap predicts death

Normal gradient between arterial and tissue pC02 = 5 mmHg

A continuous measure with good prognostic value.

Gave dobut. In early septic shock, improved microcircul flow.

Good correl between s/l capno (s/l C02 gap) and OPS (well perfused caps), lactate, gastric tonometry.

Cf to OPS, it also measures the adequacy of flow to metabolism.

Using Rivers protocol. They achieved Scv02 >70 by 6 hrs, but many still had high s/l PC02 gap. Cant be detected easily.

-Creteur

• Liver Function Tests

Normal can be seen in cirrhosis
Lactate-production (inclu liver, by aerobic and anaerobic glycolysis) and removal by liver
Gamma GT-drugs, alcohol, biliary disease

Steroids can reactivate Hep B

Treatment of alcoholic hepatitis
Steroids
pentoxyfilline

as bilirubin increases, (abdo sepsis, gram neg, etc,. due to septic liver dysfunction and cholestasis) assoc with increasing mortality.

ADMA and SDMA are good markers of liver disease.

Indocyanine green clearance test- a new, good marker (measured at finger tip), assoc. with prognosis post liver resection.

Decision re. resection:
Ascites-bilirubin-IGClearance

Receptor pathway for IGC same as bilirubin clearance.

-Wendon

• Pro-Con – Micro-circulatory alterations are adaptive
Mervyn vs Creteur

-Mervyn:
minimal DIC, minimal micro-thrombosis
Tissue p02 are elevated in septic patients
Cell death is minimal in MOF

Mitochondria shuts down. Normal that microcirculatory closes reciprocally (equivalent to brains reactivity to decrease CMR02).

Problem is 02 utilization, not delivery.

“Consider 02 ‘sucked in’ by cells when needed it, i.e., not delivery driven.”

“Maybe the toxic 02 not being used, signals to microcaps…stop sending us this, its toxic.”

Remember, 02 is a vasoconstrictor.

Ince showed that in septic animal model, the capill p02 is lower then venous p02 – i.e., a gap, i.e., shunting or heterogeneity (similar to Scv02).

How do you explain the lack of clearance of S/Lingual C02 by increase flow leading to decrease lactate and increase C02 clearance.

Ince showed GTN increases the microcircul. But not the 02 uptake. NO from GTN is toxic to mitochondria. Therefore improving microcircul. Not enough.

APC is anti inflamm. Not just anti coagul.

• Protocols

Protocol reduces variability, i.e., fewer harmed, but fewer benefit (narrows the Gaussian curve).

Greater the number in a study gives us greater confidence but not size of effect.

Evidenced based leads from the specific to the general
Inference based leads from the general (principals) to the specific (clinical problem).

Inference
Bayesian stats
It’s strength permits decisions based on principals.

Protocols may render young doctors “stupid”- JL Vincent.

- Marshall

• SARS in Toronto
New protocols were adapted very rapidly (cf. clinical setting) because v. motivated…i.e., risk of personel death.

-Stewart

• Acute Tubular Necrosis

Autopsy of sepsis with ARF…little cell necrosis but mitochondrial membrane disruption – esp early on.
If you survive, your kidneys almost always recover.
Tissue 02 in kidney goes up in ARF (rat model), esp at cortico-medullary junction where most tubules are, i.e., mitochondria are turning off.

ACEI may improve 02 in cortex (ex. in diabetes).

• Hepato Renal Syndrome

Not all ARF in jaundice is Hepato-renal syndrome

potentially reversibe
marked renal vasoconstriction, with subsequent decreased GFR.
Arterial vasodil. In splanchnics.

Diagnosis:
Increase Creatinine > 1.5
Decrease urine Na
No improvement with fluid resusc alone.
No proteinuria (i.e., not intrinsic renal disease).
No U/S evidence of obstruction

Advanced liver disease leads to severe splanchnic arterial vasodilatation with a decrease in intra thoracic blood volume which leads to marked activation of the RAA and ADA systems which leads to renal vasoconstriction.

I.e., a functional renal failure (you could transplant the kidneys and they would work!)

Type I
Develops in weeks.- Creatinine doubles in less then 2 weeks, often associated SPB. Very poor prognosis. Live on average 2 weeks.

Type II
Develops in months – slowly progressive causing refractory ascites, with no initiating event.
Similar to ARF seen in sepsis (unlike type I)

Beware of relative adrenal insufficiency.
Portal venoconstriction causes portal hypertension.

Arterial dilatation in brain, liver, kidney, adrenal causes failure (i.e., a form of MOF).

Prevention
Pentoxifylline in alcoholic hepatitis
If draining ascites, replace with albumin (I mg/kg bolus then 0.5 mg/kg/day)+/- splanchnic vasoconstrictors (terlipressin or ornipressin)

Terlipressin 2 mg which increases creatinine clearance.

(also Noradr and albumin works too)

TIPS (increases preload to heart)
N acetyl cysteine (used by some with success)

Abdo pressure an important determinant in ARF, therefore they do small volume paracentesis (large volume risks triggering RAA system).

Treatment

Prevent with albumin (I mg/kg bolus then 0.5 mg/kg/day

Once established
-Terlipressin 2-6 mg/day in divided doses
(if responds, carry on until creatinine normalizes or for a maximum of 2 weeks)

- also used terlipressin and albumin (better then terlipressin alone).

Therefore use albumin 20 – 40 gm/day – plus vasoconstrictor (i.e., terlipressin or octreotide 100 mcg tds. French use Noradrenaline).

If this doesn't work, try TIPS (contraindicated if very high bilirubin).

• CPR

Only 50% of Cardiac arrests in Seattle had myocardial damage.
The longer you wait to start CPR, the worse the cerebral blood flow- i.e., you lose diastolic (vascular tone) peripherally due to hypoxia. The onset of CPR, goes to the dilated periphery.

1970 – Seattle – 40% survived if bystander CPR.
AED installed in O'Hare airport, without a public trained. 9 arrests in one year with 9 survivors. In fact the survivors wanted to catch their flights!
But problem is that it still takes a minute or 2 to get shirt off, AED out of box,etc,.). Therefore give CPR initially (leads to much increased survival).

Compression alone – 14% survive (gasps = brain stem intact) – enhances oxygenation circulation, and ventilation.

Standard CPR – 10%

30 min CPR lay course as good as 4-5 hours (which few can afford).

6 months is the critical period for re training.

Sex steroids potential resusc drugs.
-Pepe

• SatV02 = lung – metabolism / hemodynamics X 1/ anaemia

Central venous pC02 is a reasonable estimate of arteial pC02, as is B.E.

Therefore use a pulse oximeter (gives a reasonable estimate of shunt)and central venous blood gases.

-Gattinoni

• To cool:
 use iced IV saline
N-G lavage
Surface cooling

PET scan showing marked influence of cooling on neuronal cell death.

32-34 degrees , makes defibrill. Easier (not harder), i.e., brain not only organ protected.

But increases drug ½ life by X5 (by depressing cyt p450).
- Kochanek

• Trauma

U/S – chest and abdo
Angio – if pelvic bleed (diagnosis and therapeutic)
CT – head and cervical spine (for clearing)
+/- CT angio

Damage control surgery
Reduce; hemoorhage, and contamination.

Permissive hypotension – Bicknells study, poorly controlled. Recent meta-analysis showed little difference.

• U/S and lung

Can see in pneumothorax – loss of “sliding lung” (if absent = pneumothorax)
Consolidation
Lung fluid – “B” lines (vertical lines = “comet lines”)
“A” lines (horizontal)

C.O using Simpsons method.

Can estimate LAP using trans annular doppler across mitral valve ring.

Tricuspid regurg signal gives good estimate of PAP.

• Liver failure

medical management
up to 90% go into ARF
immune failure

cerebral oedema
-give mannitol
but transplant best

increased INR are predictors of outcome except for paracetamol o/d

seronegative non A non B liver failure – poor outcome unless Tx.

Lactate v. important in prognosis.

MELD scoregood in all but paracetamol o/d

Sometimes while waiting for liver tx, we do partial hepatectomy to reduce toxic burden of necrotic liver.

Paracetamol o/d, majority get better or so sick they die.

Ongoing translocation of endotoxin leads to ongoing inflammation, leads to decreased immunity leads to increased susceptibility to infection, therefore hard to distinguish between the 2.

• Variceal hemorrhage

Portal hypertension (= >10 mm Hg hepatic venous to portal gradient)

Due to:
Increased i/hepatic vascular resistance
Increased portal venous infliow from excess NO, Carbon monoxide

Upper GI bleed:
65% oesoph varices
7% gastric varices
10% peptic ulcer
8% gastropathy

risk of death 25%

Causes of varices:
Cirrhosis
Budd-chiari
Pre sinusoidal

Portal/s. mesenteric/slpenic vein thrombosis – therefore always get U/S

Treatment
Resusc
Coag support
Endoscopic Treatment – banding, injection (few use today, increased infection risk),
Pharmaceutical treatment (terlipressin, somatostain, vasopressin plus GTN, octreotide – use very earl on..even in the community before hospitalization).

Equal efficacy between terlipressin and sclerotherapy (but increased risk of infection, sclero is less used).

-use ceftriaxone (i.e., 3rd generation cephalosporin) prior to endoscopy
-TEG – good for coagulation studies
-Intubate before endoscopy
-Omeprazole or sucralfate

Portal pressure gradient is v. important in prognosis, but rarely measured, helas.

Sengstaken tube can be life saving
- Gastric balloon – water and contrast (=250-300 ml)
- Almost never need esophageal balloon
- But up to 15% complications
- Apply traction over hepmet etc,.

Gastric varices
- Fundus
- v. liely to bleed
- Treatment: Thrombin (no longer available)
- Cyanoacryate glue
- TIPS – ideal option if you cant control bleeding after 2 endoscopies

Consider Rh VII

-Wendon

• Antibiotics in Liver failure

Acute – 25-80% get infection (20-30% are fungal)
Clinical signs (fever, increased WBCs) are absent in 30%
Therefore:
Routine culture
Reduce cross infection
Prophylactic antibiotics

Typ of m/os
Endogenous – early
Later exogenous

70-80% are Gram + (strep, staph, enterococci)
Fungal – pneumonia, blood-esp. 2nd week after admission

70% die.

Infection is risk factor for hepatic encephalopathy (due to increased cytokines)

Treament
SDD or systemic antibiotics (equally effective)
They reduce by 20-30%

Cirrhosis
Infection rate very high
Clinical signs may be absent
Suspect if ARF, hepatic encephalopathy, GI bleed
Consider 3rd generation cephalosporins
Avoid aminoglycosides (renal problems)

SBP
15% in patients with ascites
fever, abdo pain, or none
diagnosis
paracentesis (WBCs > 250/mm3)

Treatment
3rd generation cephalosporins or Augmentin

antibiotic prophylaxis if GI bleed (to prevent SPB and GI bleed)
norfloxacin or 3rd generation cephalosporins

All patients with acute liver failure get anti fungal agents

-Wendon

• ARDS

Often improves oxygenation with 1 litre of fluid (reduces dead space ventilation)

-Stewart

• STEMI

Acute Coronary Syndrome
30% STEMI (reperfusion treatment indicated)
70% NSTEMI (reperfusion treatment NOT indicated)

Pathology is similar: most rupturing plaques grow by rupture, then heal, then rupture, then heal i.e., most ruptures are asymptomatic

Shear stress “strips off” plaque cap.
NB. 2/3rds of plaques are not hemodynamically significant. Only 14% are occlussive.
Therefore exercise testing makes little sense, since it looks for hemodynamically significant plaques.

Vulnerable plaques have large lipid core (with macros and WBCs) with a thin fibrous cap. Inflammation of plaques makes them vulnerable.

Serum markers

Troponin
Stays up as long as CPK MB
By far the best

Increased in
sepsis
ARF
myocarditis

Triggers:
Within 3 hrs of awakening
Traffic
Earthquakes

Evolution - In old days
30% died (many from PE due to bed rest)
then
CCU and Beta blockers

Then
fibrinolytics up to 12 hrs post MI

Angioplasty (achieves 90% TIMI III flow-i.e., very good)
Direct
Rescue if fibrinolytics fail
Facilitated – i.e., plan to fibrinolyse then PTCA (but increased mortality so forget it)
For NSTEMI

If you can be treated within 2 hrs, then you have a 2% mortality i.e., very good. (see Lancet Bonfoy)

Aspirin
325 mg chewed (not enteric coated, a.s.a.p.)

enoxaparin slightly better then heparin
Fondaparinux best of the LMWH (increased effectiveness, decreased bleeding)

Beta blockers
Except if:
CHF
Heart block
Hypotensive
COPD (severe)

GTN for symptoms
ACEI – 25% relative risk reduction (esp if LV dysfunction)
Angio II blocker as good
Statin-a.s.a.p.(atorvastatin 80 mg)
Aldosterone antagonist (decreased mortality by 16% esp if CHF)
Mg for PVCs

Notes from Brussels 2008

• Urinary electrolytes - Gattinoni

BP determined by :
- Contractility
- Vessel tone
- Volume (we only seem to concentrate on this)

If BP/Volume is down, you get release of Vasopressin/sympathetic stimulation/RAA which lead to Na and water retention (renal success - which is why it is stupid to give diuretics).
Therefore measuring continuous urinary electrolytes has always been Gattinoni's dream. In fact the urine changes composition within minutes.

Strong Ion Difference
Cations = Na

Anions=Cl + dissociated Albumin (much is not dissocated) + HCO3 (which is a form of CO2)

the difference between Na and Cl is the buffer base (n=42). The base excess is the measured buffer base minus the normal (i.e., 42).

If you have to get rid of Cl, you maintain electrical neutrality by accompanying it with NH4+
If you have to get rid of Na, you maintain electrical neutrality by accompanying it with So4-

NB. Sigaard Anderson wes a medical student when he wrote his nomogram

3) Critique of Surviving Sepsis Guidelines - in particular Rivers Study - Perel

Most patients were Afro-Americans, from poor economic class, uninsured and 40% were alcoholics
Both control and treatment groups had very low (and atypically low) SVO2 of around 50%. (NB. high SVO2 has an increased risk of death). This is probably due to extreme hypovolaemia due to late arrival in ER.
If you look at Osman's study results of CVP and fluid responsiveness and applied them to SSGuidelines, many were non responders with low CVP and vice versa.
Therefore care must be individualised not protocolised.

NB. showed a massive decrease in mortality (30 from 46%).
Rivers did most of the care himself!

60% were transfused with blood in ER...very atypical.

• Optimal Fluid balance - JL Vincent

Time is the key parameter. IN SOAP study, positive fluid balance was the most import. factor rel to mortality. Filling pressures, intracardiac volumes are not good indicators of fluid responsiveness. (use SVV, PPV, SPV, Vena Caval Collapse- need Ultra sound) But Filling pressures good indicator of oedema formation, therefore use as a safety limit.
SSG CVP - Spont ventil = 8-12
• IPPV = 12-16

In prev healthy trauma patients, needed a PCWP = 24 to get CO to reach plateau

Once H/D stable , remove fluid ('reverse fluid challenge").
Take home message "aggressive fluid resuscitation followed by aggressive fluid removal (i.e., aim for lowest filling pressure commensurate with stable H/D.
Note if you recruit maneuvre in patients with ARDS and they don't decrease C.O., need fluid removal.

In RV failure, PEEP can paradoxically improve C.O. because of ventricula interdependance.

• Roncho RIFLE criteria

?

• ADH depends on osmolality and BP

increased in SIADH, decreased in Diabetes Insipidus
but ADH difficult to measure clinically as it attaches to platelets and rapidly removed. Therefore we measure Copeptin a segment of ADH peptide (a bit like c-peptide with insulin). This correlates with H2O deprivation (i.e. it will vary with osmolality, volume status and stress - i.e., it is a stress hormone marker as it also leads to increased ACTH (as does CRH) causing an elevation of cortisol. In fact it may be a more sensitive marker then measured cortisol.

• PPV depends on Aortic compliance and St Vol. 8 ml/kg ventil may be cut off.

assessment of preload is not assessment of preload reserve. A good dynamic test is leg raising 45 degrees for 90 sec (eg. go from semi recumbant and tilt bed down).

• How I set up PEEP forum

PEEP for: increase oxygenation/part of recruitment maneuvre in triggering to avoid gas trapping (ex. in COPD...commonly seen in NIV, therefore greater effort to trigger breath overcome by extrinsic PEEP).
can be seen in CVP trace, i.e., a large drop during triggering of ventilator, patient must go from high PEEP to pressure set on ventilator.

Kasmarek - uses high PEEP trial, then goes down to find lowest acceptable PEEP leading to improved compliance (i.e., as you go lower, you decrease compliance- you can use oxygenation, but compliance reacts quicker. NB. avoid PEEP in COPD/Asthma who are being ventilated...only use when weaning, seen in delay between when patient starts to trigger a breath and when ventilator triggers.(NB some add ex 7 PEEP to open up slow emptying airways with PEEPi in order to recruit.)
Recruit then PEEP on average 12-18 cm H20 in ARDS (some need up to 20)
8-12 cm H20 in ALI
Therefore:
actively recruit-set baseline PEEP to 26 - - then decremental PEEP trial while monitoring compliance. Once you start losing compliance, set PEEP just above this level. Leave PEEP for around 5 minutes at each level.

recruited lung potential only around 25%. Care if overdistended, causes decrease compliance and increase PVR.
Limit plateau pressure 26 cm H20.

Recruitment:
pressure 40 cm H20 for 40 seconds.

Normal lung weighs 1.2 kg, ARDS weighs 1.8 kg, if no increase in weight, then just collapse. (Gattinoni).

• Mervyn Singer

mitochondria p02 = 0.1 - 1 kPa
cell = 4 kPa

increased 02 leads to decrease glutathione in mitochondria (cells anti oxidant).

In rat model:
bleed-arterial p02 normal / tissue p02 drops
If you give high 02, arterial p02 increases but tissue p02 still drops. (i.e., arterial p02 doesnt reflect what is happening at tissue level. In fact increased 02 leads to vasoconstriction leading to drop in C.O. increase BP, decrease SV.

In animals if you increase 02, you decrease survival, decrease P/F ratio

In septic shock, if tissue 02 is high and stays high, the mortality is increased (Boekstegers, Shock, 1994).

In early sepsis, the microcirculation shuts down, add an inflammatory hit which shuts down the mitochondria, therefore the tissue 02 stays high, i,.e., 02 is not consummed.

• Pugin's Clinical Pulmonary Infection Score
(NB. > 6 correlates with the presence of pneumonia)

Criterion	***0***	***1***	***2***
Tracheal secretions	Absent	Non purulent	Purulent
CXR	No	Diffuse	Localized
Temperature	>=36.5 and <=38.4	>=38.5 and <=38.9	>=39 and <=36
WBCs	>=4000 and <=11000	<4000 and >11000	= + bands >50%
Pa02/Fi02	>240 or ARDS		<=240 without ARDS
Microbiology	Negative		Positive

• Liver encephalopathy

Acute Liver Failure - have astrocyte swelling, 30-40% mortality due to herniation.

Chronic (i.e. cirrhosis may show some swelling but generally normal ICP.

Brain is the only organ that has glutamine synthetase

GSyntetase
glutamate--->glutamine (causes swelling)
(NH3 used in reaction--detoxed)

How ammonia is produced:
Not in colon as previously taught.

Ammonia -->liver-->urea (removed). If liver fails, muscle takes over. -->glutamine-->kidney (or to lesser extent gut).

Gut ammonia is from glutamine (it needs glutaminase)
Therefore, to target ammonia:

- Volume expansion (NaCl)...-->decreases NH3 by increasing urinary excretion via kidney
- Muscle plays a key role..glutamine synthetase is an inducible enzyme
  - .55. Novel treatment is to use ornithine (to induce glutamine synthetase) and phenylacetate (which binds glutamine -->phenylacetylglutamine-->urine) i.e., these drugs mop up glutamine which then does not produce NH3.
  - .56. in pigs, these drugs reduce NH3 by 50% with massive decrease in ICP
- large bowel plays small role here
- does lactulose work...not much because of colons small role
- low protein diet...no effect and may be harmful due to negative nitrogen balance (but do NOT give glutamine in feeds)

NH3 may not be the whole story. It is probably synergistic with inflammation(-->astrocyte swelling) TNF alpha, like NH3 correlates to ICP. Therefore inflammation is a target like NH3.

- Ince (with notes from Brussels ICU book)- How 02 gets into cells ; convection (flow) and diffusion (often the rate limiting step-depends on the length of capillary squared)

NB. the glycocalyx is an important barrier (0.2 microns)
RBCs donate NO --> vasodilation (only in presence of hypoxia, i.e, only in presence of deoxyHb).

NB. post aortic X clamping--> reactive hyperaemia (but is shunted flow, not capillary flow)

Increased Hct (up to a point) will increase shear stress on the endothelium, due to increased viscosity-->decrease plasma layer next to the endothelium-->vasodilation (i.e., increased capillary density='functional capillary density' "FDC"
This increases endothelial production of NO (as the Hct increases it "overcomes" this vasodil effect)

Hemodilution - -initially causes decreased viscosity--> microvascular function is impaired (maldistribution of flow). It reduces FDC

FDC is dependant on viscosity. One can hemodilute but using a high viscosity solution, therefore you maintain the FDC. I.e., elevated viscosity maintains NO mediated dilation. NB. RBCs are NO scavengers, therefore a reduced Hct due to hemodilution increases NO availability.. FDC decreases when Hb is around 7 g/dl.

The viscosity threshold that causes decreased FCD appears to coincide with the decision to transfuse blood, i.e., the transfusion trigger may also be the viscosity trigger, some of the results obtained with a blood transfusion (which is initially poor at carrying 02) may be due to the increased viscosity. Changes in Hct may affect NO bioavailability due to changes in NO scavenging by RBCs. The width of the plasma layer should decrease when an increase in Hct brings RBCs closer to the endothelium, enhancing NO scavenging and counteracting the effects of NO production. Increasing Hct with non 02 carrying and therefore non NO scavenging, RBCs should extend the positive balance of vasodilation.
I.e., viscosity per se improves resuscitation. NB. even carbon monoxide-Hb RBCs could cause improved FDC.

