

Guidelines for Development and Implementation of ASHI Accredited Director Training Programs

Background: With the formation and implementation of the national Organ Procurement and Transplantation Network as contracted to the United Network for Organ Sharing (UNOS), it became apparent that there was a shortage of qualified histocompatibility laboratory directors who met the standards established by the (then) Health Care Financing Administration (HCFA), the American Society for Histocompatibility and Immunogenetics (ASHI), and UNOS. The need for qualified directors has been further exacerbated by the growth in bone marrow transplantation, since the National Marrow Donor Program (NMDP) also requires histocompatibility directors meeting ASHI standards. In an effort to address this shortage, UNOS established a committee to develop a post-doctoral training program for histocompatibility directors that drafted guidelines for such a program. They were not implemented by UNOS, at least in part because the committee recognized that histocompatibility testing encompasses more than support of solid organ transplantation and believed that a program under the auspices of ASHI would better ensure comprehensive training. In May 1991, at the request of UNOS, an ASHI committee was formed to establish guidelines for the implementation of a training program.

After preliminary discussion, it was decided that the most productive approach would be for ASHI to provide approval or certification of training programs. This approach would allow approval of existing post-doctoral programs, while encouraging establishment of training programs at other institutions. Initially the sole function of this committee was to evaluate and approve programs that meet established guidelines. The ASHI committee incorporated many of the recommendations from the UNOS report on a laboratory directors' training program (LDTP) into this proposal. The mandate of the committee has since expanded to include review of director qualifications and portfolios. This committee is designed to be self-supporting through application fees. Sponsorship and selection of director-trainees will remain the responsibility of the institutions approved for training programs.

The format for approved post-doctoral training programs will be a two-year fellowship in an ASHI accredited laboratory. During this time, the trainee will work under the guidance of an ASHI qualified director receiving instruction as well as "hands on" experience. This approach will provide the two years of formal training required by ASHI and UNOS standards for a histocompatibility director (Appendix A).

Purpose: To provide guidelines for the review and approval of training programs for post-doctoral candidates for histocompatibility laboratory directors and to ensure consistent quality by evaluating these programs against established criteria for curricula, requisite faculty and facilities. Completion of an approved training program should provide a candidate with two years education and experience in partial fulfillment of the requirements for a qualified histocompatibility director under CLIA/CMS, UNOS and ASHI standards. The completion of a training program is not a requirement for eligibility for the ABHI board examination for Diplomate status. Training programs, however, will be evaluated partly on the preparation provided for successful completion of this examination.

A. GUIDELINES FOR SELECTION OF CANDIDATES

At present CMS, UNOS and ASHI have standards that define the minimum training and experience requirements for histocompatibility laboratory directors (Appendix A). Completion of 4 years post-doctoral experience in immunology, two of which were devoted to histocompatibility, is a route for qualification that is common to all three sets of standards. ASHI and UNOS offer an additional, alternative route for qualification, which is by accumulating 5 years of working experience in human histocompatibility testing. Training programs approved under ASHI guidelines would provide candidates with the two years of formal training in human histocompatibility testing which is required under the first route for qualification. Accumulation of 5 years working experience would remain an option for candidate directors, but would not involve ASHI approved training programs.

Selection of candidates for training programs will be entirely the purview of the institutions or organizations sponsoring the two-year fellowship. To be approved, however, a training program should have and should submit general guidelines for candidate selection. Consideration should be given to the ability of candidates to complete the experience requirements, since all certifying agencies require a minimum of 4 years post-doctoral experience or training to qualify as a histocompatibility director and an approved training program would fulfill only the two years requirement in

histocompatibility.

B. CRITERIA FOR APPROVAL OF TRAINING PROGRAMS

1. Curriculum

Curricula for training programs should provide trainees with the necessary knowledge, experience and skills to competently fulfill the responsibilities of a histocompatibility director. Such responsibilities may be quite diverse, as illustrated in the following description (adapted from the UNOS LDTP committee) of a histocompatibility laboratory director's required expertise:

