# Development of Web-based Programs for Pathology Education

### Andy N.D. Nguyen, M.D.

Medical School, Department of Pathology and Laboratory Medicine

# 2001 Advances in Teaching & Learning



Design and implementation of three webbased programs for teaching pathology residents WEB COAG: teaching coagulation disorders

**CPCases**: archiving presentation cases

**CD MarkerDX**: teaching immunophenotype of hematologic neoplasms

### WEB COAG

# % An interactive program for teaching coagulation disorders

### KNguyen, A.N.D., Uthman, M.O., Johnson, K.A.: A web-based teaching program for laboratory diagnosis of coagulation disorders. Archives of Pathology & Laboratory Medicine. 2000; 124:588-593

### Introduction

Coagulopathy is encountered frequently in medicine, associated with high morbidity and fatality

Hany cases present a diagnostic challenge, may lead to suboptimal testing strategy or misdiagnosis

#WEB COAG: teaching laboratory diagnosis of coagulopathy (pathology residents)



**#**Three modules

# 1. <u>Coagulation profile</u>: to display typical laboratory results

2. <u>Differential diagnosis</u>: to narrow down the list of possible disorders

3. Synopsis of disorders and therapy

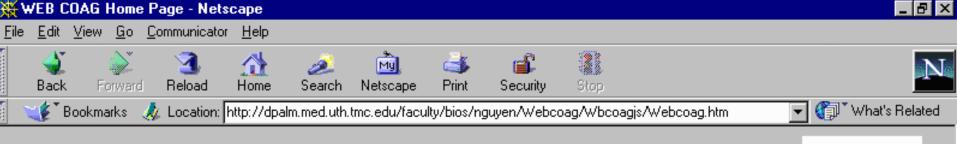
### Design (cont'd)

 Codes: Hypertext Markup Language (HTML), JavaScript (functions and subroutines)
 Servers: MS Windows NT Server 4.0 running MS Internet Information Server 4.0

# Design (cont'd)

**Knowledge** base: 41 coagulation disorders

- ₭Validation of the differential diagnosis module:
  - 61 clinical cases
  - The correct diagnosis was ranked in the list of 5 differential diagnoses in 93% of the cases [previous publication]



### WEB COAG

### **Decision Support System for Coagulopathy**



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WEB COAG is a WWW-based decision-support system for diagnosis of coagulopathy. Currently, there are three main features in this system:

- <u>Coagulation Profile</u>:displays pattern of seven screenning coagulation tests for each disorder. The tests include: prothrombin time (PT), activated partial thromboplastin time (PTT), fibrinogen (FIB), thrombin time (TT), fibrin split product (FSP), platelet count (PLT), and bleeding time (BT).
- Differential Diagnosis: displays differential diagnoses that fit the coagulation results given by the user.
- Synopsis of Coagulopathy and Therapy: displays essential information on coagulopathy and therapeutic modalities.

Back to Home Page

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### WEB COAG: SCREENNING LABORATORY PROFILES OF COAGULATION DISORDERS

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#### Select a disorder from the drop-down list to see its coagulation profile:

| Hemophilia A                                                             |                                                                                                            | • |                  |
|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|---|------------------|
| Coagulation Profile:<br>PT:  Normal Abnormal PTT: Abnormal EIR: Abnormal | TT: • Normal • Abnormal<br>FSP: • Normal • Abnormal<br>PLT: • Normal • Abnormal<br>BT: • Normal • Abnormal |   |                  |
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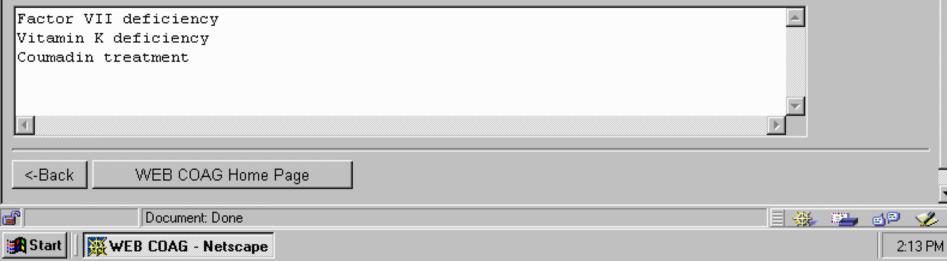
### WEB COAG: DIFFERENTIAL DIAGNOSIS

