

UNIVERSITI SAINS MALAYSIA

First Semester Examination
Academic Session of 1994/95

October/November 1994

FCP555 : Pharmacotherapeutics IV

(2 hours)

This examination consists of two sections.

Section A consists of 50 multiple choice questions.

Section B consists of two (2) long questions.

Answer ALL questions.

Answer to section A must be entered into the scripts provided.

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Section A

Mark (/) on the opposite space corresponding to a correct or most appropriate answer for each question. Each question has only one correct or most appropriate answer or statement.

1. Which of the following symptoms is least likely to respond to antipsychotic therapy?

- (a) Agitation.
- (b) Hostility.
- (c) Social withdrawal.
- (d) Hallucination.

2. What is the most important factor in selecting an antipsychotic agent for an individual patient?

- (a) Cost of therapy.
- (b) Drug side-effect profile.
- (c) Patient's past medication experience.
- (d) Type of schizophrenia.

3. Which of following pairs of drug — side-effects is appropriate?

- (a) Chlorpromazine — Low sedation.
- (b) Haloperidol — High anticholinergic effect.
- (c) Thiothixene — Low sedation.
- (d) Loxapine — High extrapyramidal effects.

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4. Which of the following is/are associated with the use of low potency antipsychotic agents?

- (i) Dermatological side-effects.
- (ii) Cardiac problems.
- (iii) Autonomic side-effects.
- (iv) Central nervous system side-effects.

- (a) (i) only.
- (b) (i) and (ii) only.
- (c) (i), (ii) and (iii) only.
- (d) (i), (ii), (iii) and (iv).

5. Which of the following is the most important monitoring parameter during the first month of clozapine therapy?

- (a) Weekly liver function test.
- (b) Daily body weight.
- (c) Weekly white cell counts.
- (d) Daily body temperature.

6. Which of the following drugs can have its serum concentration increased by chlorpromazine?

- (a) Carbamazepine.
- (b) Phenytoin.
- (c) Phenobarbital.
- (d) Diazepam.

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7. Which of the following statements regarding anticholinergic drugs is true?

- (a) Benztropine is more effective than trihexyphenidyl as an antiparkinsonism drug.
- (b) Trihexyphenidyl is less sedating than benztropine.
- (c) Euphoria and hallucination have been attributed more frequently to benztropine than to trihexyphenidyl.
- (d) Benztropine has the shortest duration of action.

8. Which of the following adverse effects is not observed in patients taking antipsychotic agents?

- (a) Drowsiness.
- (b) Hypotension.
- (c) Altered endocrine function.
- (d) Diarrhea.

9. Which of the following can cause an increase in fluphenazine clearance?

- (a) Liver disease.
- (b) Chronic smoking.
- (c) Congestive heart failure.
- (d) Alcohol consumption.

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10. Which of the following statements regarding tardive dyskinesia is true?

- (a) It abates with discontinuation of the antipsychotic therapy.
- (b) It responds favourably to levodopa.
- (c) It often persists in elderly patients.
- (d) Its severity depends on the antipsychotic agent.

11. Which of the following cranial nerves supply the muscles of the eyes?

- (i) Cranial nerve III.
- (ii) Cranial nerve IV.
- (iii) Cranial nerve VI.
- (iv) Cranial nerve V.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

12. Which of the following are features of a cerebellar lesion?

- (i) Dysarthria.
- (ii) Intention tremor.
- (iii) Nystagmus.
- (iv) Hypertonia.

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- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

13. Which of the following are features of a lower motor neuron lesion?

- (i) Fasciculation.
 - (ii) Wasting.
 - (iii) Hypertonia.
 - (iv) Exaggerated deep tendon reflexes.
- (a) (i) and (ii) only.
 - (b) (i), (ii) and (iii) only.
 - (c) (i), (ii), (iii) and (iv).
 - (d) (ii) and (iv) only.

14. Which of the following drugs is/are used in the treatment of Systemic Lupus Erythematosus (SLE)?

- (i) Methylprednisolone.
 - (ii) Chloroquine.
 - (iii) Cyclophosphamide.
 - (iv) Quinine.
- (a) (i) and (ii) only.
 - (b) (i), (ii) and (iii) only.
 - (c) (i), (ii), (iii) and (iv).
 - (d) (ii) and (iv) only.

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15. Which of the following is/are found in SLE?