The first responsibility of the Director of the Transplantation Histocompatibility Laboratory is to define the program of the laboratory by developing protocols, introducing and updating specific procedures, establishing laboratory standards with appropriate controls, and maintaining surveillance of laboratory accuracy, efficiency, and overall performance. A Director's responsibility may consist, wholly or in part, of defining phenotypical or genotypical HLA polymorphisms in samples from patients and/or donors for solid organ or bone marrow transplants, and/or from those being evaluated for disease markers linked to the HLA region, or for genetic determination of parentage. In the case of a transplantation evaluation, additional competency is required in methods of evaluating the potential for hyperacute rejection or early graft loss, as well as the biological relevancy of any pre-existing anti-HLA or tissue specific antibodies prior to transplant. Each area of evaluation may require individualized testing, depending on the tissue being transplanted, the condition of blood/tissue samples, and the clinical status of potential donors and recipients. Thus, the Director should be familiar with all relevant typing techniques to be used by the histocompatibility laboratory. These techniques focus on three major areas: serology, flow cytometry and molecular biology, one or all of which may be required to obtain clinically relevant information on HLA polymorphism. Cellular testing may also be used in some laboratories.

Importantly, as new technologies develop, the Director should be able to evaluate and apply new techniques as necessary for improved patient care.

In addition to the primary responsibility of the scientific and technical direction of the laboratory, a histocompatibility director must be able to correlate laboratory data with clinical and pathologic findings. He/she should be able to provide consultation on individual patients, recommending additional testing when appropriate. To do this effectively, the director must have some basic understanding of the clinical aspects of the patient populations served by the laboratory. Laboratory directors must also serve as manager and administrators; therefore, knowledge of management principles is essential. To ensure coverage of these important areas, each training program shall establish a curriculum that includes the following topics:

- a) **Science of histocompatibility testing: immunogenetics, immunobiology, and transplantation immunology; principles of serological, flow cytometric, cellular and DNA methods used in histocompatibility testing.** Specific topics in histocompatibility should include the genetics and biochemistry of public and private HLA epitopes; the genetics and biochemistry of other MHC components; analysis of antibody specificity; principles of immune regulation, and the principles of various crossmatching techniques. Instruction may be provided by didactic presentations/courses, seminars, reading assignments or a combination of these. See Appendix C for specific topics that should be included.
- b) **Clinical aspects of diseases for which histocompatibility testing is useful.** Histocompatibility directors should have an appreciation of the diseases that may lead to specific organ failure and the clinical management of recipients pre- and post-solid organ transplantation. Trainees should be aware of potential risk factors, such as previous sensitization, and learn what precautions or additional testing is warranted in such cases. Trainees should also become familiar with the increasing number of diseases treatable by bone marrow transplantation; the prognosis associated with these different disorders; and the comparative benefits/risks associated with related versus unrelated marrow donors. Trainees should also be familiar with diseases for which HLA associations have been demonstrated. Instruction may be provided by trainee participation in clinical rounds or seminars with clinical fellows or residents. Trainees should also participate in regular transplant conferences for the evaluation of potential transplant recipients.
- c) **Technical considerations of methods used in histocompatibility testing.** Training programs must provide "hands-on" experience in three requisite areas: serological assays, flow cytometry and DNA technology. Experience in cellular techniques may also be included, but is not required. A senior technologist or bench supervisor may conduct bench training. It is essential that trainees be given ample experience to learn the technical details and problems inherent with

test methods in order to be competent to "trouble-shoot" procedures, as well as to correctly interpret assays requiring subjective evaluation, eg. crossmatches, under the stress and time constraints which usually accompany solid organ histocompatibility testing. Details of the specific tests that should be included are given in Appendix B.

