FORM 1. SAMPLE COVER LETTER REQUESTING CLINICAL INFORMATION

WITH REQUEST FOR PATHOLOGY CONSULTATION

Consultation Information Request

Dear Colleagues;

Thank you for the opportunity to provide you with a consultation. Your patient likely has a diagnostic dilemma that entails some difficult management choices. Such cases contribute to the overall body of knowledge of hematopoietic cell transplant related complications.

In order to better serve you, we request that you provide relevant clinical details with the key issues that you want us to address in our histopathologic review of this specimen. You may do this by filling out the items in the attached questionnaire or by a narrative description. Please be sure to include the phone number, email address, and fax numbers of the clinicians who wish to be notified as well as those of the submitting pathologist.

In addition to the glass slides, including the special stains, we would appreciate receiving the representative paraffin blocks. This will enable us to make additional sections and any appropriate special stains. Serially sectioned H&E stained recuts are particularly important when evaluating the subtle changes of graft-versus-host disease.

We look forward to hearing from you soon.

Respectfully,

FORM A: LIVER CONSULTATION CLINICAL INFORMATION FORM

Patient Name: _____

Patient's Surgical Identification # (or Case #): _____

Patient's Transplant Status: Pre _____ **Days Post Transplant (or date of tx):** _____

Physician / Clinician to contact with results: (*If more than one person, please let us know*)

Name: _____ Specialty: _____

Address: _____

_____

Telephone number: ( ) ____ - _____ Fax number: ( ) ____ - _____

Email Address: _____

What are the hepatobiliary problems? (check all that apply)

☐ hepatitis B positive: ☐ HB_sAg^+ ☐ αHB_c^+ ☐ αHB_s^+ ☐ HBV DNA^+
☐ hepatitis C positive: ☐ α HCV^+ ☐ HCV RNA^+ ☐ chronic hepatocellular injury

☐ signs/symptoms of sinusoidal obstruction syndrome (VOD) ☐ assess for cirrhosis/fibrosis
☐ mass, tumor or infection in the liver
☐ GVHD ☐ other: _____

What are the current lab data?

Total serum Bilirubin	_____	mg/dL
Direct (conjugated) Bilirubin	_____	mg/dL
AST (GOT)	_____	U/L
ALT (SGPT)	_____	U/L
Alkaline Phosphatase	_____	U/L
Albumin	_____	g/dL

How was this biopsy obtained? ☐ Percutaneous Bx ☐ Transvenous Bx

Was the hepatic wedged venous pressure gradient measured? ☐ Yes ☐ No

Results: _____mm Hg

Current Immunosuppressive Therapy for GVHD:

Type: _____ Duration: _____

What specific questions do you want the pathologist to address? _____

_____

_____

FORM B. PROTOCOL EVALUATION OF LIVER BIOPSIES

Patient Name: _____ **Date:** _____

Patient ID #: _____ **Case/Surgical #:** _____

Sample Information:

Type: (i.e. needle percutaneous, FNA, transvenous needle or forceps, fixative) _____

Size and length of needle or fragments: _____

Number of portal spaces, other stains _____

Feature	Lesion description	Score Possibilities	Your Score
Bile Ducts			
Bile Duct Loss	Fraction of portal areas with an identifiable duct	%	
Bile Duct Damage-Adequacy	Not Adequate (no evaluation of injury possible=1)	0	
	Adequate	1	
Bile Duct Damage-Ductitis	None	0	
	Few ducts/focal involvement	1	
	Most ducts/diffuse involvement	2	
Bile Duct Damage-Epithelial dysmorphism: nuclear dyspolarity, segmental nuclear dropout, anisonucleosis, cytoplasmic eosinophilia	None	0	
	Few ducts/focal involvement	1	
	Most ducts/diffuse involvement	2	
Ductular reaction (bile ductule proliferation	Absent	0	
	Present	1	
Inflammation			
Periportal Inflammation	As per Modified Ishak scale[1]	0–4	
Portal Inflammation	As per Modified Ishak scale	0–4	
Lobular necroinflammation	As per Modified Ishak scale	0–4	
Central necrosis/perivenular inflammation	Absent	0	
	Present	1	
Fibrosis			
Portal based Fibrosis	As per Ludwig-Batts[2]	0–4	
Sinusoidal Fibrosis	Absent	0	
	Present	1	