#### Andy Nguyen, M.D./ UT-Medical School at Houston, Pathology/ Last Revision on: 8/10/99

| Enter Coagulation Data:  | TT: • Normal • Abnormal  |
|--------------------------|--------------------------|
| PT: O Normal O Abnormal  | FSP: • Normal • Abnormal |
| PTT: • Normal • Abnormal | PLT: • Normal • Abnormal |
| FIB: • Normal • Abnormal | BT: • Normal • Abnormal  |



#### LIST OF DIFFERENTIAL DIAGNOSES:



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### WEB COAG: Synopsis of Coagulopathy and Therapeutic Modalities

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#### Hereditary Disorders of Coagulation Proteins:

- Factor XII Deficiency, Hereditary;
- Prekalikrein Deficiency
- Factor XI Deficiency
- Factor IX Deficiency (Hemophilia B)
- Factor VIII Deficiency (Hemophilia A)
- Acquired Factor VIII Inhibitor in Hemophilia A
- vonWillebrand's Disease, type I
- vonWillebrand's Disease, type IIA
- vonWillebrand's Disease, type IIB
- vonWillebrand's Disease, type III
- Factor VII Deficiency
- Factor X Deficiency
- Factor V Deficiency
- Afibrinogenemia
- Hypofibrinogenemia
- Dysfibrinogenemia
- Factor XIII Deficiency
- Antithrombin III Deficiency
- <u>Alpha-2 Antiplasmin Deficiency</u>
- Protein C Deficiency

#### **Acquired Disorders of Coagulation Proteins:**

Coagulopathy in Vitamin K Deficiency

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### VON WILLEBRAND'S DISEASE (TYPE I)

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Biochemical aspects:

von Willebrand factor consists of a series of multimers that range in molecular weight from 800,000 to more than 12,000,000.

- Pathological Basis:
  - Mode of inheritance: autosomal dominant.
  - The biochemical abnormality in type I of von Willebrand's disease is strictly quantitative. In such patients, analysis of the multimeric structure of von Willebrand factor with crossed immunoelectrophoresis or sodium dodecyl sulfate- agarose gel electrophoresis is normal. There are concordant decreases in the levels of factors VIII R:RCo, VIII R:Ag, and VIII:C.
- Treatment:
  - ° DDAVP (1-desamino-8-D-arginine vasopressin).
  - Cryoprecipitate: 1 bag per 10 kg of body weight, twice a day.
  - Epsilon-aminocaproic acid (EACA): is a useful adjuvant in dental surgery. The usual loading dose is 5 gm, followed by 1 gm per hour for 5 - 7 days.

#### Diagnostic Criteria:

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- 1. Family\_history\_of\_coagulation\_disorders:positive
- 2. Factor\_VIII:C\_activity:abnormal
- 3. Factor\_VIII\_R:Ag:abnormal
- 4. Factor\_VIII\_R:RCo:abnormal
- 5. Factor\_VIII,cross\_immunoelectrophoresis:normal
- 6. Bleeding time:abnormal

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### PLATELET CONCENTRATE

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#### Random-donor platelet:

- Composition: platelets (>5.5\*10<sup>10</sup> /unit), WBC's, plasma, RBC's.
- Supply format: one unit (bag) contains 50 ml. One dose consists of 6 units. Shelf life is 3-5 days.
- Indication: thrombocytopenia or thrombocytopathy.
- Dosage:

For a 70 kg adult, one unit of random-donor platelets will increase the platelet count by 3,000-10,000/ul. For children, one unit of random-donor platelet will increase the platelet count by 3,000/ul per 1 kg of body weight.

