

Treatment of ITP: 1931-2017

James N. George, MD

ITP Support Association

Royal Society of Medicine

London, England

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ANNALS OF INTERNAL MEDICINE

1960; 53: 861-876

**IDIOPATHIC AND SECONDARY
THROMBOCYTOPENIC PURPURA:
CLINICAL STUDY AND EVALUATION OF
381 CASES OVER A PERIOD OF 28 YEARS**

**CHARLES A. DOAN, BERTHA A. BOURONCLE,
BRUCE K. WISEMAN, Columbus, Ohio**

ITP: Splenectomy, 1931-1959

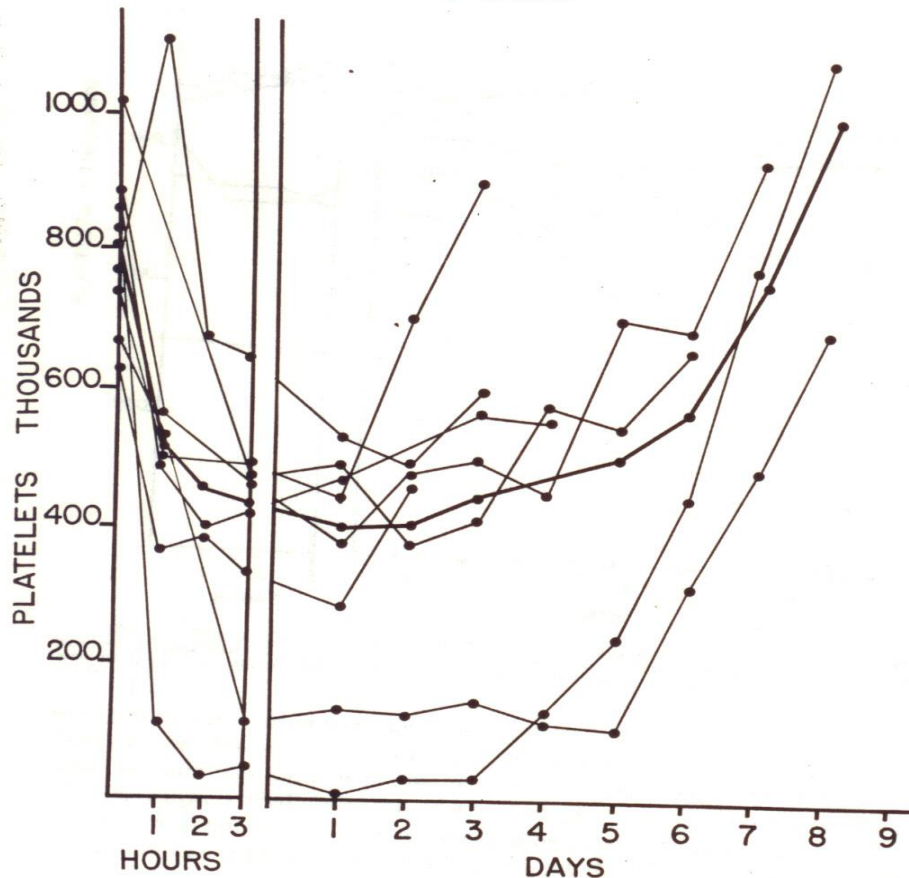
- ITP: 271 patients
 - 66 <10 yo, 42% female; 205 ≥10 yo, 74% female
- Treatment
 - Splenectomy alone: 167 patients
 - 142 (85%) durable response (plts >150, no treatment)
 - Steroids alone (*only since 1950*): 59 patients
 - 9 (15%) durable response
 - Steroids/splenectomy: 45 patients
 - Surgical mortality: 1.4%

