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H1N1 Clinical and Therapeutic Aspects

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British Columbia Society of Critical Care Medicine

Garbage bag

- http://www.youtube.com/watch?v=Mu9fICUNJtU

Overview

1. Who gets severe disease
2. What does it look like
3. How do we treat it
4. For how long
5. Special populations
6. Ongoing management of pts

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CAVEAT

Risk Factors for Severe Disease

- 70% of persons hospitalized from 2009 H1N1 influenza have had a recognized high risk condition
- Risk factors;
  - Chronic illnesses (including DM)
  - Immunosuppression
  - pregnancy
  - we think obesity
  - We think 1st nations may be at increased risk
- Those over 65 have a low risk acquiring H1N1 but if acquired, have a higher risk of complications

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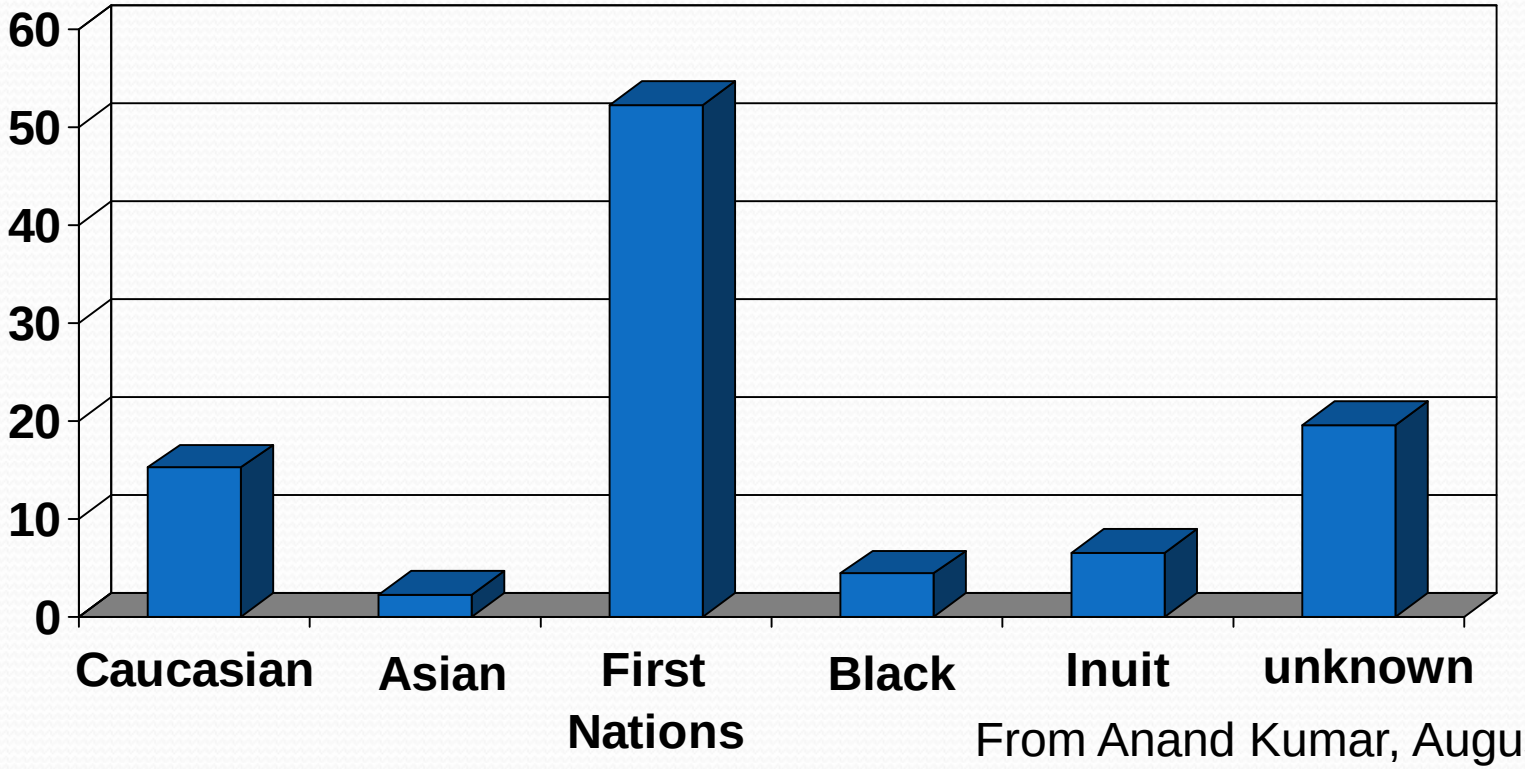
Paraphrased from CDC and WHO guidance documents