#### Single-donor platelet:

 Composition: platelets (>3\*10<sup>11</sup> /units), WBC's, plasma, RBC's.

#### Supply format:

one bag contains 300 ml. Shelf life is 24 hours.

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### Calculating Units of Cryopecipitate Needed for Fibrinogen

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| Baseline Fibrinogen Level (mg/dl): 50<br>Desired Fibrinogen Level (mg/dl): 150 |         |         |
|--------------------------------------------------------------------------------|---------|---------|
| Patient's Body Weight (Kg): 65                                                 |         |         |
| Calculate Units of Cryo Needed-> 10                                            |         |         |
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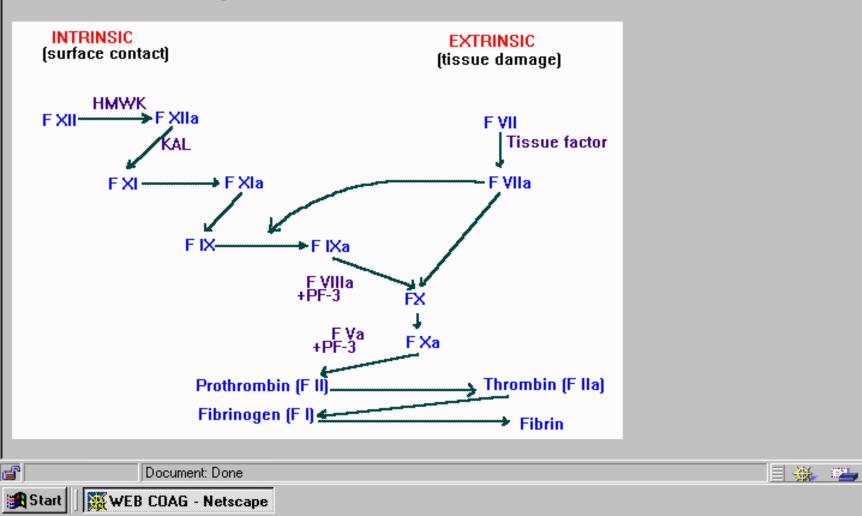
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#### **Coagulation Cascade Diagram**

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Click on the factors in the diagram below to see associated disorders



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### WEB COAG: Platelet Aggregation Patterns

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Andy Nguyen, M.D./ UT-Medical School at Houston, Pathology/ Last Revision on: 8/12/99

#### Select a disorder from the drop-down list to see its aggregation pattern:

| Storage Pool Disease                                                                         |       |
|----------------------------------------------------------------------------------------------|-------|
| Aggregation with Reagents:         ADP: O Normal O Abnormal         EPI: O Normal O Abnormal |       |
| COL: O Normal O Abnormal<br>RIS: O Normal O Abnormal<br>Show Profile Now Help                |       |
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### Discussion

WEB COAG has been used as supplemental teaching material for our residents since 1996

- Favorable response by residents and web site visitors. Comments and suggestions were incorporated
- % Other web sites on coagulation (academic, commercial)

Current project: "A comprehensive webbased program for coagulation training", grant from University Association for Research and Education in Pathology