• Singer

pV02 heart 37 mmHg (thats why the cV02 is higher the mixed venous p02, because it drains coronary sinus blood which is desaturated).
pV02 kidney 92 mmHg
pV02 gut 60 mmHg

AO2-VO2 (ml O2/100 ml blood)
Heart 10-12
Skeletal muscle (resting) 2-5
Kidney 2-3
Intestine 4-6
Skin 1-2

During hemorrhage, the Renal blood flow decreases early, but the kidney p02 stays same til late, unlike rest of body (logically with the ecrease RBF and decreased function we should get polyuria, Renal success)
Entire plasma volume filtered and reabsorbed 2X/hr

Liver shows a dramatic fall in metabolism with shock. 15% = kupfer cells-->acute phase proteins (i.e., high metabolic activity). In sepsis portal vein p02 plummets.

Muscle releases lactate as substrate for other organs (may be adaptive).

• How low can you let p02 fall in lung injured patients?

No hard evidence. End capilaary p02 is driving force.
pa02=20 mmHg is critical-below this there is not enough driving force from art -->tissue
Apnoea divers can go to pa02 to 30-35. NB. ARDS deaths, only 10-20% from hypoxia.

Some evidence that late onset neuro cognitive dysfunction if <85% sat in ARDS.

Summary of most studies:
minimal acceptable levels=p02 55-75 / Sat 88-90%

NB. p50 = 26.5 . It is one of the determinants of 02 delivery (30% of ICU patients have a L shift, 20% a R shift, to define an acceptable p02, you may have a lower Sat then acceptable (ex. <85%). i.e., take the p50 into account!

• Critical tissue p02 - Chris Ellis

mitochondia p02=<<1 mmHg
tissue p02 =around 40 mmHg (order of magnitude above mitochondria)

critical p02 in tissue is <3.0 mmHg. But Ellis believes the 'sensor' that really counts is the RBC (with NO production).

above critical level- consumption indep. of p02
below critical level- consumption decreases with dercrease p02

High flow capillaries are not functional shunts, they feed lower flow capillaries within diffusion distance.

• Grocott

02 content after 3 weeks at Everest Base Camp (5300 m) same as at sea level because of increased Hct.

Like ICU, initially "fight or flight" later "hibernation" (i.e., cel 02 consumption decreases

HAPE - above 3000m , climb 300 m /day with rest day after 1000m

Treatment:
Diamox/nifedipine/sildenafil/salmeterol/dexamethasone (also for HACE)

• Mannitol

use with filter as it crystallises.
doesnt cross intact BBB
in injured BBB, it goes down a concentration gradient-once excreted by kidneys it leaves brain-->kidney.(i.e., it can enter injured brain but leaves too)
No evidence for rebound increase in ICP

Rebound ICP probably iatrogenic, rapid fall in osmolality (i.e., give 1/2 N saline)
Dont go >320 mOsm-->ARF - No real evidence. ARF caused by mannitol by hypovolemia, therefore replace urine output.

Hypertonic saline (3% - 23.5%)

-decrease ICP - lasts longer then mannitol
-vol expander (cf. mannitol --> decreases volume)
-improves cerebral compiance (pulsatility index)
-CPP improves (similar to mannitol)
-23.5% equimolar to mannitol (i.e., 1 ml/kg = 1.5 gm/kg mannitol)

calculate osmotic gap = calculated osmol - measured osmol = difference is mannitol

• New head trauma guidelines

mostly consensus based - not a lot of evidence

new:
prophylactic hypothermia - no decrease mortality but maybe better outcome if you survive
Jug v02-50% or p02 15 mmHg = treatment threshold

Antibiotics for intubation - single dose - level II
Tracheostomy- no decrease in mortality or VAP
Can extubate even if obtunded
LMWH- seems safe level III
CPP - keep between 50 - 70 (if > 70 increased risk of ARDS)
Steroids - No ! increases mortality Level I

Nothing has decreased mortality in last 30 yrs more then 02 and intubation
Fibreoptic ICP monitor needs 40 min to calibrate. I/vent the gold standard (use rt Frontal - away from eloquence center).

ICP - no study shows improvement in outcome but consensus is yes.

Treat if > 20 mmHg
CPP 50 - 70
Brain injury - impaired autoregul.
Decompression-massive decrease ICP - but we don't know about influence on outcome
Mannitol 0.25-1 gm/kg or 2 ml/kg 7.5% NaCl
Barbs - decrease ICP but causes hypotension and is immunosuppressant (increased risk of infcetion)
Head injury has vasospasm in first 24 hrs therefore care of hyperventilation.
30 degree head up if no hypotension
avoid hypothermia - no routine prophylactic hypothermia- no decrease mortality.

• Decompression craniectomy

ongoing trial based in Cambridge - we don't know if it decreases mortality
ICP-independant predictor of mortality - sharp rise if . 20
aggressive hyperventilation reduces CBVolume by about 15 ml
Craniectomy increases capacity by 200 ml (has to be adequate size otherwise--> herniation

• Ince

Hemodilution terrible. Cell saver blood pretty good. (again a question of viscosity)
However do not hemodilute then transfuse cell saver blood (-->capillary shunting)

Criticized Hebert's study because unlike Europe, didn't use SAG Man and blood was not leukocyte depleted.

O2 supply dependancy - v. different between different organs
Heart is in a continuous supply dependant state
Kidney-02 needed mainly for Na-K pump
Monocytes-even in presence of CN stil consumes 02 if presented with antigen-i.e., used to produce 02 radicals not generate energy
Dopexamine resuscitates the mucosa not the serosa and gut

Give LPS-->decrease BP/decrease RBF/decrease creatinine clearance/but ttissue p02 stays the same (but you get increasead area of hypoxia in cortex i.e., heterogeneity of hypoxia (hidden by the mean which is OK)

2 theories:
-cytopathic hypoxia
-shunting- early (later on it is the mitochondria that is the problem - probably due to unrecognized hypoxia then reperfusion injury).

New Technique
Protoporphyria IX - naturally occurring "delayed fluorescent Lifetime" technique (DFL)
you can for the first time measure the mitochondrial p02 (the higher the p02, the slower the decay time)

At lower p02 there is hibernation --> organ function is reduced as an adaptive mechanism

In gut: 4 hrs of ischemia causes less necrosis then 3 hrs of ischemia followed by 1 hr reperfusion

• Central line

CXR will not tell you if arterial or pleural

Even with U/S, lots of examples of arterial placement

• Stretch of lung causes acidification and bacterial growth - Jerome Pugin

As you stretch alveoli, the supernatant is proportionally more acidic. This seems to be due to activation of the Na-K atpase pump (as it is abolished when given ouabain, a pump inhibitor).

As the supernatant is more acidic (below 7.2), the greater the bacterial growth. Also seen with the proliferation of fibroblasts.

In IPPV - supernatant <7.0
In spont ventil. >7.0
Therefore we should try aerosoled alkalinisation.

NB. there is no link between arterial and airway pH.

• Pro Con debate re. Steroids (Annane v Sprung)
•
• Annane:
•
• JFK was saved by postop steroids
• Sub group analysis-a non responder got noradr>0.5 mcg/kg
• they were the only group where mortality was decreased with steroids
•
• Sprung:

- steroids reversed 80% of shock, but placebo reversed 75%, but took longer(i.e., 2.5 days), but there were more super infections (33 v 26%)
-
- May have role if remain in shock >1 hr despite high dose vasopressors (seen in <10% CORTICUS)
-
- If a new drug, the FDA would never approve.
-
- In CORTICUS, gave 3 X 50 mg/day
- but still saw superinfections.

They do not do ACTH stimulation test as it is too unstandardised, also give total levels (inclu. protein bound when we want free)

NB. Annane only gives steroids if non responder to inotropes AND non responder to ACTH.

Fludrocortisone use is controversial.

- CAP - Pugin

Urine serology - legionella, pneumococcus

remember Kumars study. Once patient in shock, 6% increase in mortality for every hr delayed giving antibiotics.

“No one should die without a dose of aminoglycosides”

- Singer

Early phase is adaptive. Minimal histological evidence of cell death in MOF.
Tissue p02 is elevatedor normal (but not low)
microvascular thrombosis is rare.
Organ recovers if patient recovers (cf. glomerulonephritis)

i.e., cells go into “hibernation”

septic rats:
arterial p02 is normal -high
muscle/liver/kidney p02 drops
but at 24 hrs-->recover (i.e., adaptive) but >25% of rats die despite recovery of tissue p02.

NO competes with 02 for complex IV of mitochondria.
As you recover, the tissue 02 drops, cf. to those that die where it stays high.

If tissue not using 02, -->hyperoxia-->microvascular hypoperfusion (may be protective)
If tissue using 02, -->hypoxia-->microvascular dilates

Chris Ellis disagrees. He thinks its the m/v that starts the problem.

I.e., m/v exquisitely designed to deliver just the right amount of 02 (if increase in 02->decrease in cap dnsity)

but in sepsis, there is dysfunctional local regulation v. early on.

Why no necrosis? tissue is not anoxic- only 20-25mm Hg in hypoxic areas. We lose only about 50% of caps, i.e., there are enough caps to maintain tissue viability but at lower 02 level.

If you recover too rapidly, you get isch-reperfusion injury.

- Warfarin

It is during the first 3-6 months that the highest risk of bleeding seen, thereafter it is 1.3% / yr.

- Beale

in 30% of patients there is a significant radial-femoral artery difference >10% systolic
median systolic difference = 28 mmHg
This is exaggerated with vasopressors due to reflectance in a closed peripheral circulation.

If you give someone a high dose of vasopressor-the radial pressure may be falsely low--falsely low calculated TPR--> maintain vasopressors.

Therefore in v. sick, it may be best to use femoral artery (ex. PICCO)

• Smoke inhalation

80% of burns deaths from smoke inhal

20% of deaths are late

CO --> L shift of oxyHb curve->poor 02 off loading and binds to cytochrome in cell.
CNS signs (neg predictive value of 98%)

CN - if lactate >10 without burn, this strongly indicates CN toxicity

38% have aspiration--> sputum for microbiology

Treatment
Hydroxocobalamin-efficient and safe.
(EDTA poorly tolerated)

if inhalation, it increases need for fluid in burn by 30%

• Army treatment of burns

No crystalloid
C.A.T. device (tourniquet on for 15 min to 2 hrs)
If strong radial pulse no fluids otherwise 1 unit of hextend

FFP:Blood
1:8 67% die
1:3 35% die
1:1 <20% die

Carrico and Shires bled dogs by 70-80%

No transfusion - 70% died
returned shed blood - 60% died
returned shed blood plus 1:3 Ringers - <30% died

• Anaphylaxis - Levy

increased PVR->RVF-->increased RAP with decreased LAP (due to septal shift, i.e., RV full, LV empty...do ECHO)

NO and PG release--> vascular relaxation

Can get flash oedema
most deaths due to b/spasm esp if prior bronchoconstrictive disease.
Always rule out a pneumothorax (looks the same).

HIT-instead of neutrophils (seen in TRALI) IgG causes platelets to aggregate.

Give Vanco centrally. as it works by releasing histamine from mast cells which are in rel. high concentratin near vessels of skin (i.e., vessel not far from mast cell, therefore the vanco is in a rel. high concentration.)

Contrast media causes release of histamine esp with high ionic products..this is not a true allergy

If persistant hypotension, use terlipressin or vasopressin (V1 agents)

Vasopressin effectively reverses pathol induced vasodilation (give a couple of units to start with)

Do not forget air trapping-->increased PVR, therefore decrease i:e ratio

In one case of increased PVR and RVF, he gave ketorolac as this is thromboxane mediate and it worked!

• Liver trauma - Wendon

biliary jejeunostomy if laparoscopic trauma

beware of fatty liver of pregnancy/PET-->R lower chest pain-->spontaneous hematoma - do not heparinize (with suspicion of PE)

Blunt liver trauma-
if stable-non op treatment- interventional radiology do CT and angio (embolisation) if not pack (esp if venous bleed but do not overpack--> isch insult. Repeat packing every 48 hrs.

Stab injury-
always laparotomy

If biliary trauma, put stent across the ampulla-if that doesnt work, put naso-biliary tube (placed by endoscopist)

Beware of peudoaneurysm (1 week after trauma)--> major bleeding
check for pancreatic fracture-treat by pancreatic stenting

Radiologist very important in liver trauma

• ARDS Kacmarek

ARDS mortality=45-55%
ALI mortality = 30%

mortality prediction better if you divide patients up to ARDS, ALI, ARF (acute resp failure), after 24 hrs conventional ventilation, i.e., they seperate into 3 streams with v. differing mortality. Explains why some PEEP trials showed no mortality benefit, i.e., they would have gotten better anyway since they didnt really all have ARDS.

ALVEOLI study saw no mortality difference.

Based on the above, they will start a new study but selection of only truly sick patients i.e., only after 24 hrs treatment.
Treatment will use peak pressures at 50 cm H_2O (40 is sure to be safe, 60 associated with pneumothorax, therefore comfortable with 50) and starts with PEEP at 25.

• Status epilepticus
defined now as > 5-10 min
high mortality therefore there is a degree urgency.

seizures beget seizures, S.E. re-organizes of the neural network

3 categories:
-Grand Mal-generalized convulsive SE (can be v. subtle, eg. eyelid twitch)
-Focal S.E. - difficult to treat. Maintains consciousness
-Non convulsive S.E.-complex partial seizures (can be confused)

You can treat motor manifestations with n-m blockers but brain keeps convulsing, therefore always do a EEG

Treatment:
-Benzos
    lorazepam (6-10 mg) longest 1/2 life
    midazolam -OK but short 1/2 life (0.2 mg/kg)
-IV if rapid effect needed
    phenytoin(or fosphenytoin)
    valproate 60-70 mg/kg
-propofol
    good short term treatment, can go to burst suppression
    leave for 12-24 hrs burst suppression before weaning but ensure adequate chr. anti convulsants, follow with EEG

• Scoring systems

SAPS III
3 boxes
-previous health - accounts for 50% explanatory power
age/co-morbidity/hospital location/lead time

-ICU admission - accounts for 23% explanatory power
surgical status/

-Physiological derangment - accounts for 27% explanatory power

SMR give 95% confidence limits, if overlaps 1, not significant

• The yellow patient - Wendon

LFTs-non specific, can have cirrhosis with normal LFTs

AST/ALT-not good for cholestatic problem- good for hepatocyte damage

INR -only useful as a prognostic marker in acute liver failure

Bilirubin depends on albumin

if you look at a liver unit with its central vein and sinusoids leading to it, the area most at risk of isch./RVF/congestion is next to the central vein. This is also the area where drug metabolism and bilirubin.

Contrast CT much better then CT alone.

Screen for Hep C much worse liver problems even if not cirrhotic.

If alcohol and paracetamol - 1 gm X 3or 1 gm X 4 but give NAC (i.e., you want become glutathione depleted).

Isch hepatitis
- ex. congested liver (ex, RVF)
- U/S best diagnosis
- Treatment supportive

LPS/cytokines block uptake/excretion of bile acids-->cholestasis

Treatment-none

Fatty liver
- -increase BMI/DM/Htn (i.e., metabolic syndrome)

fat in liver- v. sensitive to oxidative stress (i.e., sepsis) --> sick liver, therefore very vulnerable-beware preop

cholestasis and feeding. Best if use enteral feed. Risk factor (TPN/sepsis)
attenuated by glutamine in TPN

Drugs
- NSAID - hepatotoxic
- TPN
- Augmentin -->cholestasis

As bilirubin increases, mortality increases

Avoid epinephrine if possible, it decreases liver circulation

Increase portal pressure--. gut congestion-->translocation of m/os

Indocyanine green clearance (ICG) is a good test, it correlates with mortality. Good for risk stratification, esp for preop hepatectomy (LFTs/Child-Pugh not sufficient)

Increased no. hepatic segments resected--> increased mortality --> liver left behind is too small for the portal flow--> liver congestion. Therefore during surgery get surgeon to measure portal pressure, if increased, clip splenic artery branch or embolise splenic artery branch.

Porto-renal reflex- as portal pressure increases--> renal vessel dilatation

• Factor V Leiden

caucasians 5-8%
not seen in Africans/Chinese/Japs

Cant be inactivated by APC

Factor V Leiden if no other risk factor: it increases risk 4-8 X
Oral contraceptive increases risk 4 X
plus Factor V Leiden (increase 35 X)

20% of VTE have malignancy
Obese-2-3 X even in young obese (5 X higher risk)
Travel >10,000 km (4.7 PE/million passenger arrivals - approx. 1/200,000)

In ICU, if prophyl it cuts DVT by 50%.

Samama NEJM 99 - Enoxaparin 40 mg decreases freq by 1/3rd (20 mg has no effect)

If needed use a filter but remove within 1 month if possible

• Massive PE

Majority of anatomically massive PE (>40%), do not have hypotension
U/S - if unexplained hypotension - if no RV dil. - not PE
Troponin - RV isch. -prognostic implications
BNP - RV stretch. -prognostic implications

thrombolytics-
indication-unstable CV

rt-PA -60mg rapidly--> 40 mg over 2 hrs (not the normal 100 mg/2 hr)

RV dysfunction
-none-no mortality
-if present, increased risk of death

TPA and heparin--> more rapid recovery of RVDys then heparin alone

If normotensive but RVDysf. --> 10% get delayed shock

If only RVDysf. - controversial if need TPA in PE without shock since vast majority do OK.
Dont forget, 1.2-3.0% get I/C hemorrhage

IVC filter, use retrievable filter.

Treatment of Rt Vent Dysf.
-Fluid - not v. effective - unless CVP < 20 (max.), beware if overloaded-->septal shift--> squeeze LV--> decrease C.O.

-Vaspressor - increase aortic diastolic pressure
-dont forget most of increased PVR is due to mediators not clot
-inotropes
-NO
Hypotension defines the best threshold for thrombolysis

Also ECMO or RV assist device work if all else fails (remember, you can do ECMO with minimal anticoagulation. Need 2-3l/min flow to empty Rt Vent-->return septum-->increase C.O. NB. Do not intubate as the crash on induction)

surgical thrombectomy if thrombolytics do not work or if C/I

Periop PE
No absolute C/I to thrombolytics

Acute RVF
Rt vent is U shaped, therefore hard to visualise in its entirety with U/S

The L side of the heart can do most of the work for the Rt side due to configuration of the fibers, i.e., a lot of R sided contraction comes from the L side (seen if you electrically stop RV from pumping but L side OK--> Rt still pumps blood as before).

Rt dilatation--> impairs L sided (which does most of the work)Therefore do not fluid overload

RV supplied by Rt coronary artery. When RV dilates, it impairs circulation of Rt Cor artery (which unlike L side, occurs during diastole and systole). Therefore doesnt do well if increase PVR --> dilation

decrease RV -->septal shift-->decrease CO-->decrease Coronary perfusion-->isch--> decrease RV

Most prognosis from U/S and biomarkers

Thickness of RV wall will tell if acute or chronic

NB. RV contraction not just dilation look for tricuspid annulus displacement also tricuspid regurg - estimates PAP

Treatment targets:
RV preload-fluid challenge but be very careful
RV contract-same inotropes as LVF, no preference for agent
minimize shunt-check to see if PFO
PA vasodilation- NO /phopsphodiesterase inhibitors/prostacyclin/Ca channel blocker/sildenafil (PDE 5 inhibitorgood in chronic-minimal effect systemically-oral only)
(NB. GTN not good on Rt heart)

If PE:
shock-->consider thrombolytics
no shock
increase troponin/BNP->ECHO-->RVDysf-->consider thrombolytics
-->no RVDysf-->anticoagul.

normal troponin/BNP-->anticoagul.

• Hepato Renal Syn

Type I-acute (weeks), severe, creat >220, 90% die
Type II - chronic (months), less severe, characterized by ascites resistant to treatment

Pathophysiol:
as ascites builds up-->neurohumoral changes-->vasoconstriction

precipitating event (variceal hemorrhage, infection, ex, SBP,) trigger -->decrease C.O.-->regional arterial vasoconstr and portal hypertension

Treatment:
-Liver Tx - do rel. well
-Terlipressin (or noradrenalin) and Albumin - improve GFR
-TIPPS-->decrease portal pressure-->increase renal blood flow but risk of encephalopathy

Notes from Brussels 2008

• Urinary electrolytes - Gattinoni

BP determined by :
Contractility
Vessel tone
Volume (we only seem to concentrate on this)

If BP/Volume is down, you get release of Vasopressin/sympathetic stimulation/RAA which lead to Na and water retention (renal success - which is why it is stupid to give diuretics).
Therefore measuring continuous urinary electrolytes has always been Gattinoni's dream. In fact the urine changes composition within minutes.

Strong Ion Difference
Cations = Na

Anions=Cl + dissociated Albumin (much is not dissocated) + HCO3 (which is a form of CO2)

the difference between Na and Cl is the buffer base (n=42). The base excess is the measured buffer base minus the normal (i.e., 42).

If you have to get rid of Cl, you maintain electrical neutrality by accompanying it with NH4+
If you have to get rid of Na, you maintain electrical neutrality by accompanying it with So4-

NB. Sigaard Anderson wes a medical student when he wrote his nomogram

4) Critique of Surviving Sepsis Guidelines - in particular Rivers Study - Perel

Most patients were Afro-Americans, from poor economic class, uninsured and 40% were alcoholics
Both control and treatment groups had very low (and atypically low) SVO2 of around 50%. (NB. high SVO2 has an increased risk of death). This is probably due to extreme hypovolaemia due to late arrival in ER.
If you look at Osman's study results of CVP and fluid responsiveness and applied them to SSGuidelines, many were non responders with low CVP and vice versa.
Therefore care must be individualised not protocolised.