Annals Internal Medicine 1960; 53: 861

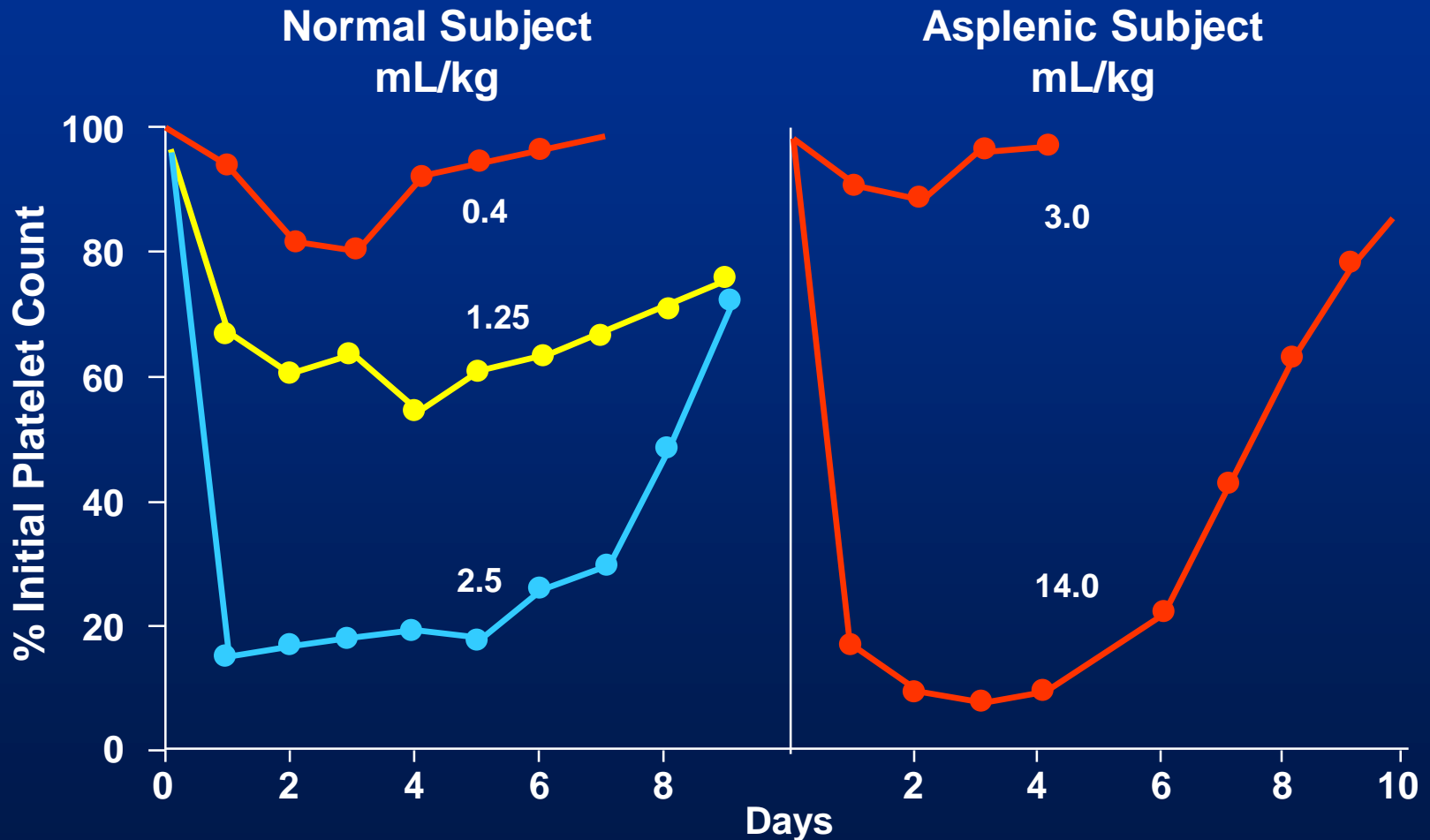
Demonstration of a thrombocytopenic factor in the blood of patients with thrombocytopenic purpura

