

Appendix Table. Histological alterations recorded after inoculation of mice with 10 50% mouse lethal doses of 2 influenza virus strains

Tissue type	Subtype H1N1 strain			Subtype H5N1 strain		
	Day 3 pi	Day 5 pi	Day 7 pi	Day 2 pi	Day 3 pi	Day 4 pi
Bronchi and bronchioli						
Lumen	Mostly granulocytic exsudate, no blood	Granulocytic/lymphocytic exsudate, no blood	Mostly lymphocytic exsudate, no blood	Empty	Empty	Some airways contain blood
Epithelium	Partial necrosis + desquamation, all airways involved	Complete necrosis + desquamation, all airways involved	Complete necrosis + desquamation, all airways involved	Intact	Intact or only some necrotic cells	Intact or only some necrotic cells
Lamina propria	Infiltration, granulocytic, lymphocytic, macrophagic, all airways involved	Like day 3 pi, but infiltrations more severe	Like day 5 pi, infiltrated cells mostly mononuclear	Normal	Normal	Normal
Submucosa (nonalveolar interstitium)	Moderate infiltrations, lymphocytic, all airways involved, no cuffs	Like day 3 pi, but infiltrations more severe	Dense lymphocytic cuffing, all airways involved	Few interspersed surnumerary mononucleated inflammatory cells	Like day 2 pi	Like day 3 pi
Arteries						
Wall	Normal	Normal	Normal	Normal	Normal	Hemorrhages, some arteries involved
Perivascular area	Moderate lymphocytic infiltration, many arteries involved	Marked lymphocytic infiltration, many arteries involved	No edema, lymphocytic cuffs, many arteries involved	Marked edema, only scattered lymphocyte infiltration, many arteries involved	Aggravated edema, few infiltrated cells, many arteries involved	Very severe edema, few infiltrated cells, all arteries involved
Alveolar ducts, sacs, and acini						
Lumen	No edema/hemorrhage, slight lymphocytic and macrophagic infiltration, only airway-adjacent acini involved	Like day 3 pi but mostly macrophage accumulation, airway-centered foci tend to spread and coalesce	Still no edema nor hemorrhages, severe lymphocytic and macrophagic infiltrations throughout the lungs	Moderate granulocytic/lymphocytic infiltration, only airway-adjacent acini involved, no edema	Like day 2 pi but airway-centered foci already coalesce, scattered flooded alveoli	Extensive edema and hemorrhages, moderate lymphocytic infiltration
Epithelium	No necrosis seen	No necrosis seen	Some necrotic cells visible, scattered hyaline membranes	Necrosis, sometimes	Multifocal necrosis, hyalin membranes	Multifocal necrosis, numerous hyalin membranes
Interstitium	Slight lymphocytic and macrophagic infiltration, only airway-adjacent acini involved	Like day 3 pi but more congestion and airway-centered foci tend to spread and coalesce	Diffuse and marked congestion, severe lymphocytic and macrophagic infiltrations throughout the lungs	Granulocytic/lymphocytic moderate infiltration, only airway-adjacent acini involved	Like day 2 pi but airway-centered foci already coalesce, diffuse and severe congestion,	Diffuse and severe congestion, hemorrhages and moderate lymphocytic infiltration
Nonrespiratory tissues						
Heart	No lesion seen	No lesion seen	No lesion seen	No lesion seen	No lesion seen	No lesion seen
Liver	No lesion seen	No lesion seen	No lesion seen	Centrolobular hydropic/granular degeneration	Centrolobular microvascular fatty degeneration + multifocal granulocytic/lymphocytic necrotizing hepatitis	Panlobular microvascular fatty degeneration + multifocal granulocytic/lymphocytic necrotizing hepatitis
Spleen	No lesion seen	No lesion seen	No lesion seen	No lesion seen	multifocal foci of	multifocal foci of

