CURRICULUM

DM CLINICAL PHARMACOLOGY

2009-10

JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION & RESEARCH (JIPMER),

PUDUCHERRY-605 006

Contents

General Conditions to be observed

1. Postgraduate medical education in the case of super-specialties shall be of three years duration after MD as prescribed.
2. Postgraduate curriculum shall be competency based.
3. Learning in postgraduate program shall be essentially autonomous and self directed.
4. A combination of both formative and summative assessment is vital for the successful completion of the course.
5. A modular approach to the core curriculum is essential for achieving a systematic exposure to the various sub-specialties concerned with the discipline of clinical pharmacology and therapeutics.
6. The training of students shall involve learning experience derived from and targeted to the needs of the community. It shall, therefore, be necessary to expose the students to community based activities.

1. Course Objectives

1.1. Training Objectives

The aim of the course is to train medical doctors in clinical pharmacology after they have obtained the requisite postgraduate qualifications. The course has been designed to impart an all-round training in scientific evaluation of drugs in man. The training provided would enable these students to

a) clinically evaluate drugs and medicinal plants in a scientific manner.

b) advise clinical specialists in medical colleges and institutes in the designing of protocols for Phase III and Phase IV clinical trials,

c) function in clinical departments of pharmaceutical companies and advise on protocol design and multi-centric trials of newer drugs.

d) impart continuing education to medical practitioners / physicians in rational drug usage.

e) teach scientific methodology of evaluation and assessment of drug treatment to postgraduate and undergraduate medical students.

f) establish pharmacovigilance centers for monitoring of adverse reactions of drugs.

g) advise drug control organizations regarding introduction of new drugs and review the performance of established drugs.

h) set up centers of therapeutic drug monitoring

i) establish drug information centers.

1.2. Components of training objectives

The three major components of the course objectives are

- Knowledge – theory & research methodology
- Attitudes – including communication skills
- Skills – Practical & Clinical

1.2.1. Knowledge

- Describe theories of drug-receptor concept, structure & action of receptors, dose-response relationships, potency and efficacy.
- Describe the principles of: correct choice of route of administration, absorption of drugs, metabolism and excretion of drugs, interpretation of drug concentration in body fluids and pharmacokinetic modeling.
- Explain the concepts of pharmacogenetics and personalised medicine.
- Demonstrate knowledge of common analytical methods and their limitations.
- Explain the mechanisms of action and modes of use of common therapeutic drugs.
- Appreciate the sources of individual variation including genetic, age and gender related (including pregnancy and lactation), and other sources of individual variation especially coexisting renal hepatic and other disease and drug interaction both beneficial and adverse.
- Demonstrate knowledge of: important (common and/or severe) adverse effects of drugs used in their area of clinical practice, common clinical presentations of ADR, ways to identify and report them and appropriate management of suspected ADR.
- Describe the principles of good laboratory practice.

- Explain the roles of national and international regulatory authorities in the process of drug approval.
- Describe the principles of controlled experiments, randomization, use of placebo and blinding.
- Describe ethical principles of research on human subjects including duties, rights and role of institute ethics committee.

1.2.2. Attitude

- Prescribe with due regard to general knowledge, as specified combined with specific patient related information relating to demographic characteristics, drug history and individual preference.
- Possess a self critical attitude and communicate effectively in drug and therapeutics & audit committee meetings.
- Alert to the possibility that clinical events might be drug-related.
- Recognise the need for individualisation of therapy where necessary.
- Respect patient/ subject autonomy, the primacy of safety of the subject and other principles of ethics.
- Contribute to public education about drugs and their utilisation.
- Appreciate the need for meticulous record keeping and research governance.
- Appreciate the importance of communicating research data orally and in written form and meticulous in writing.
- Respect the laws related to drug use in patients and also the laws related to approval process.

1.2.3. Skills

- Construct and adjust dose regimens correctly. Negotiate an acceptable regimen with the patient where appropriate.
- Select drugs and dose regimens rationally based on individual factors.
- Develop prescribing policies, formularies and guidelines.

- Evaluate guidelines on drug utilisation in the context of Drug &Therapeutics committees. Write guidelines on medicines management for evaluation by such committees.
- Make effective submissions to formulary committees and various regulatory authorities for new drugs and audit drug utilization.
- Write trial protocols and able to recruit subjects for studies and obtain valid informed consent.
- Perform PD and PK studies in human volunteers and other skills relevant to their clinical area of expertise.
- Measure end points reliably and record data accurately. Analyse data including risk-benefit analysis and dose determination for definitive phase-3 studies.
- Critically analyse papers regarding rationale, cogency, experimental design, analytical methodology, method of analysis, potential sources of bias, confounding, conflict of interest, appropriateness of discussion, validity of conclusions.
- Critically analyse advertising claims made for medicinal products.
- Able to recruit research subjects, screen potential subjects for inclusion/exclusion criteria, obtain valid informed consent.
- Arrange visits of research subject to clinical laboratory or research clinic and perform or supervise clinical measurements. Keep records to the standard required by GCP.
- Manage common and serious ADR, including anaphylaxis, appropriately. Use printed and electronic resources to identify unusual or uncertain ADR.
- Report suspected ADR appropriately. Analyse post marketing surveillance studies critically.
- Maintain up to date qualifications in resuscitation skills.
- Apply therapeutic principles in drafting management guidelines.