NB. showed a massive decrease in mortality (30 from 46%).
Rivers did most of the care himself!
60% were transfused with blood in ER...very atypical.

• Optimal Fluid balance - JL Vincent

Time is the key parameter. IN SOAP study, positive fluid balance was the most import. factor rel to mortality. Filling pressures, intracardiac volumes are not good indicators of fluid responsiveness. (use SVV, PPV, SPV, Vena Caval Collapse- need Ultra sound) But Filling pressures good indicator of oedema formation, therefore use as a safety limit.
SSG CVP - Spont ventil = 8-12
• IPPV = 12-16

In prev healthy trauma patients, needed a PCWP = 24 to get CO to reach plateau

Once H/D stable , remove fluid ('reverse fluid challenge").
Take home message "aggressive fluid resuscitation followed by aggressive fluid removal (i.e., aim for lowest filling pressure commensurate with stable H/D.
Note if you recruit maneuvre in patients with ARDS and they don't decrease C.O., need fluid removal.

In RV failure, PEEP can paradoxically improve C.O. because of ventricula interdependance.

• Roncho RIFLE criteria

?

• ADH depends on osmolality and BP

increased in SIADH, decreased in Diabetes Insipidus
but ADH difficult to measure clinically as it attaches to platelets and rapidly removed. Therefore we measure Copeptin a segment of ADH peptide (a bit like c-peptide with insulin). This correlates with H2O deprivation (i.e. it will vary with osmolality, volume status and stress - i.e., it is a stress hormone marker as it also leads to increased ACTH (as does CRH) causing an elevation of cortisol. In fact it may be a more sensitive marker then measured cortisol.

• PPV depends on Aortic compliance and St Vol. 8 ml/kg ventil may be cut off.

assessment of preload is not assessment of preload reserve. A good dynamic test is leg raising 45 degrees for 90 sec (eg. go from semi recumbant and tilt bed down).

• How I set up PEEP forum

PEEP for: increase oxygenation/part of recruitment maneuvre in triggering to avoid gas trapping (ex. in COPD...commonly seen in NIV, therefore greater effort to trigger breath overcome by extrinsic PEEP).
can be seen in CVP trace, i.e., a large drop during triggering of ventilator, patient must go from high PEEP to pressure set on ventilator.

Kasmarek - uses high PEEP trial, then goes down to find lowest acceptable PEEP leading to improved compliance (i.e., as you go lower, you decrease compliance- you can use oxygenation, but compliance reacts quicker. NB. avoid PEEP in COPD/Asthma who are being ventilated...only use when weaning, seen in delay between when patient starts to trigger a breath and when ventilator triggers.(NB some add ex 7 PEEP to open up slow emptying airways with PEEPi in order to recruit.)
Recruit then PEEP on average 12-18 cm H20 in ARDS (some need up to 20)
8-12 cm H20 in ALI
Therefore:
actively recruit-set baseline PEEP to 26 - - then decremental PEEP trial while monitoring compliance. Once you start losing compliance, set PEEP just above this level. Leave PEEP for around 5 minutes at each level.

recruited lung potential only around 25%. Care if overdistended, causes decrease compliance and increase PVR.
Limit plateau pressure 26 cm H20.

Recruitment:
pressure 40 cm H20 for 40 seconds.

Normal lung weighs 1.2 kg, ARDS weighs 1.8 kg, if no increase in weight, then just collapse. (Gattinoni).

• Mervyn Singer

mitochondria p02 = 0.1 - 1 kPa
cell = 4 kPa

increased 02 leads to decrease glutathione in mitochondria (cells anti oxidant).

In rat model:
bleed-arterial p02 normal / tissue p02 drops
If you give high 02, arterial p02 increases but tissue p02 still drops. (i.e., arterial p02 doesnt reflect what is happening at tissue level. In fact increased 02 leads to vasoconstriction leading to drop in C.O. increase BP, decrease SV.

In animals if you increase 02, you decrease survival, decrease P/F ratio

In septic shock, if tissue 02 is high and stays high, the mortality is increased (Boekstegers, Shock, 1994).

In early sepsis, the microcirculation shuts down, add an inflammatory hit which shuts down the mitochondria, therefore the tissue 02 stays high, i,.e., 02 is not consummed.

• Pugin's Clinical Pulmonary Infection Score
(NB. > 6 correlates with the presence of pneumonia)

Criterion	***0***	***1***	***2***
Tracheal secretions	Absent	Non purulent	Purulent
CXR	No	Diffuse	Localized
Temperature	>=36.5 and <=38.4	>=38.5 and <=38.9	>=39 and <=36
WBCs	>=4000 and <=11000	<4000 and >11000	= + bands >50%
Pa02/Fi02	>240 or ARDS		<=240 without ARDS
Microbiology	Negative		Positive

• Liver encephalopathy

Acute Liver Failure - have astrocyte swelling, 30-40% mortality due to herniation.

Chronic (i.e. cirrhosis may show some swelling but generally normal ICP.

Brain is the only organ that has glutamine synthetase

GSyntetase
glutamate--->glutamine (causes swelling)
(NH3 used in reaction--detoxed)

How ammonia is produced:
Not in colon as previously taught.

Ammonia -->liver-->urea (removed). If liver fails, muscle takes over. -->glutamine-->kidney (or to lesser extent gut).

Gut ammonia is from glutamine (it needs glutaminase)
Therefore, to target ammonia:

- Volume expansion (NaCl)...-->decreases NH3 by increasing urinary excretion via kidney
- Muscle plays a key role..glutamine synthetase is an inducible enzyme
  - .55. Novel treatment is to use ornithine (to induce glutamine synthetase) and phenylacetate (which binds glutamine -->phenylacetylglutamine-->urine) i.e., these drugs mop up glutamine which then does not produce NH3.
  - .56. in pigs, these drugs reduce NH3 by 50% with massive decrease in ICP
- large bowel plays small role here
- does lactulose work...not much because of colons small role
- low protein diet...no effect and may be harmful due to negative nitrogen balance (but do NOT give glutamine in feeds)

NH3 may not be the whole story. It is probably synergistic with inflammation(-->astrocyte swelling) TNF alpha, like NH3 correlates to ICP. Therefore inflammation is a target like NH3.

• Ince (with notes from Brussels ICU book)- How 02 gets into cells ; convection (flow) and diffusion (often the rate limiting step-depends on the length of capillary squared)

NB. the glycocalyx is an important barrier (0.2 microns)
RBCs donate NO --> vasodilation (only in presence of hypoxia, i.e, only in presence of deoxyHb).

NB. post aortic X clamping--> reactive hyperaemia (but is shunted flow, not capillary flow)

Increased Hct (up to a point) will increase shear stress on the endothelium, due to increased viscosity-->decrease plasma layer next to the endothelium-->vasodilation (i.e., increased capillary density='functional capillary density' "FDC"
This increases endothelial production of NO (as the Hct increases it "overcomes" this vasodil effect)

Hemodilution - -initially causes decreased viscosity--> microvascular function is impaired (maldistribution of flow). It reduces FDC

FDC is dependant on viscosity. One can hemodilute but using a high viscosity solution, therefore you maintain the FDC. I.e., elevated viscosity maintains NO mediated dilation. NB. RBCs are NO scavengers, therefore a reduced Hct due to hemodilution increases NO availability.. FDC decreases when Hb is around 7 g/dl.

The viscosity threshold that causes decreased FCD appears to coincide with the decision to transfuse blood, i.e., the transfusion trigger may also be the viscosity trigger, some of the results obtained with a blood transfusion (which is initially poor at carrying 02) may be due to the increased viscosity. Changes in Hct may affect NO bioavailability due to changes in NO scavenging by RBCs. The width of the plasma layer should decrease when an increase in Hct brings RBCs closer to the endothelium, enhancing NO scavenging and counteracting the effects of NO production. Increasing Hct with non 02 carrying and therefore non NO scavenging, RBCs should extend the positive balance of vasodilation.
I.e., viscosity per se improves resuscitation. NB. even carbon monoxide-Hb RBCs could cause improved FDC.

• Singer

pV02 heart 37 mmHg (thats why the cV02 is higher the mixed venous p02, because it drains coronary sinus blood which is desaturated).
pV02 kidney 92 mmHg
pV02 gut 60 mmHg

During hemorrhage, the Renal blood flow decreases early, but the kidney p02 stays same til late, unlike rest of body (logically with the ecrease RBF and decreased function we should get polyuria, Renal success)
Entire plasma volume filtered and reabsorbed 2X/hr

Liver shows a dramatic fall in metabolism with shock. 15% = kupfer cells-->acute phase proteins (i.e., high metabolic activity). In sepsis portal vein p02 plummets.

Muscle releases lactate as substrate for other organs (may be adaptive).

• How low can you let p02 fall in lung injured patients?

No hard evidence. End capilaary p02 is driving force.
pa02=20 mmHg is critical-below this there is not enough driving force from art -->tissue
Apnoea divers can go to pa02 to 30-35. NB. ARDS deaths, only 10-20% from hypoxia.

Some evidence that late onset neuro cognitive dysfunction if <85% sat in ARDS.

Summary of most studies:
minimal acceptable levels=p02 55-75 / Sat 88-90%

NB. p50 = 26.5 . It is one of the determinants of 02 delivery (30% of ICU patients have a L shift, 20% a R shift, to define an acceptable p02, you may have a lower Sat then acceptable (ex. <85%). i.e., take the p50 into account!

• Critical tissue p02 - Chris Ellis

mitochondia p02=<<1 mmHg
tissue p02 =around 40 mmHg (order of magnitude above mitochondria)

critical p02 in tissue is <3.0 mmHg. But Ellis believes the 'sensor' that really counts is the RBC (with NO production).

above critical level- consumption indep. of p02

below critical level- consumption decreases with dercrease p02

High flow capillaries are not functional shunts, they feed lower flow capillaries within diffusion distance.

• Grocott

02 content after 3 weeks at Everest Base Camp (5300 m) same as at sea level because of increased Hct.

Like ICU, initially “fight or flight” later “hibernation” (i.e., cel 02 consumption decreases

HAPE - above 3000m , climb 300 m /day with rest day after 1000m

Treatment:
Diamox/nifedipine/sildenafil/salmeterol/dexamethasone (also for HACE)

• Mannitol

use with filter as it crystallises.
doesnt cross intact BBB
in injured BBB, it goes down a concentration gradient-once excreted by kidneys it leaves brain-->kidney.(i.e., it can enter injured brain but leaves too)
No evidence for rebound increase in ICP

Rebound ICP probably iatrogenic, rapid fall in osmolality (i.e., give 1/2 N saline)
Dont go >320 mOsm-->ARF - No real evidence. ARF caused by mannitol by hypovolemia, therefore replace urine output.

Hypertonic saline (3% - 23.5%)

-decrease ICP - lasts longer then mannitol
-vol expander (cf. mannitol --> decreases volume)
-improves cerebral compiance (pulsatility index)
-CPP improves (similar to mannitol)
-23.5% equimolar to mannitol (i.e., 1 ml/kg = 1.5 gm/kg mannitol)

calculate osmotic gap = calculated osmol - measured osmol = difference is mannitol

• New head trauma guidelines

mostly consensus based - not a lot of evidence

new:
prophylactic hypothermia - no decrease mortality but maybe better outcome if you survive
Jug v02-50% or p02 15 mmHg = treatment threshold

Antibiotics for intubation - single dose - level II
Tracheostomy- no decrease in mortality or VAP
Can extubate even if obtunded
LMWH- seems safe level III
CPP - keep between 50 - 70 (if > 70 increased risk of ARDS)
Steroids - No ! increases mortality Level I

Nothing has decreased mortality in last 30 yrs more then 02 and intubation
Fibreoptic ICP monitor needs 40 min to calibrate. I/vent the gold standard (use rt Frontal - away from eloquence center).

ICP - no study shows improvement in outcome but consensus is yes.

Treat if > 20 mmHg
CPP 50 - 70
Brain injury - impaired autoregul.
Decompression-massive decrease ICP - but we don’t know about influence on outcome
Mannitol 0.25-1 gm/kg or 2 ml/kg 7.5% NaCl
Barbs - decrease ICP but causes hypotension and is immunosuppressant (increased risk of infcetion)
Head injury has vasospasm in first 24 hrs therefore care of hyperventilation.
30 degree head up if no hypotension
avoid hypothermia - no routine prophylactic hypothermia- no decrease mortality.

• Decompression craniectomy

ongoing trial based in Cambridge - we don’t know if it decreases mortality

ICP-independant predictor of mortality - sharp rise if . 20
aggressive hyperventilation reduces CBVolume by about 15 ml
Craniectomy increases capacity by 200 ml (has to be adequate size otherwise--> herniation

• Ince

Hemodilution terrible. Cell saver blood pretty good. (again a question of viscosity)
However do not hemodilute then transfuse cell saver blood (-->capillary shunting)

Criticized Hebert's study because unlike Europe, didn't use SAG Man and blood was not leukocyte depleted.

O2 supply dependancy - v. different between different organs
Heart is in a continuous supply dependant state
Kidney-02 needed mainly for Na-K pump
Monocytes-even in presence of CN stil consumes 02 if presented with antigen-i.e., used to produce 02 radicals not generate energy
Dopexamine resuscitates the mucosa not the serosa and gut

Give LPS-->decrease BP/decrease RBF/decrease creatinine clearance/but ttissue p02 stays the same (but you get increasead area of hypoxia in cortex i.e., heterogeneity of hypoxia (hidden by the mean which is OK)

2 theories:
-cytopathic hypoxia
-shunting- early (later on it is the mitochondria that is the problem - probably due to unrecognized hypoxia then reperfusion injury).

New Technique
Protoporphyria IX - naturally occurring "delayed fluorescent Lifetime" technique (DFL)
you can for the first time measure the mitochondrial p02 (the higher the p02, the slower the decay time)

At lower p02 there is hibernation --> organ function is reduced as an adaptive mechanism

In gut: 4 hrs of ischemia causes less necrosis then 3 hrs of ischemia followed by 1 hr reperfusion

• Central line

CXR will not tell you if arterial or pleural

Even with U/S, lots of examples of arterial placement

• Stretch of lung causes acidification and bacterial growth - Jerome Pugin

As you stretch alveoli, the supernatant is proportionally more acidic. This seems to be due to activation of the Na-K atpase pump (as it is abolished when given ouabain, a pump inhibitor).

As the supernatant is more acidic (below 7.2), the greater the bacterial growth. Also seen with the proliferation of fibroblasts.

In IPPV - supernatant <7.0
In spont ventil. >7.0
Therefore we should try aerosoled alkalinisation.

NB. there is no link between arterial and airway pH.

• Pro Con debate re. Steroids (Annane v Sprung)
•
• Annane:
•
• JFK was saved by postop steroids
• Sub group analysis-a non responder got noradr>0.5 mcg/kg
• they were the only group where mortality was decreased with steroids
•
• Sprung:
• steroids reversed 80% of shock, but placebo reversed 75%, but took longer(i.e., 2.5 days), but there were more super infections (33 v 26%)
•
• May have role if remain in shock >1 hr despite high dose vasopressors (seen in <10% CORTICUS)

•
• If a new drug, the FDA would never approve.
•
• In CORTICUS, gave 3 X 50 mg/day
• but still saw superinfections.

They do not do ACTH stimulation test as it is too unstandardised, also give total levels (inclu. protein bound when we want free)

NB. Annane only gives steroids if non responder to inotropes AND non responder to ACTH.

Fludrocortisone use is controversial.

• CAP - Pugin

Urine serology - legionella, pneumococcus

remember Kumars study. Once patient in shock, 6% increase in mortality for every hr delayed giving antibiotics.

“No one should die without a dose of aminoglycosides”

• Singer

Early phase is adaptive. Minimal histological evidence of cell death in MOF.
Tissue p02 is elevatedor normal (but not low)
microvascular thrombosis is rare.
Organ recovers if patient recovers (cf. glomerulonephritis)

i.e., cells go into “hibernation”

septic rats:
arterial p02 is normal -high
muscle/liver/kidney p02 drops
but at 24 hrs-->recover (i.e., adaptive) but >25% of rats die despite recovery of tissue p02.

NO competes with 02 for complex IV of mitochondria.
As you recover, the tissue 02 drops, cf. to those that die where it stays high.

If tissue not using 02, -->hyperoxia-->microvascular hypoperfusion (may be protective)
If tissue using 02, -->hypoxia-->microvascular dilates

Chris Ellis disagrees. He thinks its the m/v that starts the problem.

I.e., m/v exquisitely designed to deliver just the right amount of 02 (if increase in 02->decrease in cap dnsity)

but in sepsis, there is dysfunctional local regulation v. early on.

Why no necrosis? tissue is not anoxic- only 20-25mm Hg in hypoxic areas. We lose only about 50% of caps, i.e., there are enough caps to maintain tissue viability but at lower 02 level.

If you recover too rapidly, you get isch-reperfusion injury.

• Warfarin

It is during the first 3-6 months that the highest risk of bleeding seen, thereafter it is 1.3% / yr.

• Beale

in 30% of patients there is a significant radial-femoral artery difference >10% systolic
median systolic difference = 28 mmHg
This is exaggerated with vasopressors due to reflectance in a closed peripheral circulation.

If you give someone a high dose of vasopressor-the radial pressure may be falsely low--falsely low calculated TPR--> maintain vasopressors.
Therefore in v. sick, it may be best to use femoral artery (ex. PICCO)

• Smoke inhalation

80% of burns deaths from smoke inhal

20% of deaths are late

CO --> L shift of oxyHb curve->poor 02 off loading and binds to cytochrome in cell.
CNS signs (neg predictive value of 98%)

CN - if lactate >10 without burn, this strongly indicates CN toxicity

38% have aspiration--> sputum for microbiology

Treatment
Hydroxocobalamin-efficient and safe.
(EDTA poorly tolerated)

if inhalation, it increases need for fluid in burn by 30%

• Army treatment of burns

No crystalloid
C.A.T. device (tourniquet on for 15 min to 2 hrs)
If strong radial pulse no fluids otherwise 1 unit of hextend

FFP:Blood
1:8 67% die
1:3 35% die
1:1 <20% die

Carrico and Shires bled dogs by 70-80%

No transfusion - 70% died
returned shed blood - 60% died
returned shed blood plus 1:3 Ringers - <30% died

• Anaphylaxis - Levy

increased PVR->RVF-->increased RAP with decreased LAP (due to septal shift, i.e., RV full, LV empty...do ECHO)

NO and PG release--> vascular relaxation

Can get flash oedema
most deaths due to b/spasm esp if prior bronchoconstrictive disease.
Always rule out a pneumothorax (looks the same).

HIT-instead of neutrophils (seen in TRALI) IgG causes platelets to aggregate.

Give Vanco centrally. as it works by releasing histamine from mast cells which are in rel. high concentratin near vessels of skin (i.e., vessel not far from mast cell, therefore the vanco is in a rel. high concentration.)

Contrast media causes release of histamine esp with high ionic products..this is not a true allergy

If persistant hypotension, use terlipressin or vasopressin (V1 agents)

Vasopressin effectively reverses pathol induced vasodilation (give a couple of units to start with)

Do not forget air trapping-->increased PVR, therefore decrease i:e ratio

In one case of increased PVR and RVF, he gave ketorolac as this is thromboxane mediate and it worked!

• Liver trauma - Wendon

biliary jejeunostomy if laparoscopic trauma

beware of fatty liver of pregnancy/PET-->R lower chest pain-->spontaneous hematoma - do not heparinize (with suspicion of PE)

Blunt liver trauma-
if stable-non op treatment- interventional radiology do CT and angio (embolisation) if not pack (esp if venous bleed but do not overpack--> isch insult. Repeat packing every 48 hrs.

Stab injury-
always laparotomy

If biliary trauma, put stent across the ampulla-if that doesnt work, put naso-biliary tube (placed by endoscopist)

Beware of peudoaneurysm (1 week after trauma)--> major bleeding
check for pancreatic fracture-treat by pancreatic stenting

Radiologist very important in liver trauma

• ARDS Kacmarek

ARDS mortality=45-55%
ALI mortality = 30%

mortality prediction better if you divide patients up to ARDS, ALI, ARF (acute resp failure), after 24 hrs conventional ventilation, i.e., they seperate into 3 streams with v. differing mortality. Explains why some PEEP trials showed no mortality benefit, i.e., they would have gotten better anyway since they didnt really all have ARDS.

ALVEOLI study saw no mortality difference.

Based on the above, they will start a new study but selection of only truly sick patients i.e., only after 24 hrs treatment.
Treatment will use peak pressures at 50 cm H_2O (40 is sure to be safe, 60 associated with pneumothorax, therefore comfortable with 50) and starts with PEEP at 25.

• Status epilepticus
defined now as > 5-10 min
high mortality therefore there is a degree urgency.

seizures beget seizures, S.E. re-organizes of the neural network

3 categories:
-Grand Mal-generalized convulsive SE (can be v. subtle, eg. eyelid twitch)
-Focal S.E. - difficult to treat. Maintains consciousness
-Non convulsive S.E.-complex partial seizures (can be confused)

You can treat motor manifestations with n-m blockers but brain keeps convulsing, therefore always do a EEG

Treatment:
-Benzos
    lorazepam (6-10 mg) longest 1/2 life
    midazolam -OK but short 1/2 life (0.2 mg/kg)
-IV if rapid effect needed
    phenytoin(or fosphenytoin)
    valproate 60-70 mg/kg
-propofol
    good short term treatment, can go to burst suppression
    leave for 12-24 hrs burst suppression before weaning but ensure adequate chr. anti convulsants, follow with EEG

• Scoring systems

SAPS III
3 boxes
-previous health - accounts for 50% explanatory power
age/co-morbidity/hospital location/lead time

-ICU admission - accounts for 23% explanatory power
surgical status/

-Physiological derangment - accounts for 27% explanatory power

SMR give 95% confidence limits, if overlaps 1, not significant

• The yellow patient - Wendon

LFTs-non specific, can have cirrhosis with normal LFTs

AST/ALT-not good for cholestatic problem- good for hepatocyte damage

INR -only useful as a prognostic marker in acute liver failure

Bilirubin depends on albumin

if you look at a liver unit with its central vein and sinusoids leading to it, the area most at risk of isch./RVF/congestion is next to the central vein. This is also the area where drug metabolism and bilirubin.