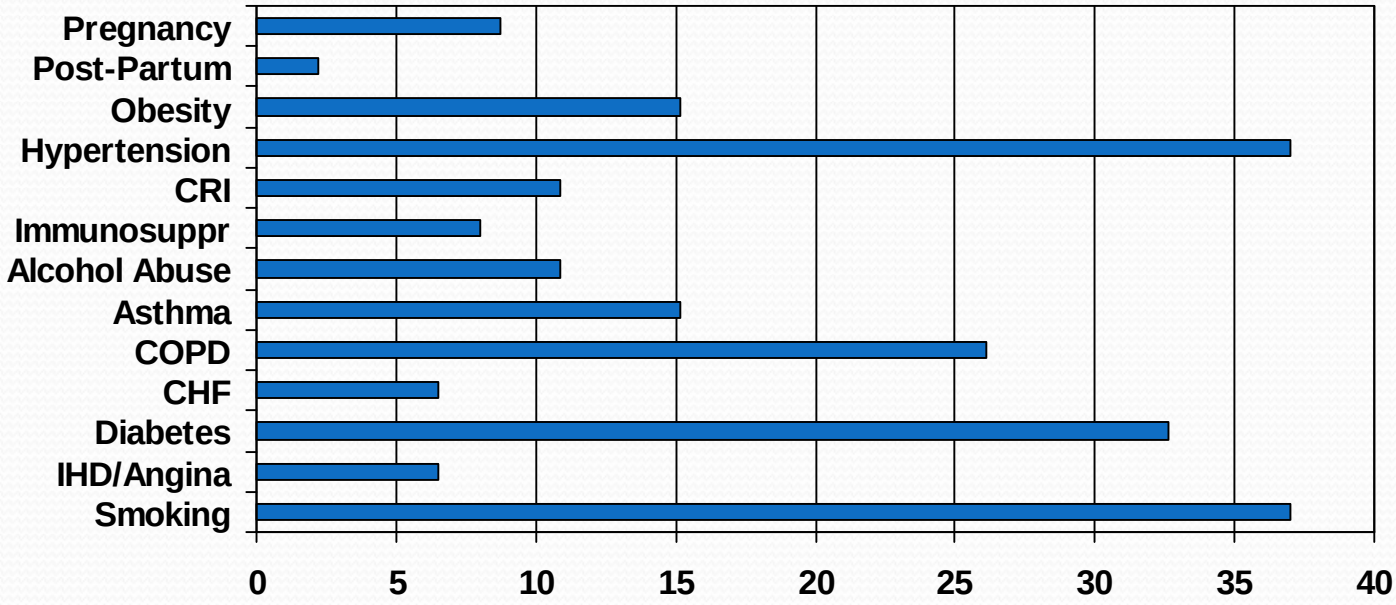
Baseline Demographics

Male	35%
Age	41.3 (29-50)
Male weight	95.7 kg
Female weight	93.2 kg



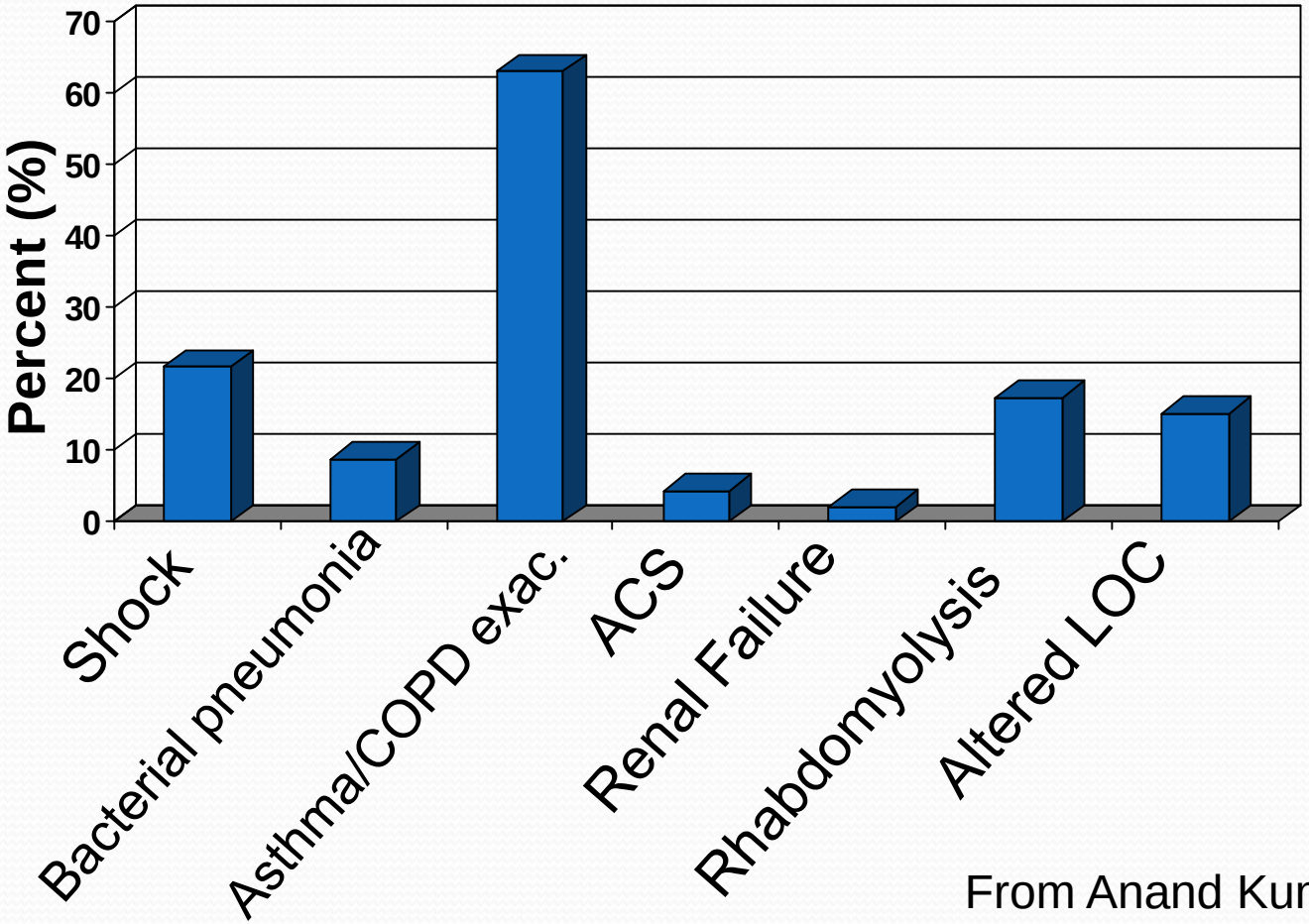
From Anand Kumar, August 09

Comorbidities



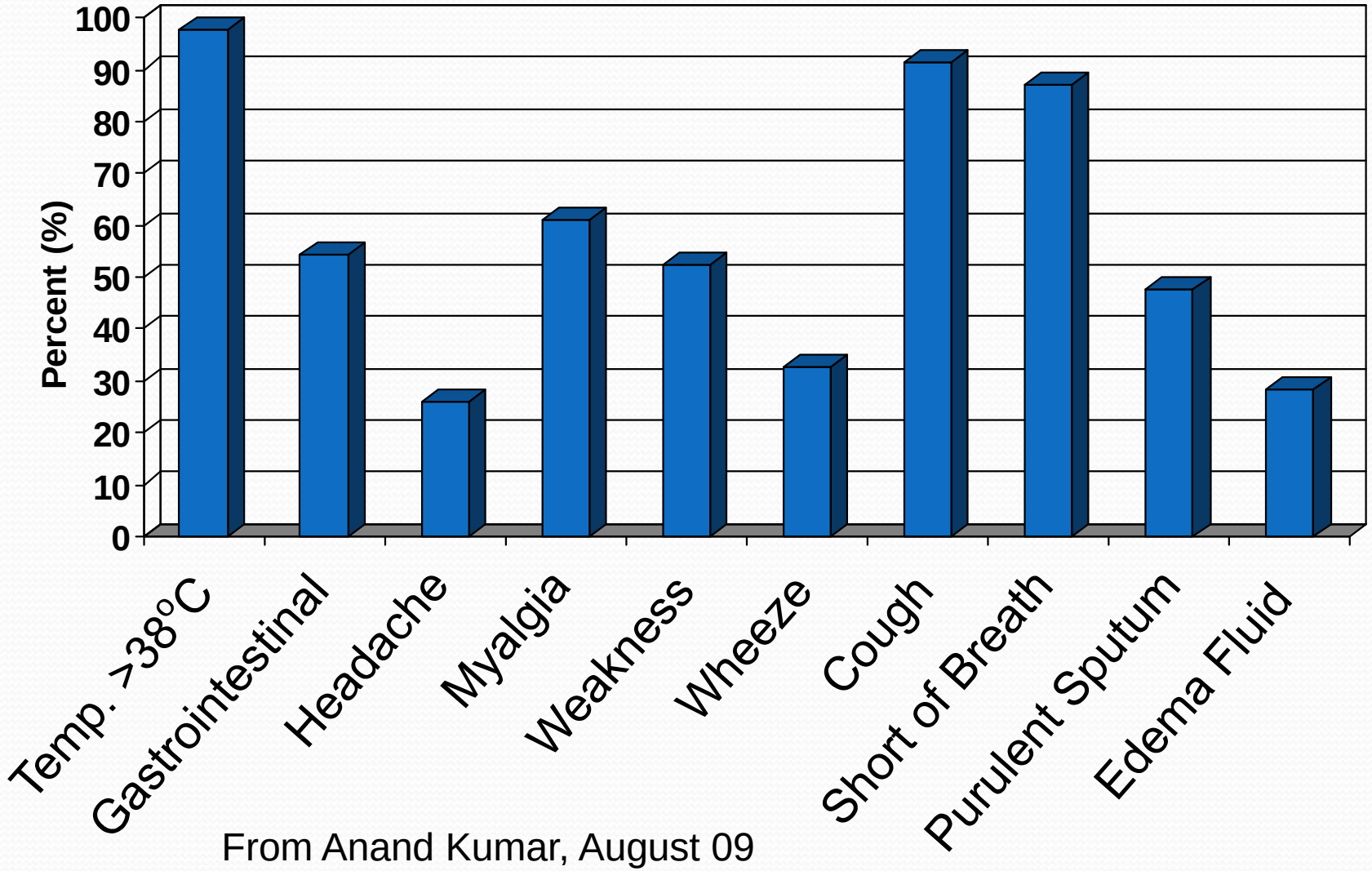
% total From Anand Kumar, August 09

Co-Presenting Illness



From Anand Kumar, August 09

Presenting Symptoms



From Anand Kumar, August 09

