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### Ask Borik (continued)

significantly associated with a risk of disease progression in asymptomatic myeloma. The presence of BJP is generally indicative of greater severity of the underlying disorder and could signal a dimmer prognosis.

Weak bands, tiny restrictions are often telling us that we are in a gray area where the adverse condition is in its infancy yet some signs might be already showing up. Without consulting the physician and knowing the clinical situation, but even then, it might be impossible to arrive to a better understanding. In view of many, we have no reliable means to distinguish an asymptomatic patient with a lasting benign monoclonal gammopathy from one in whom symptoms and malignant disease will develop. To some interpreters such uncertainty might be difficult to accept. However, the most reliable means today are periodic repeats (about 6 - 12 months) of serum and urine immunofixation to determine if the process has subsided, remained the same or progressed.

### Reference Available

Sebia's does offer one of the few electrophoresis texts available today. The book is designed to expand the reader's interpretive skills and to be used as a frequently called upon reference book to assist with difficult clinical cases as discussed above. If you would like to receive information about how to add this text to your reference library, please circle number **113**.

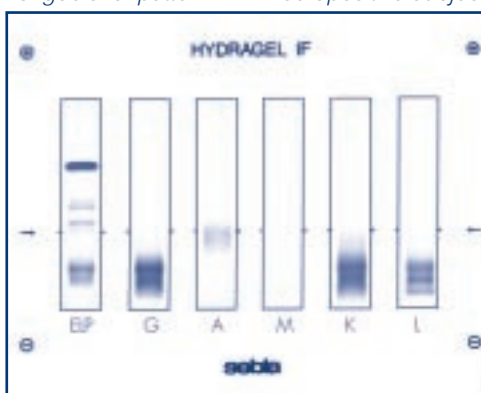
### "Serum Oligoclonal Bands" (continued)

restriction of heterogeneity of synthesized immunoglobulins.

The evolution of oligoclonal banding and any marked changes in the appearance of the bands may prove to be useful information in assessing the role of the immunosuppressive therapy.

Please circle number **112** on your Reader Response Card for more information on Sebia's IF assay.

#### Oligoclonal pattern in HIV seropositive subject



Hyper  $\gamma$  globulinemia with oligoclonal pattern involving (Kappa and Lambda) IgGs

### Distribution Services – It's More Than Just Shipping

By: Katarina Relja, Operations Manager

Much like Sebia's customer service, the expertise found in the Distribution Service Department extends far beyond the task at hand. In the effort to provide our customers with prompt and error free deliveries, the shipping department is trained in and encouraged to gain knowledge in all aspects of our industry.

Sebia's reagent shelf-life is a respectable 18 to 24 months, but due to the temperature sensitive nature of electrophoresis reagents, all orders are shipped Next Day Service. That's why no reagents are shipped on Friday. However, Saturday deliveries may be arranged at a customer's discretion provided that Saturday delivery is an option in the their area.

To assure Next Day Service, Sebia customers are encouraged to place orders prior to 4:00 PM EST. We understand in a hectic laboratory this is not always possible and urgent situations do occur. So, depending on the size of the order, Sebia is prepared to work with our customers in arranging a Next Day delivery until 6:00 PM EST.

Sebia's preferred shipping method is by UPS. In the past 2 years, UPS has proven to be a reliable method of transportation with quality service and technology. With UPS's On-Line system, Sebia is able to provide our customer's with real-time tracking and other detailed receiving information. This really comes in handy when expected shipments are mistakenly delivered to the wrong section of the laboratory. Rest assured, as good as UPS is, back-up shipping methods and services have been established so our customers never experience a stock-out situation due to shipping.

Finally, since all deliveries are generated from steamy Georgia, every box is insulated and packed with ice packs. Our customers can be assured that all orders are filled and handled on an individual basis. You're in good hands with Sebia.

# Separations

## "Serum Oligoclonal Bands"

By: Elena LoCastro, Product Specialist, Somagen Diagnostics

The use of sensitive immunofixation techniques such as the Sebia IF kit on the Hydrasys® has led to the detection and identification of several types of immunoglobulin abnormalities. These may exhibit several patterns one of which is the presence of two or more bands commonly referred to as oligoclonal bands or O-bands. These bands may be of varying intensity.

The detection and typing of these oligoclonal bands is an important part of routine immunofixation because of the high prevalence of these oligoclonal patterns in lymphoproliferative disorders. These may range from transplant patients who are given immunosuppressive drugs (and infected by CMV and EBV), patients infected with HIV, patients with certain types of cancer or patients during recovery of B-Cell function after myeloablative therapy.

The detection and follow up of oligoclonal bands is especially useful for transplant patients where pronounced oligoclonal bands may correspond to the emergence of a lymphoproliferative syndrome. At this stage, the condition may be treated by modification of the immunosuppressive therapy.