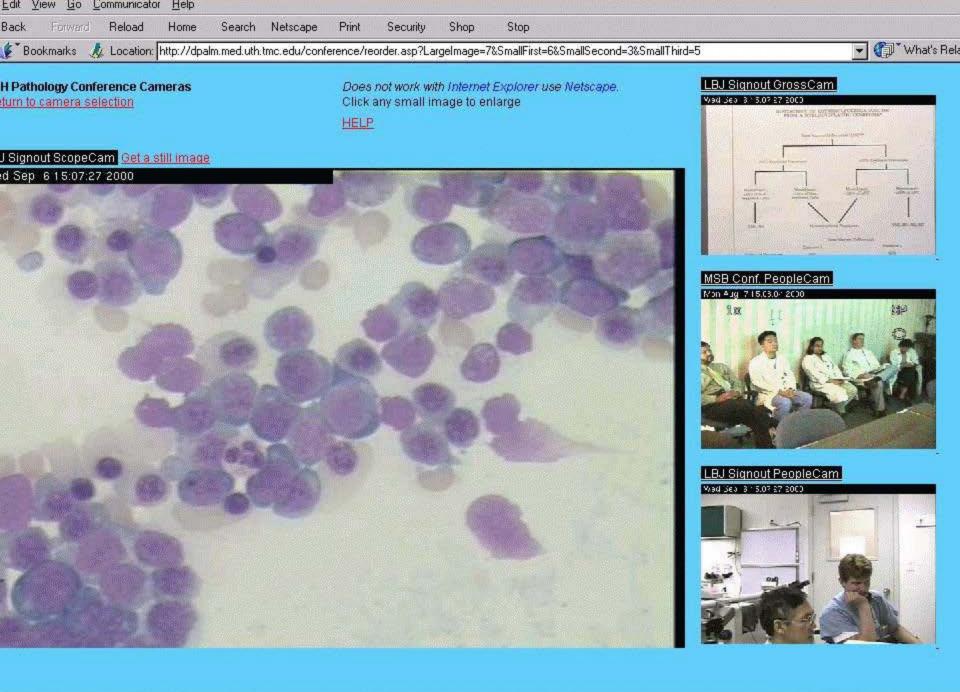


 An image database to archive cases presented in our resident teleconference
 Gupta, D., Wu, S., Nguyen, A.: An Image Database for Archived Presentation Cases. The 80 th Annual Meeting of Texas Society of Pathologists, Jan., 2001, Galveston, Texas

### **Resident Teleconference**

 Residents to share interesting cases between Memorial Hermann and LBJ
 Axis video web servers to transmit video on high-speed T1 connection (bidirectional)
 Audio communication: speakerphone





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# **Design of CPCases**

**#**Objectives:

- Save images and text data to database
- Retrieval at a later time for various uses

**#**Two components:

- Input module: to save a case
- Viewing module: to view an archived case

### Design of CPCases (cont'd)

Codes: MS Active Server Pages (ASP), VBScript, Active Data Object (ADO), structured query language (SQL)

### **Servers**:

- MS SQL Server 7.0 (database for text data)
- File server (images)
- MS Windows NT 4.0 server
- MS Internet Information Server 4.0

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### PCases: Saving the Image into Database

#### Right click on the image and save it into S:/PathImage



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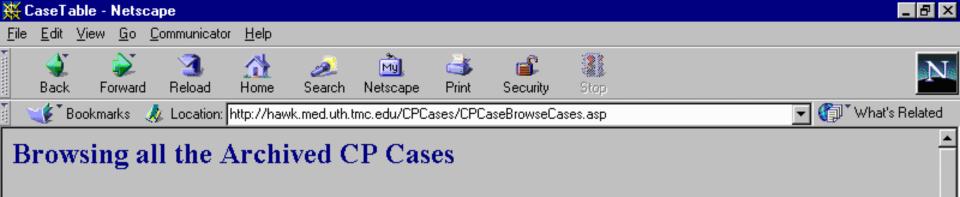
nference Date: 12/7/2000

Submit Data

Reset Input Data







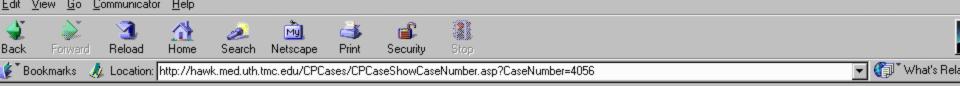
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Note: Click on any Case Number to get a full record for that case

