Course Director and Contact Information:
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Director, Peter F. Wright Immunocompromised Host Infectious Diseases Service
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Course Offerings:
Course Enrollment: up to 8 students per offering
Prerequisites:
Student Assessment: See Addendum A
Attendance Policy: See Addendum B

Course Description:
The care of patients with altered host defense is becoming increasingly complicated due to both the variety of immune-compromising therapeutic strategies and the continued spread of multi-drug resistant pathogens. To provide excellent patient care and develop new strategies in the care of immunocompromised patients, future physicians will require a solid background in basic immunology, an understanding of how both broad and targeted immune-based therapies increase infection risk, and knowledge in the diagnosis and treatment of complicated infections in these patients. Using a variety of learning formats, immersion-phase medical students will revisit foundational immunologic concepts in the clinical context of transplant immunology with special attention given to understanding infectious complications of immunosuppression. This course will provide the learner with experience, knowledge, and expertise in the care of patients undergoing hematopoietic cell or solid organ transplantation.

Course Vision:
To extend foundational knowledge in immunology and infectious diseases through immersion-phase coursework that integrates basic and clinical sciences in the context of transplant and infectious diseases subspecialties.

Course Goals:
- To review and strengthen understanding of foundational immunologic concepts with application of these concepts to the fields of transplantation and infectious diseases.
- To deepen knowledge of and rationale for immunosuppressive strategies in hematopoietic stem cell transplantation (HSCT) and solid organ transplantation (SOT)
- To strengthen understanding of the clinical presentation, risk factors, and treatment of key infections in immune-compromised hosts.
- To develop mechanistic understanding of the immunologic response to key infections that affect immune-compromised hosts.
• To understand key techniques in assessment of the immune system in transplant patients in the context of pre-transplant evaluation, post-transplant immune assessment, and infection risk.
• To improve critical reasoning skills in the setting of medically-complex patient care.
• To develop communication skills necessary to provide high quality care in a multidisciplinary setting.
• To utilize and further develop the attitudes and practices of inquisitive practice and life-long learning.

Course Objectives:

I. To review and strengthen understanding of foundational immunologic concepts with application of these concepts to the fields of transplantation and infectious diseases.
   a. Describe key steps in the development of humoral immunity and antibody responses with focus on affinity maturation, the germinal center, and B cell memory, and state pharmacologic interventions used in transplantation to modulate B cell/antibody immunity.
   b. State the basic structure, cellular distribution, and steps in antigen processing/presentation for MHC Class I and MHC Class II molecules and apply this understanding to the pathophysiology of cellular rejection in SOT and GVHD in HSCT.
   c. Know the major steps in thymic T cell development, how these impart self/non self-discrimination, and apply this knowledge to understanding of rejection and GVHD.
   d. Know the major steps in T cell activation including where and how naïve T cells interact with antigens, the requirements for successful T cell activation (three-sIGNALS), and how the T cell immune response is tuned down.
   e. Know the critical mediators of CD8+ T cell cytotoxicity and understand the importance of these for clearance of viral infection and predisposition to aberrant immune responses to viral infection.
   f. Know the major CD4+ T cell subsets and the major cytokines/transcription factors necessary for their development.
   g. Define immunologic tolerance, distinguish between central and peripheral tolerance, and state mechanisms for peripheral tolerance.
   h. State the types of immunologic pattern recognition receptors (PRRs), what pathogens these receptors recognize, and the role that PRRs play in clearance of infections and development of alloimmunity.

II. To deepen knowledge of and rationale for immunosuppressive strategies in hematopoietic stem cell transplantation (HSCT) and solid organ transplantation (SOT)
   a. SOT
      i. Describe how pre-transplant antibody screening and HLA typing are used in kidney transplantation.
ii. Compare the stringency and necessity of HLA testing pre-transplant among different organ types (Heart, Lung, Liver, Kidney) and understand the potential mechanisms/issues underlying these differences

iii. Differentiate between induction and maintenance immunosuppression and understand the mechanism of action and immunologic effects of the immunosuppression medicines used

iv. Describe the immunopathogenesis of hyperacute, acute, and chronic rejection in the SOT setting.

v. State risk factors for development of rejection

vi. Describe diagnostic and treatment strategies for antibody mediated and cellular rejection.

b. HSCT
   i. Know the importance of graft-versus-leukemia (GVL) effect, the role that stem cell source and HLA match plays in mediating this effect, and the cell-types thought to impart GVL
   ii. Describe the sources of stem cells used in HSCT and understand differences in each of these with regard to the impact on engraftment timing, GVHD, and infection risk
   iii. List clinical settings in which HSCT is used and understand how this impacts the choice of stem cell source as well as choice of both myeloablative and immunosuppression strategies
   iv. State the differences between allogeneic and autologous HSCT
   v. Know immunosuppressive medicines used, the mechanism of action of these medicines, and the timing of their use in prevention of GVHD
   vi. Know the impact of the degree of donor-recipient HLA match on transplant-related morbidity and mortality and understand the mechanisms for these effects (GVHD, Tumor Recurrence, Infections)
   vii. State the rationale for or against T-cell depletion in HSCT and the therapies used to achieve T-cell depletion.
   viii. Know the clinical presentation(s) of GVHD and the mechanism underlying GVHD development.
   ix. Understand treatment options for acute GVHD

c. SOT and HSCT
   i. Compare and contrast the immunopathogenesis of GvHD and SOT rejection.
   ii. Compare and contrast the use of HLA typing in the HSCT and SOT settings.