1.3. National Objectives

- To create trained man power in the emerging field of clinical pharmacology so as to deliver super specialty health care in the country.
- To start clinical pharmacology units in their parent institution after completing the course.

- To be able to work in any hospital with minimum facilities and facilitate the delivery of appropriate treatment regimens and work in hand with the treating physician.
- To be able to initiate an individual research project with the help of various funding agencies and aid in the improvement of health care research in our country.

2. Course Content

THEORY

General Clinical Pharmacology

A. Introduction

(a) History and development of clinical pharmacology

(b) Definition and scope of clinical pharmacology

(c) General principles in clinical pharmacology

(d) Molecular basis of drug action

(e) Mechanism of drug action

(f) Dose-response relations and effective therapeutic dose.

(g) Metabolism – e.g. route of administration, enzyme induction, absorption, distribution, biotransformation and excretion of drug.

(h) Aims of clinical trials.

(i) Problems in clinical trials.
- (i) Patient compliance
- (ii) Follow-up
- (iii) Dropouts
- (iv) Matching
- (v) Fixed combination of drugs
- (vi) Patient sensitivity
- (vii) Protocol compliance

(viii) Observer's errors.

j) Clinical Trial Reports.

k) Pharmaceutical literature.

l) Criteria for selection of investigator.

m) Principles in the design of a protocol.

n) Critical appraisal of literature.

B. <u>The Clinical Pharmacologist</u>

(a) Definition of the clinical pharmacologist

(b) Academic background.

(c) Training of the clinical pharmacologist.

(d) Role of the clinical pharmacologist in institutional / national / international setting, academia, drug industry and government.

C. <u>Drug development (making a chemical into a drug)</u>:

(a) Why a new drug.

(b) Selection of a chemical compound for screening as a potential drug.

(c) Computer assisted drug designing.

(d) General pharmacological and systemic screening

(e) Acute toxicity studies.

(f) Sub acute toxicity studies.

(h) Mutagenicity, Carcinogenicity, reproduction and teratogenicity studies.

(i) Role of government institutes, pharmaceutical houses, centers of excellence and the government in drug development collaborative efforts.

(j) Present dilemma in drug development : patent protection, price control,

generic names, national vs. multinational drug house.

(k) Orphan drugs.

(l) Role of national / international agencies.

(m) Good Laboratory Practice (GLP)

(n) Good Clinical Practice (GCP)

D. Assessment of preclinical data

(a) Animal pharmacology – effectiveness and safety.

(b) Assessment of preclinical data, adequacy of toxicity studies.

(c) Pharmacokinetic studies in animals.

(d) Selection of initial human dose from animal data.

(e) Other points :

i) Comparison with placebo / other drugs.
ii) Effectiveness.
iii) Side – effects.
iv) Carcinogenicity, mutagenicity and teratogenicity.
v) Cost.
vi) Assessment of benefit and risk.

(f) Pharmaceutical aspects – shelf life, purity, formulation, etc.

E. Ethical and legal aspects of clinical trials:

(a) Evolution, scope and membership of an ethics committee.

(b) Ethical aspects of carrying out a clinical trial

(c) Legal aspects of carrying out clinical trials.

(d) Consent of subjects – written / verbal statement given to subjects.

(e) Subjects for clinical trials.

i) Volunteers, normal, healthy

ii) Prisoners
iii) Children
iv) Mentally unsound persons
v) Pregnant women
vi) Patients
vii) Students
viii) Employees

Other aspects

(a) Drugs and the fetus.
(b) Stem cell research
(c) Payment to volunteers
(d) Compensation to subjects for injury during participation in drug trials.
(e) Insurance for doctors.
(f) Administration of drugs by non-medical personnel
(g) Assessment of risk and benefit
(h) Historical perspectives in human experimentation – experiments on prisoners at concentration camps.
(i) Helsinki Declaration
(j) Nuremberg code
(k) International perspectives (CIOMS – WHO guidelines)
(l) ICMR guidelines.

F. Types of clinical studies (trials) envisaged:

(a) Retrospective Vs. Prospective trials.

(b) Single centre Vs. Multi-centre trials.

(c) Fixed dosage Vs. Variable dosage

(d) Design of clinical trials

(e) Prophylactic drug trial

(f) Quality of life assessment trials.

G. Protocol Designing:

(a) Rationale

(b) Broad principles

(c) Development of expertise in protocol making – role of industry

(d) Designing of SOPs and CRF (case report forms)

H. Conduct of clinical trials:

(a) Principles of controlled clinical trials

(b) Investigator / centre, facilities, reputation

(c) Informed consent

(d) Institute Ethics Committee

(e) Permission from Drugs Controller

(f) Patient / volunteer recruitment, Inclusion / Exclusion criteria

(g) First administration of a chemical to the human

(h) Controlled clinical trial – sequential trials, choice of variables, crossover techniques, randomization, blind and double-blind studies.

(i) Fixed dosage Vs. Variable dosage schedule

(j) Problem faced in carrying out clinical trials

(k) Criteria for exclusion and methods to deal with dropouts with clinical trials

(l) Time phasing of trials

(m) Role of clinical pharmacologist in phase III and phase IV trials

(n) Monitoring of ADR – how and when?

(o) Statistical issues – sample size, Power of the trial

(p) Data analysis – Interim and Final

(q) Data monitoring

(r) Clinical trial registry

I. Phases of clinical trials

Preclinical requisites for phase I, II, III, and IV trials and their clinical significance.