| Case Nu                         | umber                                 | Diagnosis                                           |  |  |  |  |  |  |  |
|---------------------------------|---------------------------------------|-----------------------------------------------------|--|--|--|--|--|--|--|
|                                 | 0001                                  | Pneumocystis carinii in BAL fluid                   |  |  |  |  |  |  |  |
|                                 | 0002                                  | Mucormycosis in blood vessel                        |  |  |  |  |  |  |  |
|                                 | 0004                                  | Cryptosporidium in stool                            |  |  |  |  |  |  |  |
|                                 | 0005                                  | <u>6</u> Histoplasma in brain abscess- PAS          |  |  |  |  |  |  |  |
|                                 | 0006                                  | Histoplasma in brain abscess- GMS                   |  |  |  |  |  |  |  |
|                                 | 0007 Babesiosis                       |                                                     |  |  |  |  |  |  |  |
|                                 | 0008 HIV bone marrow                  |                                                     |  |  |  |  |  |  |  |
| <u>(</u>                        | 0008-1 Mastocytosis                   |                                                     |  |  |  |  |  |  |  |
| <u>(</u>                        | 0008-2                                | 8-2 Mastocytosis-higher magnification               |  |  |  |  |  |  |  |
| <u>(</u>                        | 0008-3 Mastocytosis-Giemsa            |                                                     |  |  |  |  |  |  |  |
| <u>(</u>                        | 0009-1 Anaplastic large cell lymphoma |                                                     |  |  |  |  |  |  |  |
| <u>(</u>                        | 0009-2                                | Anaplastic large cell lymphoma-CD30                 |  |  |  |  |  |  |  |
| <u>(</u>                        | 0009-3                                | Anaplastic large cell lymphoma-Bone marrow          |  |  |  |  |  |  |  |
|                                 | 0010 Megaloblastic changes            |                                                     |  |  |  |  |  |  |  |
| 0011 India ink for Cryptococcus |                                       |                                                     |  |  |  |  |  |  |  |
|                                 | 1012-1                                | Cryptococcus in hone marrow                         |  |  |  |  |  |  |  |
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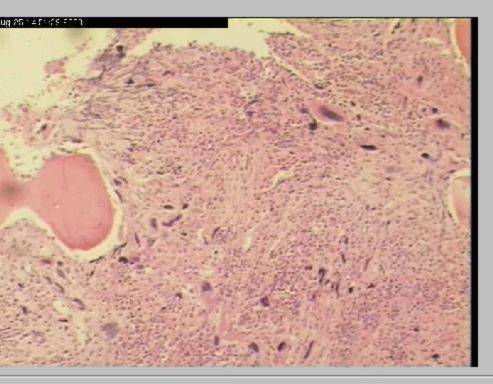
#### gnosis: Idiopathic myelofibrosis

litional Data: 55 y/o male with anemia. Peripheral blood smear showed many teardrop cells, a few blasts and NRBCs. Bone row biopsy showed diffuse fibrosis.

MED Code: M49000

hor: Andy Nguyen

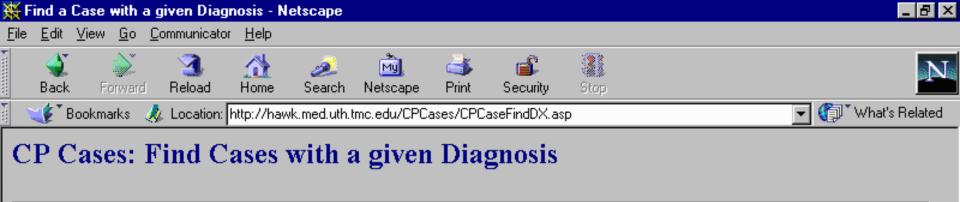
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Enter a key word then click the "Find" button:

Diagnosis: lymphoma Find

Archived CP Cases Home Page







### P Cases: Find Cases with a given Diagnosis

following matches were found:

view full image, put cursor on thumb-nail image, click the right mouse button and choose View Image)

se Number: 4074

ge Location: PathImage/4074.jpg

agnosis: Hodgkin's Lymphoma

litional Data: 22 Year Male with Hodgkin's disease Stage IV. The biopsy is hypercellular and is diffusely infiltrated by Igkin's disease. The infiltrate is comprised of Reed Sternberg cells, eosinophils, plasma cells and lymphocytes. There is fuse increase in fibro-connective tissue.