- (i) Arthritis.
- (ii) Anemia.
- (iii) Anticardiolipin antibodies.
- (iv) Raised Erythrocyte Sedimentation Rate (ESR).

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

16. Which of the following is/are (a) manifestation(s) of a pancreatic disease?

- (i) Diabetes.
- (ii) Abdominal pain.
- (iii) Constipation.
- (iv) Athralgia.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

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17. Which of the following drugs cause(s) SLE-like syndrome?

- (i) Hydralazine.
- (ii) Procainamide.
- (iii) Gentamicin.
- (iv) Carbamazepine.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

18. Which of the following statements is/are true for SLE?

- (i) Anti-DNA antibody may be present.
- (ii) There is a female preponderance.
- (iii) There is an increased incidence in relatives with other autoimmune diseases.
- (iv) Frusemide can produce an SLE-like syndrome.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

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19. Which of the following statements regarding epilepsy is true?

- (i) Juvenile myoclonic epilepsy is inherited.
- (ii) Most focal seizures are intractable.
- (iii) Temporal lobe epilepsy can present with complex partial seizures.
- (iv) Febrile convulsions in childhood usually progress to epilepsy in adult.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

20. Which of the following statements is true?

- (i) Carbamazepine is more effective than phenobarbitone in complex partial seizures.
- (ii) Clonazepam may be useful in catamenial seizures.
- (iii) Sodium valproate is the treatment of choice in focal seizures.
- (iv) Phenobarbitone may be used in the treatment of status epileptics.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

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21. Which of the following is classified as a generalized seizure disorder?

- (i) Tonic-clonic seizure.
- (ii) Absence seizure.
- (iii) Myoclonic seizure.
- (iv) Complex partial seizure.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

22. Which of the following is/are (a) part(s) of a higher mental function test?

- (i) Orientation to place, person and time.
- (ii) Immediate recent and remote memory recall.
- (iii) Cranial nerve examination.
- (iv) Examination of the primary sensation.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

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23. Which of the following is an anterior spinothalamic tract sensation?

- (i) Pain.
- (ii) Temperature.
- (iii) Vibration.
- (iv) Joint position.

- (a) (i) and (ii) only.
- (b) (i), (ii) and (iii) only.
- (c) (i), (ii), (iii) and (iv).
- (d) (ii) and (iv) only.

24. Which of the following is a goal in barbiturate coma?

- (a) To maintain intracranial pressure (ICP) between 15 to 20 mm Hg.
- (b) To achieve phenobarbital serum concentration of 20 to 40 mg/L.
- (c) To maintain mean arterial pressure (MAP) between 15 to 20 mm Hg.
- (d) To maintain mean cerebral perfusion pressure (CPP) < 50 mm Hg.

25. Which of the following agents causes more frequent rebound during the management of elevated ICP?

- (a) Glycerol.
- (b) Urea.
- (c) Mannitol.
- (d) Dexamethasone.

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26. Which of the following has delayed onset and should not be used in acute elevated ICP?

- (a) Glycerol.
- (b) Dexamethasone.
- (c) Urea.
- (d) Frusemide.

27. Which of the following is not an adverse effect associated with mannitol?

- (a) Reversible acute renal dysfunction.
- (b) Exacerbation of congestive cardiac failure.
- (c) Increased cerebral blood flow (CBF).
- (d) Decreased serum osmolality.

28. Which of the following interventions is the most effective in preventing and controlling elevated ICP?

- (a) A posture with 30° elevation of patient's head.
- (b) Hyperventilation.
- (c) Frusemide therapy.
- (d) None of the above.

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29. Which of the following is the commonest form of phobia?

- (a) Social phobia.
- (b) Simple phobia.
- (c) Agoraphobia.
- (d) Acrophobia.

30. Which of the following is the characteristic of the sleep disturbance in anxiety neurosis?

- (a) Early morning awakening.
- (b) Middle insomnia.
- (c) Late insomnia.
- (d) Early insomnia.

31. Which of the following anxiolytics is highly addictive?

- (a) Alprazolam.
- (b) Diazepam.
- (c) Midazolam.
- (d) Clobazam.

32. Which of the following antipsychotic agents is the most potent?

- (a) Chlorpromazine.
- (b) Thioridazine.
- (c) Haloperidol.
- (d) Trifluoperazine.

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33. Which of the following is a typical affect of a schizophrenic under treatment?

- (a) Flat.
- (b) Blunted.
- (c) Broad.
- (d) Restricted.