Contrast CT much better then CT alone.

Screen for Hep C much worse liver problems even if not cirrhotic.

If alcohol and paracetamol - 1 gm X 3or 1 gm X 4 but give NAC (i.e., you want become glutathione depleted).

Isch hepatitis
- ex. congested liver (ex, RVF)
- U/S best diagnosis
- Treatment supportive

LPS/cytokines block uptake/excretion of bile acids-->cholestasis

Treatment-none

Fatty liver
- -increase BMI/DM/Htn (i.e., metabolic syndrome)

fat in liver- v. sensitive to oxidative stress (i.e., sepsis) --> sick liver, therefore very vulnerable-beware preop

cholestasis and feeding. Best if use enteral feed. Risk factor (TPN/sepsis)
attenuated by glutamine in TPN

Drugs
- NSAID - hepatotoxic
- TPN
- Augmentin -->cholestasis

As bilirubin increases, mortality increases

Avoid epinephrine if possible, it decreases liver circulation

Increase portal pressure--. gut congestion-->translocation of m/os

Indocyanine green clearance (ICG) is a good test, it correlates with mortality. Good for risk stratification, esp for preop hepatectomy (LFTs/Child-Pugh not sufficient)

Increased no. hepatic segments resected--> increased mortality --> liver left behind is too small for the portal flow--> liver congestion. Therefore during surgery get surgeon to measure portal pressure, if increased, clip splenic artery branch or embolise splenic artery branch.

Porto-renal reflex- as portal pressure increases--> renal vessel dilatation

• Factor V Leiden

caucasians 5-8%
not seen in Africans/Chinese/Japs

Cant be inactivated by APC

Factor V Leiden if no other risk factor: it increases risk 4-8 X
Oral contraceptive increases risk 4 X
plus Factor V Leiden (increase 35 X)

20% of VTE have malignancy
Obese-2-3 X even in young obese (5 X higher risk)
Travel >10,000 km (4.7 PE/million passenger arrivals - approx. 1/200,000)

In ICU, if prophyl it cuts DVT by 50%.

Samama NEJM 99 - Enoxaparin 40 mg decreases freq by 1/3rd (20 mg has no effect)

If needed use a filter but remove within 1 month if possible

• Massive PE

Majority of anatomically massive PE (>40%), do not have hypotension
U/S - if unexplained hypotension - if no RV dil. - not PE
Troponin - RV isch. -prognostic implications
BNP - RV stretch. -prognostic implications

thrombolytics-
indication-unstable CV

rt-PA -60mg rapidly--> 40 mg over 2 hrs (not the normal 100 mg/2 hr)

RV dysfunction
-none-no mortality
-if present, increased risk of death

TPA and heparin--> more rapid recovery of RVDys then heparin alone

If normotensive but RVDysf. --> 10% get delayed shock

If only RVDysf. - controversial if need TPA in PE without shock since vast majority do OK.
Dont forget, 1.2-3.0% get I/C hemorrhage

IVC filter, use retrievable filter.

Treatment of Rt Vent Dysf.
-Fluid - not v. effective - unless CVP < 20 (max.), beware if overloaded-->septal shift--> squeeze LV--> decrease C.O.

-Vaspressor - increase aortic diastolic pressure
-dont forget most of increased PVR is due to mediators not clot
-inotropes
-NO
Hypotension defines the best threshold for thrombolysis

Also ECMO or RV assist device work if all else fails (remember, you can do ECMO with minimal anticoagulation. Need 2-3l/min flow to empty Rt Vent-->return septum-->increase C.O. NB. Do not intubate as they crash on induction)

surgical thrombectomy if thrombolytics do not work or if C/I

Periop PE
No absolute C/I to thrombolytics

Acute RVF
Rt vent is U shaped, therefore hard to visualise in its entirety with U/S

The L side of the heart can do most of the work for the Rt side due to configuration of the fibers, i.e., a lot of R sided contraction comes from the L side (seen if you electrically stop RV from pumping but L side OK--> Rt still pumps blood as before).

Rt dilatation--> impairs L sided (which does most of the work)Therefore do not fluid overload

RV supplied by Rt coronary artery. When RV dilates, it impairs circulation of Rt Cor artery (which unlike L side, occurs during diastole and systole). Therefore doesnt do well if increase PVR --> dilation

decrease RV -->septal shift-->decrease CO-->decrease Coronary perfusion-->isch--> decrease RV

Most prognosis from U/S and biomarkers

Thickness of RV wall will tell if acute or chronic

NB. RV contraction not just dilation look for tricuspid annulus displacement also tricuspid regurg - estimates PAP

Treatment targets:
RV preload-fluid challenge but be very careful
RV contract-same inotropes as LVF, no preference for agent

minimize shunt-check to see if PFO
PA vasodilation- NO /phopsphodiesterase inhibitors/prostacyclin/Ca channel blocker/sildenafil (PDE 5 inhibitorgood in chronic-minimal effect systemically-oral only)
(NB. GTN not good on Rt heart)

If PE:
shock-->consider thrombolytics
no shock
increase troponin/BNP->ECHO-->RVDysf-->consider thrombolytics
-->no RVDysf-->anticoagul.

normal troponin/BNP-->anticoagul.

• Hepato Renal Syn

Type I-acute (weeks), severe, creat >220, 90% die
Type II - chronic (months), less severe, characterized by ascites resistant to treatment

Pathophysiol:
as ascites builds up-->neurohumoral changes-->vasoconstriction

precipitating event (variceal hemorrhage, infection, ex, SBP,) trigger -->decrease C.O.-->regional arterial vasoconstr and portal hypertension

Treatment:
-Liver Tx - do rel. well
-Terlipressin (or noradrenalin) and Albumin - improve GFR
-TIPPS-->decrease portal pressure-->increase renal blood flow but risk of encephalopathy

Notes from Brussels 2009

• IAP – Sugrue

Normal 7-8 mm Hg
IAH=>12
IAP>16 seen in 40% of ICU patients
ACS=IAP>20 + new organ dysfunction (incidence ~3%)

Clinical measure ~60% sensitive

Can measure IAP from femoral central venous line.
(can "ballpark" it by lifting urinary catheter as a column of water).

Abdo PP = mean BP – IAP
Can use a washout urinary catheter and fit transducer to washout port.

Search for cause if raised.
Measure at operative closure, 2 hrs after entry to ICU then once a shift.

With pevic packs, very high pelvic pressure→ rectal sloughing. Measure ICP at gastric or femoral IVC.

Transmissin pressure from abdo → chest is ~ 60% (ex. if CVP = 30, IAH = 15, CVP in reality is ~15).

• IAH and chest wall – Pelosi

Trans pleural pressure (TPP) is main determinant of lung injury = pressure needed to shift lung.

Ex if "hard" chest wall ~ 15 cm H20 and TPP = 15 Paw = 30
If soft chest wall ~ 5 and TPP = 25 Paw = 30.

Anaesthesia per se doesn't change chest wall compliance, it does change lung compliance..

Obese- decrease chest wall compliance, therefore Paw doesn't reflect lung mechanics.

PEEP in obese→ shifts chest wall compliance from abnormal to normal.
Therefore, recruit then PEEP!

COPD- chest wall compliance same as normal but in ArespF it changes, therefore Paw does not reflect TPP.

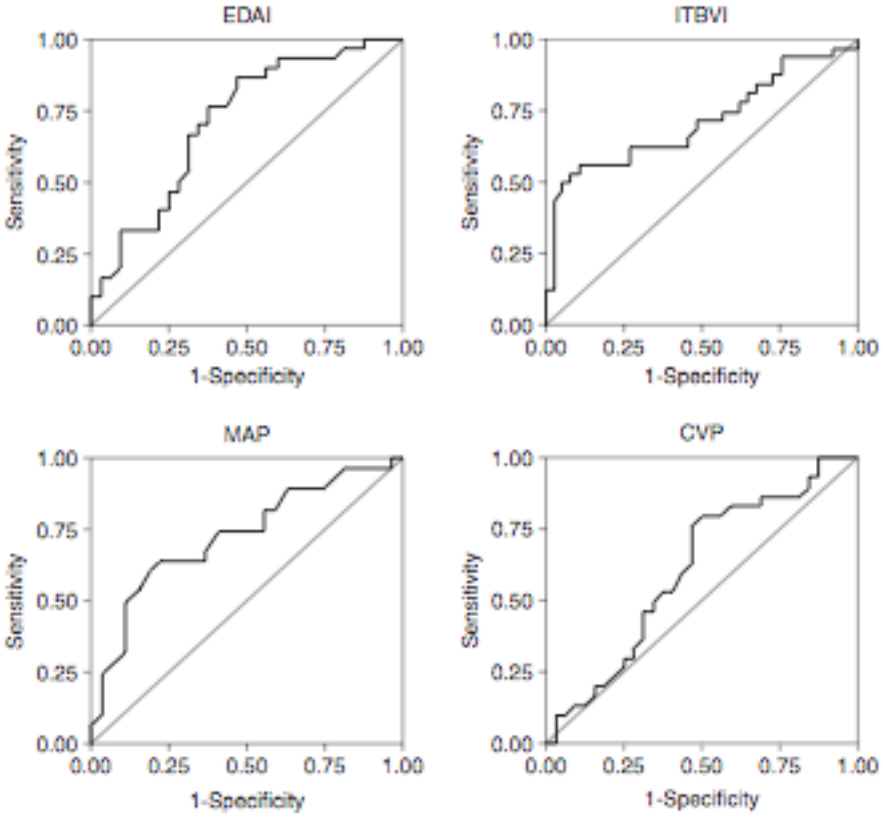
The chest wall compliance influences both lower and upper inflection points.

(The new england journal of medicine
november 13, 2008 vol. 359 no. 20 Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury) used PEEP guided by oesph pressure, i.e., used real TPP, most had IAH→increased PEEP.

IAP is main factor influencing chest wall compliance, care if > 12.

• PICCO – Perel

Preismann



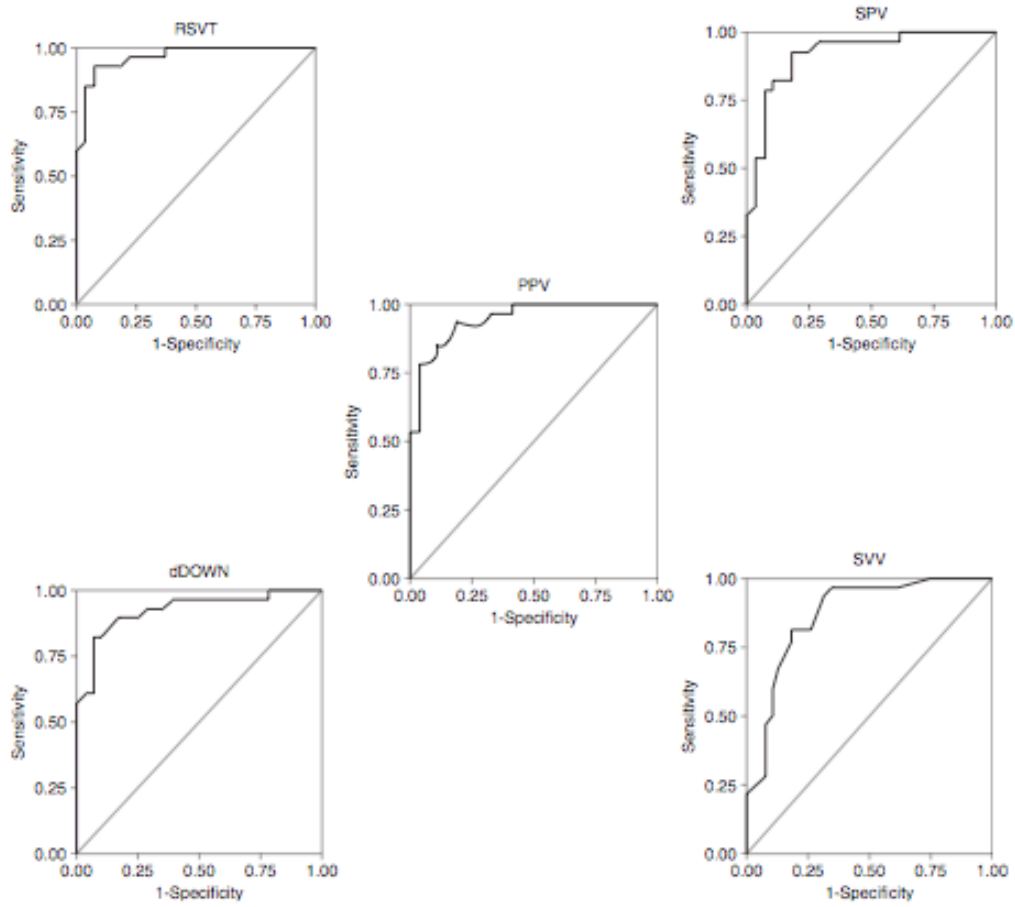


Fig 3 ROC curves for RSVT, dDOWN, SPV, SVV, and PPV.

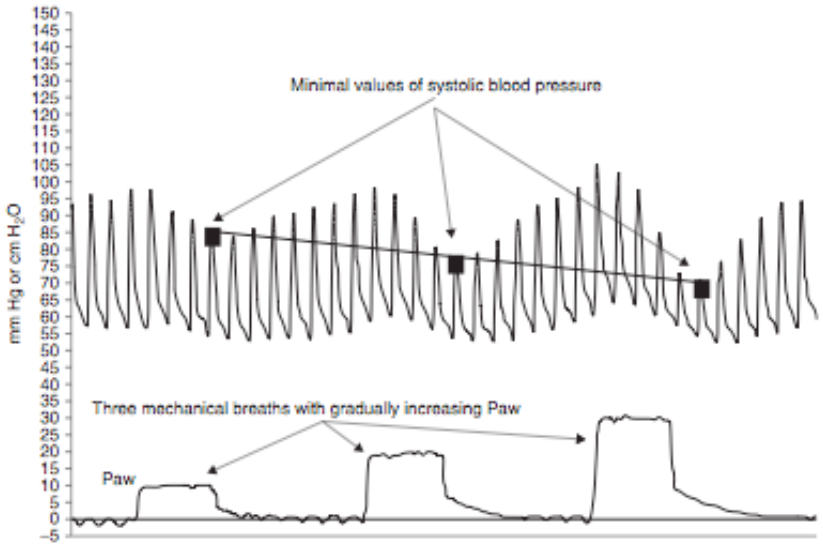
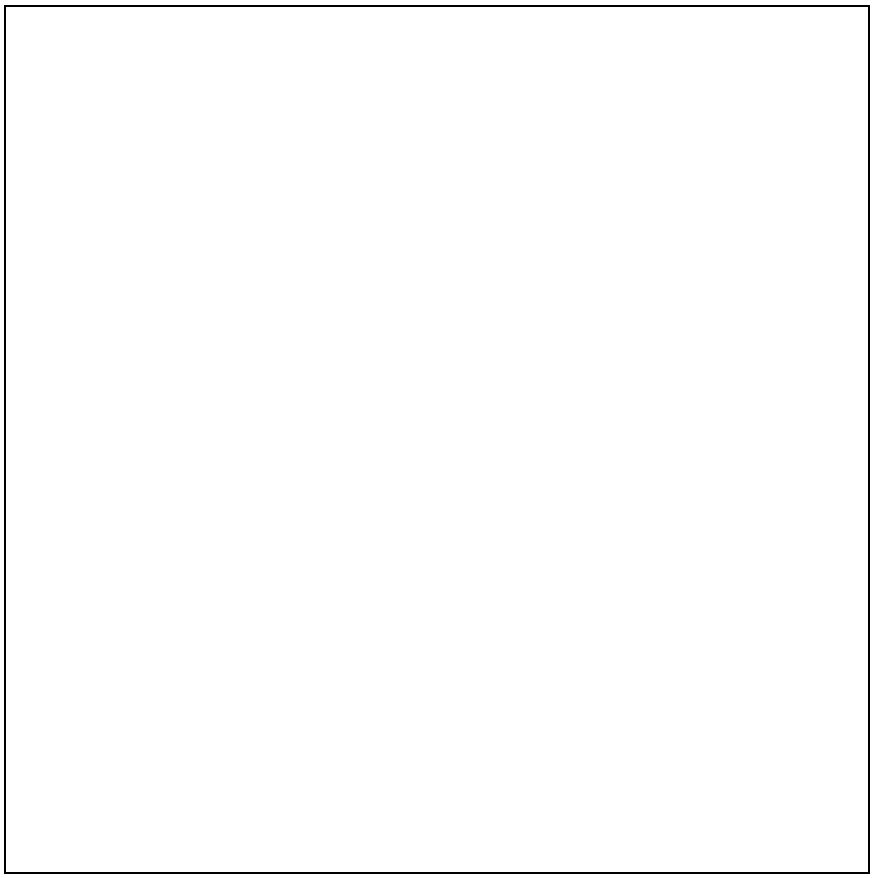


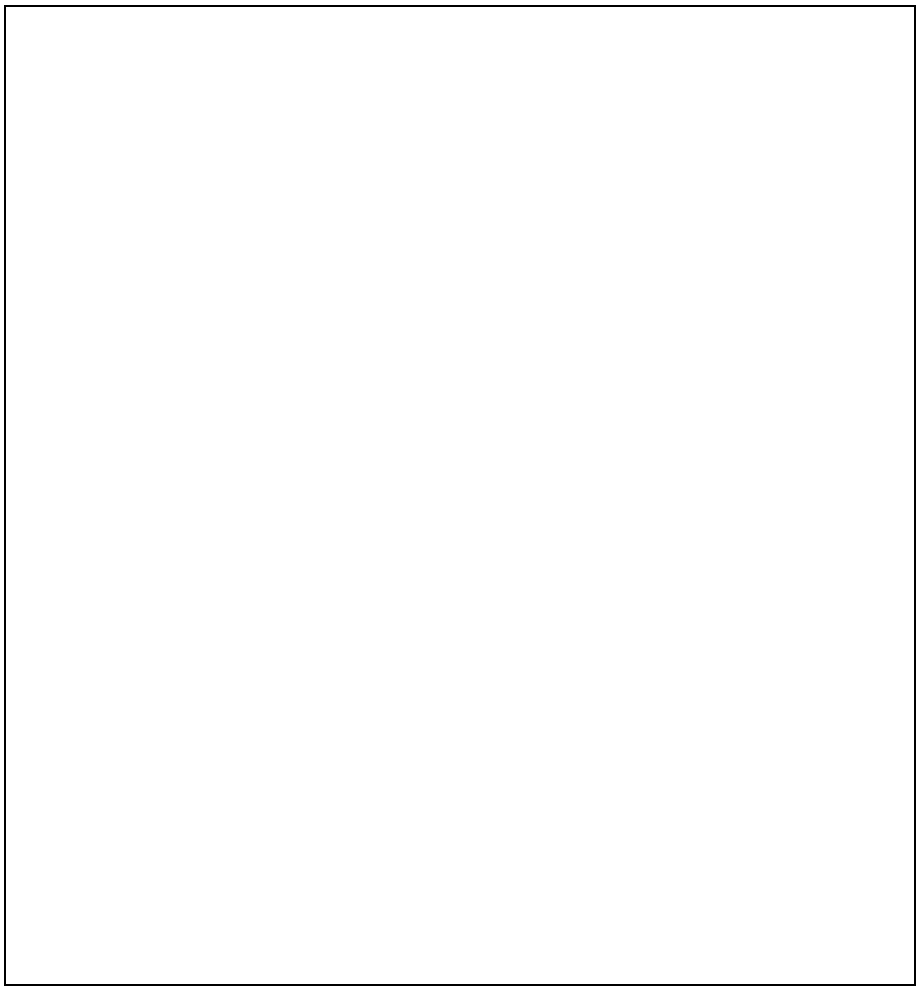
Fig 1 Response of the arterial BP to the RSVT. Three consecutive mechanical pressure-controlled breaths are delivered with inspiratory pressures of 10, 20, and 30 cm H_2O. Minimal values of systolic BP in response to each breath are recorded and then the slope of the relationship between the decrease in BP and inspiratory pressure is calculated.

C.O. can be high with low preload (high catechlamines) but adequate?