MED Code:

esenter(s): Deepali Gupta

ference Date: 9/19/2000



se Number: 2070

age Location: PathImage/2070-1.jpg

agnosis: Burkitt's Lymphoma

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### Discussion

#Our residents have saved > 100 cases to date #Future studies:

- a better index system to categorize diseases
- connection with a more sophisticated image database at the back end

### **CD MarkerDX**

△A Web-based database for diagnosis of hematologic neoplasms using results of immunophenotyping by flow cytometry. △Nguyen, A.N.D., Milam J.D., Johnson K.A., Banez E.I.: A Relational Database for **Diagnosis of Hematopoietic Neoplasms** Using Immunophenotyping by Flow Cytometry. American J Clinical Pathology. 2000; 113:95-106.

### Introduction

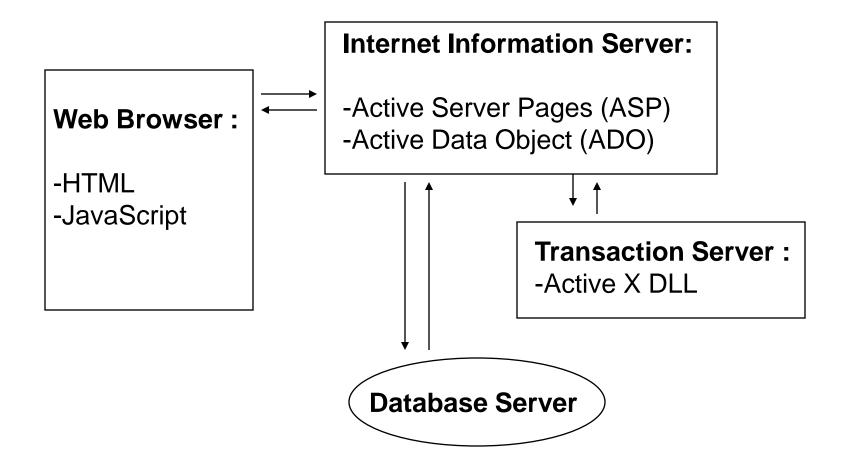
- Interpretation of immunophenotyping results by flow cytometry: pattern recognition
- Difficulty in interpretation: similar patterns, numerous markers
- CD MarkerDX: database to teach pathology residents interpret immunophenotypes

# Design

⊡ Five modules:

- Display of markers
- Display of disorders
- Differential diagnosis
- Archived cases
- Summary of results for archived cases

# Design (cont'd)



# Design (cont'd)

**Knowledge** base: 33 hematologic neoplasms.

43 immunologic markers

# ₭Validation of the differential diagnosis module:

- 92 clinical cases

- The correct diagnosis was ranked in the list of 5 differential diagnoses in 93% of cases [previous publication]

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CD MARKER DX: a dynamic Web-based database for differential diagnosis and data warehouse of hematologic neoplasms using immunophenotyping data obtained with flow cytometry

Andy Nguyen, M.D./ UT-Medical School at Houston, Pathology/ Last Revision on: 11/4/98

- 1. Differential Diagnoses
- 2. Display of Disorders
- 3. Display of Markers
- 4. Display of Archived Cases for a disorder
- 5. Display of Summary for Archived Cases

Back to Home Page

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### CD MARKER DX: List of Markers for a Disorder

Disorder:Chronic lymphocytic leukemia (B cell)/Small lymphocytic lymphoma

| CD1:   |   | CD14: |   | CD38:  |   | CD103:   |   |
|--------|---|-------|---|--------|---|----------|---|
| CD2:   | - | CD15: |   | CD41:  |   | HLA-DR:  | + |
| CD3:   | - | CD16: |   | CD42:  |   | sIg:     | + |
| CD4:   | - | CD19: | + | CD43:  | + | cIg:     |   |
| CD5:   | + | CD20: | + | CD45:  |   | PC-1:    |   |
| CD7:   | - | CD21: | + | CD56:  |   | TdT:     |   |
| CD8:   | - | CD22: |   | CD57:  |   | FMC7:    | - |
| CD10:  | - | CD23: | + | CD61:  |   | Glyco A: |   |
| CD11b: |   | CD24: | + | CD71:  |   | Keratin: |   |
| CD11c: |   | CD25: | - | CD77:  |   | CD5/19:  | + |
| CD13:  |   | CD33: |   | CD79a: | + |          |   |