III. To strengthen understanding of the clinical presentation, risk factors, and treatment of key infections in immune-compromised hosts.
   a. Describe infections that affect patients undergoing HSCT or SOT and understand key risk periods for these infections according to time period post-transplant
   b. Generate a brief infectious diseases differential diagnosis for clinical syndromes (CNS: altered mental status/fever/seizures, Pulm: cough/fever/respiratory distress,
Immunity and Infections in the Compromised Host
IDIS 5625
Course Syllabus
2015-2016

GI: diarrhea, Derm: rash/skin nodules) that present in patients with compromised immune systems.

c. Know the clinical syndromes that CMV infection in a transplant recipient can cause

d. List the indirect effects classic for CMV infection in transplant recipients

e. Understand risk factors for and presenting signs/symptoms of invasive fungal infection (focus on Aspergillosis and Candida) in the transplant recipient

f. State the spectrum of action for antifungal agents used in treating invasive fungal infection in transplant recipients

g. Describe the epidemiology, treatment, and risk factors for resistance of gram-negative bacterial infection in transplant recipients.

IV. To develop mechanistic understanding of the immunologic response to key infections that affect immune-compromised hosts.

a. Compare and contrast the clinical features of X-linked lymphoproliferative disease and post-transplant lymphoproliferative disease with attention to the role of Epstein Bar Virus in disease pathogenesis and the immunologic mechanisms underlying the development of each entity.

b. Describe the mechanisms underlying genetic predisposition to invasive Aspergillus infection in Chronic Granulomatous Disease and Hyper-IgE syndrome and link these mechanisms to defined risk factors for Aspergillus in the transplant setting.

c. Understand defects in TLR signaling that predispose to invasive bacterial infection and where in the TLR pathway these defects lie.

V. To understand techniques in assessment of the immune system in transplant patients in the context of pre-transplant evaluation, post-transplant immune assessment, and infection risk.

a. Discuss clinical utility of flow cytometric testing and outline the basic steps in it's use

b. Describe techniques used in HLA typing for HSCT and SOT patients

c. Describe the techniques used to test for pre-formed antibodies and the implications of positive tests

d. Discuss the organ specific requirements and limitations for the degree of matching needed to successful perform transplantation

e. Know which organ transplant types utilize pre-transplant antibody screening

f. Know immunohistochemical methods used in the pathologic diagnosis of rejection
Addendum A: Student Assessment

- Grading considerations
  - To pass the course, each student must pass both the quantitative and qualitative measures.
  - To obtain honors, a student should demonstrate excellent performance in all aspects of the course.
- Quantitative Assessments

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Final Examination</td>
<td>30%</td>
</tr>
<tr>
<td>Quizzes (3 per course, excluding pre-course quiz)</td>
<td>5% per Quiz (15% total)</td>
</tr>
<tr>
<td>Final Presentation</td>
<td>20%</td>
</tr>
<tr>
<td>Translational Journal Club</td>
<td>15%</td>
</tr>
<tr>
<td>TBL PID-ID Sessions (5% each)</td>
<td>10%</td>
</tr>
<tr>
<td>Immunology Talk</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

- Qualitative Assessments
  - Competency milestone data about each student will be collected from 2 unique observers per week (e.g. clinical faculty, residents, teaching faculty). These observers will assess student performance in key competencies during the activities of the course. Competencies measured in this course are defined below.
  - Course directors will synthesize this input into a final, summative assessment for each competency domain (in gray below).
  - Competency domains and milestones that are required for student assessment in the ISC's

<table>
<thead>
<tr>
<th>MEDICAL KNOWLEDGE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Integration</td>
<td>MK2a</td>
</tr>
<tr>
<td>Depth</td>
<td>MK2b</td>
</tr>
</tbody>
</table>
Frequency of assessment and feedback of the above milestones:

<table>
<thead>
<tr>
<th>When assessment occurs</th>
<th>Who assesses?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-course</td>
<td>Course Director, Clinical Faculty, Residents, Peer and/or Self</td>
</tr>
<tr>
<td>End of course</td>
<td>Course Director and Clinical Faculty (Residents optional)</td>
</tr>
</tbody>
</table>

Table 3

Assigning a final grade

Students’ final grades should use their performance on quantitative measures as a foundation for final grade assessment that should be adjusted, as appropriate, to reflect their performance on competency domains (Table 4).

