Tumor Markers

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IDEAL TUMOR MARKERS

- Be specific to the tumor
- Level should change in response to tumor size
- An abnormal level should be obtained in the presence of micrometastases
- The level should not have large fluctuations that are independent of changes in tumor size
- Levels in healthy individuals are at much lower concentrations than those found in cancer patients
- Predict recurrences before they are clinically detectable
- Test should be cost effective

COMMON TUMOR MARKERS

Analyte	Cancer Use
CEA	Monitor colorectal, breast, lung cancer
CA-125	Ovarian cancer monitoring
CA15-3, 27. 29	Monitor recurrences of breast cancer
AFP	Germ cell tumors, liver cancer
Total PSA	Screen and monitor prostate cancer
Free PSA	Distinguish prostate cancer from BPH
HCG	Germ cell and trophoblastic tumors
Hormone receptors	Breast cancer therapy
NMP 22, BTA FDP	Monitor recurrences of bladder cancer

SCREENING TESTS

- Cancer must be common
- The natural history of the cancer should be understood
- Effective treatments must be available
- The test must be acceptable to both patients and physicians
- The test must be safe and relatively inexpensive

CEA

- Described by Gold and Freedman in1965 as a marker for Colorectal Cancer
- Molecular mass of approximately 200,000 kA
- Glycoprotein with a carbohydrate composition ranging from 50 - 85% of molecular mass
- CEA levels 5 - 10 times upper limit of normal suggests colon cancer
- CEA is not used to screen for colon cancer

CEA Distribution In Healthy Individuals and Patients with Non-Malignant Conditions

	% Distribution of CEA		
	ng/mL	ng/mL	ng/mL
Healthy Subjects	0-3.0	3.1-10	>10.0
Non Smokers	96	4	0
Smokers	80	19	1
Non-Malignant Diseases			
Cirrhosis	**53**	**42**	**5**
Ulcerative Colitis	**65**	**26**	**9**
Rectal polyps	**78**	**19**	**3**
Pulmonary	**52**	**39**	**9**
Gastrointestinal	76	21	3

CEA Distribution In Patients With Malignant Disease

	% Distribution of CEA		
	0-3 ng/mL	3.1-10 ng/mL	>10 ng/mL
Colorectal	28	20	52
Breast	50	27	23
Ovarian	80	16	4
Pulmonary	39	29	32

CA-125

- CA-125 glycoprotein molecular weight 200-1,000 kda
- Introduced in 1983 by Bast for ovarian cancer
- In the US, in 1998 25,400 new cases will be diagnosed and 14,500 women will die as a result of this disease
- 70% of the women with ovarian cancer are over the age of 50
- One half of patients with stage 1 ovarian cancer have elevated CA-125 levels and a five year survival rate of 90%. In late stage disease, the five year survival rate is from 4-30%
- Worldwide incidence is highest in industrialized countries and lowest in Japan and India

SYMPTONS OF OVARIAN CANCER

- ASCITES
- ABDOMINAL and PELVIC PAIN
- ABNORMAL UTERINE BLEEDING
- GASTROINTESTINAL DISCOMFORT
- WEIGHT LOSS
- URINARY FREQUENCY

RISK FACTORS

INCREASED RISK	DECREASED RISK
Family History	Oral Contraceptive
Advanced Age	Breast Feeding
Infertility	Tubal Ligation
Nulliparity	

CA-125 Distribution In Healthy Subjects and Patients with Non-Malignant Conditions

	% Distribution of CA-125		
	<35 u/mL	35-65 u/mL	>65 u/mL
Healthy Individuals	98	1.7	1.3
Non-Malignant Conditions			
Pregnancy	73	22	5
Cirrhosis	30	13	57
Pulmonary Disease	94	0	6
Pelvic Inflammatory Disease	76	3	21
Endometriosis	86	11	3
Ovarian Cysts	90	7	3
Uterine Fibroids	77	13	10
Breast Fibroids	100	0	0

CA-125 Distribution In Patients With Malignant Disease

	% Distribution of CA-125		
Cancers	<35 u/mL	35-65 u/mL	>65 u/mL
Ovarian	14	9	77
Lung	56	19	25
Breast	82	8	10
Endometrial	70	8	22
Cervical	66	15	19
Colorectal	76	11	12

CEA - CAP Proficiency Survey

	#Labs	Mean ng/mL
Abbott AXSYM	689	11.14
Bayer ACS 180	73	8.63
Bayer Centaur	240	8.50
Bayer Immuno-1	34	7.71
Beckman Access	201	7.86
DPC Immulite 2000	78	11 .60
Roche Elecsys/E170	105	11.27
Tosoh AIA-Pack	33	18.76
J&J Vitros ECI	97	13.17

