Welcome & Introductions

Dr. Lamar’s slides are available for download at www.LLS.org/programs, under the program listing.

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Redox Biology and Medicine Center
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Winston-Salem, NC
Disclosures

• Zanetta S. Lamar, MD, has affiliations with Seattle Genetics (*Consultant, fees waived*).
Learning Objectives

• We will discuss
  • History of Hodgkin
  • Epidemiology, presentation, diagnosis
  • Management of early and advanced disease
  • Emerging therapies
  • Shared decision making
ON THE PATHOLOGICAL CHANGES IN HODGKIN'S DISEASE, WITH ESPECIAL REFERENCE TO ITS RELATION TO TUBERCULOSIS.

BY DOROTHY M. REED, M.D.,

Fellow in Pathology, Johns Hopkins University.

[From the Pathological Laboratory of the Johns Hopkins Hospital and University.]

(Plates IV-VII.)

HISTORICAL.—It is seventy years since Hodgkin' called the attention of the medical world to the peculiar enlargement of the lymphatic glands, which has since been designated by his name. Hodgkin's original paper was a simple report of seven unusual cases, which had come under his observation as pathologist at Guy's Hospital. He noted that the cases agreed in glandular tumors and were frequently associated with enlargement of the spleen. He did not attempt any critical analysis of his material, and undoubtedly had no conception that, in one or possibly two of his cases, he was dealing with a peculiar and rare disease. The other cases have no interest for us in this connection, as they are instances of tuberculosis, syphilis and possibly leukemia.

Reed Sternberg cell
Epidemiology

- 8,260 cases diagnosed in 2017
- Represent 0.5% of all new cancer cases
- Five years after diagnosis 86.4% remain alive

Based on November 2016 SEER data submission.

Presentation

Lymph node groups

PET scan

Hoppe, 2007, Hodgkin Lymphoma,
LWW p125
Bone marrow biopsies are no longer routinely performed
The distant past….

Hodgkin disease is a systemic disease and invariably fatal

Laparotomy and splenectomy are required for best results
The distant past….

Hodgkin disease is a systemic disease and invariably fatal. Laparotomy and splenectomy are required for best results. Wide-field high dose irradiation is treatment of choice for Stage I-III disease.

Adapted from Saul A. Rosenberg.

The distant past….

Chemotherapy is reserved for patients with advanced disease.

Adapted from Saul A. Rosenberg.
The distant past….

Laparotomy and splenectomy are required for best results. Wide-field high dose irradiation is the treatment of choice for Stage I-III disease. Chemotherapy is reserved for patients with advanced disease. MOPP-like chemotherapy is the treatment of choice. Infertility, leukemia and heart disease are acceptable toxicities.
Early stage favorable Hodgkin
### Early stage favorable Hodgkin

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCIC</td>
<td>IA or IIA</td>
<td>ABVD x 4 – 6 cycles</td>
<td>94% at 12 years</td>
</tr>
<tr>
<td>HD.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Excluded for bulky disease, ≥3 nodal areas, elevated ESR

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### Can we safely reduce the chemotherapy or radiation doses?

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
<th>Study findings</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD10</td>
<td>IA-IIA*</td>
<td>ABVD x 2 cycles then 20 Gy radiation</td>
<td>91% at 5 years</td>
</tr>
<tr>
<td>HD13</td>
<td>I-IIA</td>
<td>ABVD x 2 cycles then 30Gy radiation remained standard. Cannot routinely omit Bleomycin or dacarbazine</td>
<td>93% at 5 years</td>
</tr>
</tbody>
</table>

* Excluded for bulky disease, ≥3 nodal areas, elevated ESR

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Wake Forest Baptist Medical Center
Can we safely use a PET scan to guide therapy?

Early stage favorable Hodgkin PET directed therapy trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPID</td>
<td>IA – IIA Non-bulky</td>
<td>ABVD x 3 cycles if PET scan (-) (Deauville 1 or 2)</td>
<td>91% at 3 years</td>
</tr>
<tr>
<td></td>
<td>I–II</td>
<td>ABVD x 2 cycles if PET (-) then ABVD x 1 and involved node radiation (INRT)</td>
<td>99% at 5 years</td>
</tr>
<tr>
<td>EORTC H10</td>
<td>I–II</td>
<td>ABVD x 2 cycles if PET scan (+) then escalated BEACOPP x 2 cycles and INRT</td>
<td>91% at 5 year</td>
</tr>
</tbody>
</table>

* Excludes for bulky disease, ≥3 nodal areas, elevated ESR
### Pet scan Deauville score