Progression of symptoms

Date of symptom onset to date of hospital admission	6.2 days (±7.9)
Date of hospital admission to date of ICU admission	1.2 days (±1.4)

From Anand Kumar, August 09

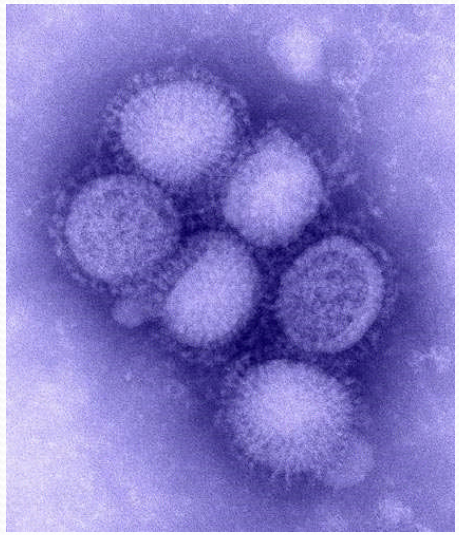
Influenza ICU Clinical Syndromes

1) Destabilization of chronic disease ie CHF, CRF, cardiopulmonary disease, coronary syndromes, diabetes –CXR variable; do well clinically

2) Severe COPD or asthma exacerbation –lasts for weeks, CXR clear

Influenza ICU Clinical Syndromes

3) Severe bacterial pneumonia complicating H1N1 infection (lobar or bronchopneumonia) –typically involve S. pneumoniae or S. aureus and may have septic shock



4) Rapidly progressive bilateral diffuse viral pneumonitis – potentially very severe with some requiring advanced ventilatory techniques.