These serum oligoclonal bands are usually related to IgG immunoglobulins but may rarely be seen as IgMs or IgAs. It is important to differentiate these oligoclonal bands from multi-band patterns observed when several polymerized units are seen, namely with IgM and IgA immunoglobulin or when excess free light chains are noted. When treated with BME (beta-mercaptoethanol), the oligoclonal band pattern stays identical and the intensity does not change. This differentiation of an oligoclonal banding pattern from a polymerized monoclonal band is of importance since this pattern may be useful to

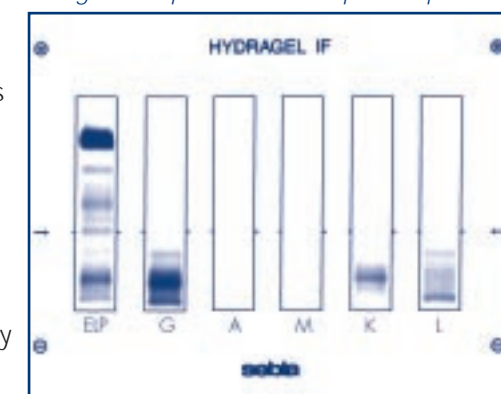
indicate that one of several conditions is responsible for the oligoclonal bands ranging from benign and transient conditions to pathological conditions.

Usually associated with immunodeficiency, the origin of the immunosuppression may be:

- congenital: in children with immune combined deficiency (rare cases)
- therapeutic: in cases of organ or bone marrow grafts
- viral: in AIDS
- cancer: found in certain types autoimmune diseases

In the case of transplant patients, the presence of oligoclonal banding in serum immunofixation may serve as a marker for the subsequent development of a post transplant lymphoproliferative disorder, such as non-Hodgkins malignant lymphoma, which may be encountered associated with EBV. The mechanism for the

#### Oligoclonal pattern in a transplanted patient



Oligoclonal pattern involving (Kappa and Lambda) IgGs

appearance of these bands is not well documented. They may correspond to a transient synthesis of specific antibodies directed against the viral agent or to a limited synthesis of antibodies resulting from a defective immune system.

The investigation of oligoclonal bands for transplant patients serves to indicate a

continued on back



result from a response of the immune system to an antigenic stimulus. This and other unusual presentations are infrequent but frequent enough to cause continuous concerns about proper interpretation.

Having wetted your appetite, I have to disappoint you. Due to limited space, I will deal this time only with the troublesome small restrictions or weak M-bands on immunofixation gels. Discussion of "weird" bands will appear in the next issue of Separations.

**"WEAK" AND "WEIRD" BANDS OF IMMUNOFIXATION**

Life would be considerably more simple if immunofixation patterns of patient's serum were clearly either negative or showed distinct bands of heavy and light chain monoclonal components. But, alas, life is rarely simple. The bands are often weak and not distinct. Even when we exclude possible artifacts (e.g., caused by inappropriate sample concentration or handling of samples) the immunofixation patterns may be complicated due to the properties of immunoglobulins. Monoclonal immunoglobulins can polymerize (e.g., IgA, IgM and free light chains), form aggregates (e.g., cryoglobulins, IgG), form complexes with various proteins or polyclonal immunoglobulins, and undergo post-translational modifications. Furthermore, a clone producing complete monoclonal proteins can yield excessive amounts of free light chains or it can produce two types of heavy chains (only one light chain).

In true monoclonal gammopathies a single clone or several single clones of plasma cells or B-lymphocytes produce excessive amounts of immunoglobulin, but not in response to an immunogen. However, there is a group of conditions associated with M-components that possess activity against various immunogens. Therefore, they appear to

**Reporting of "Weak" IF Bands**

Questions come up quite often about the clinical significance of weak, single or multiple restrictions, such as those associated with MGUS or restricted heterogeneity patterns. How the small bands should be reported without unnecessarily alarming the physician and causing psychological burden to the patient, while not ignoring the possibility of a serious disorder at its onset, are frequently grounds for conflicting arguments. With more sensitive electrophoretic and immunofixation techniques becoming the standard of clinical laboratories, the share of detected small M-components has considerably increased.

It has been reported that about 60% of detectable M-components are too small to be quantifiable by densitometry and another 20% are at a concentration of <50 mg/dL. About 15% and 25% in these two groups, respectively, are associated with BJP in urine; K and L free light chains are equally represented. Interestingly, in about 10% of the BJP positive urines, both K and L are present (believed not to be due to a ladder effect).

When a monoclonal protein is detected in serum by EP at a level of <50 mg/dL (i.e. as a weak band approximating the intensity of a-1 antitrypsin in normal

serum) and confirmed by IF it is usually reported similar to this: "small restriction (band), significance not clear; suggest serum follow-up and urine testing for BJP". Similarly, it seems perfectly adequate to call multiple weak bandings as "restricted heterogeneity consistent with autoimmune, infectious, immunodeficiency and immunosuppressive conditions; presence of M-component(s) cannot be excluded".

**Significance of "Weak" IF bands**

Additional insight into the significance of weak (small) restrictions is obtained by examining the entire gamma zone in the serum pattern. If the polyclonal immunoglobulins (gamma zone) are normal or increased, the likelihood of a malignant lymphoproliferative process is low. Tiny restrictions on a normal or increased polyclonal background suggest a likelihood of a polyclonal process leading to restricted heterogeneity. Small monoclonal band(s) associated with a polyclonal decrease is likely to signal a malignant lymphoproliferative process.

