1. Figure 1 shows an electron micrograph of a glomerular capillary loop (rbc=red blood cell, B=basement membrane, US=urinary space). Which of the following is most likely?

A. By light microscopy glomerulus would show complete replacement by hyalin
B. The patient has membranous glomerulonephritis
C. The glomerulus contains "wire loops"
D. The capillary loop shown is normal
E. The findings resulted from rheumatoid arthritis

2. Which of the following findings is most likely in the patient corresponding to the kidney biopsy shown in Figure 1?

A. Decreased serum C3
B. Acute rheumatic fever
C. Atherosclerosis
D. Destructive arthritis
E. Anti-centromere antibodies

3. Figure 2 shows a mitral valve at autopsy. Which of the following is most likely?

A. The patient died from acute rheumatic fever
B. The pulmonic valve is probably abnormal
C. The patient has Libman - Sacks endocarditis
D. The aortic valve may be abnormal
E. The function of the mitral valve would be normal
4. Which of the following is most likely to be present in histologic sections of the valve shown in Figure 2?

A. Fibrinoid necrosis
B. Fibrin deposits
C. Bacterial antigens
D. Immune complexes
E. Hyalinized collagen

5. Which of the following statements is most likely correct about the glomerulus shown in Figure 3?

A. It shows proliferative glomerulonephritis
B. It contains immune complex deposits
C. It shows a crescent
D. The patient has Wegener's granulomatosis
E. It shows fibrinoid necrosis

6. Clinical condition/problem most likely to be present in the patient corresponding to Fig 3:

A. Crippling arthritis
B. Verrucous endocarditis and skin rash
C. Granulomatous inflammation of the lung
D. CREST syndrome
E. Malignant hypertension

7. Figure 4 (blood vessel at low magnification) shows which of the following?

A. Histologic changes compatible with scleroderma
B. A fatty streak
C. Fibrinoid necrosis
D. A healed Aschoff body
E. A complicated atherosclerotic plaque
8. **Least likely** to be present in the patient corresponding to Figure 4:

A. An auto-antibody
B. Arthritis
C. Ischemia involving a visceral organ
D. Immune complexes
E. Sclerodactyly with dermal collagen deposition, epidermal atrophy and loss of dermal appendages

9. Figure 5 shows an opened segment of the abdominal aorta (clamps at renal artery bifurcations). Which of the following is **most likely** to be correct?

A. The abnormal findings may have been caused by polyarteritis nodosa
B. Aortic regurgitation could develop as a result of the lesion(s) shown
C. Circulating immune complexes were involved in the pathogenesis of the lesion(s)
D. Atrophy would be present in an abnormal area of this aorta
E. The disease(s) shown would be more prevalent in females

10. **Least likely** to be present on histologic examination of the aorta shown in Figure 5:

A. Angiogenesis
B. Excess deposition of elastic fibers
C. Fibrosis
D. Thrombus
E. Lymphocytes
11. Figure 6 shows a prostate biopsy. Which of the following diagnoses is most likely to be correct?
   A. Leiomyosarcoma
   B. Squamous cell carcinoma
   C. Well differentiated adenocarcinoma
   D. Poorly differentiated adenocarcinoma
   E. Lymphoma

12. Which of the following is the most likely consequence of this neoplasm?
   A. Formation of an ulcerated mass involving the anterior bladder
   B. Obstruction of the prostatic urethra
   C. Obstruction of the ureter
   D. Hematuria
   E. Direct invasion of the seminal vesicles

13. Figure 7 shows a biopsy from a mucosal surface. Which of the following diagnoses is correct?
   A. Hyperplasia
   B. Squamous metaplasia
   C. Preinvasive neoplasia
   D. Adenoma
   E. Healing ulcer

14. Most likely etiology of the findings in Figure 7:
   A. Acute inflammation
   B. Viral infection
   C. Hormone imbalance
   D. Ischemia
   E. Inherited mutation of a tumor suppressor gene
15. Best interpretation for the findings in Figure 8:
   A. Dysplasia
   B. Fibrosarcoma
   C. Neurofibroma
   D. Adenoma
   E. Squamous carcinoma