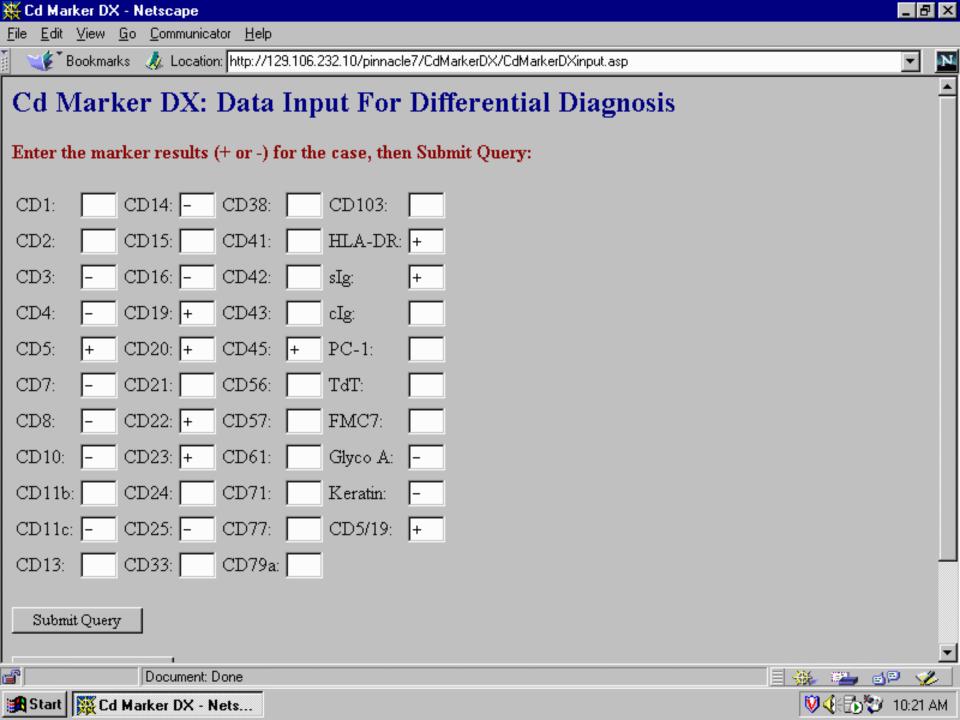
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### Cd Marker DX: Differential Diagnosis

| DISORDER                                                         | C    | M-N | M  | N |
|------------------------------------------------------------------|------|-----|----|---|
| Chronic lymphocytic leukemia (B cell)/Small lymphocytic lymphoma | 1    | 13  | 13 | 0 |
| Prolymphocytic leukemia (B cell)                                 | 1    | 12  | 12 | 0 |
| Mantle cell lymphoma                                             | 0.88 | 7   | 8  | 1 |
| Diffuse, mixed cell lymphoma                                     | 0.87 | 6   | 7  | 1 |
| Large B-cell lymphoma                                            | 0.85 | 5   | 6  | 1 |

#### Legends:

M= the number of attributes of a disease that match the input data

N= the number of attributes of a disease that do not match the input data

(M-N)= M minus N

C= matching factor, defined as the ratio of M/(M+N)