Harrington, Minnich, Hollingsworth, Moore

IDIOPATHIC THROMBOCYTOPENIC PURPURA
8 CASES



Response to Different Doses of ITP Plasma from One Patient



Shulman NR, et al. *Trans Assoc Am Phys* 1965; 78: 374

Management of ITP: 2017

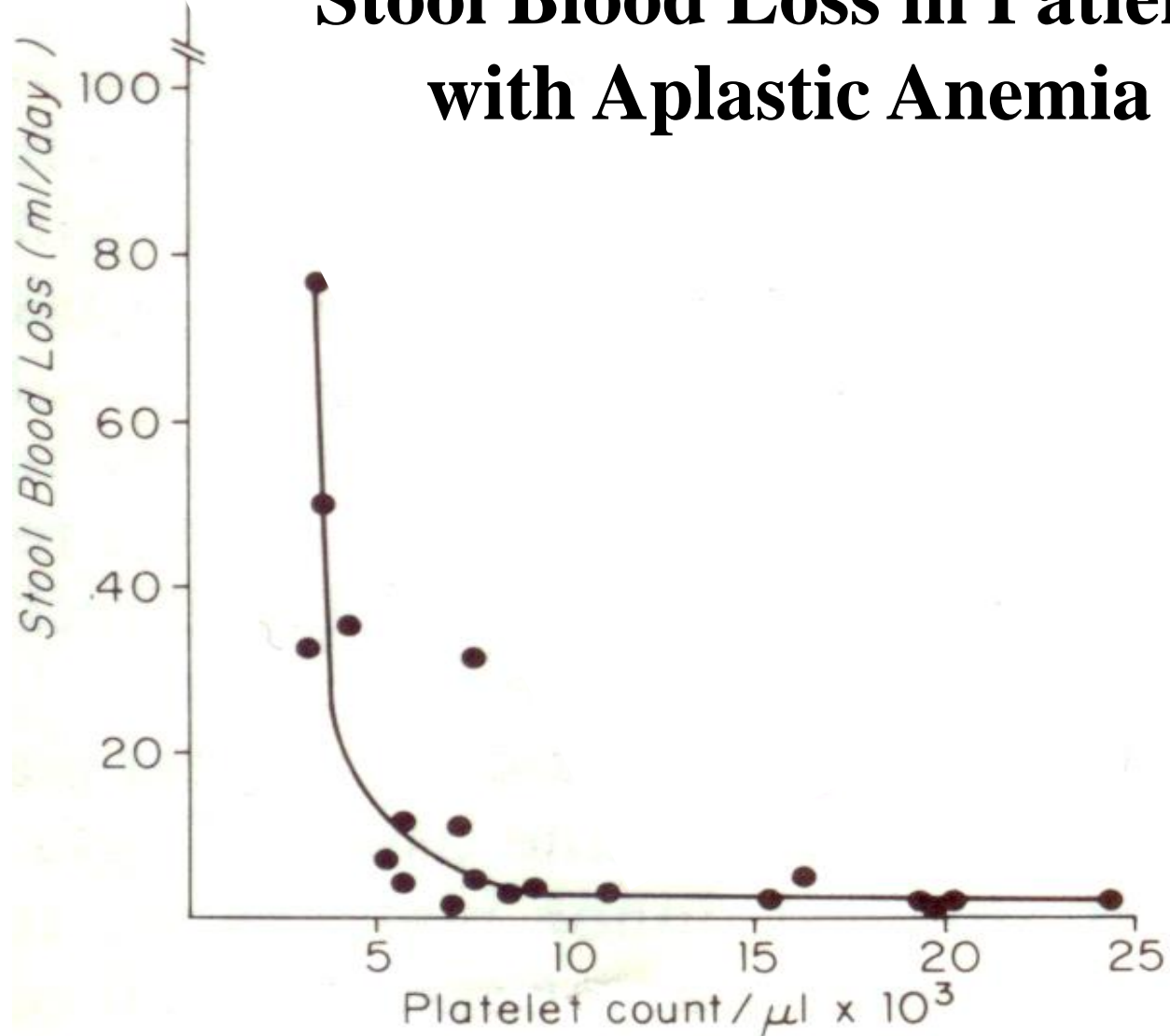
Treatment of Severe Bleeding

- **Platelet transfusion**
- **IVIg: 1 gm/kg (repeat next day if platelet count <50,000)**
- **Corticosteroids**
 - **Methylprednisolone: 1 gm/d x 3 days**
 - **Dexamethasone: 40 mg/d x 4 days**
- **Romiplostim: 500 µg SQ (approx 7 µg/kg)**

Initial Management of ITP: 2017

- **Platelet count >30,000: observation**
- **Corticosteroids**
 - **Prednisone (e.g., 1 mg/kg/day)**
 - **Dexamethasone (40 mg/d x 4 days, may repeat)**
- **IVIg: appropriate for treatment of overt bleeding, because of rapid response (“rescue therapy”)**

Stool Blood Loss in Patients with Aplastic Anemia



Slichter, Harker. *Clinics Haematol* 1978;7:523

Steroid Treatment of ITP

The Patient's Perspective

- **Patients often consider the treatment of their ITP worse than their disease**
- **Hypotheses:**
 - **Patients are more concerned about steroid side effects than their doctors**
 - **Doctors are more concerned about risk for bleeding than their patients**