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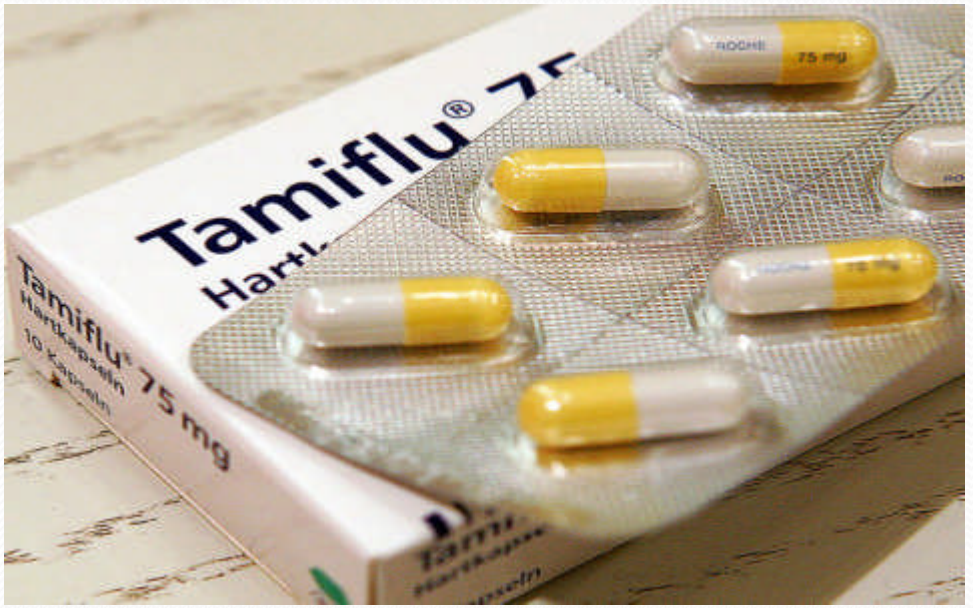
From Anand Kumar, August 09

Treatment- General

- Initiate treatment as early as possible
- In a pandemic DON'T wait for laboratory confirmation
- 1st line therapy is Oseltamivir.
- Zanamivir is the second line agent and can be difficult to administer as it is inhaled.

Treatment- Osteltamivir

- A neuramidase inhibitor
- Only available formula is oral
- Standard dose is 75mg NG BID for 5 days.



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Treatment - Dosing

- Unclear what the optimal dosing is, studies are planned.
- Many use 150mg BID as it is well tolerated.
- Early reports from the Winnipeg experience indicate that in critically ill patients adequate serum levels are obtained with 75mg NG BID.

Renal Failure and Oseltamivir dose Standard dose

Use of Oseltamivir in Patients with Renal Impairment
Amended Guidelines

Creatinine clearance	Recommended treatment dose (5 days)	Recommended prophylactic dose (10 days)
> 30 ml/min	75mg twice a day	75mg once a day
10 – 30 ml/min	75mg once a day Or 30mg twice a day	75mg every second day Or 30mg once a day
< 10 ml/min (not on dialysis)	75mg as a single dose	30mg once a week (2 doses)

Osteltamivir use in pt with Cr Cl <10 ml/min is an unlicensed use

Haemodialysis	**High-flux**	75mg three times a week after each dialysis session	75mg three times a week after each dialysis session
	Low-flux	30mg three times a week after each dialysis session	30mg three times a week after each dialysis session
Peritoneal Dialysis		30mg once a week (1 dose)	30mg once a week (2 doses)