16. Most likely primary organ/site of origin for the lesion depicted in Figure 8:
   A. Epidermis
   B. Colon
   C. Breast duct
   D. Subcutaneous fibrous connective tissue
   E. Peripheral nerve

17. Most likely presenting signs/symptoms for the neoplasm shown in Figure 9:
   A. Abnormal mammogram
   B. Enlarging mass in leg muscles
   C. Enlarging lymph node
   D. Paraneoplastic hypercalcemia
   E. Polypoid mass in colon

18. Best criterion to employ in order to determine whether the neoplasm in Fig 9 is malignant:
   A. Presence of nodal metastasis
   B. Mitotic rate
   C. Invasion of the epithelial basal lamina
   D. Size of the lesion
   E. Presence of a genetic alteration
19. Most likely diagnosis for figure 10:
A. Squamous dysplasia
B. Sarcoma
C. Lymphoma
D. Adenocarcinoma
E. Squamous carcinoma

20. Most likely clinical presentation/history of this patient:
A. Positive test for occult fecal blood
B. EBV infection in immunosuppressed host
C. Abnormal squamous cells detected on Pap smear
D. Invasion of periosteum noted on x-ray
E. Lightly pigmented Caucasian with unprotected sun exposure

21. Which of the following is most likely to be paraneoplastic syndrome?
A. Pneumonia in a patient with lung cancer
B. Anemia in a patient with colorectal carcinoma
C. Hypercalcemia in a patient with osseous breast carcinoma metastases
D. Thromboembolism in a patient with pancreatic carcinoma
E. Bleeding tendency in a leukemic patient

22. Incorrect statement about colorectal adenocarcinoma:
A. May be associated with inherited gene mutation
B. It is common for cases to occur without familial predilection
C. Most hematogenous metastases involve the liver
D. Disease recurrence may be associated with elevation of a serum tumor marker
E. Most tumors evolve from polyps comprised of metaplastic epithelium
23. Feature which is not necessarily attributable to invasive growth in epithelial neoplasia:
   A. Atrophy of parenchymal tissue surrounding the neoplasm
   B. Irregular or ill-defined interface between neoplasm and host
   C. Desmoplasia
   D. Neoplastic cells disposed individually or in small nests
   E. Interruption of the epithelial basal lamina

24. Not observed with invasive epithelial neoplasia:
   A. Angiogenesis
   B. Partially differentiated cells
   C. Inflammatory cell infiltrates
   D. Differentiation of neoplastic cells into fibroblasts
   E. Remodeling of extracellular matrix

25. Which of the following is most likely to be observed in a pannus?
   A. Anitschkow's cells
   B. Angiogenesis
   C. Hyperplasia of cartilage
   D. Liquefactive necrosis
   E. Atrophic synovium
26. Which of the following statements concerning neoplasia epidemiology/pathogenesis is correct:

A. Most malignancies arising in adults are associated with inherited mutation of a known tumor suppressor gene

B. Neoplasia accounts for less than 1% of mortality in the pediatric age group

C. The incidence of a given type of neoplasm within a population may vary as a function of time

D. Inheritance of Rb-1 is associated with development of retinoblastoma but not with occurrence of other forms of neoplasia

E. Retinoblastomas do not occur when there is not an inherited mutation of Rb-1

27. Correct statement about human papilloma virus (HPV):

A. Genotype of the virus determines degree of infectivity but not degree of oncogenicity

B. Evidence of HPV infection may be observed in Pap smears

C. Infected cells demonstrate eosinophilic viral inclusions

D. Infection in a normal host usually results in squamous carcinoma of the uterine cervix

E. Virus encoded proteins disable the myc gene product via binding interaction

28. Correct statement about p53:

A. It acts as an oncogene

B. In order to function properly, the wild type gene product must accumulate and remain in the cytoplasm of a damaged cell

C. Cells with p53 mutation fail to express any gene product

D. Normally, p53 expression would antagonize the activity of bcl-2

E. Physiologic expression is greatest in normal, terminally differentiated cells
29. **Correct** statement about ras:
   
   A. It may act as a participant in autocrine growth stimulation pathways
   
   B. It is most commonly altered in neoplasms via a chromosomal translocation
   
   C. When activated, it translocates to the cell nucleus
   
   D. It is commonly altered in animal, but not human, neoplasms.
   
   E. The inactive form binds to extracellular growth factors

30. A forty-five year old woman presents with Raynaud's phenomenon, cough, finger ulcerations and autoantibodies directed against DNA topoisomerase I. Which of the following disease complications is most likely?
   