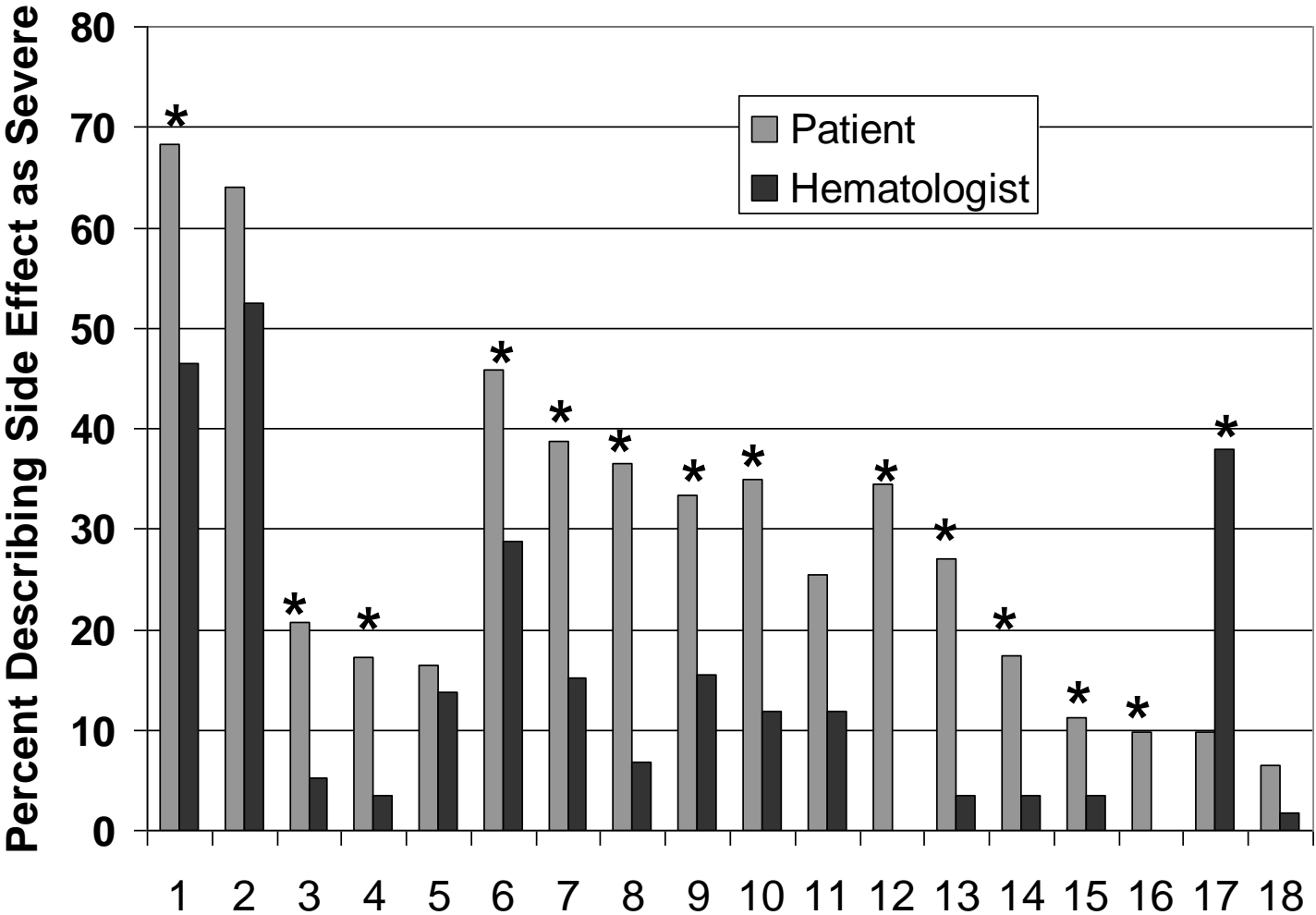
Europ J Haematol 2009; 83: 175

Steroid Side Effects:

Patient and Hematologist Perspectives

- **Survey ITP patients and hematologists in Oklahoma about occurrence and severity of 18 steroid side effects**
- **Patients reported the occurrence of “bothered a lot” more often than hematologists for 13 side effects ($P < 0.05$)**
- **Hematologists reported the occurrence of “bothered a lot” more often than patients for 1 side effect ($P < 0.05$)**

Perception of Severity of Corticosteroid Side Effects by Patients and Hematologists



Treatment of ITP: 2nd-line, Subsequent Treatments

- **Rituximab**
 - It's not surgery
 - It's a familiar drug (for hematologists)
- **Splenectomy**
 - Established record of success
 - It's forever; rare risk for severe sepsis
- **TPO receptor agonists**
 - May be required forever

Rituximab

- **Initial response (Plts >50): 57%**
- **Response sustained at 1 year: 38%**
- **Response sustained at 5 years: 21%**