Phase 0 (micro- dosing studies)

Phase I :(a) Human pharmacological studies, dosage fixation, tolerance, single dose / multiple dose, dose escalation.

(b) Determination of signs, symptoms and lab parameters of drug safety

(c) Human pharmacodynamic studies

Phase II A : (a) Clinical trials – selection of subjects

(b) Dose determination

(co) Design / parameters to be observed / duration / variables

(d) Detailed pharmacokinetics

II B: (a) Selection of subjects

(b) Dose determination for use in phase III

(c) Safety parameters

Phase III (a) Clinical trials – selection of subjects / design / parameters /duration / variables / safety parameters / single or multi centric

(b) Dosage fixed / variable

(c) Randomisation – types, methods, tackling problems

(d) Use, active/inert placebos, ethics

Phase IV : (a) limited marketing permission coupled with mandatory post marketing surveillance

(b) Types of phase IV clinical trials

(c) Design of phase IV clinical trials

(d) Selection of subjects / parameters to be observed / duration

(e) Extended phase IV or field trials.

J. <u>Multi-centric Trials</u>:

a) Indications for multi-centric trials

b) Organization

c) Number of centres

d) Quality control at different centres / training facilities / protocol compliance

e) Standardization

f) Data processing – coordinating centre / role of computers

g) Experience of pharmaceutical organizations

h) Experience of World Health Organization / ICMR

i) Problems of multi-centric trials.

K. Withdrawals and dropouts in clinical trials:

a) Reasons for dropouts

i) drug related

ii) non – drug related

iii) random

b) Reasons for withdrawals

c) Selection and exclusion criteria

d) Duration of trial, extended due to lack of subjects

e) Patient does not co-operate – physician's choice

f) Loss to follow up

g) Patient gets seriously ill / slow improvements

h) Patient gets concomitantly other drugs contrary to protocol

i) Bio-statistical treatment of dropouts

L. Washout & run in period

a) Necessity

b) Ethical aspects

c) Duration

d) Problems in cross-over trials

M. Special features of clinical trial with plant / herbal products

a) History of the use of plant products

b) Present status

c) Standardization

e) Preclinical evaluation and toxicity requirements –

Problems, WHO recommendations

f) Ethical aspects – preclinical requisites

g) Advantages and disadvantages

h) Problems

i) Coordination of clinical trials of plant products –

Collection, transport, extraction and storage of plant

material, role of pharmacognosists etc.

j) Consultation with Ayurvedic and Unani practitioners of medicine

N. General problems in organization and carrying out clinical trials:

a) Preparation of a flow chart for the entire trial – initiation to completion

b) Collaboration between different departments involved in the trial

d) Collaboration with the manufacturer / supplier of the drug to ensure uninterrupted regular supply of drugs.

e) Incentive / payment to investigator / volunteers.

f) Medical insurance – investigator / volunteers

g) Compilation of forms in time

h) Regular and phased processing of data, publication of results.

O. Pharmacokinetics

(a) Absorption, distribution, biotransformation and excretion of drugs.

(b) Studies on bioavailability of drugs.

(c) Population pharmacokinetics

(d) Interaction between the drug and other drugs

(e) Interaction with various physiological systems

(f) Enzyme induction

(g) Trial of multiple combinations

(h) Therapeutic drug monitoring

(i) Setting up of a bioavailability and bioequivalence study centre

(j) Good laboratory practice – Quality assurance.

(k) Newer drug delivery systems

P. Pharmacogenomics:

Role of Pharmacogenomics in

a. Drug metabolizing enzymes and transporters

b. Drug response

c. Drug development and therapy

d. Personalised drug therapy

e. Pharmacovigilance

Q. Pharmacoepidemiology:

(a) Prescribing habits.

(b) Provision of drug information

(c) Drug utilization studies.

(d) Pharmacoeconomics.

(e) Essential Drug List & P drug concept.

(f) Hospital Formulary.

(g) Rational drug use.

R. ADR monitoring - Pharmacovigilance

a) Definition and classification

b) Prediction of adverse effects and interactions of a particular potential drug from the chemical structure and animal studies

c) Methods for ADR monitoring

d) Monitoring of commonly observed side effects

e) Monitoring of rare side effects in marketed drugs

f) Hospital monitoring systems

g) Maintenance of an Adverse Drug Reaction Registry - hospital / regional / national/ international (data base)

h) Drug surveillance

i) Measurement of drug levels in plasma for monitoring side-effects

j) Investigations of cause and effect relationship, therapeutic challenge.