Whenever a monoclonal gammopathy (MGUS or malignant) is indicated or suspected, or small M-bands are present, testing for BJP in the urine should be considered. Although presence of BJP is no longer considered an indication of malignant monoclonal gammopathy, detection of BJP can significantly contribute to the patient's diagnostic picture. BJP in low concentrations are found relatively often, alone or in combination with MGUS. Unfortunately, similar to monoclonal components in serum, there is no defined threshold of BJP concentration indicating malignancy or assuring benign character of the condition. However, BJP >20 mg/dL is much more likely to indicate a malignant B-cell proliferation than lower concentrations. BJP excretion >50 mg/day is

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In the meantime, keep sending in those questions. You may send them to me by mail at Sebia, 190-6611 Bay Circle, Norcross, GA 30071, attn. "Ask Borek", by fax at 770-446-8511 attention "Ask Borek", or by e-mail at [bjanik@sebia-usa.com](mailto:bjanik@sebia-usa.com). Whichever method you choose, include your name, laboratory name and phone number should I have questions for you.



That's the game plan for most every health care system today...and the University of Michigan Hospitals — part of the University of Michigan Health System — is no exception. When the organization merged three separate labs into one, technologists faced heavier volumes — but there were no extra players to hand off the extra work to.

"At the time of the transition, we were using a manual electrophoresis system that was very labor intensive and time consuming," explains Mara Williams, Supervisor of Special Chemistry. "We began searching for an automated solution to improve our efficiency so that we could effectively handle the increased workload."

Williams' team reviewed different options and found Sebia's HYDRASYS® to be "worlds apart" from its competitors in terms of gel quality, resolution and 'user-friendliness.' Designed as a 'walkaway' system, the HYDRASYS rapidly performs all phases of electrophoresis — from sample application to migration to incubation to staining, destaining and drying.

She adds that throughout hundreds of runs performed on the HYDRASYS since

**You know the drill: 'Do more with less'**

University of Michigan Hospitals in Ann Arbor, Michigan

July 1998, the Sebia gels have never failed her lab. "Sebia's product is consistently good. With our old system, we always had a certain number of repeats because something didn't look quite right — but with Sebia, we've eliminated that problem."



"By automating electrophoresis, the lab has freed up man-hours for other tasks."

Williams also likes the fact that since most of the reagents come already prepared, prep work is fast and easy. Not only that, the gel combs can be set up ahead of time and stored up to eight hours before they're run on the HYDRASYS — further optimizing the workflow.

By automating electrophoresis, the lab has freed up man-hours for other tasks. "Now one technologist can accomplish the same amount of work that used to be handled by two techs," Williams says. "That means we can assign people to other tasks." After the samples are put through

**"One of the first things that struck us was that even though the Sebia gels are very small, the resolution is so good and clear," says Williams. "It was unanimous among our staff that Sebia offered the best 'readability' of the solutions we looked at — and that helps to ensure utmost accuracy."**

electrophoresis, another Sebia system helps technologists analyze the results. The HYRYS™ Densitometer makes sense of the various readings and presents results and parameters using different color shades for fast, easy interpretation. The instrument allows for fast scanning — less than two seconds per sample — and enables storage of up to 20,000 curves and results on the hard drive and another 20,000 on a ZIP disk.

"With the HYRYS, we can edit patterns right on-screen, which is a real plus," Williams notes. "And the quality of the printed reports are great — they're extremely easy to read and digest."

By employing Sebia systems, the University of Michigan Hospitals' core lab has evolved in terms of workflow and the level of service it provides to hospital staff and patients. "The merger of three departments into one was a very stressful undertaking, but these automated systems have helped to ensure speed and quality despite a huge increase in volume," says Williams. "It was a nice surprise when we realized that our goals weren't unreasonable...that we could accomplish more with less."

**About the University of Michigan Hospitals**

Located in Ann Arbor, the University of Michigan Hospitals — part of the University of Michigan Health System — comprises three inpatient facilities with 872 licensed beds. These include: University Hospital, C.S. Mott Children's Hospital and Women's Hospital. As a teaching resource for the University of Michigan Medical School, the Hospitals organization trains approximately 4,000 students each year in the techniques of modern clinical medicine.

The Health System consistently ranks among the nation's best health care institutions. In 1999 the system was highlighted by U.S. News & World Report as one of the "best hospitals in the United States" and the number 10-ranked medical school in the country.

**We Need Your Feedback**

In order to better serve you, we constantly update our **Sebia Separations** Mailing list. Please complete this card and return to us.

Please circle the reader service numbers of those items on which you would like more information.

article 112

article 113

Number of electrophoresis tests run per week.

Protein\_\_\_\_ Immunofixations\_\_\_\_ Hemoglobin\_\_\_\_

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Thank You for Your Assistance

**"It was unanimous... Sebia offered the best 'readability' of the solutions we looked at."**  
 —Mara Williams,  
 Supervisor of Special Chemistry  
 University of Michigan Hospitals  
 University of Michigan Health System