   A. Crippling arthritis
   
   B. Glomerulonephritis
   
   C. Cardiac valve deformities
   
   D. Thrombocytopenia
   
   E. Difficulty with swallowing

31. **Incorrect** statement about oncogene amplification:
   
   A. It may be observed in epithelial neoplasia
   
   B. It results in increased expression of the gene product
   
   C. It has been observed to involve growth factor receptor genes in human neoplasms
   
   D. It may be caused by point mutation
   
   E. It may be associated with abnormalities present on a karyotype
32. **Incorrect** statement about angiogenesis in neoplasia:
   A. It requires interaction between neoplastic and host cell populations
   B. It facilitates growth of the primary tumor but not metastasis
   C. It is facilitated by host macrophages and/or fibroblasts
   D. It is mediated by growth factors which are active in physiologic angiogenesis
   E. It is required for supply of oxygen and nutrients to the growing neoplastic population

33. Neoplasm which is most strongly associated with exposure to a chemical carcinogen:
   A. Prostate carcinoma
   B. T cell lymphoma
   C. Thyroid carcinoma
   D. Transitional carcinoma
   E. Fibrosarcoma

34. **Incorrect** statement about dysplasias (i.e. preinvasive epithelial neoplasia):
   A. They are premalignant
   B. They may be precursors in neoplasms associated with chronic/persistent inflammatory states
   C. They may form glands
   D. They contain cells with DNA mutations
   E. It is not possible to predict which dysplastic lesions would be most likely to become invasive carcinomas
35. **Least** likely to be a critical event in the etiology or pathogenesis of a lymphoma:
   A. Viral infection
   B. Preinvasive growth phase
   C. Chromosomal translocation
   D. Increased myc expression
   E. Increased expression of bcl-2

36. **Least** likely to occur with prostate carcinoma:
   A. Positive serum tumor marker
   B. Nodal metastasis
   C. Metastases to bone
   D. Squamous differentiation
   E. Grade dependent prognosis

37. A patient of yours presents with ascites and multiple serosal implants comprised of neoplastic cells. Which of the following is **most** likely?
   A. The patient has a cystic pelvic mass
   B. The neoplasm is HPV-associated
   C. The patient probably has hematuria also
   D. The patient has a positive PSA
   E. The patient has a Stage I pancreatic carcinoma

38. A patient of yours has a neoplasm which exhibits a doubling time of 30 days. Which of the following is **most** likely?
   A. Breast carcinoma
   B. Colon carcinoma
   C. Embryonal carcinoma
   D. Thyroid carcinoma
   E. Low grade lymphoma
39. **Least** likely to be a progression-related event for an invasive carcinoma:

A. Clonal heterogeneity  
B. Ulceration  
C. Clonal expansion  
D. Cooperative intercellular interactions between neoplastic and sub-populations  
E. Cooperative intercellular interactions between neoplastic and host populations

40. **Correct** statement about chemical carcinogenesis:

A. Initiation, once completed, may be reversed  
B. Tumor promoters act via oxidative DNA injury  
C. Cells with DNA alterations are considered to be initiated  
D. Transformation may occur if there is a lengthy interval between initiation and promotion  
E. In some cases, initiation may follow promotion in the transformation process

41. **Correct** statement about virus-associated neoplasia/ carcinogenesis in humans:

A. Viral infection alone is sufficient to result in malignancy  
B. It requires completion of the viral life cycle  
C. It occurs only with retroviruses  
D. It occurs without altering the host cell DNA  
E. Virus encoded proteins may disable apoptosis in host cells
42. Which of the following features would distinguish invasive carcinoma from dysplasia with the greatest degree of specificity?
   A. Degree of nuclear hyperchromasia
   B. Mitotic rate
   C. Nuclear to cytoplasmic ratio of neoplastic cells
   D. Degree of differentiation
   E. Presence of vascular invasion by neoplastic cells