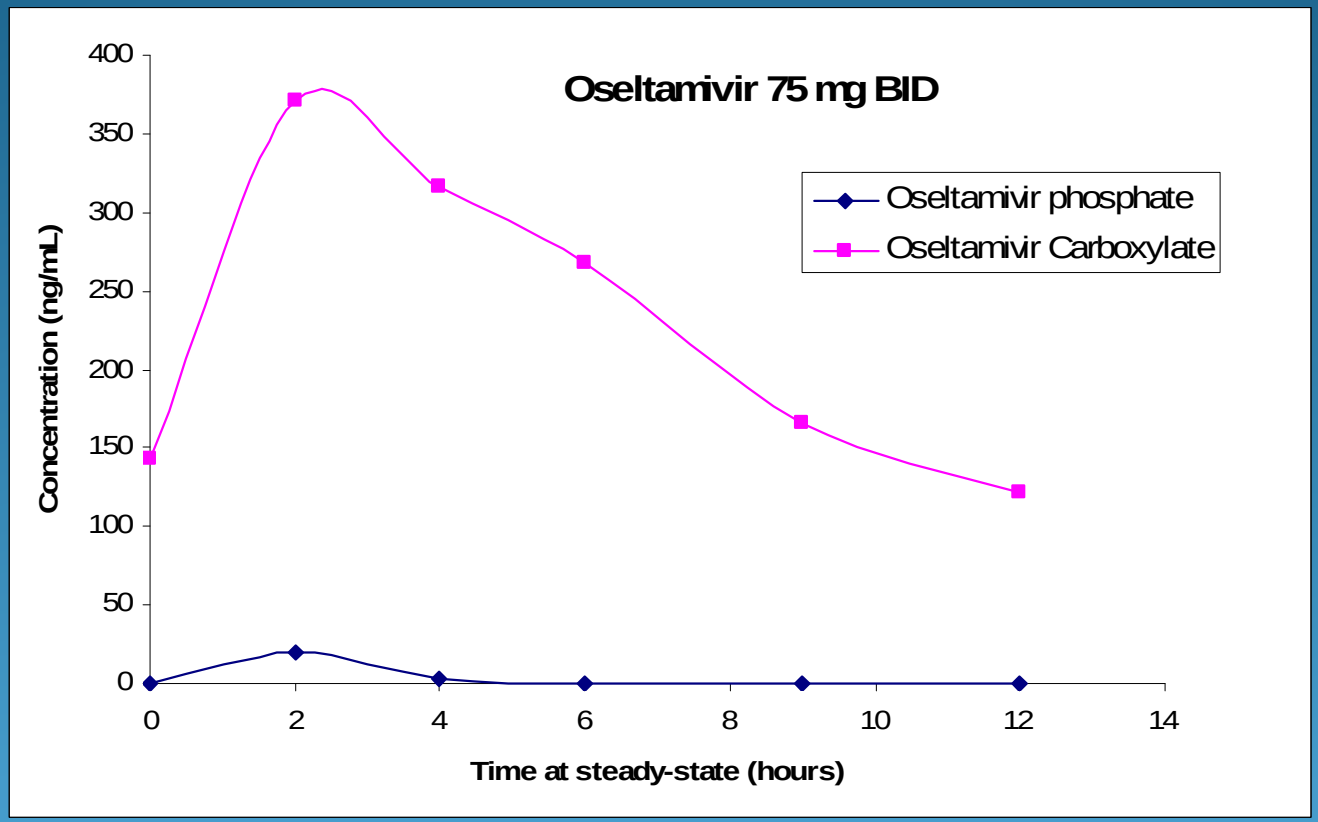
Renal Failure and Osteltamivir dose Double dose

Creatinine clearance	Recommended treatment dose (5 days)
> 30 ml/min	150mg twice a day
10 – 30 ml/min Including patients on CAVH / CVVH / CAVHD / CVVHD	75mg twice a day

From the Guidance document prepared by the
UK Renal Association Clinical Affairs Board, updated Aug3rd 2009

Patient examples:

Patient 01-017 33 yo female, 116 kg, creatinine = 34 umol/L



IC95 = 30 ng/mL

Kumar, submitted

Treatment - Duration

- Duration of treatment in critically ill patients is unclear as well.
- Standard duration of therapy is 5 days.
- There have been reports of “clinical rebound” in patients who had shown some modest improvement and worsened again after the cessation of osteltamivir at 5 days. Significance of this is unclear.
- Strong considerations needs to be given in continuing the course of therapy past the standard 5 days in critically ill patients who are slow or poorly responsive to initial osteltamivir.

Treatment - Duration

- Longer duration of therapy may be required in patients who persistently shed virus or who are immunosuppressed.