Final grad assessment based on quantitative and qualitative scores:
### Table 4

<table>
<thead>
<tr>
<th>Final Grade</th>
<th>Quantitative Score</th>
<th>Summative Competency Ratings (Qualitative Score) (6 domains assessed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of Failure</td>
<td>&lt;70%</td>
<td>Any Sub-Threshold OR &gt;2 Thresholds</td>
</tr>
<tr>
<td>(course director discretion)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pass</td>
<td>At least 70%</td>
<td>No more than 2 Thresholds All others at Target or above</td>
</tr>
<tr>
<td>High Pass</td>
<td>At least 80%</td>
<td>At least 3 Reaches All others at Target</td>
</tr>
<tr>
<td>Honors</td>
<td>At least 90%</td>
<td>Nothing below Target 5 Reaches</td>
</tr>
</tbody>
</table>

### Student grievance concerning grades

Students can seek redress of a problem with a grade no later than four weeks after the grade is released. Students with a grievance should confer directly with the ISC Director. Every effort should be made to resolve the problem fairly and promptly at this level. If the student and ISC Director cannot resolve the problem through discussion, the student can formally request an appeal, within two weeks of talking with the course director, from the Associate Dean for Medical Student Affairs (ADMSA). Appeal will prompt a review of the course’s assessment practices by the Standing Assessment Committee, as well as a review of the individual student’s situation by the ADMSA, the Associate Dean for Undergraduate Medical Education, and a neutral faculty reviewer. If resolution is still not achieved, the ADMSA will make a recommendation to the Senior Associate Dean for Health Sciences Education, who will make the final decision.
Addendum B: Attendance Policy (Copied from VUSM Immersion Phase Absence Policy and Procedures)

INTRODUCTION

This policy pertains to all MANDATORY learning experiences (didactic, small-group, clinical, etc.) that take place during the Immersion Phase of the VUSM MD degree program. Students are expected to attend all required sessions as described in the course syllabus. However, because specific situations may arise where a student may need to miss a required session, the following policy applies.

Planned absence (pre-approval required):

- Interviews
- Religious holy days
- Presentations of work at an advertised external scholarly meeting

Emergency absence (approval required post facto if necessary):

- Serious medical issues
- Family emergencies

You may submit a request to be absent for other life events, however these absences are highly discouraged and are likely not to be approved, given their impact on both the student learning experience and the clinical learning environment. Students are encouraged to plan their flex months to accommodate these events.

- Weddings
- Family events (non-emergency)
- Any other activities falling on required sessions

ADDITIONAL CONSIDERATIONS:

- Students should not make travel arrangements prior to receiving notification of the outcome of their request. Approval will not be granted just because travel arrangements have been made.
- Denied absences will not be allowed the option to make up course work or clinical time, and the student’s grade will be affected.
- Students who are approved to miss more than two clinical days per course must make up the missed clinical time.
- Students will be held responsible for didactic material they miss during approved absences. Make-up work for other activities may be required by course faculty/directors.
- Only two absences can be approved during any course (total). Students who take more than two absences per Immersion Phase course or who miss blackout periods (below) may fail the course.

***Examples of situations in which make-up work will not be allowed, and the student’s grade will be affected include***:
Absences for which no request was made
Absences for which a request was made and denied.

REQUEST PROCESS:

Students may request advanced permission to miss required educational activities due to circumstances outlined above. To make such a request, a student must:

1. Request permission from the course director using the *VUSM Immersion Phase Absence Request Form* at least 4 weeks in advance of the start of the course.
2. Email the signed *VUSM Immersion Phase Absence Request Form* to the Associate Dean for Medical Student Affairs or Assistant Dean for Assessment for approval.
3. Contact appropriate parties regarding the absence (i.e., course/block director, small group facilitator, peers, FHD course and block directors, Research area heads, and/or supervising clinician, as appropriate).
4. Student will be notified by course leadership regarding required make-up work.
5. Students will be notified by email regarding whether their request is approved or denied.

If the absence is due to a health or family emergency (i.e., less than four weeks in advance), the students must:

1. Contact the course leadership (i.e., course/block director, small group facilitator, FHD course and block directors, Research area heads, and/or supervising clinician, as appropriate) as soon as possible about their situation.
2. Submit the *VUSM Immersion Phase Absence Request Form* to the course director.
3. Submit the signed *VUSM Immersion Phase Absence Request Form* to the to the Associate Dean for Medical Student Affairs or Assistant Dean for Assessment for approval.
4. Student will be notified by course leadership regarding required make-up work.
5. Students will be notified by email regarding whether their request is approved or denied.

REQUIRED SESSIONS

Absences during/on the following required sessions are likely not to be approved, given their impact on both the student learning experience and the clinical learning environment. **Students who miss mandatory educational activities without approval in an Immersion Phase course on/during a required session may fail the course.** Required sessions include the following, unless indicated by course director:

- First day of class
- Orientation
- Examinations
- Any day that extends a school holiday (except normal weekend breaks if they occur during a course)
- Learning Communities face-to-face College sessions
- FHD monthly face-to-face session
- Research mandatory sessions
- Other sessions as determined by course leadership/administration as described in the course syllabus