FORM B. PROTOCOL EVALUATION OF LIVER BIOPSIES (continued)

Patient Name: _____ **Date:** _____

Patient ID #: _____ **Case/Surgical #:** _____

Feature	Lesion description	Score Possibilities	Your Score
Cholestasis			
Acute parenchymal	None	0	
	Zone 3	1	
	More extensive than zone 3	2	
Cholangiolar	Absent	0	
	Present	1	
Chronic cholestasis	Absent	0	
	Present	1	
Fatty liver changes			
Steatosis, degree	None	0	
	<5% parenchyma	1	
	5-33% parenchyma	2	
	34-66% parenchyma	3	
	≥ 67% parenchyma	4	
Steatohepatitis	Absent	0	
	Present	1	
Iron			
Hepatocellular iron accumulation	As per MacSween[3]	0-4	
Reticuloendothelial iron	Absent	0	
	Present	1	
Vascular changes			
VOD/SOS-like changes	Absent	0	
	Present	1	
Other findings			
Extramedullary hematopoiesis	Absent	0	
	Present	1	
Final Diagnosis			
	No GVHD	0	
	Possible GVHD	1	
	Probable GVHD	2	
	GVHD	3	

Term definitions and other notes (Liver)

Bile duct loss: A portal area without any identifiable main duct (using artery as size guide), disregarding ductular reaction (formerly referred to as ductular proliferation) around edge of portal area. This should be recorded as a visual estimate the percent of portal areas with ducts remaining, rounded to the nearest 10%. If immunostains are used to enhance detection of residual ducts, this should be stated.

Bile duct damage-adequacy: Adequacy may be affected by duct loss, the size of the biopsy or other factors. If the biopsy is judged inadequate for evaluation of duct damage, the next two items should be left blank.

Bile duct damage-ductitis: infiltration of duct by mononuclear cells. Any degree of infiltration should be scored positively.

Bile duct damage-epithelial dysmorphism: This includes a variety of reactive changes, including nuclear pleomorphism, cytoplasmic vacuolation/eosinophilia, nucleolar enlargement, architectural alterations.

Fibrosis: Fibrosis should be evaluated on an appropriate connective tissue stain, rather than on H&E.

Acute parenchymal cholestasis: Evidence of cholestasis in the hepatic parenchyma, including canalicular cholestasis, hepatocellular cholestasis, accumulation of macrophage foam cells.

Cholangiolar cholestasis: Dilated periportal bile ductules filled with inspissated bile.

Chronic cholestasis: marked ballooning with central hepatocellular lysis and pseudoxanthomatous hepatocyte changes.

Steatosis: Involvement of the liver by steatosis should be judged at low to medium magnification (no more than 100x total magnification). Finely vesiculated microsteatosis may be underscored, but microvesicular steatosis should probably be separately recorded.

References

1. Ishak KG e al. Histologic grading and staging of chronic hepatitis. J Hepatology 1995;22: 696-699.

2. Batts KP, Ludwig J: Chronic hepatitis: an update on terminology and reporting. Am J. Surg Pathol 1995; 19:1409-1417.

3. Searle JW, et al., “Iron storage Disease” in MacSween RN, Burt AD, Portmann BC, Ishak KG, Scheurer PJ, Anthony, P. Pathology of the Liver, 4th ed 2002, Churchill Livingston, Table 5.1, p 260-261.