43. Most likely to be a criterion for stage in a lung carcinoma:
   A. Mitotic count
   B. Presence of hypercalcemia
   C. Invasion of pleura
   D. Coughing up blood
   E. Length of time the patient has been symptomatic

44. Correct statement about tumor grade:
   A. The difference in survival between a well and a poorly differentiated colon carcinoma is 80-90%
   B. It is a better predictor of outcome than stage
   C. It is inversely correlated with stage
   D. Clinical significance of grade depends on the tumor type or primary organ
   E. In colon carcinoma, the depth of invasion is a grading criterion

45. Most likely to be a feature of malignancy in a breast lump:
   A. Cystic character
   B. Liquefactive necrosis
   C. Mushy consistency on palpation
   D. Biphasic differentiation
   E. White-grey firm, gritty surface on cut section
46. A male patient of yours presents with a "poker spine", aortitis and uveitis. Which of the following is most likely in this patient?

A. Sacroiliitis  
B. The patient has HLA-D4  
C. The serum is positive for rheumatoid factor  
D. Sjogren's syndrome  
E. Circulating immune complexes

47. Correct statement about the natural history of a breast carcinoma:

A. The interval from tumor inception to clinical presentation averages about one year  
B. Hematogenous metastasis does not occur until the tumor reaches a palpable size  
C. The time interval from inception to presentation is generally longer than the time interval from presentation to recurrence  
D. Presence of angiolymphatic emboli implies that metastasis has occurred  
E. Mammography lessens the interval from tumor inception to diagnosis by 80%

48. A benign neoplasm comprised of gland forming epithelial cells is called:

A. Adenoma  
B. Leiomyoma  
C. Choristoma  
D. Hamartoma  
E. Squamous papilloma
49. Most common histologic type of neoplasm which causes mortality in Americans who are greater than 50 yrs of age:
   A. Malignant melanoma
   B. Adenocarcinoma
   C. Sarcoma
   D. Transitional carcinoma
   E. Lymphoma

50. Least likely to be observed in a pleomorphic adenoma:
   A. Epithelial basal lamina
   B. Genetic alterations
   C. Neoplastic population less mature than corresponding normal cell population
   D. Neoplastic cells present in lymphatic vessels
   E. Neoplastic cells which exhibit differentiation toward stromal (connective tissue) elements

51. Correct statement about metastasis:
   A. Nodal metastasis is required for distant metastasis to occur
   B. Nodal metastasis implies incurable disease
   C. Nodal metastases are more frequent with sarcomas than carcinoma
   D. The spleen is one of the most common sites for hematogenous metastases
   E. A small percentage of tumor cells which intravasate form metastases
52. **Not** a factor that impacts the organ which is involved by hematogenous metastases:
   A. Type of vasculature in the secondary organ
   B. Cardiac output to secondary organ
   C. Tumor cell-host cell interaction at secondary organ
   D. Anatomy of lymphatic drainage from the primary organ
   E. Anatomy of venous drainage from the primary organ

53. **Not** a feature of sarcomas:
   A. Angiogenesis
   B. Nuclear hyperchromatism
   C. Invasion through basal lamina by neoplastic cells
   D. Greater incidence in pediatric (vs adult) age group
   E. Origin from non-invasive precursor lesion

54. **Best** definition for neoplasia:
   A. Loss of maturity among existing functionally differentiated cells
   B. Incomplete maturation of stem cell progeny
   C. Over-proliferation of mature cells
   D. Lack of recognizable cellular differentiation
   E. Inappropriate tissue organization

55. A patient of yours, as a child, experienced acute rheumatic fever and now presents with heart disease many years later. Which of the following lesions/findings would be **least** likely in this patient (i.e. at the present time):
   A. Thromboembolism
   B. Myocardial scarring
   C. Calcification in valve leaflets
   D. Pericardial adhesions
   E. Tricuspid valve fibrosis
56. You examine a lung mass which is comprised of mature columnar epithelium with normal stromal cells and fully differentiated cartilage. The most likely diagnosis is:

A. Choristoma
B. Hamartoma
C. Pleomorphic adenoma
D. Chondroma
E. Fibroadenoma

57. Which of the following is not more likely/more frequent in a poorly differentiated (vs a well differentiated) adenocarcinoma?