- d) **Interpretation of test results and recommendations for further testing.** A most important area of training is the actual participation by the trainee in the interpretation of test results and consultation with physicians regarding further recommended testing or follow-up studies. Because transplantation is such a large component of histocompatibility testing, sufficient experience should be obtained by trainees such that they will be competent to: 1) Develop a patient file according to the individual needs of each type of transplant operation; 2) Interpret the patient file by analyzing the composite results and provide a clinically useful assessment of these data to the managing physician; and 3) Provide pre- and post-transplant monitoring. Experience in this area is best gained by co-reviewing cases with the director of the training program. Trainees will be required to compile a portfolio of cases (see Appendix B).
- e) **Management Principles.** Each training program must offer trainees instruction in basic management principles, as well as in topics unique to histocompatibility/transplantation laboratories. Because many histocompatibility labs are now independent, rather than hospital or university based, knowledge of laboratory management is vital to trainee-directors since they may not have institutional managers to assist in the administration of their future labs. Instruction may be provided by seminars, existing courses, or by sending trainees to management workshops. The following topics should be included:
- Federal, state and other accreditation regulations and standards.
 - Development of contracts, cost centers, referral basis.
 - Personnel management - recruitment, selection, training, and continuing education.
 - Organization of laboratory - effective use of personnel, distribution of workload.
 - Employee benefits, health plans.
 - Personnel Health and Safety - OSHA standards; safeguards for biologic, chemical, and radioactive hazards.
 - Details of ESRD Cost Report
 - Fee scheduling, cost accounting, budget preparation
 - Risk Management
 - Legal/professional liability
- f) **Patient files: data management and analysis.** A laboratory director must have ready access to both the laboratory data and pertinent clinical information in order to provide meaningful consultation on individual patients. For transplant patients, this information will include: HLA phenotype or genotype; level and specificity of any antibodies; medical history and primary diagnosis; prior transplants, transfusions, pregnancies, medications or other risk factors. Because ready access to this information is vital, it is best stored and classified in computer programs. The trainee should be given the opportunity to design or assist in the design of necessary data base files. Utilizing these files or pre-existing ones, the trainee must have the opportunity to analyze the data and their statistical significance. If needed, the trainee should be encouraged to take courses in the basic principles of statistics, computer operations, and programming.
- g) **Research and Development.** Because histocompatibility testing is continually evolving, each trainee should be given the opportunity to pursue a research project. This project could be in the development and standardization of new techniques, or in clinically applied research, but should be relevant to clinical applications of histocompatibility.

2. Faculty

Each training program shall be directed by an individual who is qualified by ASHI Standard B 1.000 to direct a histocompatibility laboratory. The director should have expertise in all areas of the training curriculum or there should be other, appropriately qualified, doctoral level personnel available. The director(s) shall be available throughout the two-year training for regular tutorial sessions with the trainee(s) to review and discuss test results and interpretations. The interaction

of the trainee with the laboratory director is an important component of the training program; therefore, at least 50% of the Director's time should be committed to laboratory activities. There should be at least a 10% time commitment to the training program that can be divided among participants if multiple directors are involved in the program.

3. Facilities

To be approved, a training program must be centered in an ASHI accredited laboratory currently holding approval in the categories of:

Serological Typing
 Renal and Non-Renal, Solid Organ Transplantation
 Bone Marrow Transplantation
 DNA Typing - HLA
 Flow Cytometry

The laboratory should have sufficient space and equipment to permit bench training and research by the trainee(s).

Alternate Sites: If not all categories are held by the training program laboratory, it is acceptable to arrange for the trainee to spend time in another laboratory that is accredited in the appropriate category (ies). Because it is beneficial for trainees to be exposed to different programs, reciprocal arrangements between training laboratories will be encouraged. It is suggested that applicants for training program approval consider including in their curricula 1-2 short (1-4 weeks) rotations in other approved laboratories.

C. SUGGESTED FORMAT FOR TRAINING CURRICULUM

It is recognized that training programs may emphasize different areas depending upon individual research interests and clinical services. However, there are certain fundamental areas where sufficient time must be spent to ensure adequate training, and certain topics may require exposure throughout the course of the two-year program. For example, the basics of serologic typing procedures can be learned during a six-month rotation, but interpretation of problematic crossmatches and analysis of antibody screening results should be performed throughout the two-year fellowship to provide a sufficient number of cases. Programs should be designed to include, on a regular basis throughout the program, routine review of test results and compilation of case files. Such review can be done concurrently with other areas of work. Similarly, the research or development project can be done concurrently with other rotations, and any area in the curriculum can be expanded into the research focus.

As long as all topics are adequately covered in a training program curriculum, no specific time frames will be required. Moreover, because trainees will differ in their educational backgrounds and training, the curriculum may be modified to meet the individual needs of a particular trainee. For example, if a trainee has a strong background in immunology, the curriculum should be adapted to reduce the time spent in lectures or review of immunobiology and increase the time available for other areas, eg. genetics or molecular biology. The following is a suggested, general format that would be suitable for most trainees:

<u>Topic:</u>	<u>Time Commitment:</u>
Serological Assays	6 months
Cytotoxicity	
Genotyping	
Crossmatch assays	
Antibody Screening	
DNA Technology	6 months
DNA Isolation	
DNA amplification	
Electrophoresis	
Typing technologies (SSP, SSOP, etc)	
Specialty Assays - Immune Monitoring	1 month
OKT3, CD3	

IL-2R	
CD34	
Flow Cytometry	3 months
Flow crossmatch	
Flow PRA	
Immunophenotyping	
Optional Rotation in another lab or area	1 -4 weeks
Engraftment	
Sequencing	
Cellular Assays	

On-going Activities throughout two-year fellowship:

Lectures, seminars in basic immunobiology (Appendix C)

Participation in Clinical rounds, conferences

Review, interpretation of tests; consultation with physicians regarding further testing; compilation of case files.