Patel, et al., *Blood* 2012; 119: 5989

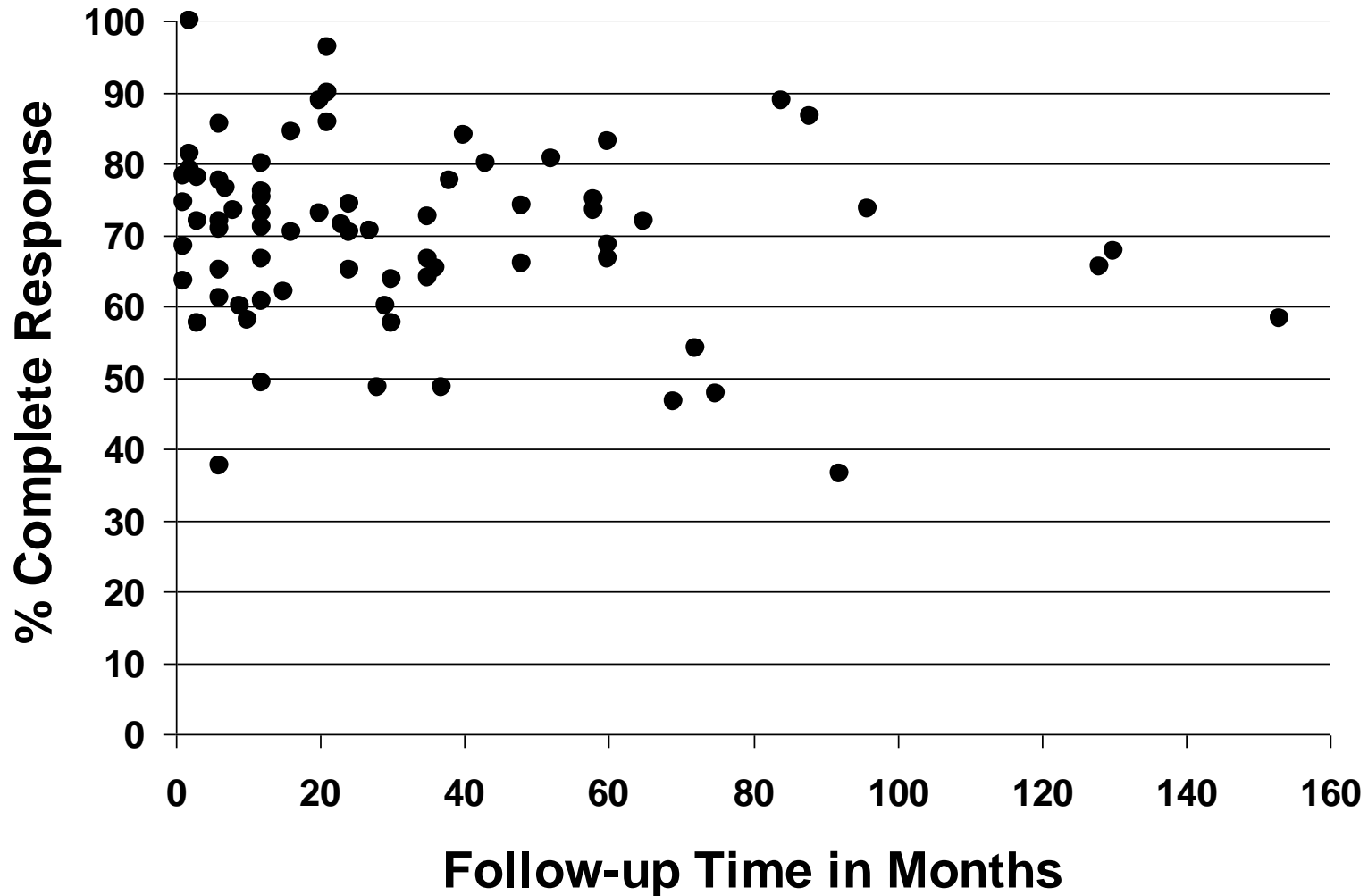
ITP: Response to Splenectomy

47 adults-only case series (N = 2623)

- 1731 (66%) with CR (Plts >150, no treatment)**
- 577 (22%) with PR (Plts >50, no treatment)**
- Follow-up 1-153 mo (median, 29 mo)**
- % CR not related to duration of follow-up**

Kojouri, et al., *Blood* 2004;104:2623

Splenectomy for ITP



Long-term Complications Following Splenectomy

- **Bacterial infection (sepsis)**
 - **Lifetime risk: 1-3%, lifetime (this estimate precedes current pneumococcal and other immunizations)**
- **Thrombosis**
 - **Both arterial and venous thrombosis: increased risk, 1.4, lifetime**

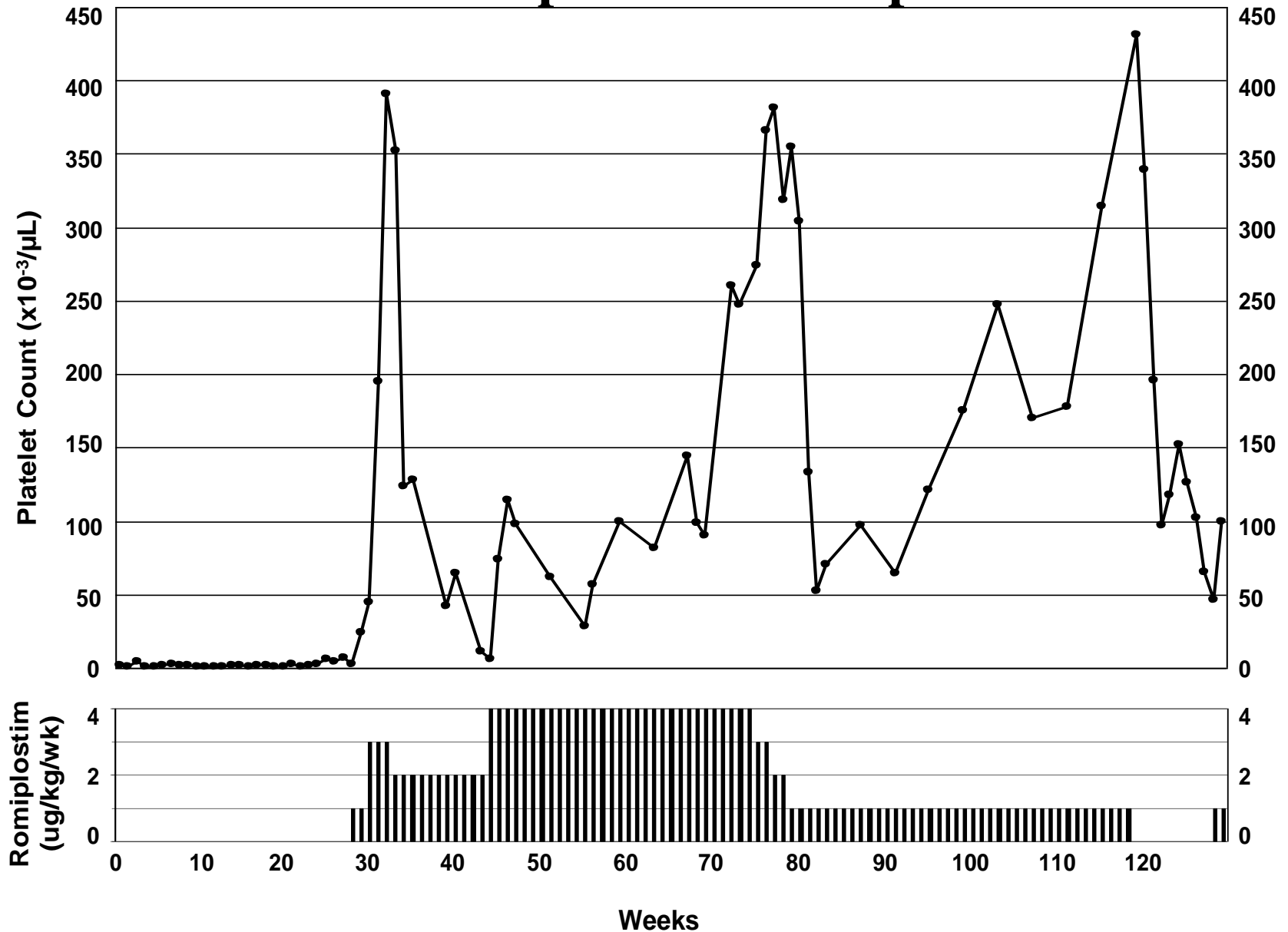
Prevention and Treatment of Post-Splenectomy Sepsis (US)