In practice use PICCO when:
Co-morbidities (ex. CCF)
Therapeutic conflict (ARDS and Sepsis)

Can get Pulmonary Permeability Index to separate hydrostatic from permeability oedema.
Monnet “Pulmonary Permeability Index”





• Fluid optimisation – Hamilton

Oesophageal doppler – 9 outcome studies/920 patients -> little mortality benefits but decreased LOS and morbidity

Target - > 10% S Vol (measure FTC)

Maintenance – crystalloid 1-2 ml/kg/hr
Colloid bolus

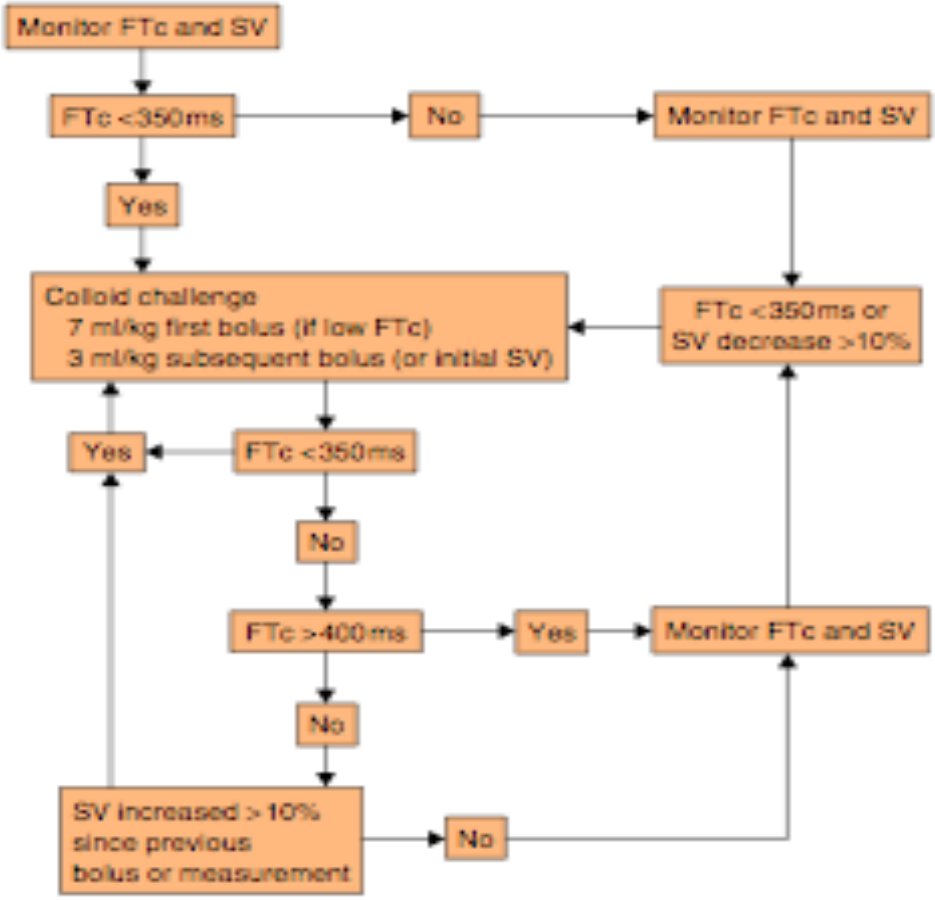


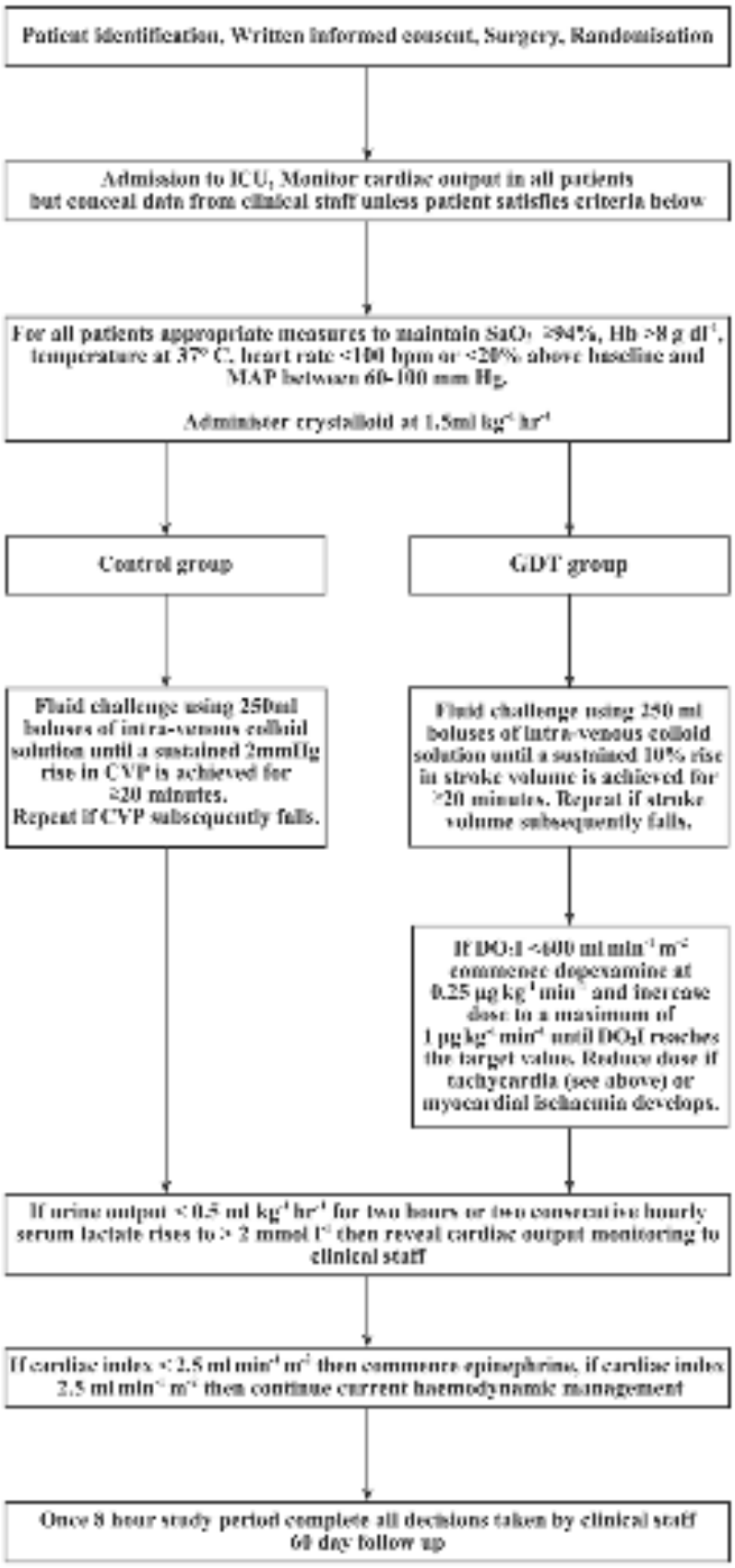
Fig. 1 Fluid administration algorithm. FTc, descending aortic corrected flow time; SV, stroke volume

www.bjs.co.uk *British Journal of Surgery* 2006; **93**: 1069–1076

Timing important-similar volume between treatment group and control. The difference was in timing.

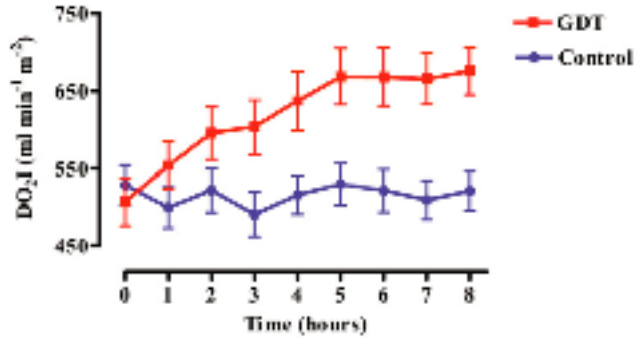
Postop Lidco Plus – target SV >10% (give 250 ml colloid /5 min) – once Svol maxed, look at 02 del (ideal =600 ml/m/m2) if not achieved – dopexamine (max. 1 mcg/kg/min)

• Fluid optimisation Pearse



Cardiovascular treatment protocols for goal-directed therapy (GDT) and control groups. DO_2I, oxygen delivery index; Hb, haemoglobin; SaO_2, arterial oxygen saturation.

Figure 3



Oxygen delivery index for goal-directed therapy and control groups during the 8-hour study period. Results are means ± SEM. DO_2I, oxygen delivery index; GDT, goal-directed therapy.

Mortality for non cardiac, major surgery far higher then cardiac surgery.

Aim is D02 = 600 ml/m/m2 – most benefit is a decrease hospital acquired infection

Control vs treatment group
Similar BP/CVP
Increased lactate, a very late sign
Treatment group a much better D02

Therefore optimise fluids using inotropes if need be (at a low dose), up to 8 hrs post op.
Monitor with PICCO/Lidco/ScvO2

• Intraop H/D Green

Uses:
BIS
Lidco Rapid (for pre induction baseline)
LMA (Proseal) for ALL ops!

Problem with oesoph doppler- gives a baseline after induction (can drop 45%), which is taken as normal.

Uses less fluid
Ignores CEPEX (Old study, never repeated) Keeps stable whatever the CEPEX. Doesn't optimise preop.
Fluid challenges must be gven quickly (not over 15 min)

• Optimising high risk surgical patient Vallet

Vialle

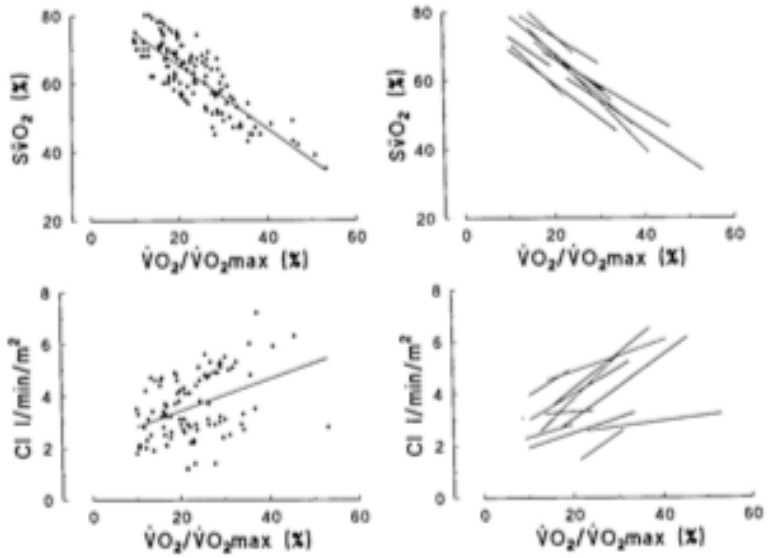


Fig. 2. (*Top*) Correlation between mixed venous oxygen saturation ($S\bar{v}_{O_2}$) and oxygen uptake expressed as the percentage of preoperatively measured maximal oxygen uptake ($\dot{V}_{O_2}/\dot{V}_{O_2}$max, %) (*Top left*) All data points are shown ($n = 136$), $r = -0.82$ ($P < 0.0001$). (*Top right*) Individual lines of correlation are shown. Correlation coefficients ranged among patients from −0.67 to −0.99. Slopes and y intercepts ranged from −0.78 to −1.3 and from 79.2 to 96.9, respectively. (*Bottom*) Correlation between cardiac index (CI) and $\dot{V}_{O_2}/\dot{V}_{O_2}$max (%). (*Bottom left*) All data points are shown ($n = 98$), $r = 0.40$ ($P < 0.05$). (*Bottom right*) Individual lines of correlation are shown. Correlation coefficients ranged among patients from 0.24 to 0.98. Slopes and y intercepts ranged from 0.01 to 0.17 and from −1.1 to 3.7, respectively.

Assess risk
- Stair climb
- CPEX
- POSSUM (ASA doesn't take into account type of surgery)

Preop preparation
Regional anesth
Early removal of drains and mobilise

Avoid tissue 02 debt→ increase inflam and cytokines→ alters microcirculation

PPV close to SVV (Finapress pretty good for PPV)

Masino pulse oximeter→ "Pleth. Variability Index"

Treatment Algorithm

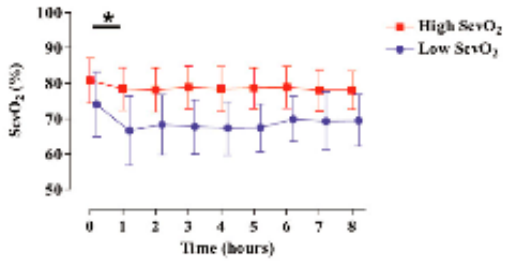
	OK	Add Vol
MAP (>70?)	Vasopressor	Give Vol (+/- inotrope)
		PPV (<12 ?)

But vasopressor will → increased stressed volume → will correct PPV

How about DO2

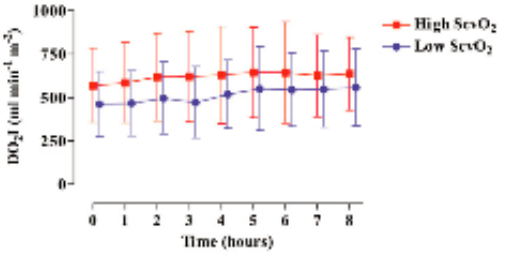
Pearse

Figure 1



Central venous saturation ($ScvO_2$) in the 8 hours after major surgery. Results are means ± SD. *$p < 0.0001$ for low $ScvO_2$ group; $p = 0.02$ for high $ScvO_2$ group. The difference between the high and low groups is significant overall and for each individual time point ($p < 0.0001$).

Figure 2



Oxygen delivery index (DO_2I) in the 8 hours after major surgery. Results are means ± SD. The difference between the group with high central venous saturation ($ScvO_2$) and the low $ScvO_2$ group is significant overall ($p = 0.005$) but not for individual time points 7 and 8.

Best outcome with higher Scv02 post op – optimal cutoff 73%

Donati

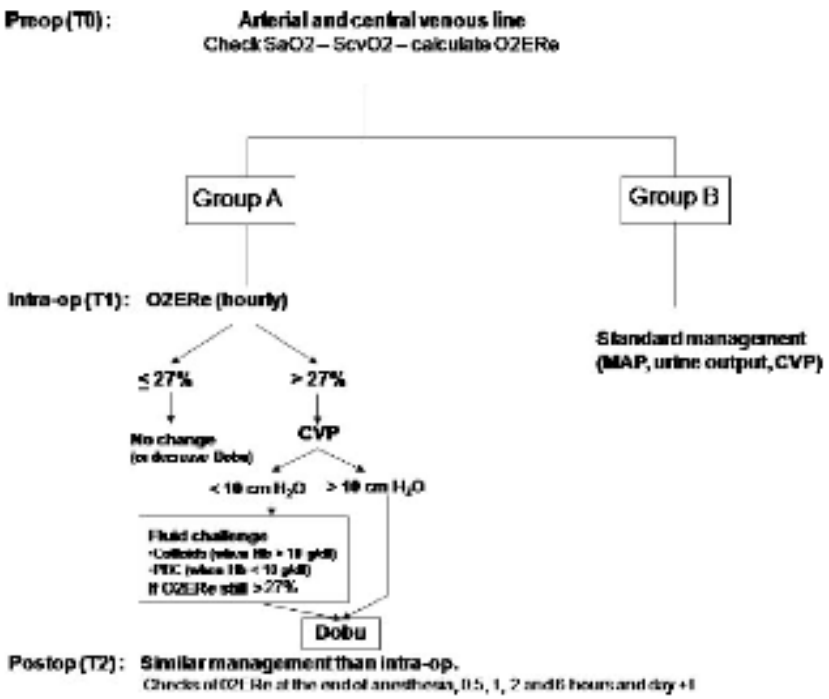


FIGURE 1. Therapeutic protocol. In addition to the standard management (group B), a standardized therapeutic protocol designed to restore and/or keep O_2ERe < 27% was applied to patients randomized to group A. Intra-op = intraoperative; Preop = preoperative; Postop = postoperative.

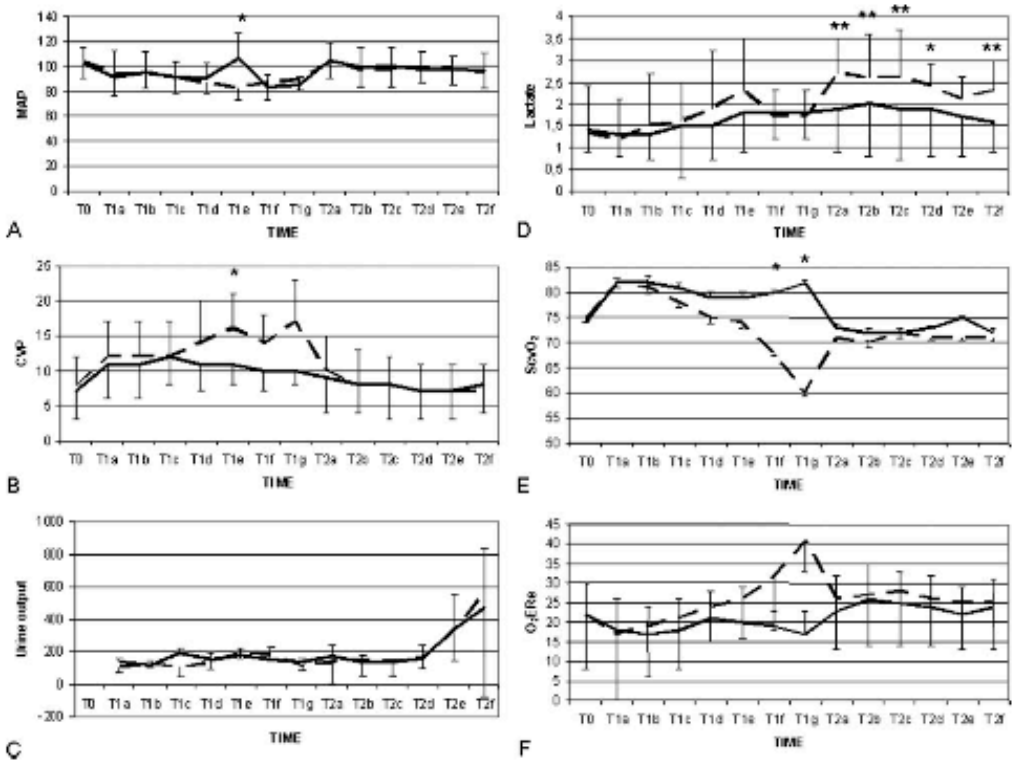


FIGURE 3. Time course of MAP (mm Hg), CVP (mm Hg), urinary output (mL/h), blood lactate (mmol/L), $ScvO_2$ (%), and O_2ERe recorded after induction of anesthesia (T0), hourly after cutaneous incision (T1a–f), throughout surgery, during the first 6 h of the postoperative period (T2a–f), and on postoperative day 1. Group A (O_2ERe group) is represented by solid line, and group B (standard management group) is represented by dotted line. Data are shown as mean ± SD. *$p < 0.05$ and **$p < 0.01$ between groups.

Pinsky

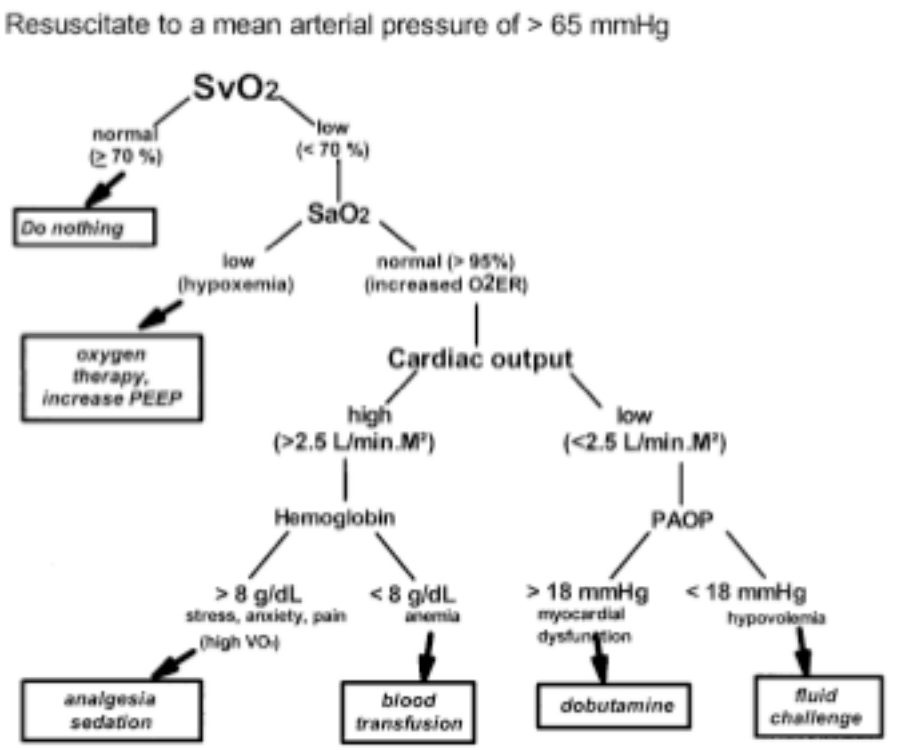


Figure 1. Diagnostic and therapeutic algorithm based on mixed venous oxygen saturation (SvO_2) measurements: therapeutic options to be considered are presented in the rectangles. SaO_2, arterial oxygen saturation; O_2ER, oxygen extraction ratio; *PEEP*, positive end-expiratory pressure; *PAOP*, pulmonary artery occlusion pressure; VO_2, oxygen consumption.

Aim for SVV or PPV <10%
Scv02 >75%

• Marinin

Used v. high doses of insulin in beta blocked overdoses. Up to 600 u.hr (1-2 u.kg/hr progressively increased). → increased CO and decreased TPR in refreactory shock.

• Goal directed therapy Pearse

254 million surgical procedures world wide.
Low dose dopexamine 0.5 mcg/kg/min → decreased mortality (high dose → increased mortality).

Effect of fluid and inotrope → drmatic effect on D02, Scv02, microvascular flow cf to fluid alone. NB. Dopexamine has potent vasodilator effects.

V. large difference in CO but none in CVP nor BP.

No change seen in global inflammatory markers after GDHT

(NB. Therefore beta agonists and antagonists seems to influence outcomes)

• Pinsky

PPV-SVV predict preload responsiveness. 34 papers prove it!

• Scv02 Perel

If CO looks good but Scv02 not high→ may need to increase CO.

Scv02 directed GDHT several recent papers show it can decrease in 1st hours post op (due to increase metabolism).

NB. Rivers mean Scv02 was 50%! (most were v. hypovolemic) in sepsis, most are increased or normal.