<table>
<thead>
<tr>
<th>Score</th>
<th>Pet scan findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No uptake</td>
</tr>
<tr>
<td>2</td>
<td>Uptake is ≤ mediastinal (chest region) blood pool</td>
</tr>
<tr>
<td>3</td>
<td>Uptake is ≥ mediastinal blood pool but ≤ liver</td>
</tr>
<tr>
<td>4</td>
<td>Uptake more than the liver</td>
</tr>
<tr>
<td>5</td>
<td>Uptake markedly higher than liver +/- new disease sites</td>
</tr>
</tbody>
</table>

#### Complete response

#### Partial response or progression

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Baseline PET scan

2 cycles ABVD

- **Deauville 1 or 2**
- **Deauville 4**
- **Deauville 5**
# Early stage treatment

<table>
<thead>
<tr>
<th></th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABVD</strong></td>
<td>Associated with high cure rates</td>
<td>Side effects, bleomycin lung toxicity</td>
</tr>
<tr>
<td></td>
<td>Low risk of infertility</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Better tolerated</td>
<td>Results improved with radiation</td>
</tr>
<tr>
<td><strong>Radiation</strong></td>
<td>Associated with high cure rates</td>
<td>Associated with increased risk of future cancers</td>
</tr>
<tr>
<td></td>
<td>Doses of radiation has decreased significantly</td>
<td></td>
</tr>
<tr>
<td><strong>Stanford V</strong></td>
<td>Associated with high cure rates</td>
<td>Results similar to ABVD</td>
</tr>
<tr>
<td><strong>BEACOPP</strong></td>
<td>Associated with high cure rates</td>
<td>Risk of secondary malignancies, infertility, premature menopause</td>
</tr>
</tbody>
</table>

## ABVD side effects

- Decreased blood counts
- Hair loss
- Nausea/vomiting
- Neuropathy

![Chemotherapy](image)
• Early unfavorable and advanced stage Hodgkin
# Treatment options for early unfavorable or advanced Hodgkin

<table>
<thead>
<tr>
<th>Name of study</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG 2496</td>
<td>ABVD x 6 cycles</td>
<td>74% at 6 years</td>
</tr>
<tr>
<td>Viviani</td>
<td>BEACOPP x 8 cycles +/- radiation</td>
<td>85%</td>
</tr>
<tr>
<td>RATHL</td>
<td>ABVD x 2 cycles, PET scan (-) then AVD x 4 cycles</td>
<td>84% at 3 years</td>
</tr>
<tr>
<td>ECHELON-1</td>
<td>Brentuximab and AVD</td>
<td>82% at 2 years</td>
</tr>
</tbody>
</table>

ECHELON

Stage III-IV Hodgkin
N = 1334

- **ABVD**
  - N = 670
- **Brentuximab + AVD**
  - N = 664
Advanced stage treatment

<table>
<thead>
<tr>
<th></th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABVD x 6 cycles</td>
<td>High cure rates</td>
<td>Bleomycin toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Side effects worse in &gt;60 yrs</td>
</tr>
<tr>
<td>BEACOPP x 8 cycles</td>
<td>Better disease control</td>
<td>Toxic, less experience in the US</td>
</tr>
<tr>
<td>ABVD x 2 cycles, PET scan (-)</td>
<td>Slightly reduced risk of</td>
<td>If PET scan positive, ideal</td>
</tr>
<tr>
<td></td>
<td>bleomycin toxicity</td>
<td>treatment less clear</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brentuximab and AVD</td>
<td>No risk of bleomycin</td>
<td>Cost of brentuximab</td>
</tr>
<tr>
<td></td>
<td>toxicity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>May be slightly more effective</td>
<td>Requires growth factor</td>
</tr>
<tr>
<td></td>
<td>than ABVD</td>
<td>Risk of neuropathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More follow up needed</td>
</tr>
</tbody>
</table>
• What if the cancer does not go away or what if it comes back………

AETHERA TRIAL

329 patients with high risk Hodgkin

Risk factors:
- No complete remission
- Remission < 1 year
- Extranodal involvement

Transplant

Brentuximab
1.8mg/kg
N = 165

Brentuximab consolidation = 42.9 months

Placebo
N = 164

Placebo = 24.1 months

PD-1 inhibitors

- Also called checkpoint inhibitors
- Acts as gatekeepers on T cell function
- Nivolumab
- Pembroluzimab