- **Immunizations**
 - Pneumococcal vaccine (every 5 years)
 - *H. flu* type b (Hib) vaccine
 - Meningococcal vaccine
 - Influenza vaccine (every year)
- **Keep antibiotic (amoxicillin or a fluoroquinolone) at home**
 - Take one tablet immediately for fever with chills (before calling a doctor)
 - See a doctor immediately

Romiplostim Treatment of ITP

- **63 yo man diagnosed in 1991**
- **Transient responses to prednisone, dexamethasone, danazol, and splenectomy**
- **Then intermittent steroid treatment; platelet count always <10,000; only minor purpura**
- **Randomized to placebo for 6 months, 2001**
- **Then treated with romiplostim**

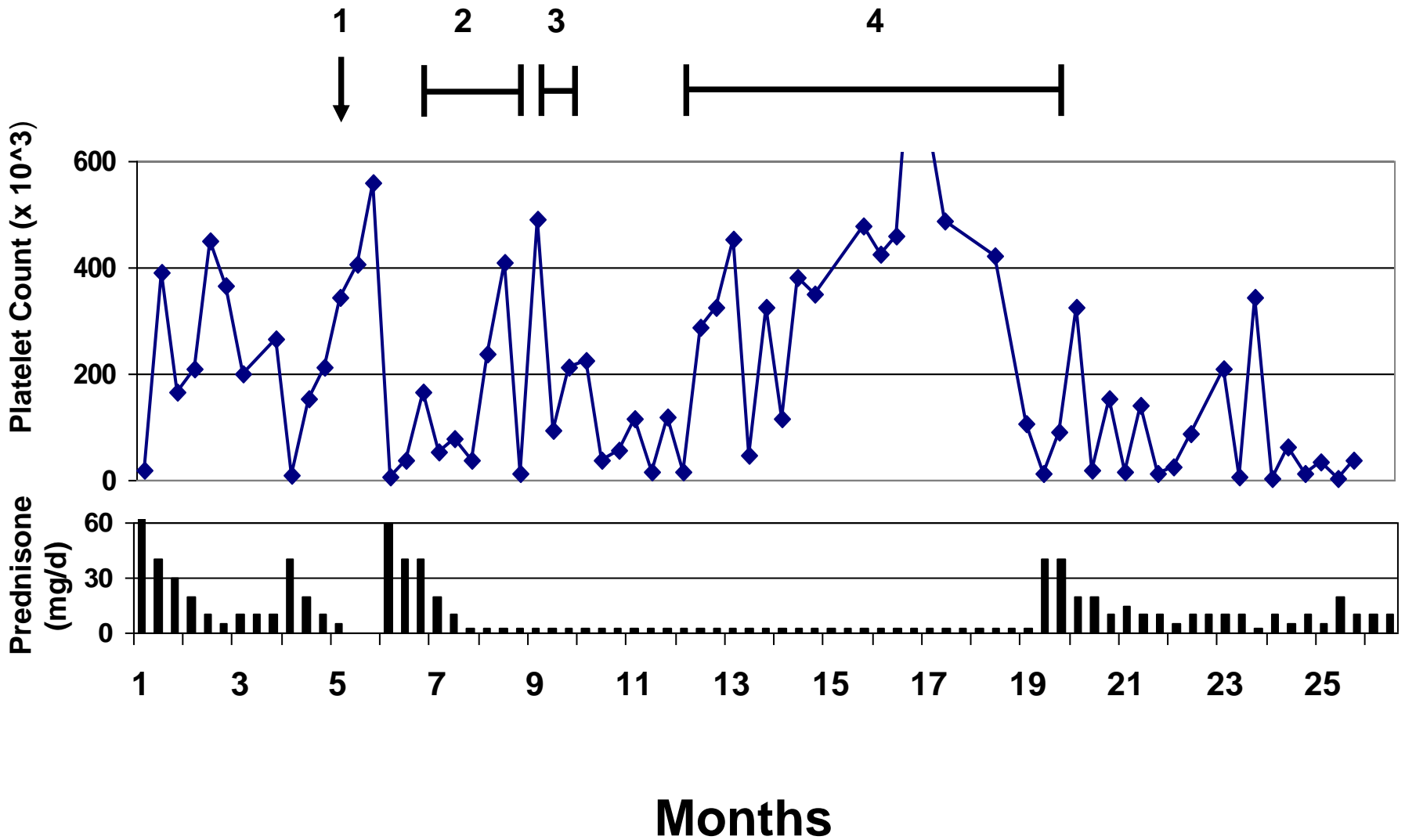
ITP: Response to Romiplostim



Romiplostim Treatment of ITP

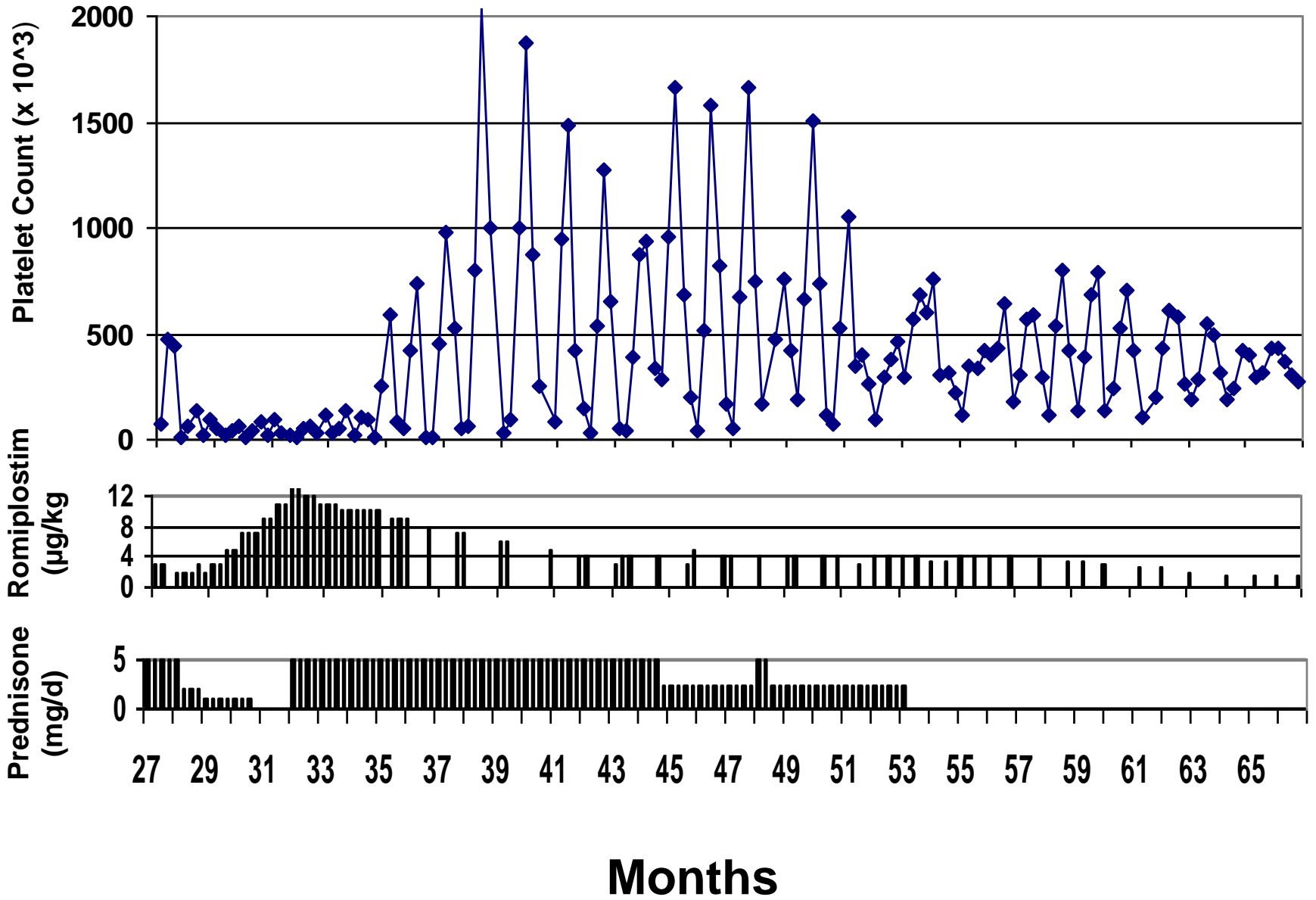
- **79 yo woman diagnosed Dec 2003; purpura, rectal bleeding, platelet count 16,000**
- **Transient responses to prednisone, IVIG, splenectomy, rituximab, azathioprine, danazol**
- **Referred for romiplostim trial; failed to qualify 9 times because platelet count not consistently <30,000 throughout screening**

79 year-old Woman with Refractory ITP



Romiplostim Treatment of CTP

- **January 2006, 3 week cycles of thrombocytopenia recognized**
- **February 2006, enrolled on romiplostim “single patient protocol”**
- **Initial weekly dosing; then 1.5 µg/kg every 3-4 weeks**
- **Stopped romiplostim in 2009; normal platelet counts at annual visits**



Management Choices for Adults With ITP

Survey of Oklahoma Hematologists-Oncologists

Question 3:

- **28 year old previously healthy woman (A+), platelet count 9000**
- **Initial good response to steroids**
- **Steroids tapered and stopped after 3 months**
- **4 months later, platelet count 9000 with epistaxis**
- **IVIg effective for short times**

Amer J Med Sci 2014; 347: 190

Management Choices for Adults With ITP

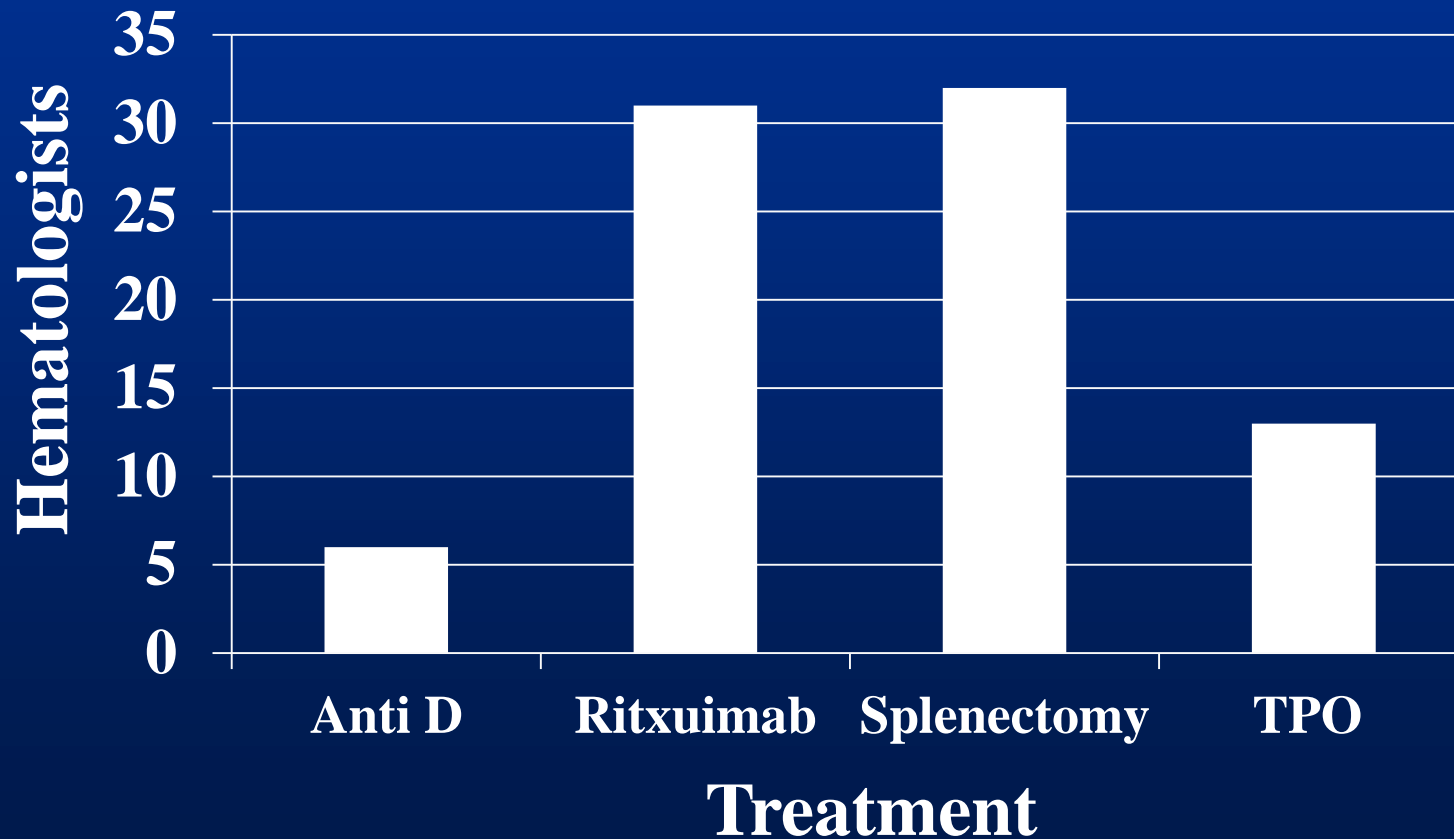
Survey of Oklahoma Hematologists-Oncologists

Question 3: Treatment options

- Anti-D
- High-dose dexamethasone
- IVIg
- Observation
- **Rituximab**
- **Splenectomy**
- **TPO receptor agonist**

Oklahoma Hematologists-Oncologists: 2012

Question 3



Oklahoma Hematologists-Oncologists: Response to Question 3

Treatment	Years in practice		
	<5	5-20	>20
Rituximab	11	12	7
Splenectomy	8	8	16

P = 0.047

Amer J Med Sci 2014; 347: 190

Conclusions

- **Splenectomy**
 - The 1st effective and still the most effective long-term treatment for ITP; risk of surgery and long-term risks of infection and thrombosis
- **Rituximab**
 - Avoids surgery; less durable response; maybe less risk than splenectomy
- **TPO receptor agonists**
 - Avoids surgery; very effective; no (or rare) sustained response when treatment stopped; long-term risks uncertain, probably negligible