34. Which of the following is termed a negative symptoms of schizophrenia?

- (a) Delusion.
- (b) Pressure of speech.
- (c) Looseness of association.
- (d) Mannerism.

35. Which of the following is a typical antipsychotic drug?

- (a) Buspirone.
- (b) Fluoxetine.
- (c) Sertaline.
- (d) Clozapine.

36. Which of the following is a characteristic of endogenous depression?

- (a) Psychosis for agitation.
- (b) Middle insomnia.
- (c) Weight loss.
- (d) Apathy.

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37. Which of the following is not a tricyclic anti-depressant?

- (a) Mianserin.
- (b) Amitriptyline.
- (c) Imipramine.
- (d) Dothiopin.

38. Which of the following is the drug of choice for complex partial seizures?

- (a) Phenytoin.
- (b) Carbamazepine.
- (c) Valproic acid.
- (d) Phenobarbitone.

39. AA has been on phenytoin (PHT) PO 300 mg daily for his generalized tonic-clonic seizures. He has been seizure-free for the last 1 year and there is no evidence of side-effects. The TDM lab reported PHT concentration of 7 mg/L. The most appropriate action would be to

- (i) check plasma albumin concentration.
 - (ii) check whether AA has been compliant.
 - (iii) check for proper sampling time.
 - (iv) recommend to increase dose because PHT concentration was not in the "therapeutic range.
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- (a) (i) and (ii).
- (b) (ii) and (iv).
- (c) (i), (ii) and (iii).
- (d) (i), (ii), (iii) and (iv).

40. Which of the following adverse effects of phenytoin is not related to its plasma concentration?

- (a) Nystagmus.
- (b) Drowsiness.
- (c) Gum hypertrophy.
- (d) Ataxia.

41. Which of the following can precipitate seizures in predisposed individuals?

- (i) Lack of sleep.
- (ii) Emotional stress.
- (iii) Hyperventilation.
- (iv) Too high antiepileptic drug (AED) concentrations.

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- (a) (i) and (ii).
- (b) (i), (ii) and (iii).
- (c) (i) and (iii).
- (d) (i), (ii), (iii) and (iv).

42. Which of the following is not true about trihexyphenidyl (Artane) in the treatment of Parkinson disease?

- (a) It acts by replacing dopamine neurotransmitter.
- (b) It is more effective in tremor and rigidity than in bradykinesia.
- (c) It should not be stopped abruptly to avoid rebound effect.
- (d) Its side-effects include delirium, disorientation and decreased memory.

43. Which of the following is not a clinical feature usually associated with Parkinson disease?

- (a) Intentional tremor.
- (b) Rigidity.
- (c) Bradykinesia.
- (d) Postural difficulties.

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44. Which of the following statements regarding levodopa therapy in Parkinson disease is/are true?

- (i) Concurrent use with MAOI can cause hypertensive crisis.
- (ii) Anticholinergics are effective as adjuncts.
- (iii) The use of carbidopa and levodopa combination reduces peripheral conversion of dopamine.
- (iv) There is no loss of efficacy with long-term use.

..... (a) (i) and (ii).

..... (b) (i), (ii) and (iii).

..... (c) (i), (ii), (iii) and (iv).

..... (d) (ii) and (iv).

45. Rank in order of increasing severity in the extra-pyramidal side-effects for the following neuroleptics.

- (i) Haloperidol.
- (ii) Clozapine.
- (iii) Chlorpromazine.
- (iv) Trifluoperazine.

..... (a) (i), (ii), (iii) and (iv).

..... (b) (ii), (iii), (iv) and (i).

..... (c) (iii), (iv), (i) and (ii).

..... (d) (iv), (i), (ii) and (iii).

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46. Which of the following is the most common cause of death in patients with myasthenia gravis?

- (a) Liver dysfunction.
- (b) Renal failure.
- (c) Respiratory weakness.
- (d) Cardiovascular problems.

47. Which of the following is used in the diagnostic test in myasthenia gravis?

- (a) Pyridostigmine.
- (b) Edrophonium.
- (c) Neostigmine.
- (d) Prednisone.

48. Which of the following extra-pyramidal side-effects is the result of cholinergic underactivity?

- (a) Pseudo-parkinsonism
- (b) Acute dystonia
- (c) Tardive dyskinesia
- (d) Akathesia

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49. Which of the following statements is not true regarding plasmapheresis for myasthenia gravis?