Slide A Chen, et al, JCO 2017
## Therapy combinations under investigation

<table>
<thead>
<tr>
<th>Brentuximab +</th>
<th>Nivolumab+</th>
<th>Pembroluzimab+</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICE</td>
<td>AVD</td>
<td>Acalabrutinib</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>Ibrutinib</td>
<td>Brentuximab</td>
</tr>
<tr>
<td>Dacarbazine</td>
<td>ICE</td>
<td>Lenalidomide</td>
</tr>
<tr>
<td>Ipilumumab</td>
<td>Ipilumumab</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab</th>
<th>Lenalidomide</th>
<th>Lenalidomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brentuximab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dacarbazine</td>
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</tr>
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### The future is here

**Chimeric antigen receptor (CAR) T cell**

1. **IN THE BODY**
   - Blood is drawn from the patient.
   - T cells are separated from the blood and reinfused into the body.
   - CAR T cells identify the cancer cells with the target antigens, and kill them.
   - CAR T cells may remain in the body for some time to help prevent the cancer cells from returning.

2. **IN THE LAB/MANUFACTURING FACILITY**
   - An inactive virus is used to insert genes into the T cells.
   - The genes cause the T cells to make special receptors, called CARs, on their surfaces.
   - Modified T cells (also called CAR T cells) are multiplied until there are millions of these attacker cells.
   - CAR T cells are put back into the patient’s bloodstream, typically after chemotherapy is given to make space, and continue to multiply.
Shared decision making

- Newly diagnosed
  - How will treatment affect….
    - Fertility, cardiovascular disease, risk of another cancer (skin, breast, lymphoma)
    - Finances??
    - Herbal supplements…
  - Interim PET scan
    - Will treatment change based on the results?

- Post-treatment
  - How often will scans be performed?
  - How long will I deal with memory problems, sexual dysfunction, fatigue, peripheral neuropathy?
  - When should I transition to primary care?
The present....

Hodgkin is curable

The present....

Excisional biopsy preferred for diagnosis
The present....

Treatment based on early PET scan findings will evolve

Chemotherapy remains standard but immunotherapy is an emerging treatment
The present....

The treatment of choice for Hodgkin is likely to change in the next few years

The treatment goal is not only cure of Hodgkin but also improving quality of life during and after therapy
The Future

WAKE TEAM LYMPHOMA

Medical Oncology
Maurizio Bendandi
Rakhee Vaidya
Kathryn Mercer

Radiation Oncology
Karen Winkfield

Nursing
Tonya Johnson
Stephanie Bollinger

Hematopathology
David Grier
Michael Beaty
Stacey O’Neill

Robert McCall
Nancy Rosenthal

Pharmacy
Jessica Duda

LeAnne Kennedy

Thanks to my team and thank you for listening
Living with Hodgkin Lymphoma

Q&A Session

Ask a question by phone:
- Press star (*) then the number 1 on your keypad.

Ask a question by web:
- Click “Ask a question”
- Type your question
- Click “Submit”

Due to time constraints, we can only take one question per person. Once you have asked your question, the operator will transfer you back into the audience line.

The Leukemia & Lymphoma Society Offers:

- **LLS Information Specialists:** Master’s level oncology professionals who can assist you through cancer treatment, financial and social challenges, and give accurate up-to-date disease, treatment, and support information.
  ➢ EMAIL: infocenter@LLS.org
  ➢ TOLL-FREE PHONE: 1-800-955-4572

- Free Education Booklets:
  ➢ [www.LLS.org/booklets](http://www.LLS.org/booklets)

- Free Telephone/Web Programs:
  ➢ [www.LLS.org/programs](http://www.LLS.org/programs)

- Live, Weekly Online Chats:
  ➢ [www.LLS.org/chat](http://www.LLS.org/chat)
The Leukemia & Lymphoma Society Offers:

- **Support Resources**: LLS Community, discussion boards, blogs, support groups, financial assistance, and more: [www.LLS.org/support](http://www.LLS.org/support)

- **LLS Podcast, The Bloodline with LLS**: Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: [www.thebloodline.org](http://www.thebloodline.org)

- **Education Video**: Free education videos about survivorship, treatment, disease updates, and other topics: [www.LLS.org/educationvideos](http://www.LLS.org/educationvideos)

- **Patti Robinson Kaufmann First Connection Program**: Peer-to-peer program that matches newly diagnosed patients and their families: [www.LLS.org/firstconnection](http://www.LLS.org/firstconnection)

- **Free Nutrition Consults**: Telephone and email consultations with a Registered Dietitian: [www.LLS.org/nutrition](http://www.LLS.org/nutrition)

- **What to ask**: Questions to ask your treatment team: [www.LLS.org/whattoask](http://www.LLS.org/whattoask)

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**THANK YOU FOR PARTICIPATING!**

We have one goal: A world without blood cancers