TROPONIN I - CAP Proficiency Survey

	# Labs	**Mean ng/mL**
Abbott AXSYM	**1228**	**3.93**
Dade Dimension	**706**	**0.43**
Dade Stratus	**229**	**0.40**
Beckman Access	**307**	**0.24**
Bayer Centaur	**144**	**1.22**
Bayer ACS 180	**173**	**1.12**
J&J Vitros ECI	**81**	**0.16**
DPC Immulite	**23**	**2.90**

GUIDELINES FOR ORDERING/ INTERPRETING TUMOR MARKER TESTS

- Never rely on the result of a single test
- Order every test from the same laboratory
- Consider half-life of the tumor when interpreting the result
- Consider how the Tumor Marker is removed or metabolized
- Consider Hook Effect
- Consider presence of HAMA antibodies

MULTIPLE MYELOMA

Multiple Myeloma - proliferation of a single clone of plasma cells that produces a monoclonal protein

Annual Incidence - 4 in 100,000

Number of cases per year - 13,000

Represents 1% of all malignant diseases

Median age at diagnosis - 65 years

Median survival - 3 years

ETIOLOGY OF MULTIPLE MYELOMA

Radiation Exposure

Agriculture - Farming & Pesticide Use

Chemicals - Benzene

Not Related to Smoking or Alcohol Consumption

Monoclonal Gammopathy of Undetermined Significance

Defined as the presence of a serum monoclonal protein at low levels

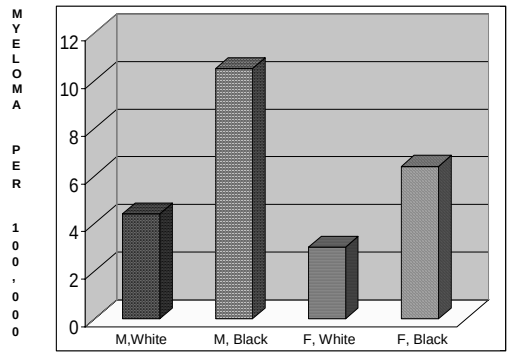
Number of cases per year - 750,000-1,000,000

54% Men 46% Women

Occurs in 2% of persons over 50 years, 3% over 70 years

Median age at diagnosis - 72 years

Median survival - 12 years



SYMPTOMS OF MULTIPLE MYELOMA

Bone Pain - Back, Ribs
Osteoporosis
Bone Fracture
Fatigue
Anemia
Renal Failure
Infections

Clinical Laboratory in Multiple Myeloma

-Biochemical -

Serum monoclonal proteins >3.0 g/dL
Polyclonal Immunoglobulin Decreased
Proteinuria, Bence-Jones Protein present in urine
BUN, Creatinine ⇧
Calcium ⇧ ,N

- Hematological -

Hemoglobin Decreased
Anemia - Normochromatic, Normocyte
ESR Increased

Major Laboratory Features of MM

Findings	% of MM patients affected
Hemoglobin ≤12 g/dL	65
Serum calcium ≥11.0 mg/dL	14
Serum creatinine ≥ 1.7 mg/dL	23
Serum M-protein present	92
Urine M-protein present	75
M-protein in serum or urine (or both)	99
Bone lesions	75
Bone marrow plasma cells ≥10%	90

Monoclonal Gammopathy of Undetermined Significance

Serum monoclonal protein <3.0 g/dL

Stability of monoclonal protein during long term follow-up

<10% Plasma cells in bone marrow

None or a small amount of Bence-Jones protein in urine

Absence of lytic bone lesions

Serum calcium, BUN, creatinine - Normal

Hemoglobin - Normal

Laboratory Data at Diagnosis for MGUS

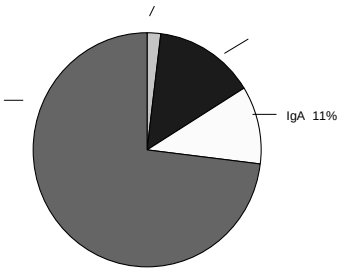
Serum concentration of the uninvolved immunoglobulin is decreased in 38% of patients

Urine - Kappa Bence-Jones Protein 21%
Lambda Bence-Jones Protein 10%

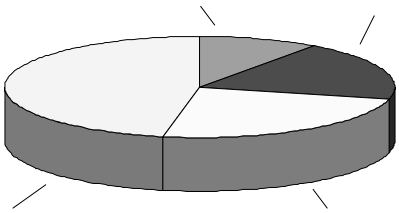
For most of the patients, the concentration of the Bence-Jones protein was <150 mg/24 hr

No light chain was detected in 69% of the patients

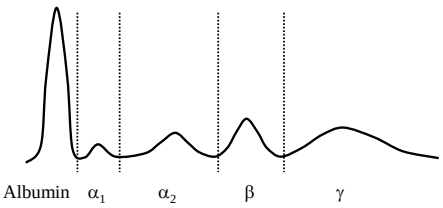
Distribution Frequency of Monoclonal Proteins In MGUS



Clinical Course of 241 Patients with MGUS



Normal SPE



Monoclonal gammopathy

Albumin decreased
Sharp peak in gamma region