S. Drug interactions

a) Definition

b) Classification :

i) Drug host interaction
ii) Drug disease interaction
iii) Drug-drug interaction
iv) Drug-food interaction
v) Drug environment interactions

vi)Drug - gene interaction

c) Mechanisms

d) Clinical relevance

T. Biostatistics & Data Handling

a) Role of biostatistician in protocol designing

b) Sample size calculation

c) Choice of biostatistical technique

d) Use of statistical software (e.g.. SPSS)

e) Data dredging

f) Duplicate copies of records

g) Data processing – verifying analysis

h) Documentation

i) Writing up the results of the trials by whom – Investigator / Sponsor

j) Life Tables

U. Iatrogenic Disease

a) Definition

b) Occurrence, incidence, causes, morbidity, mortality

c) Investigation to definite casual relationship, therapeutic challenge

d) Role of the clinical pharmacologist

V. Drug regulation – National:

a) Definition and evolution of drug regulation

b) Requirement for introduction of a new drug

c) Requirement for new use of existing drugs

d) Requirements for altered dosages and new combinations

e) Quality control procedures

f) National regulatory agency / state regulatory agency.

g) Laws related to drugs and cosmetics Act

W Drug regulation – International :

a) Acceptance of data obtained in one country by the drug regulatory agency of another country for use of the drug in another country (racial / genetic / nutritional differences)

b) Special problems in clinical evaluation of plant medicines

c) Administration of drugs by trained paramedical personnel

d) Laboratory facilities essential for clinical evaluation of drug – Phase II and III

e) Extended phase IV trials

f) Drug regulations of India and some other countries (USA, UK, Japan &EEC)

g) Role of World Health Organization

X. Centres for clinical pharmacology – training / research

a) Need

b) Development of new centres – personnel, facilities

c) Requirement : Personnel, equipment, beds

d) Existing centers – national / international

e) Future.

Y. Pharmaceutics

a) Drug formulation

b) Pharmaceutical equivalence – Disintegration and dissolution

c) Good manufacturing practice (GMP)

d) Bioavailability and Bioequivalence

e) New drug delivery systems.

SPECIAL CLINICAL PHARMACOLOGY

A. Preclinical evaluation of new drug dossiers

i) Animal pharmacology – general, specific, ED50

ii)Adequacy of data

iii)Toxicology data

iv) Animal pharmaceutical data / aspects

v) ED50, LD50, therapeutic index

B. Pathophysiology of specific diseases and clinical pharmacology of drugs used in

a) Ischaemic heart disease

b) Epilepsy

c) Hypertension

d) Heart failure

e) Oedema

f) Circulatory shock

g) Cardiac arrhythmias

h) Psychosis

i) Anxiety and affective disorders

j) Diabetes mellitus

k) Sleep disorders

l) Rheumatoid arthritis

m) Bronchial asthma

n) Peptic ulcer

o) Malignant diseases

p) Autoimmune disorders

q) Ocular conditions

r) Dermal diseases

s) Migraine

t) CNS degenerative disorders

u) Stroke

v) Hyperlipidemia

C. Fundamental principles involved in chemotherapy of microbial/ parasitic disease

a) Antimicrobials

b) Anti-malarial drugs

c) Anthelminthic drugs

d) Antiviral drugs (Dynamics / Kinetics)

e) Antifungal drugs

f) Antitubercular drugs

g) Antileprosy drugs

h) AIDS

D. Drug usage in

a) Renal failure

b) Hepatic failure

c) Cardiac failure

d) Extremes of ages

e) Pregnancy and lactation

f) Malnutrition

E. Clinically important drug interactions

a) Antiepileptics , hypnotics and psychoactive drugs

b) Cardiovascular drugs

c) Anti-inflammatory and analgesic drugs

d) Antimicrobials

F. Clinical pharmacology of contraception

a) Contraceptive agents

b) Assay of reproductive hormones

c) Metabolic and biochemical changes associated with oral contraceptives

d) Recent advances in contraceptive technology

e) Clinically important drug interactions of steroidal contraceptive.

G. Special problems in clinical trials

a) Prophylactic drug trial

b) Oral contraceptives and intrauterine devices

c) Central nervous system drugs

d) Cardiovascular drugs including diuretics

e) Drugs in tropical diseases

f) Acid peptic disease drugs.

H. Miscellaneous Topics

a) Transfer of drugs across blood-brain barrier

b) Gene-based therapy

c) Poisoning and its management

d) Products of recombinant DNA technology

e) Haematopoietic growth factors

f) Immunomodulators

g) Use of drugs for diagnostic purposes.

PRACTICALS

I Practical exposure to conduct an on-going clinical trials in one of the following areas :

a) Cardiovascular pharmacology

b) Reproductive pharmacology

c) Neuropsycho pharmacology

d) Gastroenterology

e) Renal pharmacology

f) Tropical medicine

g) Rheumatology

II. Visits to pharmaceutical companies / institutes / laboratories for training in area of drug developments.

III. Exposure to laboratory techniques and patient management

To be undertaken during clinical posting in Internal Medicine and

Emergency Department.

Laboratory Techniques :

a) Haematology	: Complete haemogram, prothrombin time	
b) Liver function tests	: SGOT, SGPT, Alk. Phosphatase, Serum bilirubin,	
c) Kidney function tests	: Urine analysis, Blood urea, Uric acid, Creatinine clearance	
d) Special tests	: Glucose tolerance test, Oral / I.V., Blood cholesterol, Triglycerides	
e) Clinical Biochemistry	: Blood / urine – electrolytes, blood glucose	
f) Hormone Assay	LH	Progesterone
	FSH	Estradiol
	hCG	Testosterone
	hPL	T3, T4
	TSH	Insulin
	ACTH	Cortisol

V. List of practicals to be demonstrated / carried out by the residents:

A. Pharmacodynamics

1) Methodology of recording blood pressure by NIBP & ambulatory B.P apparatus
2) Chronobiology of blood pressure and heart rate
3) Recording of E.C.G. and measuring heart rate
4) Effect of mental stress on blood pressure and heart rate