• Gut failure Malbrain

= intolerance to fed + IAH

should be incorporated into SOFA

• IAP Sugrue

normal 7-8 mm Hg (at end expiration, supine)
IAH > 12
ACS = > 20 + new organ dysfunction

You can use the IVC from femoral line (can also use washout urinary catheter)

Abdo PP = mean BP – IAP (aim for > 60 measure once a shift)
Transmission of abdo pressure→ chest (~ 60%) (ex if CVP is 30, IAH is 15, therefore CVP is ~ 15).

• IAH and chest wall Pelosi

Trans pul pressure is main determinant of lung injury = pressure needed to shift lung
PEEP in obese → shift chest wall compliance from abnormal to normal
COPD – in acute resp failure chest wall compliance changes

• Temporary abdo closure De Weele

all have faults:
Bogota bag
Vicryl mesh
VAC pack
VAC abdo drainage is best. Sucks out around 2-3 l / day.

• ICP Menon

CPP = 60 (higher CPP → increased resp/CV complications) but if lots of ischemic brain volume – seen on PET scan→ benefit from an increase of CPP ex 90. Therefore balance risks vs benefits for individual. Danger of one size fits all protocol.

• Bed rest

decrease lean body mass
if steroids added → great decrease in lean body mass.

Also associated with left lower lobe collapse as dependant heart crushes the lung.

• Patient ventilator assynchrony Brochard

Controlled ventilation → dramatic decrese in diaphragmatic force (cf. assisted ventilation)

Too little support → increase WOB
Too much → diaph atrophy
Assist-control ventil. – same breath given by ventilator but the machine breath can be triggered by patient.

Keep peak flow high (~60l/min) it decreases WOB

If assynchrony:
Adjust the exp. Trigger (or % of peak flow-usually 25%..the higher the %, the sooner the cycling from inspir to expir).

External PEEP – rarely works

Distinquish the respiratory rate on ventilator from the total (i.e., machine plus patients ineefective resp rate)

Best modes on horizon:
NAVA (EMG run)
PAV (proportional assist ventil)
- Cycles at end of patient flow
- Triggers-flow or pressure
- Pressure proportional to flow and volume

• REDOX Tim Evans

Albumin – v. important anti oxidant (may be be redox therapy rather then volume support)
Acute phase proteins – transferrin/haptoglobin – v. important anti oxidants

Thioredoxin-an intracellular protein, upgraded in sepsis. Important actor in redox.
(Macrophage inhibiting factor- a member of thioredoxin family)

Albumin will bind free Hb→ decrease neutrophil activity and SIRS
(SAFE- increase in mortality in head injury only. It increases aPTT and bleeding)

• Mitochondrial dysfunction Mervyn

Acute phase (Early) fight mode- increase energy need by 40%

Chronic phase – decrease energy need (i.e., goes to sleep – hibernation – survival benefit)
- At rest energy expenditure only 15% above normal, healthy people
- Decrease hormonal level → anti inflamm. Phase
- The sicker the patient the less energy expended

Recovery phase
- Increase in energy expenditure by 60% cf. to control
- Turned on by lots of factors (NO, estrogens, exercise)

• Checklists Dale Needham
FAST HUG 7 compounds
<10% of nurses understood patients goals
Michigan Central line checklist study – blood stream infection went from 7.7→1.4 at 18 months (no Hawthorne effect – i.e. sustained)

• Gattinoni

Normal lung weighs 800-1000 gm

ARDS lung weighs ~1700 gm (i.e., 2X)

The greater the oedema→the greater the collapse→the greater the recruitability→the greater the severity→ the higher the mortality

If you have a need for a high PEEP of 60, you may have a TPP of 40. Therefore the subjects heart and venous return are exposed to 40. Therefore you give lots of fluid to stop the decrease in O2 delivery…but within minutes, you will get lung oedema. Therefore PEEP will work, but "non-sensical".

Atalectasis → high load on rt ventricle. Therefore recruitment may have a beneficial effect on hemodynamics.
Above 55 cm H2O (ex PEEP 35→Paw 20 = 55).No change in BP but TEE showed marked decrease in CO (ex. 40%)→ rapid recovery after.
In obese, re-expand lung→ decrease RV afterload

Abandon sustained recruitment Use cyclical, ex. progressively increasing PEEP.

• Calcitonin Beat Muller

Normally calcitonin and pro calcitonin only produced in thyroid. In sepsis, all tissues produce calcitonin and pro calcit. In response to cytokines = hormokines

C-GRP – most potent vasodilator in body- a calcitonin peptide – increased by cutokines.

CT – a family of peptides- can be used for prognosis and response to treatment.

Pro-adrenomedulin – a very good prognostic marker.

• Ince
Old blood loses around 30% of its O2 carrying capacity.

• Nitric oxide Mervyn

NO- a by-product of: Arginine to citrulline

-endothelial NO – eNOS
-neurtonal NO – nNOS
-inducible NO – iNOS (inhibited by LNMMA – monomethyl arginine)

Sepsis-> large increase in production→ increase eNOS –minutes, peaks in hours, wanes in 12 hrs

Also increases in cardiogenic and hemorrhagic shock but to a lesser extent.

Role in sepsis:
-vasodilates
-myocardial depression
-potent inhibitor of mitochondrial respiration
(NO competes with O2 in complex lV, blocks complex l, increases with increased severity)

Methylene blue- scavenges NO-> increase TPR-> reduces distributive shock (as does synthetic Hb solutions).

• NICE Sugar vs Leuven

NICE Sugar Leuvan

No		3500	6100
Target BSL		180-215	140-180
Feeding	fed		hypocaloric
Insulin		continuous	cont+bolus
Mortality		<3%	>3%

Finfer
"lesson for people who write guidelines…do not ignore negative studies before generalizing"

K-Meier
Mirror image of V den Burgh study, i.e., late difference in mortality

Inclusion criteria
"death not imminent (NB. 3000 expected to die in 24 hrs, i.e., ICU is now a place to die).

Used time weighted glucose.

More people in intensive group, control group had more steroids.

Cause of death- cardiovascular (distributive shock) , no difference in new organ failure.
Subgroup analysis-tend to be overanalysed-should be before data collection.

Increased severe hypoglycemia.

"glucose control…its like titrating a noradr infusion using a sphygmomanometer every 4 hrs.

3 studies: (multicentered – show increased mortality
Glucontrol
VISEP
Nice sugar

VdBurgh-one center-sub group analysis:
- -surgical ICU
- > 3 days
- Cardio-thoracic surgery

Feeding-different in NICE SUGAR and VdBurgh but VISEP similar to VdB

We need real time, continuous plasma glucose

"NICE SUGAR is a study of tight vs medium glucose control"

• Cancer patients in ICU Azoulay

- More specific, effective less toxic, targeted chemotherapy (ex. mortality of CML is much better now cf. with 80s)

CHOP and Rituximab for B cell lymphoma much better with fewer side effects.
Over last few years, cancer patient shows an increased survival of 20%, inclu in ICU.

"Golden hour, do not leave intubation for > 3 days if on NIVentil.- they all die."

-neutropenia-no effect on mortality
-solid vs haematological cancer-no difference re. prognosis

Antibiotics- avoid aminoglycosides – toxic but no effect on survival

85% do not need anti fungals

Admit to ICU earlier, not when moribund (which is why mortality in ICU is so high).

• Elderly in ICU – Boldt

Blunted beta responsiveness
Earlier activation of inflammatory cascade and blunted anti inflammatory response. Therefore more likely to suffer from sepsis.

>85 yrs old -if need IPPV – 85% die
-if need inotropes, 100% die

• ICU and pregnancy Poldermanns

ICU studies exclude pregnant patients
Largest risk to fetus at 8-10 wks (before protective placenta is complete – filters out molecules > 500D)

CO ~ 6l/min – majortiy have systolic murmurs, blood volume increases 35%, plasma 45%, with a concomitant decrease in Hct

CO can decrease by 20-39% when supine – 20% goes to uterus.

Increase Vt 40%, increase O2 demand, increase Min vol 50%, increase GFR-> decrease urea/creatinine/albumin
Increased clearance for many drugs (ex. ampicillin has an AUC decrease of 30%)
NB. All inotropes are category C (i.e., we don't know).

• MET teams
Little evidence (see MERIT study, NICE guidelines)
"It is ifinitely harder to resuscitate a dead patient, then a sick one" Bellomo
(> 3 beeps to surgeon..if no response-> MET team)

• Identifying cardio-pulmonary insuff at bedsied Pinsky
"Biosign index" (BSI) – neural networks and pattern recognition (even if all values are normal)

Don't eyeball intermittently- patients tend to get worse-> better ->worse -> better ->crash!

Only 40% of of patients written up for pulse oximetry
73% of UK hospitals have outreach
78% of thresholds not called

Cochrane and MET – mixed results (from Canada)
20% for end of life issues
20% need to go to ITU
50% appropriate
25% ridiculous
25% v. late

(often no one in room when MET team arrives…dumbing down a risk).

K. Hillman
50% of calls for "worried"
<5 % need ITU transfer
<50% had vital signs monitored

• Coagulation Levy

Natural anticoagulants – attached to endothelium
APC
Tissue factor inhibitor (TFPI)
Anti thrombin

Glycocalyx "fixes" the above if lost->coagulation
Hyperglycemia-> loss of glycocalyx
Sepsis-> loses almost all glycocalyx-> activation of coagulation
TNF inhibition-> protects glycocalyx
Experimentally the glycocalyx can be restored in 1-2 hrs (i.e., very dynamic) (measure using radio labelled dextrin)

• Blood viscosity Intaglietta

FCD = determinant factor for survival in haemorrhage

Best way to recruit -> increase viscosity
Even non transporting Hb (ex metHb) -> increase viscosity-> increase FCD

Increase Hct-> increased CO by 20%

In severe anemia, small change in Hct (<20%) -> important delta SVR
Increase viscosity-> increase shear stress-> regulates production of NO -> vasodilation

FCD depends on viscosity-> increase shear stress-> increase NO -> increase diameter (up to a point).

Ince – in Everest extreme -> sub lingual SDF-> slow moving RBCs (sludging) -> more time to offload O2.

• Microcirculation and mitochondria Mervyn

Sepsis – Rare microcirculatory thrombus
Minimal cell death – failed organ recovers quickly if patient survives
Increase in tissue pO2

Sepsis plus ARF – No ATN
Histology is unremarkable, necrosis uncommon (increase pO2, decreased global O2 del – but cells don't die – why? Because of metabolic shutdown

Sepsis – phases
Early – myocardial depression
Macrovascular hit
Microvascular hit
Late – (24 hrs) – mitochondrial hit – increased tissue pO2 (i.e., cells not using O2) -> vasoconstriction to lower tissue O2 at microvascular level

Recovery (or not) – mitochondrium picks up -> decreased tissue pO2 (vasodil)

• ARF Kellum

25-30% will die (but only 25% get CRRT)
(if you witheld ventilation from a resp failure patient -> criminal) But we reserve CRRT for only sickest -> 40% mortality) (patient with a similar severity of illness but no ARF – 5% die)

Those that recover without CRRT-> longer period of uremia
Therefore filter early! – but no real evidence ("start at the injury level of RIFLE")

35 ml/kg/hr – probably best starting dose – but no data – await "IVORY" study

In practice most get 18-20 hrs CRRT/day at 20 ml/kg/hrs.

Kellum starts with 20 ml/kg/hr -> goes up if it can decrease vasopressors (ex. refractory shock – we use convection rather then CVHDF

• Gattinoni

Chloride – main way the kidney maintains SID is via Cl

Hypervolemia (increase Na) -> (RAAS) -> increased NaU -> increased SID Ur -> increased Urinary pH

Hypoventil -> increased pCO2 -> increased NH4+ (instead of Na+ and Cl- NH4+ and Cl-) to maintain SID

Begins immediately but takes 2-3 days to complete since v. big volumes.

Diuretics -> alkalosis because of chloride loss

• NIV Jolliet

25% of IPPV on PSV have assynchrony
43% of non intubated on NIV have assynchrony

NIV specific problems:
- Trigger – as you increase leak -> increase auto trigger (i.e., interpreted as inspiratory leak -> delay)

- Slope of pressure wave – recommended that it be steep but if too steep -> increase leaks

- Level of pressure support
too little -> tachypnoea (increased Workload)
too much -> delayed cycling, increase iPEEP, late cycling, leak (increased Workload)

- Cycling – v. influenced by leaks (-> lengthening of pressure) (delayed cycling – could time cycle to correct)

In practice, COPD -> if too much pressure support ->iPEEP
8ml/kg Vt is reasonably good (listen for leaks)

• Limitations of NIV Kacmarek

In acute hypoxic resp failure – maybe we prolong NIV too long

Risk factors for failure:
- PF <175 after 1 hr i.e., lack of response
- Pneumonia/CAP – with caution

Acute respiratory failure –if failed (40% failed) -> 47% died
-if didn't fail (5% died)

Don't use NIV in patients with post extubation problems -> hypoxemic resp failure -> increased mortality (25% vs 14%)

When to use:

Postop resp failure
Immunosuppressed
Postop lung resection (keep PAW < 20)
CAP with caution
ALI with caution

Don't use:
Post extubation hypoxia

Trigger to say we failed:
Hypoxemia -don't worry about hypercarbia
Evaluate clinical signs (and P/F ratios) after 1-2 hrs if no change (intubate)

• APC PROWESS Ranieri
Compound production changed during trial
European drug agency mandated more trials
Lily paying for another study

• Round table on NIV
We should monitor re-intubation rate – if re-intubated (-> increase SOFA)
Brochard has a 15% rate
First high Vt (open alveoli) -> PEEP

• Age of RBCs Ince
In US they don't use leukodepleted blood -> most studies from US
(i.e., problem is the WBCs)

CPDA may not be good
RBC deformability – use "LORCA" to measure
28 day old blood -> corrects venous pO2 but not micro circulatory pO2 and decreases deformability

Fresh blood -> corrects all

Rat RBCs get older quicker then humans (7 day old in rats = 21 days in humans) – all studies use rat RBCs

RBCs in humans not effected by storage

Hypoxic RBCs donate NO and cause vasodilation
Take fresh RBCs - make them hypoxic – add nitrite-> they produce NO. If done to old RBCs – expected less NO to be produced but produced even more NO !! (unexpected finding!) since we thought the lack of NO produced by old RBCs caused no recruitment of caps.

Could excess NO be harmful? In stored RBCs, seem to form metHb (due to excess NO) when exposed to hyoxia-> no capillary resuscitation.

We can rejuvenate the RBCs with (?) in lab -> works like fresh blood.

"Give blood for microcirculation – remember old RBCs carry 30% less O2 then fresh blood – still better then nothing (ex. R/lactate)
-plus- RBCs viscous nature recruits m/circul.

Experiment on rat kidney microcircul. Get BP up to normal (or high) with fluids, no improvement in cap pO2 – give blood, and it returns to normal.
Hct <30% deleterious to capillary – even if SvO2 is normal

• ARDS Gattinoni

Steps:
History
Length of time
Ventil settings
NB low Vt is normal Vt for non ventilated
Listen all over with stethoscope -> ex inspir creps = opening and closing of alveoli

2ary ARDS
have higher abdo pressure -> increased TPP
therefore always look at the abdo – the bigger,the higher the PEEP

Measure O2 sat and venous blood (not arterial) : pH same as arterial +0.1/ pCO2 same as arterial +3-4 mmHg

U.O.

CT scan
Take to CT to see if big recruiter or not. If big recruiter, advises prone position (plus add 15 or more of PEEP esp. if big belly -> look at ScVO2 – if decreased the decreased O2 delivery (i.e., find best PEEP).

• How to recruit Gattinoni

2 trials show that 40 X 40 doesn't work

Gattinoni takes an ambu bag and stethoscope. He likes to feel while the nurse listens for the distinctive sound of alveoli opening.
If low TPP (ex. big belly), high airway pressures probably don't matter.
(i.e., you have to take into account chest wall elastance

But even low TPP but high Paw -> dangerous hemodynamic consequences (i.e., not just lungs to consider`)

Positive pressure in lungs always -> retain Na and H20 (liters) in lungs

Once intubated, you lose 30% of lung vol, therefore PEEP at once.
Opening pressure for 80% of alveoli is 10 cm H20

Accept if 10% of lung is collapsed – cost too high for the remaining 10%.

He starts with CMV for 2-3 days to give patients a rest with absolute sedation (decreases O2 consumption) yes you pay a small price but so what? After go to assisted ventilation.

Permissive g=hypercarbia – absolute pH not the problem, it's the rate i.e., body adjusts by dumping Cl- in the urine.

Tracheo in 4-5 days if predicted to be > 10 days.

• CAP Niedermann

Prior antibiotics – i.e., 3 days of antibiotics in last 6 months -> increase risk of multi resistant m/o's.

• Heart failure Peacock

Diagnosis:

ECG non diagnostic in 98%
Exam non diagnostic in 33% (S3 sensitivity 20%, specificity 95% -if present, its good, but only 1 in 5 have this)
CXR non diagnostic in 25%

• Hemodynamic bundles Jonas
UK training – used to be 7-8 years, now -> 5 years
NCEPOD – average patient waits ~ 12hrs between admission and seeing a consultant.

Decreased experience -> care bundles = "substitute for medical education"

Improve selection- CEPEX detects those who cant clear O2 debt
Periop care - individualize goal directed therapy

Postop care – DO2 targeting (speed at which you repair debt reel to morbidity / mortality).

NB. Major surgery -> increased VO2 of 40-50%

• Microcirculation DeBaker

Mandatory plasma layer – lines the blood vessel wall. The smaller diameter vessels have relatively more plasma to RBC -> decrease in Hct.

Microcirculation have different pO2s because of branch points.

Control of microcirculation = pi/8 x radius4/2 x 1/n x pressure gradient
i.e., radius is more important than pressure.

2 reasons for increased ScvO2
1) hibernating mitochondria
2) heterogeneity of microvascular flow

No link between achievement of Rivers goals and microvascular recovery (in press).
i.e., you need to resuscitate the microvascular circulation and not just the BP.

• Pugin 40% of patients with fulminant pneumonia do not have fever.

• PCT Beat Muller

allows you to safely reduce antibiotics by 50%

" A fool with a tool, is still a fool"

ROC curve for diagnosing severe sepsis, clinician ~ CRP, PCT is better then either..

"antibiotic resistance is not the fault of the ICU, but the fault of primary care use."

PCT-better tool for diagnosis of COPD recrudescence cf. to Antonsen's clinical criteria (increase cough/ green sputum).

The more severe the illness, the less likely you are to need PCT, to make diagnosis but the more to decide when to stop antibiotics.

PCT after endotoxin,it rises v.quickly. Much more quickly then CRP (but CRP stays up longer). PCT rises at same rate as cytokines.
• Impact of tight glucose control on cerebral glucose metabolism.

Tight control -> "local hypoglycemia and increased local lactate -> increased mortality even without systemic hypoglycemia – (co-authored by Peter LeRoux)

• Polytrauma Kaplan
Pan scans – i.e., stem to stern scans now take 7 secs!
Don't need pelvic film nor C-Spine if CT.
Blunt aortic trauma – get rid of aortography -> TEE or CT chest +/- contrast
(more stents, more wait and see before op).

• CPR Nolan
2008
survival to discharge=7.9% (incidence 56/100,000)
bystander CPR=30%
Vt/Vf is decreasing -23% PEA=20%, asystole 40% (60% total)
40% of cardiac arrests admitted to ICU will survive to hospital discharge.
Arizona protocol – 200 compressions before assessing rhythm and shocking -> much better outcomes (esp in VF).

Mechanical device – "autopulse"-backboard and wrap around chest that pumps.
"LUCAS" active comression/decompression

Major change in protocol – going away from 3 stacked shocks -> 1 shock. Keep pre-shock pause -> less then 10 sec (longer pause -> less chance of successful defib.)

New Norweigen study suggests adrenaline doesn't help.
"FEER" –focused ECHO during CPR to detect reversible causes (PE/hypovol) use a sub xiphoid view.

Post resusc phase:
Hypothermia
Early coronary re-perfusion (as important as hypothermia!)
IABP
Inotropes – dobut/ nor – if reverible dysfunction
Anti-arrht/pacemaker – control seizures

Consider post cardiac arrest centers (cf. trauma centers).

• Hepato-renal syndrome
SBP and cirrhosis
Give 1.5 gm.kg albumin -> then 1 gm/kg at 48 hrs
Aggressively search for infection – culture ascites, etc,.
H-R syndrome – only after excluding all the other causes of renal damage (NSAIDS, proteinuria, hypovol, etc,.)

Vasoconstrictor and albumin – reverses splanchnic vasodilation and fall in RBF. Doesn't recommend Renal replacement therapy early on.

TIPS contraindicated in late, decompensated severe liver failure.

Vasoconstrictors: (goal is a decrease in creatinine)
Terlipressin (best)
Noradrenaline
Octreotide

• Renal failure and sepsis Kellum

65% of critically ill in the ICU – get AK injury
Casts are poorly prdictive of ATN (you need a biopsy – which we rarely do).

There is a family in US with congenitally v. low albumin – they live to a ripe old age!

• Frusemide and ARF

Pro:
Increase in tubular flow-> washout casts
No decrease RBF
Decrease O2 demand by 20% by decreasing Na reabsorption (but unlikely to be important. We would see ARF on Everest if kidney were so senstive to hyoxia.

Con:
No relief of tubular obstruction
Excess preload reduction
No improvement of RBF (RAAS)
ANP -> diuresis but no decrease in Na reabsorption – no decrease O2 demand
Mannitol -> diuresis but increase in Na reabsorption – increase O2 demand
(meta analysis – no use in aortic surgery)

Diuretics only for fluid balance, not to increase UO (you lose a good diagnostic tool). No evidence it helps to:
Avoid ARF, avoid RRT, shorten RRT

• Stewart approach to acid base

H+ depends on:
- pCO2 (not bicarbonate – a dependant variable)
- SID
-A tot (esp albumin…a weak acid, therefore in hypoalbuminemia, there is an increase in base excess).