Clinical research/development project(s): Clinical research is encouraged, but primary emphasis should be on clinical testing. Ongoing research might be about 20-25% of the trainee's time.

Additional responsibilities, eg. provision of "on-call" coverage, assistance to lab director, etc., may be designated by individual training programs, particularly if the institution is funding the training fellowship equivalent to a resident or "house staff" position.

D. DIRECTOR TRAINING REVIEW COMMITTEE

The committee will be comprised of at least 5 members in addition to the chair, all of who will be directors of ASHI accredited laboratories and hold the Diplomate, ABHI board certification.

Committee Responsibilities: The Director Training Review committee will evaluate all applicant training programs for their qualifications and ability to meet the established guidelines. The period of accreditation or approval for training programs successfully meeting the guidelines will be for five years. The initial evaluation will include an on-site inspection for evaluation of facilities and to meet and discuss the curriculum with the program faculty. The committee will also be responsible for reviewing and revising the guidelines for training programs as technology or clinical service needs change.

E. APPLICATION PROCEDURE

Applicants wishing to submit post-doctoral training programs description to be considered for approval should submit the following:

1. Program Curriculum.

A two-year curriculum should be submitted with details of each rotation or lab experience that will be available for trainees. The description should include the proposed time to be spent in each rotation. Any special courses or seminars to be taken by trainees should also be included, as well as rotations in other laboratories. The scope and level of activity in each program area must be adequate for comprehensive training. The application must include a copy of Subpart B, Laboratory Activities, from the most recent ASHI Accreditation renewal.

2. Program Director and other personnel.

The application should include a list and description of responsibilities for the program director and other pertinent personnel, eg. Associate Directors, laboratory supervisors, or senior technologists. Curriculum vitae should be included for the Program Director/Laboratory Director and for any other personnel with major teaching responsibilities. A list of any past

pre-and post-doctoral trainees, their training periods, and current positions should be provided. Letters of commitment, which define the extent of support through clinical rounds, conferences, etc., should also be included from the director(s) of transplant program(s) and organ procurement agency.

3. Facilities.

A brief description of laboratory space and equipment should be included and should also indicate the availability of research/development space. A description of past and current research and development projects should be provided, including titles of funded grants and/or contracts.

4. Program Funding.

The application should indicate support for the training program, including: fellowship or stipends available for trainees; support available for trainee research projects; and funds available for rotations in other approved laboratory training programs.

5. Institutional Approval.

As required by each institution, each application should include letters of commitment from the appropriate institutional official(s). These letters should state institutional non-discrimination policies, citizenship requirements, etc., which may affect candidate selection.

6. Application fee.

An initial application fee of \$1500 will be charged to cover the costs of the on-site review. At the end of the five-year period of approval, all programs must fully reapply and submit another application fee.

7. Application submission.

The original copy of the application should be sent to the ASHI Executive Office and a copy to the Chair of the Director Training Review Committee. If available an electronic copy should be sent to the committee chair. If an electronic copy cannot be sent, 8 additional copies must be sent to the ASHI office.

F. APPLICATION REVIEW

Upon receipt of an application, the Committee Chair will review each application for completeness and obtain additional information as needed. The full committee will review the application and provide comments to the chair regarding the appropriateness of the application. One committee member will be responsible for scheduling a site visit to evaluate the facilities and to review the proposed curriculum with the laboratory director and other training program faculty. A second committee member may participate in the site visit. A summary report of the site visit and an overall evaluation for each applicant will be distributed to the entire committee for review. The Chair will assess the opinion of the committee for the final decisions on the approval of training programs by email or the chair may convene the committee through a conference call. To be approved, at least three-fourths of the committee members must vote favorably for a program. The committee may give provisional approval to programs if there appear to be only minor deficiencies with the proposed curriculum or facilities. In such cases, applicants will be notified in writing of the committee's evaluation and suggestions. Upon receipt from the applicant of a modified curriculum or correction of any deficiencies, the program may be fully approved. If an applicant is denied approval, the decision of the Training Program Review Committee may be appealed to the ASHI Board. A letter requesting review by the Board must be sent to the ASHI President within 30 days of the receipt of the committee's decision.