5) To study the effect of hand grip exercise on blood pressure and heart rate

6) To study the comparative effect of propranolol and labetalol on cold – stress induced increase in arterial blood pressure

7) To study the effect of sublingual nitroglycerin tablet on blood pressure and heart rate

8) To study the effect of sublingual isoprenaline on heart rate

9) To study the effect of beta-blockers on exercise tolerance in volunteers utilizing treadmill

10) To study the effect of sublingual nitroglycerin on haemodynamic changes in exercise

11) To study the haemodynamic effects of exercising on a treadmill

12) Assessing effect of drugs on psychomotor performance

13) Assessing analgesic effects of drugs in human volunteers

14) Spirometry and Respiratory function tests and effect of bronchodilators

15) Assessing the effect of diuretic on urinary volume and sodium, potassium excretion

16) Effect of NSAIDs on diuretic action in volunteers

17) To demonstrate the mydriatic, miotic and cycloplegic effect of drugs in volunteers

18) Effect of beta-blockers on isometric exercise induced increase in blood pressure

19) Effect of anticholinergic drugs on salivation, pupillary size, heart rate and memory

20) Effect of antihistaminic drugs on histamine-induced wheal and flare response

21) Assessment of sleep pattern in healthy human volunteers

22) Effect of sedative hypnotic on sleep architecture and pattern in healthy volunteers

23) Study of sleep pattern in insomnia and other sleep disorders and the effect of drugs on sleep pattern in them

24) Effect of drugs on pulse plethysmography in humans

B. <u>Pharmacokinetics</u>

1) To study the pharmacokinetics of paracetamol in healthy volunteers using HPLC method

2) To study the pharmacokinetics of sulphonamides in healthy volunteers using Spectrophotometic method

3) To assess the acetylator status of a patient / volunteer using isoniazid by spectrofluromteric /HPLC method

4) Monitoring of plasma levels of lithium in patients

5) Methods for estimation of sodium, potassium using flame photometry technique

6) Cumulative urinary excretion of drugs (sulphonamides) for estimation of pharmacokinetic parameters

7) To study the pharmacokinetics of aspirin in volunteers using spectrofluorimetric methods

8) To measure the hormone/drug levels by radio-immuno assay

9) To study the kinetics of phenytoin by HPLC method

10) To study the pharmacokinetics of carbamazepine by HPLC method

11) To study the pharmacokinetics of phenobarbitone by HPLC method

12) To study theophylline pharmacokinetics by HPLC method

13) Bioavailability and bioequivalence studies in volunteers

C. Pharmacogenomics

1) Extraction of DNA by phenol chloroform method

2) Quantitative analysis of DNA by spectrophotometry

3) Standard PCR procedure for CYP2C9*2

4) Setting up restriction digestion reaction – CYP2C9*2

5) Polyacrylamide gel electrophoresis – casting, loading, gel documentation

6) Web based design of PCR-RFLP for CYP2C9*2

3. Recommended Textbooks and Journals

The following is only a partial recommended list of the prevailing text books and journals at the time of the compilation of the syllabus. As and when new textbooks or journals become available, the candidates would be appraised accordingly.

3.1. Textbooks

1. Guide to Clinical Trials Bert Spilker, Raven Press, New York
2. Patient compliance in medical practice and clinical trials Bert Spilker, & Joyce Cramer, Raven Press
3. Data collection forms in clinical trials Bert Spilker, and John Schoenfelder Raven Press
4. Methodology of Clinical Drug Trials Alain Spriet, Dupin Spriet, Pierre Simon. Karger Publisher.
5. Techniques of Patient oriented research Charles Y C Pak, Perrie M Adams. Raven Press, New York.
6. Designing Clinical Research, Stephen B Hulley, Steven R Cummings. Williams & Wilkins
7. Drug treatment by Avery, ADIS publications.
8. Therapeutic Drugs Sir Collin Dollery , Churchil Lilvingstone.
9. Drugs in use Lina J Dodds.The pharmaceutical press.
10. Drug interaction Facts. David S Tatro. Facts and Comparison
11. Pharmacokinetics Made Easy. Donald J Birkett. The McGraw Hill Company Inc.
12. Clinical Pharmacokinetics Concepts and applications.Malcom Rowland. B.I.Waverly Pvt Ltd.
13. Clinical Pharmacology. DR.Laurence.Churchil Livingstone
14. Pharmacoepidemiology. Brain L Strom. Wiley Publishers.
15. Biostatistics a foundation for analysis in the health sciences. Wayne W Daniel. Wiley Publishers