- (a) It requires specialized equipment and personnel.
- (b) Complications are more common in the elderly.
- (c) It provides long-term benefit.
- (d) It has a very short onset of action.

50. Which of the following is not true regarding a generalized anxiety disorder?

- (a) It has a gradual onset.
- (b) It occurs both in children and in adults.
- (c) It may be presented with sweating or gastrointestinal upset.
- (d) It occurs more often in women.

(50 marks)

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Section B.

Question 1.

A 24 year-old female presented to the psychiatric clinic with the complaints of sleep disturbances and worries for unknown reason. After a thorough assessment she was diagnosed to have anxiety neurosis.

- (i) List 6 other symptom of anxiety neurosis you would expect to find in this patient.

(3 Marks)

- (ii) List two medical conditions you would consider in the differential diagnosis.

(2 Marks)

B. She was to be treated as an outpatient and was willing to come for regular follow up.

- (i) Name 3 groups of drugs appropriate for the treatment.

(2 Marks)

- (ii) Among the groups of drug you mentioned in B (I) above, which would you recommend as the group of choice? Give 3 examples of drugs in the group.

(3 Marks)

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C. It was decided to put her on diazepam 5 mg TDS.

- (i) Comment on the dose and frequency of the diazepam used.

(3 Marks)

- (ii) List 4 side effect of diazepam.

(2 Marks)

D. After 5 days of treatment, she still complained of sleep disturbances. In addition she also complained of drowsiness during the day.

- (i) How you would manage her at this stage without using additional drug?

(5 Marks)

E. At the end of two months of treatment, you noticed that the dose of diazepam has been increased to 10 mg TDS. The patient however claimed that the drug was not effective anymore and requested for further increase in the dose.

Comment on the above condition. How would you further manage her?

(5 Marks)

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Question 2

GG was a 26 year-old man weighing 45 kg who was admitted to HUSM emergency room (ER) for status epilepticus. His record indicated that he had primary generalized tonic-clonic seizure and was initially treated with phenytoin (PHT) PO 200 mg nocte. At this dose his attacks were not controlled and his steady-state PHT concentration was 9 mg/L. His dose was then increased to 260 mg PO daily and his attacks became well controlled. Phenytoin plasma concentration measured on January 1, 1994 was 15.1 mg/L and on March 12, 1994 it was 14.9 mg/L.

For the past one week, GG had been eating a lot of durian. According to his mother, GG believed that his epilepsy had been cured since he did not have any more attacks. Furthermore he thought that taking PHT and durian at the same time could make him hot.

- A. Define status epilepticus.

(1 Marks)

- B. What was the most likely cause of GGs status epilepticus

(1 Mark)

- C. What would be your recommendation regarding initial drug therapy in the ER?

Give name of drug, dose and route of administration.

Why would you choose that drug?

(5 Marks)

- D. Calculate V_m and K_m of PHT for GG.
(You may use the graph paper supplied)

(3 Marks)

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- E. The ER physician had just received the PHT plasma concentration he requested earlier and it was reported as 2 mg/L. He would like to give an intravenous PHT loading dose to this patient and he asked for your recommendation. Write a complete order (show all calculations and state any assumptions you make).

(8 Marks)

- F. Give 2 adverse effects of PHT that are not related to its plasma concentration.

(1 Marks)

- G. Describe the effect on phenytoin plasma concentration from the interactions with the following drugs.

- (i) Cimetidine
- (ii) Carbamazepine
- (iii) Antacid
- (iv) Valproic acid

(4 Marks)

- H. After 2 days in the hospital GG was going to be discharged home. What would you tell him during your discharge counseling?

(2 Marks)