FORM C. GASTROINTESTINAL BIOPSY CLINICAL INFORMATION

Patient Name: _____

Patient's Surgical Identification # (or Case #): _____

Patient's Transplant Status: Pre _____ **Days Post Transplant (or date of tx):** _____

Physician / Clinician to contact with results: (*If more than one person, please let us know*)

Name: _____ Specialty: _____

Address: _____

_____

Telephone number: ( ) ____ - _____ Fax number: ( ) ____ - _____

Email Address: _____

What are the patient's dominant symptoms? (Check all that apply)

- ☐ Nausea ± vomiting
- ☐ Anorexia ± satiety
- ☐ Abdominal pain
- ☐ Diarrhea
- ☐ GI bleeding
- ☐ other: _____

What was seen at endoscopy?

EGD		**Colon**
☐	Mucosal edema ± erythema	☐
☐	Erosion(s)	☐
☐	Ulcer(s)	☐
☐	Vascular ectasia	☐

What cultures were done using biopsies taken at this endoscopy? *Please note any positive results.*

_____

_____

_____

_____

Current Immunosuppressive Therapy for GVHD:

Type: _____ Duration: _____

What specific questions do you want the pathologist to address?

FORM D: PROTOCOL EVALUATION OF GUT BIOPSIES

Patient Name: _____

Patient's Surgical Identification # (or Case #): _____

Sample Locations: _____

Number of biopsies: _____

Number of serial sections, other stains _____

Feature	Lesion description	Score Possibilities	Your Score
Apoptosis	None	0	
	Spotty/isolated	1	
	Multiple per crypt	2	
Crypt/pit loss	None	0	
	Single/focal destruction	1	
	Extensive	2	
Inflammatory infiltrate-mononuclear	None to sparse	0	
	Focal/peri-crypt	1	
	Diffuse	2	
Inflammatory infiltrate, eosinophils	Absent	0	
	Present in Lamina propria	1	
	Present in Lamina propria and crypts	2	
Eosinophilic Crypt Abscesses	Absent	0	
	Present	1	
Inflammatory infiltrate- neutrophils	Absent	0	
	Present in Lamina propria	1	
	Present in Lamina propria and crypts	2	
Neutrophilic Crypt Abscesses	Absent	0	
	Present	1	
FINAL DIAGNOSIS:			
	No GVHD	0	
	Possible GVHD	1	
	Probable GVHD	2	
	GVHD	3	

Comments: differential diagnosis, issues with the sample, reasons for favored diagnosis, other

_____

_____

_____

Confounding pathology should be noted separately. This pathology may include a variety of findings such as bowel prep colitis, CMV, cryptosporidia, focally enhanced gastritis,[1] mycophenolate mofetil focal colitis,[2] and C. difficile. Apoptosis has also been described with the use of proton pump inhibitors.[3]

Term Definitions and Other Notes (GI)

Apoptosis: Apoptosis should only be evaluated within pits or crypts and should reflect apoptosis of epithelial cells. Surface epithelial apoptosis is not recorded.

Crypt/pit loss: "Extensive" means at least a short stretch of mucosa with most or all of the crypts/pits missing.

Inflammatory infiltrate-mononuclear: focal accentuation above normal (or above background) or diffuse infiltration that is greater than normal (or background). In heavily immunosuppressed patients, the level of "background" inflammation may be very low.

Inflammatory infiltrate, eosinophils: Since a certain number of eosinophils may be normal in the lamina propria, the infiltrate should be increased enough so that it is recognizably above a normal level. Any infiltration of eosinophils into crypt epithelium should be scored as positive for eosinophilic cryptitis.

Eosinophilic crypt abscesses – One or more eosinophils in a crypt lumen should be recorded as a positive finding.

Inflammatory infiltrate- neutrophils: Any degree of infiltration of neutrophils into crypt epithelium should be called positive for cryptitis.

Neutrophilic Crypt Abscesses – One of more neutrophils in a crypt lumen should be recorded as a positive finding.

References

1. Xin, W, Greenson, JK. The Clinical Significance of Focally Enhanced Gastritis. Am J Surg Pathol 2004: 28;10:1347-1351.