16. Principles of Pharmacology Basic concepts and clinical Applications .Paul L Munson Chapman & Hall.

17. Integrated Pharmacology. Page .Curtis Mosby Publishers

18. Conns Current Therapy. W B Sanders company

19. Davidson's Principles and practice of Medicine. C R W Edwards. Churchil Livingstone

20. Goodman & Gilman's The Pharmacological Basis of Therapeutics. Brunton LL, Parker KL.

21. Harrison's Principles of Internal Medicine. Harrison. McGraw Hill

22. Pulmonary and Antiallergic drugs. Delvin P John. Wiley & Sons

23. Patient package insert as a source of drug information. Bogaert Marc etal. Excerpta Medica

24. Introduction to drug metabolism .Gibson G, Gordon and Skett Paul. Chapman and Hall.

25. Techniques of patient oriented research. Pak Y , C. Charles , Akams M Perrie. Raven press

26. The Broad range of clinical use of Phenytoin. Barry H Smith. Dreygus Medical Foundation

27. Clinical Pharmacy and Therapeutics. Walker Roger and Edwards Clive. Churchil Livingstone

28. Pharmacology. Goth Andrews, Vessel S Elliot. C.V. Mosby Company

29. Modern Pharmacology. Craig R Charlges, Stitzel E Robert. Little Brown Company.

30. Drug Induced liver disease. Farrel C Geoffrey. Churchil Livingstone

31. Human Pharmacology. Brody M Theodore et al.C.V. Mosby.

32. Principles of Clinical Toxicology. Thomas A, Douglas J Bricker. Raven Press.

33. Cardiovascular Drug Therapy. Messel H Franz. W.B. Sanders.

34. Assessing Causes of Adverse Drug Reactions. Vanulet Jan. Academic Press Subsidiary of Hart court Bruce Jovenic Publishers

35. Handbook of Clinical Research. Liyod Julia. Churchil Livingstone

36. Basics and clinical Pharmacology. Katzung G Bertram. Appleton & Lange

37. Drugs in Pregnancy and Lactation. Bridges G. Gerald et al .Williams and Wilkins

38. Cardiovascular Pharmacology and Therapeutics. Bramah W Singetal. Churchill Livingstone

39. Meyler's Side effects of Drugs. Dukes MNG. Elseiver Publications

40. Evaluations of Drug Interactions Shinn F Arthur & Shrewsbury P Robert. C.V. Mosby Company

41. AMA Drug evaluations. AMA division of drugs .W.B. Sanders Company

42. Clinical Toxicology. C.J. Poison et al. Pitman Publications

43. Board Review series Pharmacology. Rosenfeld. Williams & Wilkins.

44. Manual of antibiotics and infectious Diseases. Conte. Williams & Wilkins.

45. Clinical Pharmacology made Ridiculously Simple. Olson. McGraw Hill.

46. Topics in Clinical Pharmacology and Therapeutics. Maronde F Robert. Springer Verlag.

3.2. Journals

1. British Journal of Clinical Pharmacology
2. European Journal of Clinical Pharmacology
3. Clinical Pharmacology and Therapeutics
4. Nature Reviews Drug Discovery
5. Drugs
6. Pharmacotherapy
7. Annual Reviews of Pharmacology and Toxicology
8. Journal of Clinical Pharmacology
9. International Journal of Clinical Pharmacology
10. Annals of Pharmacotherapeutics

11. Applied Clinical Trials
12. Postgraduate Medical Journal
13. Therapeutic Drug Monitoring
14. The Lancet
15. American Journal of Medicine
16. Annals of Internal Medicine
17. British Medical Journal
18. New England Journal of Medicine
19. Journal of Cardiovascular Pharmacology
20. Pharmacogenetics & Pharmacogenomics
21. Pharmacogenomics
22. Journal of Pharmacogenomics
23. Clinical Pharmacokinetics
24. Journal of Chromatography and Biomedical Applications
25. Indian Journal of Experimental Biology
26. Indian Journal of Medical Research
27. Archives of Internal Medicine
28. Drug Safety

4. Mode of Selection

4.1. Selection – Guidelines

1. Students for DM (Clinical Pharmacology) shall be selected strictly on the basis of their academic merit.

2. For determining the academic merit, the Institution may adopt course :- (i) On the basis of merit as determined by a competitive test conducted by a competent authority on a national level.

4.2. Eligibility

1. Candidates should have passed M.D degree in Pharmacology or General Medicine or Pediatric Medicine from any University recognised by the Medical Council of India.

2. Candidates should have passed DNB in Pharmacology or General Medicine or Pediatric Medicine with thesis approved.

3. Candidates appearing for M.D Pharmacology/General Medicine/Paediatric medicine or DNB Pharmacology/General Medicine/Pediatric Medicine examination and expecting results before admission may also submit their application subject to the condition that they pass their qualifying examination before admission.

4.3. Procedure for selection

1. There will be an Entrance Examination conducted by the Institute on a National Level at JIPMER, Pondicherry in the month of June/July. The advertisement for the same would be published in all the leading national newspapers and employment news in the month of April/May.

2. The written examination would consist of 100 MCQs (75 in Pharmacology, 25 in General Medicine & Pediatrics). The duration of the examination will be $1^{1/2}$ hours.

3. The correct answer should be blackened with black ball point pen.

4. Each answer with correct response will carry 4 marks and one negative mark for wrong answer and no negative mark for unanswered question.

5. After the written examination there will be a personal interview for the merit listed candidates at the rate of 5 candidates for one seat.

6. The personal interview will carry 20 marks.

7. The final merit list will be drawn on the basis of marks obtained both in written examination and in personal interview.

8. A detailed prospectus would be published and sent along with the application form giving all details of the mode of eligibility of admission, submission of application, procedure for selection, date of joining, contract and emoluments, leave during residency, accommodation, duties and responsibilities, hours of work, leave, certificates, fees etc.

9. The course would commence ordinarily on 1st August.

4.4. Sample MCQs for D.M. (Clin. Pharm) Entrance Exam

1. A 160 mg dose of a drug was administered i.v, and 80 mg was eliminated during the first 120 minutes. If the drug follows first order elimination kinetics, how much of the drug will remain 6 hours after its administration ?