1. Program responsibilities:

Accreditation will be for 5 years. During that time, the training program director should notify the DTR committee chair when trainee directors begin and end training programs.

2. Renewal of Program Approval.

The Program Directors from each approved program will be required to submit a renewal application every five years. This renewal application must contain the same information as required in the initial application and should indicate any changes in the curriculum, key personnel or facilities. The same deadlines and procedures for committee review will apply to renewal applications as for initial ones. Evaluation of renewal applications will be on the same basis as for initial applications.

APPENDIX A

Standards for Histocompatibility Laboratory Directors

1. HCFA Standards (effective September 1, 1992)

493.1443 (o) If the laboratory performs tests in the specialty of histocompatibility, the individual functioning as the technical supervisor must either—

- (1)
 - (i) Be a doctor of medicine or osteopathy licensed to practice medicine or osteopathy in the state in which the laboratory is located; and
 - (ii) Have training or experience that meets one of the following requirements:
 - *(A) Have 4 years of laboratory training or experience, or both, within the specialty of histocompatibility; or
 - *(B)
 - (1) Have 2 years of laboratory training or experience, or both, in the specialty of general immunology; and
 - (2) Have 2 years of laboratory training or experience, or both, in the specialty of histocompatibility; or
- (2)
 - (i) Have an earned doctoral degree in a biological or clinical laboratory science from an accredited institution and
 - (ii) Have training or experience that meets one of the following requirements:
 - *(A) Have 4 years of laboratory training or experience, or both, within the specialty of histocompatibility; or
 - *(B)
 - (1) Have 2 years of laboratory training or experience, or both, in the specialty of general immunology; and
 - (2) Have 2 years of laboratory training or experience, or both, in the specialty of histocompatibility.

2. ASHI Standards

B1.000 A Director/Technical Supervisor must hold an earned doctoral degree in a biologic science, or be a physician, and subsequent to graduation must have had four years experience in immunology or cell biology, two of which were devoted to formal training in human histocompatibility testing. Credit toward this 96 weeks can be applied at the rate of 19 weeks for each year of appropriate working experience in human histocompatibility testing. The Director must have documentation of professional competence in the appropriate activities in which the laboratory is engaged. This should be based on a sound knowledge of the fundamentals of immunology, genetics and histocompatibility testing and reflected by external measures such as participation in national or international workshops and publications in peer-reviewed journals. He/she is available on site commensurate with workload at the laboratory, provides adequate supervision of technical personnel, utilizes his/her special scientific skills in developing new procedures and is held responsible for the proper performance, interpretation and reporting of all laboratory procedures and the laboratory's successful participation in proficiency testing.

3. UNOS Standards

B1.000 Consistent with current Clinical Laboratory Improvement Act (CLIA) regulations, the laboratory must have a Director, a Technical Supervisor, and a Clinical Consultant. When the appropriate criteria are met as defined by CLIA '88, one individual may serve in 1, 2 or all 3 capacities, i.e., Laboratory Director, Technical Supervisor and Clinical Consultant.

B2.000 A Director/Technical Supervisor must hold an earned doctoral degree in a biologic science, or be a physician, and subsequent to graduation must have had four years experience in immunology or cell biology, two of which were devoted to formal training in human histocompatibility testing. Credit toward these two years can be applied at the rate of 0.4 years for each year of appropriate working experience in human histocompatibility testing. The Director must have documentation of professional competence in the appropriate activities in which the laboratory is engaged. This must be based on a sound knowledge of the fundamentals of immunology, genetics and histocompatibility testing, and reflected by external measures such as participation in national or international workshops and publications in peer-reviewed journals. He/she is available on site commensurate with the workload at the laboratory, provides adequate supervision of technical personnel, utilizes his/her special scientific skills in developing new procedures, and is held responsible for the proper performance, interpretation, and reporting of all laboratory procedures and the laboratory's successful participation in proficiency testing.