2. Papadimitriou JC, Cangro CB, Lustberg et al. Histologic Features of Mycophenolate Mofetil-Related Colitis: A Graft-Versus-Host Disease-like Pattern Int J Surg Path 2003: 11, 295-302.

3. Welch DC, Goldenring JR, Ness EM, et al. Gastric graft-versus-host disease revisited: does proton pump inhibitor therapy affect endoscopic gastric biopsy interpretation? Am J Surg Pathol 2005; in press.

FORM E. CUTANEOUS CONSULTATION CLINICAL INFORMATION FORM

Patient Name: _____

Patient's Surgical Identification # (or Case #): _____

Patient's Transplant Status: Pre _____ Days Post Transplant (or date of tx): _____

Physician / Clinician to contact with results: (*If more than one person, please let us know*)

Name: _____ Specialty: _____

Address: _____

_____

Telephone number: ( ) ____ - _____ Fax number: ( ) ____ - _____

Email Address: _____

What are signs and symptoms are currently present? (check all that apply)

- ☐ rash, lichenoid and or erythema
- ☐ sclerosis
- ☐ pruritis
- ☐ fasciitis
- ☐ erythema

Immunosuppressive Therapy for GVHD:

Type: _____ Duration: _____

What specific questions do you want the pathologist to address?

FORM F. PROTOCOL EVALUATION OF CUTANEOUS BIOPSIES

Sample Type, i.e. punch, ellipse, shave	Size , WxD mm	Number of serial sections, other stains

Epidermis			
Thickness			
Basilar Vacuolopathy	Normal	Atrophic	Hyperplastic
Apoptosis	Yes	No	
Spongiosis	Yes	No	
Keratinocytic Atypia	Yes	No	
Exocytosis			
Lymphocytes	Yes	No	
Other Inflammatory Cells	Yes	No	
Thickening of basilar lamina	Yes	No	

Follicular Epithelium		
Basilar Vacuolopathy	Yes	No
Apoptosis	Yes	No
Exocytosis		
Lymphocytes	Yes	No
Other Inflammatory Cells	Yes	No

Eccrine Epithelium		
Basilar Vacuolopathy	Yes	No
Apoptosis	Yes	No
Exocytosis		
Lymphocytes	Yes	No
Other Inflammatory Cells	Yes	No

Subcutaneous Tissue / Septae		
Collagen Sclerosis	Yes	No
Inflammation:		
Cell Type:		
Lymphocytes	Yes	No
Plasma Cells	Yes	No
Eosinophils	Yes	No
Neutrophils	Yes	No

Comments: (differential diagnosis, issues with sample, reasons for favored diagnosis, other)

Dermis		
Papillary Dermis		
Collagen Sclerosis	Yes	No
Melanophages	Yes	No
Inflammation:		
Cell Type:		
Lymphocytes	Yes	No
Plasma Cells	Yes	No
Eosinophils	Yes	No
Neutrophils	Yes	No
Distribution:		
Perivascular	Yes	No
Periadnexal	Yes	No
Interstitial	Yes	No
Band-like	Yes	No

Reticular Dermis		
Collagen Sclerosis		
Upper Reticular	Yes	No
Lower Reticular	Yes	No
Widening of Reticular Dermis	Yes	No
Fascial	Yes	No
Inflammation:		
Cell Type:	Yes	No
Lymphocytes	Yes	No
Plasma Cells	Yes	No
Eosinophils	Yes	No
Neutrophils	Yes	No
Distribution:		
Perivascular	Yes	No
Periadnexal	Yes	No
Interstitial	Yes	No
Band-like	Yes	No

Minimal criteria suggested for the diagnosis of cutaneous lichenoid chronic GVHD: Epidermal hyperkeratosis, hypergranulosis and acanthosis, apoptosis of epidermal keratinocytes in basal lower stratum spinosum layer or along outer root sheath of follicles, ± bandlike infiltrate along dermal epidermal junction, ± apoptosis or inflammation of eccrine coils.