   A. None B. 10 mg

   C. 20 mg D. 40 mg Ans: C. 20 mg

2. Intravenous administration of epinephrine to a patient results in severe decrease in diastolic pressure & an increase in cardiac output. Which of the following drugs might the patient have previously taken that could account for this effect?
   A. Propranolol B. Atropine
   C. Phenylephrine D. Prazosin Ans: D. Prazosin

5. Training

5.1. Period of Training

The period of training for obtaining the degree of D.M in Clinical Pharmacology shall be three completed years (including the examination period) after obtaining M.D degree, or equivalent recognised qualification.

5.2. Training Programme

1. All the candidates joining the D.M (Clin Pharm) training programme shall work as full time senior residents during the period of training , attending not less than 80%(Eighty percent) of the training during the calendar year, and given full time responsibility, assignments and participation in all facets of the educational process.
2. They shall maintain a log book and record of the work carried out by them and the training programme undergone including details of the procedures done in ward postings, various labs, etc.
3. During training for the D.M (Clin Pharm) there shall be proper training in basic medical sciences related to clinical pharmacology. Emphasis to be laid on drug therapy and emergency care services.

4. The D.M (Clin Pharm) student shall be required to participate in the teaching and training programme of undergraduate and postgraduate students in the departments of pharmacology, medicine, pediatrics etc.
5. Training in medical audit, management, health economics, health information system, basics of statistics, exposure to human behaviour studies, knowledge of pharmacoeconomics and introduction to non linear mathematics shall be imparted.
6. Students will be given graded responsibility in the management and treatment of patients entrusted to their care
7. They will participate in seminars, journal clubs, group discussions, clinical meetings, grand rounds and conferences, advanced diagnostic, therapeutic & laboratory techniques.

5.3. Teaching Learning Schedule

5.3.1. Clinical / Laboratory Postings

Year	No.of months	From …To	Posting
First	1	Aug	Clinical Pharmacology Lab
	1	Sep	HPLC Lab
	2	Oct & Nov	Medicine
	1	Dec	Drug Information Centre
	1	Jan	Emergency medicine
	2	Feb & Mar	Clinical Trial Room
	2 weeks	Apr	Medical ICU
	2 weeks	Apr	Paediatrics
	1	May	ADR monitoring
	1	Jun	Pharmacogenomics Lab
	1	July	Sleep lab
Second	2	Aug & Sep	Pharmacogenomics Lab
	1	Oct	Cell Culture Lab
	2	Nov & Dec	Clinical Pharmacology lab
	1	Jan	Psychomotor Testing Lab
	1	Feb	RIA Lab
	2	Mar & Apr	Clinical Trial Room

	1	May	Immunology – Ward & Lab
	1	Jun	Pharmacodynamics Lab
	1	July	Psychiatry
Third	1	Aug	Pharmacovigilance centre
	3	Sep – Nov	Pharmacogenomics Lab
	1	Dec	Drug Industry / CRO
	3	Jan – Mar	Clinical Pharmacology Lab
	1	Apr	Clinical Trial Room
	1	May	LC-MS Lab
	1	Jun	Drug Information Centre
	1	July	Exam

5.4. Academic Programme

5.4.1. Departmental

- **Journal Club** – Critical appraisal of original research article published in peer reviewed national / international journals. The presenter will be assessed by all the faculty and marks recorded in log book.
- **Subject Review** – Complete updated review of literature with critical analysis of major topics in clinical; pharmacology and therapeutics. The abstract of the review should be circulated at least one week prior. The presenter will be assessed by all the faculty and marks recorded in log book.
- **Lectures / Practical Demonstrations** – Lectures in statistics and research methodology will be conducted periodically. Students have to complete and submit the given assignments regularly. The clinical pharmacology experiments will also be demonstrated. Students have to practice and familiarize these experiments. The clinical pharmacology experiments and procedures performed by the students should be recorded in the log book. A record should also be maintained.
- **Symposium** – A broad topic will be selected and each part will be dealt by a postgraduate student. It should be a complete, systematic, evidence based review of the topic. The session will be moderated by a Professor.

5.4.2. Interdepartmental

- **Interdepartmental Colloquium -** Monthly meetings between the departments of Medicine, Cardiology and Clinical Pharmacology Unit of Department of Pharmacology.
- **Modular Teaching -** Participation in Undergraduate Modular Teaching in the subjects of Clinical Pharmacology and Therapeutics.
- **Bed-side Clinics** - For postgraduates in the various clinical departments.

5.4.3. Central (Institutional)

- Monthly meeting of JIPMER Scientific Society
- Monthly Medical Review Meeting
- Death Audit Meeting

6. Examination & Evaluation

6.1. Evaluation of the student during the course

The student will be assessed continuously during the training program.

6.1.1. Log Book & Practical Record

The student's monthly performance is recorded by the faculty of the department / laboratory where he / she has worked. The students have to maintain a log book and get it signed from the faculty periodically. Their performance in clinical postings, departmental activities like journal club, subject review etc. will be assessed and included for internal assessment marks. They will be assessed on attendance, sincerity, skills learnt. Objective evaluation, based on scores for mastering particular skills will be done whenever possible.

All students have to maintain a practical record and get it signed periodically by a faculty.