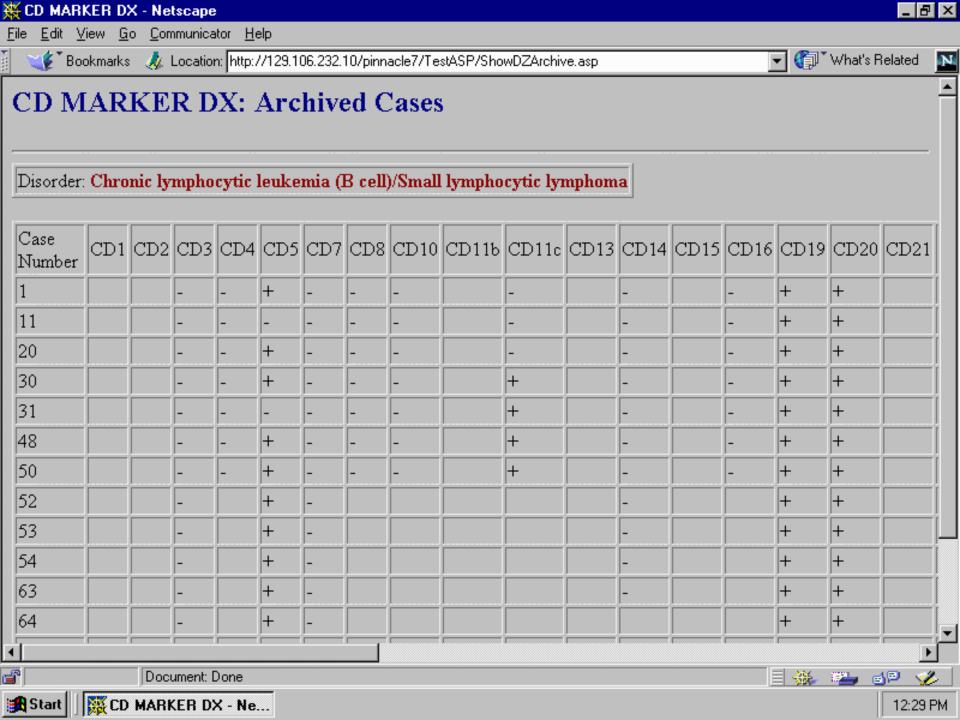
Notes: the higher the values of C and (M-N), the higher the probability of a disease.

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### **CD MARKER DX: Summary of Results from Archived Cases**

Disorder:Chronic lymphocytic leukemia (B cell)/Small lymphocytic lymphoma

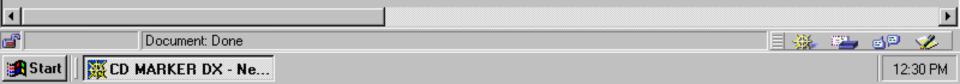
| Markers                | CD1 | CD2 | CD3 | CD4 | CD5 | CD7 | CD8 | CD10 | CD11b | CD11c | CD13 | CD14 | CD15 | CD16 | CD19 | CD20 | CD21 | C |
|------------------------|-----|-----|-----|-----|-----|-----|-----|------|-------|-------|------|------|------|------|------|------|------|---|
| Diagnostic<br>Criteria |     | -   | -   | -   | +   | -   | -   | -    |       |       |      |      |      |      | +    | +    | +    |   |
| No of<br>(+)Cases      | 0   | 0   | 0   | 0   | 11  | 0   | 0   | 0    | 0     | 4     | 0    | 0    | 0    | 0    | 13   | 13   | 0    | 7 |
| No of<br>(-)Cases      | 0   | 0   | 13  | 7   | 2   | 13  | 7   | 7    | 0     | 3     | 0    | 12   | 0    | 7    | 0    | 0    | 0    | 0 |

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CD MARKER DX Home Page





CD MarkerDX has been used as supplemental teaching material for pathology residents since 1998

Future project: data warehouse of clinical cases for marker analysis-> to fine-tune the diagnostic criteria

### CONCLUSION

Here web-based programs for pathology education

**#**Minimum hardware requirement

**#**Work on all operating systems, all browsers

Favorable response from residents (clinical use/ scientific presentations/ articles)

# CONCLUSION (cont'd)

Advantages of web-based programs: access from anywhere, any computer platforms, ease of updating materials

- ₩ Web-based education may eventually form the core materials for life-long learning, especially at the point-of-service
- **#**Our web site: http://dpalm.med.uth.tmc.edu/