Minimal criterion for the diagnosis of cutaneous sclerotic chronic GVHD: Homogenization (sclerosis) of most of papillary and/or reticular dermal collagen.

Final Diagnosis	
No GVHD	0
Possible GVHD	1
consistent with GVHD	2
GVHD	3

FORM G. ORAL MUCOSA CONSULTATION CLINICAL INFORMATION FORM

Patient Name: _____

Patient's Surgical Identification # (or Case #): _____

Patient's Transplant Status: Pre _____ Days Post Transplant (or date of tx): _____

Physician / Clinician to contact with results: (*If more than one person, please let us know*)

Name: _____ Specialty: _____

Address: _____

_____

Telephone number: ( ) ____ - _____ Fax number: ( ) ____ - _____

Email Address: _____

What are the oral problems? (check all that apply)

- ☐ lichen-like changes
- ☐ keratosis
- ☐ ulcerations
- ☐ pseudomembranes
- ☐ salivary dysfunction
- ☐ sensitivity to food
- ☐ mouth pain

What cultures have been taken? Please note any positive results.

_____

_____

Type: _____ Duration: _____

What specific questions do you want the pathologist to address?

FORM H. PROTOCOL EVALUATION OF MUCOSAL BIOPSIES

Notes:
Recommend incisional biopsy (non-ulcerated site to include underlying gland lobules). Minimum of 5 lobules of salivary glands must be submitted.

Is biopsy site clinically	Normal	Erythematous	Keratotic
Mucositis	Yes	No	
Erythema			
	Yes	No	
Clinical Keratosis			
	Yes	No	
Ulcerations			
	Yes	No	
Xerostomia			
	Yes	No	
Sclerodermatous mucositis			

Epithelium

	Normal	Atrophic	Hyperkeratosis	Acanthosis
Thickness				
	Yes	No		
Basilar Vacuolopathy				
	Generalized	Localized		
If yes…				
	Yes >1/10x field	Occasional <1/10x field	None	
Apoptosis / Eosinophilic Bodies				
	Yes	No		
Spongiosis				
	Yes	No		
Keratinocytic Atypia				
Exocytosis (5 lymphocytes/10x field)	Yes	No		
Lymphocytes				
	Yes	No		
Other Inflammatory Cells				
	Yes	No		
Thickening of basilar lamina				

Lamina Propria

	Generalized	Localized
Inflammation		
Cell Type	Yes	No
Lymphocytes		
	Yes	No
Plasma Cells		
	Yes	No
Eosinophils		
	Yes	No
Neutrophils		
	Yes	No
Mast Cells		

Distribution	Yes	No
Perivascular		
	Yes	No
Periductal (excretory)		
	Yes	No
Interstitial		
	Yes	No
Bandlike (interface, submucosal, obscuring the junction)		

Glands (Intralobular)

	Yes	No
Periductal lymphocytes ONLY with exocytosis into duct		
	Yes	No
Periductal mixed chronic infiltrate		
	Yes	No
Lymphocytes (only) around & migrating into acinar units		
	Yes	No
Apoptotic cells in ducts / acini		
	Yes	No
Periductal Fibrosis		
	Yes	No
Acinar degeneration / interstitial fibrosis/ductal ectasia		
	Yes	No
Oncocytic Metaplasia (in children)		
	Yes	No
Loss of polarity of ductal epithelial cells		

Width of mucosal surface	Number of minor salivary lobules	Number of serial sections, other stains

Final Diagnosis	No GVHD	0
	Possible GVHD	1
	Probable GVHD	2
	GVHD	3

Comments:	
DDX	
Reasons for favored Dx	
Issues with sample	
Other	

Minimal criteria for mucosal chronic GVHD:
Epithelial changes (localized or generalized) similar to those described in cutaneous GVHD and/or presence of intralobular, periductal lymphocytes (only), and exocytosis of lymphocytes (only) into intralobular ducts and acini. Periductal fibrosis (not generalized interstitial fibrosis).