6.1.2. Internal Assessment

Notified written tests and practical will be conducted on different topics followed by a viva voce. Two tests will be conducted per year with an additional send-up exam in the final year. The internal assessment marks will be calculated from the best 5 performances out of six notified tests (excluding send up examination).

The maximum marks for the internal assessment is 200 (theory-90, viva-10, Practical-80, records-20). They should score at least 50% to appear for the final examination.

6.1.3. Dissertation

Each student will carry out a clinical research work under the supervision of a eligible faculty member of the Pharmacology department. The dissertation will be reviewed by all faculty members of the department once in 6 months. The dissertation will be submitted to the institute and will be evaluated by a panel of examiners appointed by the Institute. The candidate should score at least 50% of marks for acceptance of his dissertation work. Acceptance of dissertation will be a prerequisite for the candidate to appear in the final examination.

6.2. Scheme of Theory, Practical and Oral Examination

6.2.1. Attendance

The candidate will have to put in 80% attendance each year and show satisfactory progress as evidenced by the internal assessment. In case of unsatisfactory attendance/progress, the candidate may be withheld from appearing for the university examination.

6.2.2. Dissertation

Dissertation will be evaluated by two different examiners and not by the examiners for theory and practical exam. The examiners should be given minimum of three weeks to evaluate them and send their marks with the specific comments. The candidate should score at least 50% of marks for acceptance of his dissertation work. Acceptance of dissertation will be a prerequisite for the candidate to appear in the final examination.

6.2.3. Board of examiners

Board of examiners will consist of four members. The examiner should be clinical pharmacologist with at least 10 years of teaching experience and should not be below the rank of associate professor of the four, two will be internal examiners and other two will be external examiners.

6.2.4. Theory examination

It consists of four papers (to be conducted in four days). Each paper carries the maximum of 100 marks. The duration of each paper is three hours.

Paper-IGeneral Clinical Pharmacology

Paper-II Methodology in clinical drug evaluation

Paper-III Systemic clinical pharmacology

Paper IV Recent advances in therapeutics

Each paper will have ten short note questions of ten marks each.

6.2.5. Practical Examination

Day I - Forenoon

One pharmacodynamic experiment followed by viva-voce (maximum: 50 marks)

Day I - Afternoon

a. Designing a phase I/II/III/IV clinical trial. The aim of the trail will be given and any necessary information asked by the candidate (maximum: 50 marks).

b. Problem solving exercises in clinical pharmacology – 5 problems (maximum: 25 marks).

Day II - Forenoon

One pharmacokinetic experiment followed by viva-voce (maximum: 50 marks)

Day II – Afternoon

a. Defense of dissertation - The candidate will be required to defend his dissertation in front of all four examiners (maximum: 25 marks).

b. Oral examination - All four examiners seated together will hold oral examination (maximum: 100 marks).

6.2.6. Total Marks

Theory	400
Practical	200
Oral	100
Dissertation	100
Internal assessment	200

Total marks **1000**

6.2.7. Minimum Requirement to Pass

Theory and viva 50%

Practical 50%

Dissertation 50%

6.3. Model Theory Question Paper

D.M. (Clinical Pharmacology)

Paper I – General Clinical Pharmacology

Time: 3 hours *Answer all questions* *Max. marks: 100*

Write short notes on:

1. Clinical significance of plasma protein binding of drugs
2. Polymorphisms of drug metabolizing enzymes
3. Two compartment pharmacokinetic model
4. $t_{1/2\alpha}$ and $t_{1/2\beta}$.
5. Ligand gated ion channels
6. Methods to improve adherence to medication
7. Strategies to minimize adverse drug reactions
8. Drug dose adjustments in renal failure
9. Prescription event monitoring
10. Target concentration intervention (TCI).

D.M. (Clinical Pharmacology)

Paper II – Methodology in Clinical Drug Evaluation

Time: 3 hours *Answer all questions* *Max. marks: 100*

Write short notes on:

1. Phase 0 clinical trials
2. Lead identification and optimization
3. Sequential design in clinical trials
4. Safety monitoring in clinical trials
5. Schedule Y
6. Methods to minimize bias in clinical research
7. Regulatory requirements for starting Phase I clinical trial for a new chemical entity
8. High throughput screening
9. Postmarketing surveillance
10. Clinical trials registry

D.M. (Clinical Pharmacology)

Paper III – Systemic Clinical Pharmacology

Time: 3 hours *Answer all questions* *Max. marks: 100*

Write short notes on:

1. Common adverse drug reactions of antiepileptics
2. Coanalgesics
3. Concerns in using thiazolidinediones
4. Cell cycle specific anticancer agents
5. Methods to counteract drug resistance ti antimicrobials
6. WHO ladder for management of pain
7. Renin inhibitors
8. Treatment of hypertensive emergencies
9. Ways to minimize adverse drug reactions to corticosteroids
10. Heliox

D.M. (Clinical Pharmacology)

Paper IV – Recent Advances in Therapeutics

Time: 3 hours *Answer all questions* *Max. marks: 100*

Write short notes on:

1. CGRP antagonists for migraine
2. GINA guidelines for treating bronchial asthma
3. Newer antianginal agents
4. Nanomedicine
5. Recent guidelines for managing heart failure
6. Novel insulin analogs
7. Newer drug targets for rheumatoid arthritis
8. Current concepts in management of deep vein thrombosis
9. Neuroprotective therapy for parkinsonism
10. Tumor vaccines