Based on physico-chemical properties…is more mechanistic.
Why use it?
Ex. Metabolic alkalosis associated with a decreased albumin
Ex. mechanism of hyperchloremic acidosis
-has refined detecting unmeasured ions where traditional calculations of anion gap needs correction for albumin

• CPR training Pepe

1 in 5 in community die from sudden death (average age is 62)
- very reverible

survival drops to 0 by 5 min without CPR
survival drops to 0 by 15 min with CPR

Seattle – 1970s all school children learned CPR. If v. rapid – 70% can survive (teach your spouse)

Kouwenhoven in 1960 – started CPR with chest compression only Most in OR, most survived.
In dogs with chest compression only, can keep alive 30 min.

Today, 20% only will get bystander CPR.

Heart O2 delivery same if you breath or not.
40% gasp, CPR -> oscillatory ventilation.

Survival	Compression only	compression+ breath	No CPR
	15%	16%	6%

Rescue breathing not necessary for 7 min.

• CPR and airway Nolan

~ 30% regurgitated
gastro-oesoph pressure barrier drops from 30 -> 5

oesoph intubation ~ 4-7% -> 100% fatal

anesth residents need 60 intubations to be deemed profficient
75% of paramedics do 1 /yr!
ETT – no change in survival
Guedel and O2 via mask seems very good.

• Vasopressin in trauma

Small dose Nr + fluids -> best survival (high dose nor very poor).
Causes an increased stressed vol. -> limits coagulopathy with increased fluid administration.

Keep BP ~ 80-90

Use nor ~ 0.1 mcg/kg/min only if fluid alone (1-1.5 l doesn't work)

BP : No brain injury -> SAP 80-90
With brain injury -> SAP 120 (controversial, LUND found no outcome difference if MAP 45-50).

Noradrenaline

Dose (mcg/kg/min)	0.05	0.1		2.0
Receptor	Beta 1		alpha 1	
Action	inotropy	decrease venous cap		No decrease CO

• Damage control
Originally a naval term applied to damaged ships
Harlan Stone = truncated laparotomy
Rotondo- 1993 J. Trauma best evidence
Keep operation < 2 hrs

Techniques;
Vascular – ligation/shunting (good to excellent results in military)
GI – oversaw/staple resection without anastomosis
Decompress abdomen – decreased pCO2, decreased intracranial pressure
FFP: RBCs (1:1)

Abdo packs -> increased WBC respiratory burst + WBC activation -> MOF (later).
-Ureter/bladder – repair rapidly
Early EN) feed -> decreased pneumonia (use N-J tube. Percut tubes -> entero-cutaneous fistula).

Most abdo ops now done in ICU.

• Liver trauma Wendon

Grade severity by CT
If CPB clipped during lap chole. -> fever/free fluid -> be aggressively diagnostic
Treat with hepatico-jejeunostomy

No liver biopsy if INR < 1.5 platelets <76

Use TEG rather then routine tests – which underestimate coagulation factors needed.

Pregnancy – think of liver hematoma, not just PE

CT angio – lap + packing (around liver – not into liver. Control venous bleeding
Selective emboliz. (micro coils) but cause hepatic necrosis post emboliz. (esp. gall bladder necrosis) supplied by R hepatic artery.

Bile duct injury -> ERCP – stent sphincter of Oddi – if no ileus! If ileus, (increased pressure, therefore wont drain) -> naso-biliary tube (i.e., must drain into low pressure system).

If no embol. -> repeat CT after 1 week looking for pseudo aneurysm.

• Spinal cord trauma
3% of trauma
50% cervical (most C1-2 high, or C6-7 low).
HALO best or full backboard
CT better then Cerv XR
Injured area loses autoregulation-i.e., BP dependant
Steroids- benefit (Bracken study) refuted after re-analysis of data (in fact may be harmful).

• Lessons from combat Pepe
Tourniquet (C.A.T. =Combat Application Tourniquet) on 15 min – 2 hr…no resulting amputation

Topical products
Quick clot – expensive
Haemocon = chitosan ~$100 a pop, decrease concentration -> cheaper, and generates less heat.

Golden hour box = keeps cool for 3 days (FFP + 2 units RBCs)

Ratio: FFP: RBC	Mortality
1:8	67%
1:3	35%
1:1	19%
2:1	under investigation

PYNG=interosseous devive -> sternum
EZ-IO=tibia (drill, hand applied)
Can use : tibia, humeral head, sternum
ER teams in Texas use instead of IV.

• VASST study Whalley

No difference in mortality in severe sepsis (i.e. vasopressin)
Most difference in mortality in less severe sepsis, seen on day 10 in Kaplan-Meier curve.

Vasopressin vs noradr – decreased progression to ARF + RRT by 2X
Vasopressin – less constriction of afferent glomerular arteriol cf.to nor
more constriction of efferent glomerular arteriol cf.to nor

vasopressin + steroids may be most beneficial
higher vasopressor levels if steroids
v. low vasopressor levels if noradr

Use it early – not as a rescue treatment.

Notes from Brussels 2010

• Gattinoni

More severe ARDS is inflammatory, less atalectatic, is more recruitable. Therefore use higher PEEP (ex. +15) and prone (which doesn't work in milder forms).

Evolution of ARDS
12-15 ml/kg – advised in NEJM in the 1970's
ECMO – rest "baby lung" (Gattinoni, Lancet 1980's)
Permissive hypercapnia
Low tidal volumes (ARDSNet)

Future-> we should measure TPPressure – ex. H1N1, mainly obese, pregnant..30 cmH20 may not be enough inflation pressure as TPP high.

Proning stiffens the chest wall-> redistributing ventilation from good to badly ventilated regions.

• Roncho – AKInjury has strong implications for prognosis, you don't need failure.

• Dellinger – Thrombolysis in PE
Indictions:
Persistent hypotension
Persistent hyoxemia (severe)

New guidelines from last year are much more prudent re. thrombolysis since high risk of intracranial bleed. Debat whether to use if RVDysfunction but no hypotension. Maybe mechanical disruption in cath lab is best but little evidence either way.

• PE – Evans

Clot lasts >72 hrs at least
Only 1/3rd normalise at 30 days.

Pregnancy U/S first line

D-dimer – high sensitive, low specificity if pre test probability is likely, no point in doing the test.

Post op d-dimer is not useful

V/Q is fraction of the radiation cf to CT.

• VAP – Chastre

oral chlorhexidine – we need more RCT.

SDD – confirmed in the literature to decrease the VAP and mortality only technique that is confirmed in the literature, but increase in resistance including digestive m/os.
But after stopping→ rebound in digestive tract.

• H1N1 round table

ECMO – 50 – 50 re need for ECMO - need more RCTs.

Use < 7 days because if used later, the outcomes are very poor.

Steroids - some patients in an anti inflammatory state, some pro-inflammatory, not enough data. Consider statins.

Young patients tolerate S02 of 80% - ie permissive hypoxemia (but we don't know if long term IQ is affected).

Many had pneumothoraces despite low pressures. Many were very compliant.

• Canneson

One reason that static measures don't work, is that the Starling curve is pump dependant – i.e., you may be on the flat part of the curve (ex. heart failure).

CVP is needed for calculating perfusion pressure of organs as well as telling you the back pressure (therefore keep <12).

PPV tells you if fluid responsive, i.e., (preload dependant) not if output is adequate (ex preload independent).

PPV may be inaccurate in RVF.

• Pearse

Increase in FiO2 often dramatically improves the ScV02 ("why?").

Don't forget the venous saturation will depend on the position of the O2 saturation curve (ex. pH, pCO2).

Use low dose dobutamine for postop optimisation – i.e.,
< 1 mcg/kg/min. This improves microcirculatory flow cf. to just fluid.

• Kacmarek

Recruitment only works in early ARDS.

Once recruited use a decreasing PEEP trial – looking for optimal P/F and compliance (if using compliance add +2 to the PEEP at optimal compliance – why?).

Don't disconnect→derecruitment (Andy was right!)

Occassionally you need to recruit with pressures up to 50. Gattinoni says that it might rarely raise pO2 but you only recruit ~2% of atalectatic lung.

• Ince
Shear stress important in microcirculation recruitment by increasing NO.
Glycocalyx like a gel. It occupies 20-30% of intravascular volume.

James-"no science to support volume limitation with voluven."

Hyperoncotic colloid (ex. 20% albumin) increases risk of renal injury.

FFP causes much more TRALI then RBCs.
Hyperchloremic acidosis→ decreased RBC deformability. For microcirculatory recruitment, the Hct should be above 30. Beware of too much hemodilution (see SDF slide after CPB).

RBCs are larger then capillaries therefore they must deform.

Glycocalyx protected by steroids and HES. It is damaged by oxidative stress, hyperglycemia, etc., this is where adhesion molecules act.

4-5 mmHg difference between the capillary and the mitochondria. (Protoporhrin IX quenching was used to measure mitochondrial p02.

RBCs
Rat's RBCs age is 2X faster then humans.
Europe transfusion of WBC containing blood is outlawed. Hebert's study used blood containing WBCs and citrate (a poor additive).

Transfused RBCs carry ~30% less 02 but infintely better then clear solution because they -> increased viscosity->increase sheer forces->recruit capillaries->decrease diffusion distance->decrease local tissue hypoxia.

If capillaries unrecruited, blood will be shunted . Therefore not fully offloading of 02-> higher 02 saturation returning to the heart.

In ICU we take ~ 50 ml blood /day

• Gattinoni

Prone and ARDS. Only useful in severe ARDS i.e., P/F <140. Keep prone for 20 hrs/day for ~ 6 days. “Real” ARDS- low P?F, low compliance, recruitable – i.e., inflammatory oedema, not just atalectasis.

Results of proning diluted with mild ARDS where little benefit.

• Dellinger

inhaled NO in ARDS – it attracts blood flow to ventilated units (i.e., it lifts vasoconstriction) but little difference in outcome.

Titrate daily.

Prostatacylcin may be cheaper.

• Mechanical ventilation in H1N1

pressure control ventilation did not work well.
Pressure regulated volume control (pressure controlled, volume guaranteed) better.

HFO- = sub dead space
Higher PEEP
Lower plateau pressure with higher mean pressures
Lower the frequency, the higher the pCO2 elimination.

ECMO – 11% of ANZAC patients with H1N1 needed ECMO.

For alveolar capillary leak, some try beta agonists (or human growth hormone).

• Pinsky
Early identification of patients outside the ICU
Prof. Tarrasenko at Oxford university used mathematical models to set up a “biosign” neural network using complex systems looking for patterns of changing parameters → danger. Derive an integrated “Biosignal”. The biosign alerted team 6.3 hrs Before MET criteria were met. Cut off of BSI number is 3 (i.e., call a code if greater).

In spontaneous ventilation, look for a drop in CVP >=2 cm.
They are fluid responsive.

Pulsus paradoxus = increase in respiration->decrease in CVP->increase venous return (see venous return curve)->increase rt ventricular volume-> interdependence-> decreased LV compliance->decrease stroke volume out of LV (ex. in asthma)

Kussmaul-increase CVP on respiration- the opposite to fluid responsiveness-> decrease CVP (ex. cor pulmonale).

One cant predict fluid responsiveness by looking at the size of the heart (small may be non responsive; big may be). Therefore echo not very good – also depends on compliance.

• Michard
SPV- but 1.3rd due to diastolic pressure variation.
SPV and PPV are surrogates for SVV

Brain dead organ donors who are optimised re. fluids (ex. SVV) have a greater number of useful organs.

New software removes the problem of most arrhythmias (not AF) by cutting out the ectopic beat and replacing it.

Definition of fluid responsiveness = increase of CO by 15%.

Pumps give 999ml/hr

Use a CVP increase of 2cm H20, to guarantee that enough fluid hs been given to then go and assess fluid responsiveness using dynamic parameters, i.e., has the rt atrium been stretched enough. He does not rely on the `cvp to see if fluid responsive, only if enough fluid has been given to then go on to further assess, i.e., it is a pre-requisite.

• Angus

Only well proven effect of ICU on mortality is the ICNARC study showing withdrawal (i.e., removing) ICU at night → increased mortality.

• O Brien

When not to admit the cirrhotic patient

For ICU:
Variceal bleed
Sepsis
Encephalopathy
Renal failure
Post op
Bridge for transplant

>35% of total ICU costs for cirrhotics is for non survivors.

Very poor prognosis:
Sepsis
Organ failure kidney failure

Variceal bleed-definetly admit. Intubate in ITU ~12-15% die.
Alcoholic aetiology makes no difference (ex. cf. to viral hepatitis).

SOFA a good predictor (better then APACHE which is poor for liver patients – underestimates).

Post surgery- outcome relative to severity.Pneumonia most common problem.

Those that survive ITU and do not go onto transplant, quality of life poor.

Admit but do not escalate:
Sepsis
Need inotropes (v. poor prognosis).

Don't admit:
MOF
Esp renal replacement – only if bridge to tx
Advanced liver disease

• Julia Wendon
Bleeding varices

Liver offers variable resistance despite fibrosis
HVPG >10 mmHg (=hepatic vein to portal gradient)
Always look for non-cirrhotic cause – eg. portal vein thrombosis
Banding is the treatment of choice.

Always intubate before endoscopy****

Give terlipressin early (in France given by SAMU).
25% re-bleed, therefore start on beta blocker early.
Terlipressin as good as octreotide. Keep terlipressin on for 48 hrs after banding.

Sepsis-> increase cytokines-> hepato sinusoides constrict-> increase portal pressure->bleed. Therefore give antibiotic prophylaxis. Give Ceftriaxone as more resistance to norfloxacin is being seen.

Try to endoscope within 15 hrs.
Good beta blocker is carvidalol (recent data).

If Child C – you should do a TIP shunt after endoscopy – v poor prognosis.

Sengstaken- potentially life saving but can be very dangerous. Always intubate and ventilate. Leave in no more then 24 hrs.

Gastric varices – very difficult to treat. Glue probably best (also consider TIPS) but you cant extrapolate above considerations for oesophageal varices to gastric varices as the studies excluded gastric varices.

TIPS- keep an eye on the CVP, if too high, TIPS wont work.

NB>

Metabolic syndrome-> fatty liver-very susceptible to oxidative stress or ischemic injury. We fill-> increase RAP-> makes things worse from back pressure -> liver blood stasis.

• Teboul
Passive leg raising gives an increase CO if responder, but need to use continuous CO measure.
Occluded PEEP for 15 sec also predicts fluid responsiveness.

• Malbrain
IAP – 50% of IAP is transmitted to the thorax, therefore influences cardiac transmural pressure.

• Mythen
On summit of Everest, some had a p02 of ~ 20mmHg, but no renal failure-i.e., what hits the kidney? Many animal models called hypoxic renal damage, but with p02 well above this, therefore differentiate acute from chronic hypoxia when looking at models.

• Azoulay
Haematological malignancy and lung injury in ICU

Diagnosis of lung injury:
Induced sputum-look for pneumocystis (also PCR-good negative predictive value)
Nasopharyngeal swabs-for virus
CT-look for lymphocytic infiltration
Antigen in urine-esp for legionella
BAL-occ. Esp if suspected pneumocytis

Invasive aspergillosis-if decreased WBCs for a long time.

No case for NIV if severly hypoxic (ex. pneumocystis)
Mortality was 100%, now 40%!

• Mirski
Tracheostomy

Previous tracheostomy is not a contraindication
Many are doing PEG at same time.
In some countries, they do a cervical-pharyngostomy fro feeding tube placement-very superficial and easy.

• Always drain parapneumonic effusions “before the sunsets” …risk of developing an empyema is high.

To determine if you need to drain a pneumothorax, 2 cm distance from lung wall to chest…no longer speak in terms of %.

Site of tube is more important then the size (14-16 F is usually OK, less pain).

If pleural effusion, get all the fluid out. At John Hopkins, they drain up to 6 l but measure pleural pressure to be sure they don’t create a great vacuum ->neg. pressure plumonary oedema (which they feel is over stated), i.e., its not the volume drained but the negative pressure.

If loculated,-> put finger in to break down the loculations.

• ARDSNet
early on the, the compliance and P/F ratio are better using a high tidal volume, but more died. Therefore one may have to live with lower parameters to stop later damaging the lungs by over inflation.

APRV is like old fashioned long I:E ratio, i.e., hold in inspirationwith short expiratory breaks-can breath during, therefore comfortable.

HFO=CPAP with a “wiggle”. OK in some hands, but a steep learning curve. Therefore not for everyone.

ECMO-like Leicester, Michigan trial showed many were transferred but stayed on conventional ventilation.

H1N1-difficult to recruit.

How long do you leave HFO/ECMO-wait til the Fi02=.5 and PEEP=<15 then ->APRV->conventional ventilation

C02 removal vs. ECMO-don’t worry about increase C02..it may downregulate cytokine system.

• Marini-

None of the studies of plateau pressure looked at trans pulmonary pressure
Even if you do measure it, it is heterogenous.

Stress = unit of force/unit of area – TPP is a unit of stress
Marini criticises esophageal balloon:
-it gives the pressure in only one area
-intrapleural pressure is not exactly the same as the interstitial pressure, i.e., the pressure surrounding the alveolus.

The esophageal balloon measures the mean changes (not absolute value), The interstial prssure is different and it is what counts. Also patient position changes the value of the esophageal balloon pressure.

APRV=BIPAP+spontaneous breathing in terms of benefits.

• Gattinoni

Balance R/lactate has an SID of ~ 19 but has to to maintain electrochemical neutrality ("otherwise it is a battery")
Lactate is metabolised – if not (liver problems)-> lactic acidosis.

• Lipman
Antibiotics

We are grossly underdosing. Ex. amikacin is 15mg/kg, it should be much higher.
Vancomycin has poor lung penetration, therfore either increase vanco dose and add rifamycin; or use linezolid.

Linezolid-> drop in WBCs after 1 week.
Teicoplanin-can be used as a bolus if no time for vancomycin.
Give cephalosporins by continuous infusion – or at least shorten the interval.

If antibiotics given for too long, -> always increase resistant m/os in gut.
Staph aureus (not albus) v. sticky, therefore use longer duration if blood stream infection. Lipman always does an echo if staph aureus seticemia looking for SBE……..

Lipman advises to look for an increased creatinine clearance (i.e., need a higher dose) by clamping the urinary catheter from midnight until 08:00 then urine, serum creatinine to calculate the creatinine clearance.

Higher creatinine clearance is not rare (often 130-150%)-> underdosing.

One dose of aminoglycosides does no harm to the kidney even if there is renal injury or old patient.

CVVH-a real pharmacokinetic mess, we don't know what to do.

Reduce duration of antibiotic but only if you have source control.
(ex. use long duration if mediastinitis, SBE, etc,. i.e., where you don't have source control.)

• Propensity score is used to remove bias in observational studies.

CCf-first see if fluid retention – often in pul oedema..they may be normo or hypovolemic! Despite a very wet CXR.

• Body tries to limit uptake of Fe if infection, i.e., to discourage bacterial growth. Some say Fe supplementation contraindicated if infection.

Brussels 2014

Candida -higher baseline TNF but less increase of TNF if stimulated (i.e., immunosuppressed)

Mervyn- Increased PCT in all forms of inflammation, not just bacterial.

ALung CO_2 removal uses 15.5 F catheter (VasCath uses 13-14 F)

Hunt If sitting for 90 minutes, you decrease blood flow in the popiliteal veins by 50%

Marshall – Abdo pack – leave 24-48 hrs
At 4 days, colonized
At 72 hrs- fibrin deposit leads to bleeding on removal
He uses Factor VIIa in “heroic cases” (can be occ. Life saving but difficult to show in RCTs)

Kacmarek
iPEEP in COPD. To trigger, patient needs to drop Paw a lot, causing an increased WOB, therefore add some PEEP.
In patient-ventil asynchrony, often best to **drop** assistance.
Consider Po.1-therefore it takes 150-250 mSec for brain to realize asynchrony, so why does it matter..J. Marini

Look at flow to see asynchrony of effort

Kacmarek- APRV – CPAP of +30 and oesophageal pressure of -5 to -15 leads to a TPP of 35-45.

Liver clears lactate at ~ 1 L/min that’s why only high dose CVVH will drop lactate. i.e., CVVH not very important cf. to liver.

Pancreatitis-necrosis gets infected in 2-3 weeks, therefore do not do a FNA before 2 weeks.
EVERESt trial of H2O removal in CCF showed it’ s Na+ removal that counts, not H20 removal.

ISICEM 2016 - Best of Brussels

• Remote ischaemic preconditioning
only works in high risk
Propofol negates effect (so look for this in studies)

• Kellum – saline -> increase Na to distal tubule -> increase glomerular tubule feedback -> decrease GFR
Frusemide stress test – negative after give low dose frusemide (1.0 - -1.5 mg/kg -> 100ml UO/hr) to oliguric patient = tubule cells are injured.

• Timsit – Previous use of antibiotics -> 10X risk of MDRs.
"mutant prevention concentration" = 8-32 X MIC -> decrease risk of MDRs.
Give loading dose of antibiotics 1-2 hrs before continuous infusion.
You need the MIC, ex. if strep.pyogenes has an MIC of 0.1, any dose will do; if pseudo. MRSA, etc, MIC 4-8, the dosing is very important.

Jean Carlet showed :
inadequate antibiotics and no source control = 100% deaths
adequate antibiotics and no source control = 90% deaths

Infection severity does not equate with resistance (ex. strep pneumonia).
98% negative predictive value if MRSA nasal PCR is negative in pneumonia or soft tissue infection.

• Mervyn – Kumars paper. 585 patients excluded (given antibiotics before onset of shock -> 5.5% died which is higher then those given after a few hours delay once shock has set in!

Bloos showed that source control is the only factor associated with death if delayed > 6hrs (increase of 2.5X). Most studies looking at timing of antibiotics did not look at the timing of source control.