APPENDIX B

I. Technical Function of the Clinical Histocompatibility Laboratory

A. Basic and Required

1. Lymphocyte, lymphocyte subset, and monocyte cell separation techniques.
2. Serologic typing for Class I (HLA-A, B, and Cw) locus antigens.
3. Serologic typing for Class II (HLA-DR, DQ, and DP) antigens as they evolve.
4. Characterization of HLA antibodies.
5. Ability to identify and correct problems ("trouble shoot") the typing and crossmatching techniques and their components (including both serologic reagents and complement as well as molecular testing).
6. Performance and interpretation of results from techniques related to crossmatching, including complement mediated flow cytometry, autotoxicity testing, absorption/elution techniques, antibody isotype, and blocking and augmentation of cytotoxic reactions.
7. Techniques for molecular genetic analysis, including DNA isolation, amplification, electrophoresis, binding to primers and probes.
8. Correlation and comparison of results using different technologies (molecular vs. serology, cytotoxic vs. flow).

B. Additional techniques which may be covered

1. Production/characterization of monoclonal antibodies as HLA reagents.
2. Mixed lymphocyte culture
3. Primed lymphocyte typing (PLT) for typing HLA-DP antigens.
4. HLA-Dw typing by means of homozygous typing cells (HTC).
5. Cell-mediated cytotoxic responses against Class I and Class II antigens.
6. T-cell cloning
7. Post-transplant immunologic monitoring, if appropriate, by techniques including phenotyping of lymphocyte subpopulations by flow cytometry, quantitation of lymphokines, procoagulant activity, expression of differentiation and activation antigens, and growth factor receptors.
8. Engraftment: STR, VNTR, etc
9. Sequencing

II. Clinical Aspects of the Transplantation Histocompatibility Laboratory

An important function of the laboratory is to maintain contact with the clinical aspects of the transplant program (s). This will need to be developed along lines consistent with the policies and programs of the transplant centers, but it should include attendance at clinical transplant meetings of both administrative and medical/surgical personnel. It is recommended that trainees be given the opportunity to observe an organ recovery and a transplant operation; to make rounds at least once a month with the transplant team.

III. In order to document the trainee's experience, it is required that he/she maintain reviewed cases of personally studied patient work-ups and follow-up studies. These should include demographic, pre- and post-transplant clinical information, serum screening analysis, crossmatching evaluations, HLA typing and antigen/haplotype matching, any other pertinent data (e.g. transplant biopsy data), appropriate literature references, and the program-director's signature indicating review. It is recommended that this include:

1. Fifty cadaver renal transplants, including non-renal solid organ transplants
2. Fifty living related renal transplants of different races (with haplotype analysis)
3. Fifty bone marrow transplants
4. Additional cases in other areas of histocompatibility testing should be included as applicable to the program including Disease Associations, Transfusion Support, and Genetic Identity

These cases may be used for the new director's portfolio.

APPENDIX C

Subject Matter to be Covered in Lectures and Seminars for Trainees

1. Basic immunobiology topics:
 - Overview of cell interactions in the immune system
 - Cells and organs of the immune system
 - Antibody structure - isotypes, idiotypes, allotypes
 - Immunoglobulin genes and gene expression
 - Antigen-antibody reactions
 - Major histocompatibility genes and proteins
 - Mapping of the MHC genes by function and gene product
 - Antigen recognition by T-cells
 - The thymus in the development and differentiation of T-lymphocytes
 - T cell receptor genes and proteins
 - Adhesion/accessory molecules
 - CD markers and nomenclature
 - Macrophages and antigen processing/presentation
 - Lymphokines, monokines, and other regulatory substances
2. Immunogenetics
 - Review of basic principles of genetics (if needed)
 - Population genetics
 - Immunoglobulin allotypes and other genetic matters
 - Biostatistics including: Bayes theorem, probability analysis, chi square, correlation coefficient
 - MHC genetics and polymorphism
 - Immunoglobulin and TCR gene rearrangement; generation of diversity
3. Basic Principles of Molecular Biology
 - Chemistry of DNA, RNA
 - Gene regulation
 - Transcription, translation
 - Recombinant DNA technology

Gene therapy

4. Clinical Topics in Histocompatibility and transplantation

Mechanisms of organ allograft rejection

Immunologic tolerance to allogeneic tissue; specific and nonspecific immunosuppression

Clinical aspects of solid organ transplantation (diseases leading to specific organ failure, recipient selection and preparation, donor selection, transplant surgery, post-operative management, follow-up procedures, outcomes)

Clinical manifestations and management of rejection

Clinical aspects of bone marrow transplantation (diseases treated by marrow transplantation, recipient selection and preparation, donor selection, transplant procedures, post-operative management, follow-up procedures, outcomes)

Graft versus Host Disease

Pathology of human allograft rejection

Autoimmunity

Molecular basis for HLA/Disease associations

Engraftment

Genetic identification

Revised October, 2002