A. Mitotic figures
B. Angiolymphatic tumor cell emboli
C. Nodal metastases
D. Genetic alterations
E. Gland formation by tumor cells

58. A female patient of yours presents with chest pain, a fever, purpura and painful, swollen joints. Splenomegaly and pleural friction rub are noted on physical exam. Which of the following tests is most likely to reveal a functionally and diagnostically significant abnormality?

A. Serum rheumatoid factor determination
B. Urinalysis
C. HLA - DR3 test
D. Joint fluid analysis
E. Serum ASO titre
59. A neoplasm with desmoplasia would be:
   A. Soft
   B. Bloody
   C. Very firm
   D. Necrotic
   E. Preinvasive

60. Correct statement about growth rate for breast carcinomas:
   A. It is dependent on tumor grade
   B. For a given tumor, it routinely fluctuates markedly on a daily basis
   C. It would be more rapid, on average, than an acute leukemia
   D. It is essentially similar between individual cases
   E. It increases after clinical diagnosis

61. A skin biopsy shows mononuclear cell infiltrates around dermal appendages with liquefactive degeneration of the basal layer of epidermis and immunoglobulin deposits at the dermal-epidermal junction. Which of the following is the most likely diagnosis?
   A. Generalized scleroderma
   B. Rheumatoid nodule
   C. Ankylosing spondylitis
   D. Systemic lupus erythematosus (SLE)
   E. Scleroderma, limited form
62. Correct statement about the natural history of an adeno-carcinoma:
   A. Genetic structure of the neoplastic cells remains stable once invasion has occurred
   B. Most evolve from histologically completely benign neoplasms
   C. They are comprised of multiple unrelated and functionally independent clones
   D. Selection pressures imposed by the host or by therapy contribute to progression-related events
   E. Genetic alterations occur, but do not affect the behavior of the tumor cells

63. A patient of yours has abnormal blood levels of lipoprotein Lp(a). Which of the following is most likely correct?
   A. The patient has SLE
   B. The patient is at increased risk for developing a myocardial infarct
   C. The patient has a neoplasm
   D. The patient has a history of rheumatic fever
   E. The patient has polyarteritis nodosa

64. Antibody virtually diagnostic of systemic lupus erythematosus:
   A. Rheumatoid factor
   B. Anticentromere
   C. Anti-Smith (Sm)
   D. P-ANCA (perinuclear antineutrophil cytoplasmic auto-antibody)
   E. JO-1 antibody (t RNA synthetase)
65. Antibody present in more than 95% of patients with drug-induced lupus erythematosus:
   A. Anticentromere
   B. Antiphospholipid
   C. C-ANCA (cytoplasmic antineutrophil cytoplasmic autoantibody)
   D. Rheumatoid factor
   E. Antihistone

66. Disabling of joint function is not found in:
   A. Rheumatoid arthritis
   B. Generalized (diffuse) scleroderma
   C. Mixed connective tissue disease
   D. Rheumatic fever
   E. Ankylosing spondylitis

67. Important mediator of both the inflammatory process and acute coronary syndromes:
   A. Platelet activating factor (PAF)
   B. Leukotriene B₄ (LTB₄)
   C. Basic fibroblast growth factor (bFGF)
   D. Nitric oxide
   E. Histamine
68. Oxidized LDL contributes to atherogenesis by all of the following except:

A. Being readily ingested by macrophages through the scavenger receptor.
B. By increasing monocyte adhesion
C. By stimulating release of growth factors and cytokines
D. By being cytotoxic to both endothelial and smooth muscle cells
E. By increasing the motility of macrophages in the lesions

69. The currently favored and modified response-to-injury hypothesis of atherogenesis includes all of the following except:

A. The development of focal areas of chronic endothelial injury and/or dysfunction
B. Increased accumulation of lipoproteins into the vessel wall, especially oxidatively modified LDL and VLDL.
C. Cellular interactions in the foci of injury involving endothelial and smooth muscle cells, monocytes/macrophages and T lymphocytes
D. Repeated episodes of thrombosis and organization as the initiating event
E. Intimal smooth muscle cell proliferation with formation of extracellular matrix

70. Which of the following is not considered a manifestation of complicated atherosclerotic plaques?

A. Development of a necrotic lipid pool
B. Surface ulceration
C. Dystrophic calcification
D. Thrombosis overlying the plaque
E. Hemorrhage into the plaque
71. Which of the following is least likely to be a location of an atherosclerotic plaque?