• Coopersmith – Future of ITU
Florence Nightingale arguably created the first ITU by cohorting patients next to the nurses station.
Surviving sepsis compliance was 15-25% only. But strongly associated with mortality. Compliant death rate = 30%, non compliant = 40% death.
In US only 33% of patients cared for by a trained intensivist, therefore telemedicine may be the answer, or physician assistants/nurse practitioners (they already place 70% of CVCs, chest tubes, etc in Coopersmiths ITU). They care for 90% (heavily protocolised), he takes care of the 10% sickest.

Adaptive trials compare cancer trials, where they characterise by stage, Herceptin receptor, genotype, etc. We just say “sepsis”. Cancerlogists laugh at us.We should be looking at “omics” (genomics, proteomics, etc).
Microbiome- 100 trillion microorganisms in gut. Increased diverse of microbiome -> increase 3 yr survival on bone marrow transplant patients. In ITU we decrease microbiome diversity. Low gut phosphate -> increased virulence of microbiome (? Give phosphate in gut in future?).
Anti PD1 immunotherapy (used to treat Jimmy Carter’s melanoma)success depends on the make up of the microbiome.

• Hopkins – post ITU neuro imaging
Susceptibility MRI-you can see punctate haemorrhages that are not seen on CT, esp if hypoxia (ex. ARDS), esp in basal ganglia and hypocampus and temporal lobes. 5% healthy older people have white matter lesions, which is much increased in post ITU. Also see lots of cerebral atrophy (look at lateral ventricles), these progress over years. Higher procalcitonin (>2) -> increased hippocampal atrophy post ITU. Quantitative MRI-=”Free surfer”. The longer the delirium in ITU = increased atrophy post ITU also decreased white matter connectivity, all leading to decreased cognitive function.

• 20% Albumin is salt poor. Different manufacturers produce v different albumin compositions.

• Difficult intubation in ITU
Obese – in OR 2-3% are difficult; in ITU = 40-60%.

Tracheostomy in Europe survey performed between 15-21 days.
Use of fibreoptic (bet 3.6 or 5.0 Fr) increases Paw. 1 year mortality of trachea patients in Italy was 80%! With very poor quality of life.

When and how to decannulate a tracheo – very little evidence.
Tube capping trial > 24 hrs.

Diaphragmatic atrophy is linear and seen histologically from from day 1

Oscilliate trials used lots of sedation (benzos and NMBs).

• Hall – “applying the protocol at the bedside is the art of EBM.”
After Leuven 1, there was lots of adoption of tight glucose control, after NICE Sugar there was not de-adoption, just a slowing of the rise in adoption.

40-45% of studies later shown to be wrong.

ITU trials : 56% not yet reproduced; 26% have not been reproducible when tried.

• ITU study of duration of ward round in Canada found a mean time of 15 minutes / patient.

• Mebazaa – COPD and RV Function

Avoid hypotension, even in the absence of CAD, a low BP will decrease coronary artery flow and further impair RVF.

Increased pl. proteins during weaning is due to weaning induced pulmonary oedema. COPD exacerbations very frequently (30%) associated with heart failure and CVD.

Copeptin is a very good acute and transient marker of stress. It is increasingly used in the ER with troponin to rule out MI.
Exacerbated COPD on a ventilator use antibiotics v Pseudomonas (esp if NIV failure) plus methylpred (100-200mg/day) (Brochard disagrees).

• Gattinoni – CO2 removal

You lose N2 in exchange -> atelectasis (which requires high Paw to recruit -> damage. Therefore add N2 to sweep gas. If you lower the RQ (i.e., remove too much CO2) you need to increase the FiO2. Be careful, this is not a benign technique. The anticoagulation side is potentially dangerous. Plus the physiology is complex.

• The Targeted Temperature Trial (36 degrees) kept patients at controlled temperature for 72 hrs!

• Brochard – High Flow O2 (HFO)

Mechanism-He thinks it's the flow more then the 02. Need a non-condensing circuit. Breathless patient breathes at 1L/sec (= 60L/min). We classically give 15L of 02 via a Hudson mask (1/4 of needs, therefore more airis entrained). We need 44mg/L of H20. It probably gives a CPAP of <5 cm H2O (difficult to measure – depends if mouth open or closed). The resp rate almost always drops (sometimes dramatically – ex. 2/min – we don't know why) Min volume drops with a maintained pCO2 (probably due to dead space washout)-> decrease work of breathing. NIC (CPAP) injects high flow of gas in front of patient, not into the naso-pharynx. Hi Flow -> a stable pCO2 and an increased pO2. If failed HFO, early failure (40% die); late failure (i.e., >48 hrs) ->66% die (still holds even after propensity scoring for severity.

“Florali” study (NEJM) the first study looking at intubation rate between O2 mask and NIV. It showed no difference. HFO showed better outcome cf. to Hudson mask and NIV.

If hypoxaemic and hypercapnic, use HFO with lower FiO2, but we do not know if this works.

• Angiotensin II
Needs ACE, which is located in the endothelium of lung. Therefore in severe ARDS, this is destroyed therefore ACE activity is lost -> Angiotensin insufficiency. This is need by kidney -> harm with a decreased BP. Therefore there may be a role for extraneous Angio II. (which also recruits capillaries (has an important micro vascular effect).

• Jan Bakker Vasodilators (e-mail for slides)
• De Baker
Low pO2 -> increased NO in RBCs -> vasodilation (produced from nitrites) (?SNO)

• Mervyn B Blocker and sepsis
In mouse model, beta blocker benefited the sickest but harmed the less sick. Therefore important to choose the right patient (the esmolol study used very sick patients – another good reason to risk stratify).

• NIV and pneumonia – round table

In patients with malignancy, resp. failure requiring ETT doubles mortality cf. to non malignancy patients who are intubated.

Re. CO2 removal, Brochard says wait for trials. Beware, Mebazaa showed that COPD patients admitted often die of cardio-vascular problems. Recent studies of CO2 removal shows lots of vascular complications.

• Calandra – Kumar study (time to antibiotic therapy has been refuted in numerous recent studies.

De-escalation showed a decrease in mortality in some studies.

• JL Vincent Major traumatic haemorrhage.

-Do not use Ringer lactate in TBI (is hypo-osmolal).
2 strategies in major haemorrhage :
- FFP Plasma:RBC at least 1:2. Aim for PT/PTTr <1.5.
- Fibrinogen concentrates +RBCs if Fibrinogen <1.5 – 2.0

Tranexamic acid – load 1 gm over 10 minutes followed by 1 gm over 8 hrs within 3 hrs of trauma.
Platelets keep above 50 (100 if TBI). 4-6 units or 1 thrombopheresis.
If on anti-platelet drugs, give platelets.
PCC if on Vit K antagonists or NOACs (now called DOACs = direct oral anticoagulants). Some hospitals can now measure plasma levels of DOACs, or Thrombin time or aPTT for Dabigatran.

Thromboprophylaxis within 24 hrs once bleeding stops.

When should we trigger a MHP (i.e., start thawing FFP), JLV says using lactate and clinical impression.

• Michard – Goal directed therapy
Best is probably SV optimization with fluids +/- inotropes. Beware of BP too, it is important. Therefore vasopressors if BP too low (see Sessler on influence of even short episode of periop hypotension – 6 minutes of hypotension (<55 MAP) -> 25% increase of complications.

• Reuter – looked at cardiological literature of "normal physiologic values" from Europe, Brazil, Korea -> very variable depending on sex, age, region, ethnicity). Therefore given the large variations, we must individualise goals. He described his pancreatitis in pig study, showing the harmful effects of pushing to the top of the Starling curve with maximum stroke volume. He showed in this study the damage to the glycocalyx (i.e., increased heparin sulphate) in the SVol maximised group!

• Molnar – UK anesthetic mortality <1%; in high risk group it is >10% (hidden in mass of large number of low risk cases). IPPV is a series of Valsalva manoeuvres. There is no correlation between CI and MAP.

• ScVO2 round table – V. low incidence of low ScVO2 . Venous blood vs arterial blood : difference in pH = 0.03 ; pCO2 =~3 mm Hg.
"MIA" = measure, interpret, apply.

- pCO2 gap is a surrogate for cardiac output
- pCO2 gap = PcvCO2 – PaCO2
- pCO2 gap >6 mmHg suggests a persistent shock state that may be amenable to fluid resuscitation +/- inotrope support
- a "ScvO2-cvaCO2gap-guided protocol" has been proposed by Vallet et al (2013) to guide the management of septic shock

RATIONALE

From Vallet et al (2013):

- CO_2 is the end product of aerobic metabolism
- PCO_2 in the venous blood reflects the global tissue blood flow relative to metabolic demand
- CO_2 is about 20 times more soluble than O_2 so it more reliably diffuses out of ischemic tissues into the venous effluent making it a sensitive marker of hypoperfusion
- in situations where an O_2 diffusion barrier exists (e.g. non-functional and obliterated capillaries), "masking" poor O_2 extraction (O_2ER) and increased tissue O_2 debt, CO_2 still diffuses to the venous effluent, "unmasking" the low perfusion state for the clinician when venous-to-arterial CO_2 difference is evaluated
- the gap is a marker of adequacy of venous blood flow to remove CO_2 produced rather than a marker of tissue hypoxia or dysoxia

PCO_2 GAP IN DIFFERENT SHOCK STATES

From Vallet et al (2013):

Shock type	**Lactate**	**O2ER**	**ScvO2**	**cvaCO2gap**
Cardiogenic or hypovolemic	HIGH	HIGH	LOW	HIGH
Anemic or hypoxemic	HIGH	HIGH	LOW	LOW
Distributive	HIGH	LOW	HIGH	HIGH
Cytopathic	HIGH	LOW	HIGH	LOW

EVIDENCE

- early days, mostly small proof of concept studies in humans so far

Severe sepsis and septic shock

- some authors suggest targeting a PCO_2 gap <6mmHg as an index of adequate tissue perfusion
- supported by observational data suggesting a role in identifying patients with ScvO2 >70% who are still inadequately resuscitated (Vallee et al, 2008) and predicts lactate clearance (Mesquida et al, 2015 and Mallat et al, 2014)

Lactate drops in 2 phases:
- flow dependent
-metabolic recovery; liver takes time to 'mop up' lactate. 50% of survivors had a high lactate at 24 hrs. Another cause of a low ScVO2 is micro-circulatory disturbance.

NB. Pressure support ventilation increases O2 demand by 20%.

Gattinoni – cellular hypoxia must have a base deficit, not just caused by lactate.

• Torres – See new VAP guidelines from ESICM in 2016.
Used PICO to prepare guidelines (Population, intervention, comparison, outcome)

Suggestion > 10 days antibiotics if MDRs.

• Azoulay – The 3 days ITU trial is no longer valid! (i.e., 8 days of IPPV, the mortality was the same as on admission)

Cancer and ITU – mortality was 90% -> now 45-50%. But have to admit early!

Candidaemia in cancer patients, you must remove the CVC.

• Sepsis 3

Kaukonen – great variability in definition (ex. ICD codes, etc) and control group mortality in RCTs of sepsis but trend shows a decrease mortality in all studies. Kaukonens paper showed a decrease mortality (using Bones criteria) from 35% -> 18% (SMR (APACHE II) decreased to 0.5.

• Mervyn see video www.jamasepsis.com

Big data : 90% outside ITU; of 5 million, 850,000 had sepsis ; 11% treated for infection; of these, only 4% of the 11% died (from what, we do not know); 1 in 200 of the entire population studied died in hospital. Not massive. qSOFA needs validation outside the USA. Therefore keep MEWS score (see what qSOFA adds to MEWS).

SIRS as good as qSOFA. SOFA/qSOFA will be applied retrospectively – we may pick up patients who are already sick, therefore too late, therefore keep SIRS.

Overall infection mortality studied (of the whole population of 1.3 Million EHR) 0.5%.

qSOFA and mortality
0 organs = <1%
1 organs = 2-3%
2 organs = 8%
3 organs =>20%

• Rowan

UK poor cousin re. ITU beds/population. England has fewer then Scotland, Wales Ireland.

• Finfer – Contests inclusion of lactate in septic shock. He sees patients on vasopressors but with a normal lactate. They still have (according to Finfer) septic shock.

• Derek Angus – qSOFA positive -> 10 X more likely to die irrespective of age, lactate, etc. (lactate doesn't add much). See www.qsofa.org

• Flail chest – NICE says you should use surgical fixation.

• Meningitis – a clinical diagnosis. Mortality is 20%. The most important prognostic factor is the GCS. Speed of treatment is of the essence. 1 hour delay -> a 30% increase in deaths!

CT before LP if new seizure. Debatable if decreased GCS a contraindication to LP (Swedes say no). Get antibiotics in first. Do not wait! Brain abscess ruptures in 7%. Give steroids BEFORE antibiotics or forget it. Use high dose dexamethasone (Dex 10mg every 6 hrs for 4 days) risk of rebound deterioration, therefore taper dex. Only use dex in pneumococcus (if not, stop).
Hydrocephalous in 10% (cerebral complications in 5-15%). In ITU treat as TBI. If unconscious consider ICP measurement.
For Listeria, use high dose Ampicillin (>> 2 gm). Re. LP after 5-7 days (controversial), esp if not responding. Stiff neck in only 40%,

• Chastre – Unnecessary antibiotics -> increase MIC in stable COPD patients. Only 30% of antibiotics in ITU had hard evidence of infection.

Antibiotics to treat proximal airway colonization -> increase in MDRs and superinfection.

VAP – if BAL is negative and clinically low suspicion -> stop antibiotics (Bayes approach).

Stop Vanoc/Linezolid if MRSA is not identified.
A too long course of antibiotics -> increased MDRs.

PCT in recent study (De Jong) decreased mortality.

• Abdo sepsis – 30% of septic shock are from abdominal sources. Abdominal infection has highest mortality.
Procalcitonin fails to predict treatment response (cf. LRTI).50% are surgically cured despite a persistently high PCT and vice versa.

Timing of surgery vital : < 2 hrs – all survived ; >6 hrs all died.

• Timsit – CRBSI

If CVC + and blood - -> do an U/S look for thrombosis (heart too).
Erythema is not a risk for infection, only pus and pain at CVC site.

If CVC + and blood – with Staph. Aureus (or acinetobacter/ MDR Pseudomonas) -> v. high bacteraemia later if not treated.

If CVC + and blood - - with candida = unclear. Probably another candida site, i.e., seeding.
Very debatable if we should routinely culture the tip if patient well and CVC removed (Chastre disagrees).

• CRE MDRs

High dose Tigecycline/Colistin (official dose too low), Colistin does not penetrate lung well. Aerosol is better, but the right device is a real problem (we do not know really).

High dose Meropenem plus extended infusion – use combo even if resistant.
Speaker uses 2 different carbapenems for KPC (serine based activity even if resistant (not for NMD= metallo beta lactamase activity).
Fosfomycine-never alone.

• P. Montravers – "avoid carbapenems" – Tazocin in ESBL might be OK if MIC 2-4 (20% not getting high enough levels with intermittent infusions. Therefore high dose (4 not 3 x/day) plus extended infusion plus dosing levels.

Add an aminoglycoside – v. successful except in ESBL E.Coli (75% success).

• MDR VAP - Niedermann
Tigecycline, if used needs combo plus high dose.
MRSA- prefers Linezolid.
All presenters agree on high dose plus extended infusion.

2 conflicting studies on continuous infusins (BLISS v BLING). The negative study had patients on RRT, which negates the benefit of continuous infusion.

Aerosol -> increased efficacy plus no new resistance. Many patients with MDRs are only lacking in host defences, therefore not salvageable.

If using a combo therapy, once you get susceptibility test, drop the other antibiotic (except aminoglycoside).

• Surveillance cultures (only for MDRs) = detecting MDRs that are not yet causing infections.
Risk of MDR (most important):
-length of hospital stay > 7 day
-prior antibiotics
-positive surveillance culture

Colonization preceeds infection, therefore surveillance is important.
Frequency – 2X /week (nasal/tracheal) (only 1X/week for rectal) (blood/urine only if indicated)
If pre test probability 20% ->post test probability
-> surveillance + = 70%
-> surveillance - = 8%

Invasive potential = we can have colonized lungs with Pseudomonas but rarely becomes invasive – if so long after.

Rates of appropriate antibiotic are higher if surveillance used. High rate of negative predictive value – saving antibiotic use cf. with empiric therapy. Only use latest surveillance culture. If surveillance culture is positive, do not necessarily treat (a clinical decision-ex candida in sputum) (takes 2-3 days to get back).

• Timsit ESBL colonised

Only 16% become infected, but if so, has a high mortality.
Carriage without infection -> no increase in mortality but an increased LOS and increased risk of receiving a carbapenem (by day 3 -> increased MDR in microbiota). Therefore we must reduce use of carbapenems in colonised.

Contact isolation – increased medication errors, lots of errors (see ref on slide). If not isolated -> increased colonisation -> increased LOS -> less place in ITU.

• Decontamination of surfaces – Must engage with cleaning ladies – may be afraid to touch equipment etc. Spanish in doing so have halved MDRs.

• Chastre – Anti virulence treatments

Most antibiotics were "invented" by micro organisms. Target virulence factors of m/os (ex. antibodies to type III injector system – injects toxins, Quorom sensing, etc). By doing so, we respect the guts microbiota. At present we can only target specific serotypes, ex. St aureus alpha toxin (USA 300) in both MSSA and MRSA.

• DIC Hunt –
Exercise ->increases adrenaline -> increased TPA -> fibrinolysis (increased by adrenaline, aDH and thrombin).
Plasmin -> breaksdown extracellular cement too.
Old model talked of primary and secondary fibrinolysis. In DIC, we need fibrinolysis to break down clot, therefore do **not give tranexamic acid**.
Commonest cause of DIC in world is snake bite.

Thrombomodulin in presence of TNF is endocytosed, therefore not available to activate protein C (that's why we gave activated protein C).
DIC – give FFP (20ml/kg), Fibrinogen, platelets, but not tranexamic acid nor factor VII. aPTT is prolonged, therefore if you do give a small dose of heparin (no proof) measure anti Xa.

• Coagulation in trauma – fibrinolytic shutdown -> reconsider use of tranexamic acid (see slide).

• Wendon – coagulopathy of liver disease
Factor VIII/Protein C ratio is important. Measure fibrinogen (v. important). We should give DVT prophylaxis in cirrhosis -> reduces portal vein thrombosis. Best clinical test is a decrease fibrinogen and decreased platelets (i.e., now are not in balance).

• Peter - great talk

Evidence that clinicians change practice if RRR >8-10%

• Wendon – AoCLD
Do not admit to ITU if inexorable decline, but hard to know who that is (see slides on website). Mortality in cirrhosis admitted to ITU is ~40-60% and declining, but sepsis is a killer in cirrhosis. They tend to get MDRs (18%) ex. VRE. CRP doesn't help (Liver produces CRP). Time is of the essence. Pre emptive antimicrobials improved mortality in variceal bleed.
Alcoholic hepatitis – no role for pentoxyfylline, but a role for NAC (short term).
Steroids clearly showed a benefit- if bilirubin doesn't decrease by day 7 – stop, it isn't working.

HRS – 15% survive at 3 months. But rel. rare ~ 10%.

Definition : withdraw diuretics and fill; no proteinuria nor RBCs; normal U/S. 90% are non HRS. 70% survive. Therefore -> RRt, terlipressin, albumin. Look for proteinuria-> predicts AKI-> therefore terlipressin and albumin earlier.

Acute ascites (cf chronic) -> IAH -> AKI. Therefore increase BP +/- small volume ascites (1-2 L) paracentesis. -> increase RBF (give 1 mg terlipressin X3 +/- albumin pre and post paracentesis.
Kidney clears ~ 20% ammonia, therefore in AKI -> increased ammonia -> encephalopathy. Therefore RRT and they wake up.

Normal creatinine in cirrhosis is 65, therefore look at delta creatinine. RRT also controls hyponatremia. Cerebral oedema is rare in AoCLF (cf. ALF), many have brain atrophy, therefore lots of space, but risk of intra cerebral haemorrhage, therefore look for localising signs.
Treatment of encephalopathy – ventilate; standard feed; lactulose (cleans and acidifies – but abdo distension); rifaximin (improves microbiome- but not proven in ITU patients); albumin (controversial).
Upper GI bleed – aim for Hb ~ 8 gm. Band oesophageal varices; glue for gastric varices. Always with ETT. Early TIPS if failed (X1).
Cirrhotics get pulmonary hypertension, if so, TIPS doesn't work, i.e., doesn't decrease pressure in portal vein.
To assess , use SOFA-CLIF score. Sepsis is key to prognosis.

• VAP
If VAT untreated -> 1/3rd go on to get VAP (see Martin Loeches)
How to diagnose VAP (Chastre), **3 days mechanical ventilation -> 90% have colonisation of upper airway**. Do not treat (leads to MDRs). Blind BAL usually samples RLL.

• From the Newsletters

Brochard –
more then 10% of ITU patients have ARDS
more then 25% of ventilated patients have ARDS

Driving pressure = Vt/compliance (surrogate of strain), the most powerful predictor of mortality due to VILI.

Shapiro – Fluids

Look at the study vs control group fluid administered
ARISE Δ 0.2L (4.3l vs 4.5L)
PROCESS Δ 0.7L
PROMISE Δ 0.2 L

Opal – Sepsis
5.3 million deaths world wide annually from sepsis

Niedermann- 50% of VAP is preventable (only).

Jaber – Re-intubation for ARF post-operatively pushes mortality from 0.3% to 16%.

De Wit – Detect alcohol use with CDT (carbohydrate deficient transferrin).

Maggiore – changing the HME to heated humidifier reduces the Vt from 9ml/kg to 7 ml/kg.

Herridge – Post ITU survivors have cognitive impairment (irrespective of age) equivalent to mild to moderate Alzheimers or moderate TBI.