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Treatment - Resistance

- Consider osteltamivir resistance for patients who fail to respond to initial therapy.
- Particularly if they are;
  - immunocompromised,
  - have received osteltamivir prophylaxis,
  - have received a prolonged course of osteltamivir
  - or if increased osteltamivir resistance is known to be circulating in the community

Treatment - Pregnancy

- Osteltamivir is Pregnancy category C (ie no studies to assess safety)
- Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use.

Treatment – bacterial co-infections

- Bacterial co-infections with respiratory pathogens (ie CAP/HAP/VAP) may be present and appropriate antibiotics should be used empirically both initially and at the time of a clinical worsening.

- Stop empiric antibiotic therapy in a patient who is H1N1 PCR positive and microbiologically negative.

Treatment - ventilation

- Standard treatment of hypoxemic respiratory failure
  - Many pts are young and may require high doses of 2 or 3 sedatives to suppress respiratory drive
  - Variations in PEEP (high PEEP may or may not be effective)
  - ARDSnet ventilation
  - BIPAP is unlikely to be of benefit and can be an effective means of aerosolization
  - Unclear but reasonable to adopt a fluid restrictive stratgey (FACT)

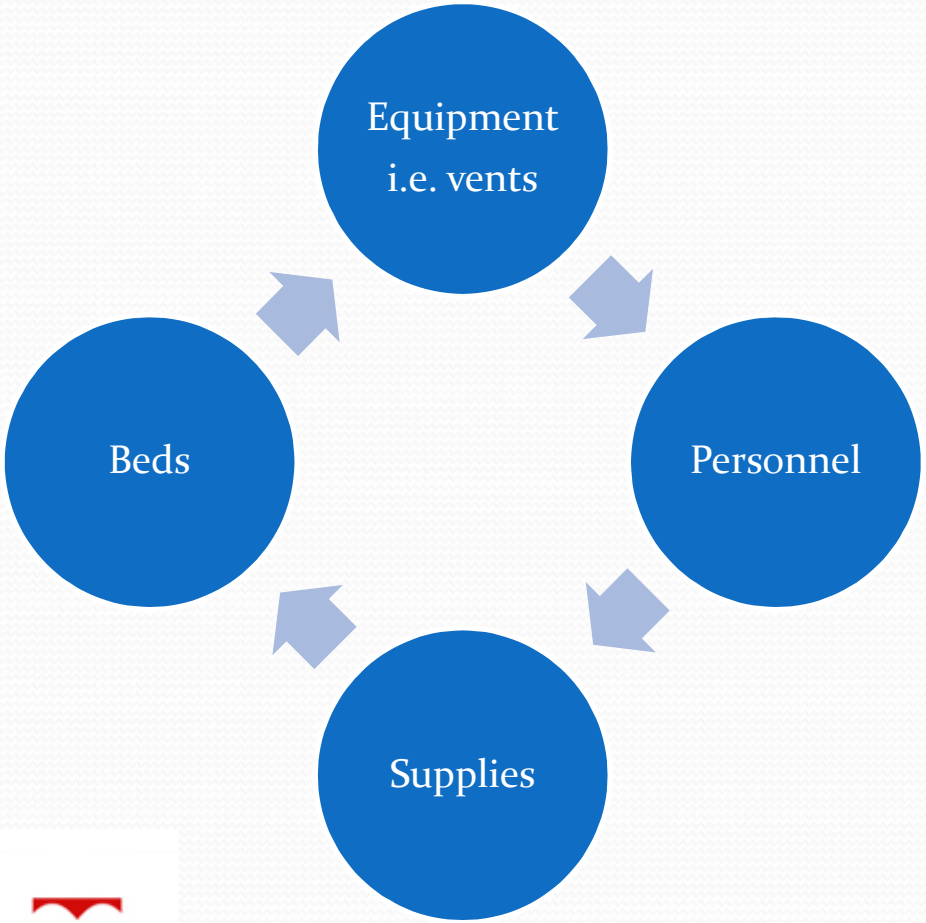
Treatment- ICU standard care

- Maintain gut motility as osteltamivir is administered via NG
- In the chaos of a pandemic attempt to try and maintain standard ICU care (ulcer prophylaxis, feeding, DVT prophylaxis etc)

Treatment- Adjunctive and Desperation measures

- Consider NO, flolan, proning, HFO, occasionally ECMO used

Local Surge Planning



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- http://www.youtube.com/watch?v=E7FhpRMc2no