A. Circle of Willis
B. Near the ostia of vessels which branch from the thoracic aorta
C. Internal carotid artery
D. Aortic arch
E. Proximal coronary arteries

72. Which of the following events is most closely related to the conversion of a fatty streak into an atheromatous plaque?

A. Injury to the endothelium
B. Occlusion of more than 80% of the vessel's lumen
C. Proliferation of smooth muscle cells
D. Phagocytosis of lipids by macrophages
E. Phagocytosis of lipids by smooth muscle cells

73. Which of the following is a major risk factor for the development of atherosclerosis?

A. Elevated HDL level
B. Hyperuricemia
C. Insufficient physical activity
D. High dietary carbohydrate intake
E. Hypertension
74. Correct statement about fatty streaks:
   A. They contain large cholesterol crystals which result in clear "clefts" in tissue sections
   B. Some undergo regression
   C. They have the same anatomical distribution as atherosclerotic plaques
   D. They may be associated with decreased blood flow through the affected vessel
   E. They contain abundant extracellular lipid

75. The following list contains events which may, or may not, be involved in the pathogenesis of rheumatoid arthritis.

Choose the answer (A-E) which orders events in the most correct pathogenetic sequence.

   1 - synovial cell proliferation
   2 - cartilage destruction
   3 - activation of CD4+ cells
   4 - development of auto-antibodies to complement
   5 - activation of macrophages

A. 4 to 5 to 1 to 2
B. 3 to 5 to 1 to 2
C. 5 to 3 to 4 to 1
D. 5 to 3 to 2 to 1
E. 2 to 1 to 3 to 5
DIRECTIONS: Match the neoplasm (76-80) to the etiologic factor (A-E below). Use each choice once only:

A. Basal cell carcinoma
B. Small cell carcinoma
C. Lymphoma
D. Thyroid carcinoma
E. Gastric adenocarcinoma

76. Carcinogen exposure
77. Ultraviolet light exposure
78. Persistent inflammation
79. Viral infection
80. Ionizing radiation

DIRECTIONS: Match the gene (81 - 85) to the most appropriate direct function (A-E below):

A. Growth factor binding tyrosine kinase activity
B. Up-regulates transcription of cyclins
C. Deactivation of ras
D. Induces apoptosis
E. Down regulation of cyclin-cdk complex activity

81. bax
82. NF-1
83. p21
84. ERBB-2
85. myc
DIRECTIONS: Match each option (86–90) with the best alternative listed (A–G below). Each alternative may be used once, more than once or not at all.

A. Rheumatic fever
B. Ankylosing spondylitis
C. Mixed connective tissue disease
D. Polyarteritis nodosa
E. Generalized (diffuse) scleroderma
F. Polymyositis/dermatomyositis
G. Inclusion body myositis

86. Pulmonary disease mediated by endothelin-1
87. Association with a malignant tumor
88. Pancarditis
89. HLA-B27 serotype
90. Migratory polyarthritis
DIRECTIONS: Match each option (91-95) with the best alternative listed (A-G below). Each alternative may be used once, more than once, or not at all.

A. Systemic lupus erythematosus
B. Polymyositis/dermatomyositis
C. Ankylosing spondylitis
D. Rheumatoid arthritis
E. Wegener's granulomatosis
F. Generalized (diffuse) scleroderma
G. Rheumatic fever

91. "Heliotrope" skin rash
92. C-ANCA (perinuclear antineutrophil cytoplasmic autoantibody)
93. Necrotizing lesions of upper respiratory tract
94. Immune complex nephritis
95. Malignant hypertension-like small vessel disease

DIRECTIONS: Match each cell (96-100) with its appropriate product listed (A-E below). Each alternative may be used once only.

A. Thromboxane A$_2$ (TX A$_2$)
B. Prostacyclin (PG I$_2$)
C. Oxidatively modified LDL
D. Interferon-gamma (IFN-gamma)
E. Extracellular matrix

96. Lymphocyte
97. Endothelial cell
98. Smooth muscle cell
99. Monocyte/macrophage
100. Platelet