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Appendix

Normal Laboratory Values

1.	Ammonia	80-110 mcg/dl	or	47-65 umol/L
2.	Amylase	4-25 IU/ml		
3.	Billirubin			
	- Direct	0-0.2 mg/gl		0-3 umol/L
	- Indirect	0.2-0.8 mg/dl		30-14 umol/L
	- Total	0.2-1 mg/dl		30-17 umol/L
4.	CO ₂	20-30 mEq/L		24-30 mMol/L
5.	pCO ₂	35-45 mmHg		
6.	CI	100-106 mEq/L		100-106 mMol/L
7.	Cpk	50-170 U/L		
8.	Creatinine (SCr)	0.6-1.5 mg/dl		60-130 umol/L
9.	Random blood sugar	70-110 mg/dl		3-10 umol/L
10.	Iron	50-150 mcg/dl		9.0-26.9 umol/L
11.	Lactic dehydrogenase	70-210 IU/L		
12.	Magnessium	1.5-2.0 mEq/L		0.8-1.3 mMol/L
13.	pO ₂	75-100 mmHg		
14.	pH	7.35-7.45		
15.	Acid phosphatase			
	Male	0.13-0.63 IU/ml		36-176 nmol s ⁻¹ /L
	Female	0.101-0.65 IU/ml		2.8-156 nmol s ⁻¹ /L
16.	Alkaline phosphatase	39-117 IU/L		
17.	Phosphorous	3.0-4.5 mg/dl		1.0-1.5 mMol/L
18.	Potassium (K+)	3.5-5.0 mEq/L		3.5-5.0 mMol/L
19.	Calcium (Ca ²⁺)	8.5-10.5 mg/dl		2.1-2.6 mMol/L
20.	Sodium (Na+)	135-145 mEq/L		135-145 mMol/L
21.	Bicarbonate (HCO ₃ -)	24-38 mEq/L		24-28 mMol/L

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22.	Protein		
-	Total	6.0-8.5 g/dl	60-85 g/L
-	Albumin	3.5-5.0 g/dl	35-50 g/L
-	Globulin	2.3-3.5 g/dl	23-35 g/L
-	Transferrin	200-400 mg/dl	2.0-9.0 g/L
23.	Transaminase (SGOT)	0-40 IU/L	0-0.32 $\mu\text{mol s}^{-1}/\text{L}$
24.	BUN	8-25 mg/dl	2.9-8.9 mMol/L
25.	Uric Acid	3-7 mg/dl	0.18-0.42 mMol/L
26.	Blood Pictures		
	Red blood cell (RBC)		
	Male	4.8-6.4 $\times 10^6/\text{mm}^3$	
	Female	4.2-5.4 $\times 10^6/\text{mm}^3$	
	White blood cell (WBC)	4.0-11.0 $\times 10^3/\text{mm}^3$	
	P	60-75%	
	L	20-40%	
	M	4-8%	
	B	0-1%	
	E	1-3%	
	Platelet (Plt)	200-400 $\times 10^3/\text{mm}^3$	
27.	ESR		
	Male	0-10 mm/jam (Wintrobe)	
	Female	0-15 mm/jam (Wintrobe)	
28.	Hematocrit		
	Male	45-52%	
	Female	37-48%	
29.	Hemoglobine (Hgb)		
	Male	13-18 g/dl	
	Female	12-16 g/dl	
30.	Prothrombin time (PT)	75-100% baseline	
31.	APTT	25-37 sec.	
32.	Creatinine Clearance (CrCl)	105-150 ml/min/1.73 m^2	
33.	TT ₄	3.0-7.5 mcg/dl	
34.	RT ₃ U	25-35%	
35.	FTI	1.3-4.2	

...27/-

NORMAL HEMODYNAMIC VALUES AND DERIVED INDICES

Normal Value Units			
BP S/D/M	Blood Pressure Systolic/Diastolic/Mean	120/80/93	mm Hg
CO	Cardiac Output	4-6	Liters/min.
RAP	Right Atrial Pressure (Mean)	2-6	mm Hg
PAP S/D/M	Pulmonary Artery Pressure Systolic/Diastolic/Mean	25/12/16	mm Hg
PCWP	Pulmonary Capillary Wedge Pressure (mean)	5-12	mm Hg
CI	Cardiac Index	2.5-3.5	Liters/min/m ²
	$CI = \frac{CO}{\text{Body Surface Area}}$		
SV	Stroke Volume	60 - 80	ml/beat
	$SV = \frac{CO}{\text{Heart Rate}}$		
SVI	Stroke Volume Index	30 - 50	ml/beat/m ²
	$SVI = \frac{SV}{\text{Body Surface Area}}$		
PVR	Pulmonary Vascular Resistance	< 200	dynes.sec.cm ⁻⁵
	$PVR = \frac{MPAP - PCWP}{CO} \times 80$		
TPVR	Total Peripheral Vascular Resistance	900-1400	dynes.sec.cm ⁻⁵
	$TPVR = \frac{MBP - RAP}{CO} \times 80$		
LVSWI	Left Ventricular Stroke Work Index	35-80	gm-m/m ² /beat
	$LVSWI = (MBP - PCWP) (SVI) (.0136)$		