



Northwestern University: Division of Immunotherapy

***Crohn's: immunology and
therapy***

Theory

- Ablation of aberrant immune system with elimination of auto-destructive T-cells
- Reconstitution with new immune system

Theoretical Objections

- Persistent antigen (bacterium, virus, etc) with re-exposure to trigger
- Leaky intestinal epithelium with increased access to noxious antigens

Risk HSCT vs. Crohn's Disease

- Mortality rate of Crohn's-little data
- Farmer, large series, Gut 1985, 6%
- Recent Copenhagen study, also 6%
- Mortality probably higher in selective series
- Risk autologous HSCT less than 1%
- Serious morbidity Crohn's
 - Fistulae, abscesses
 - Eye, skin, joint, hepatic
 - Recurrent surgery, short bowel, HPN
 - Abdominal pain, drug addiction

HSCT Methodology

- Mobilization of HSC
- CD34⁺ selection
- Conditioning regimen



HSCT criteria for Crohn's

- < age 60
- Failed prednisone, azathioprine, 5-ASA metronidazole, anti-TNF alpha
- CDAI between 250-400



HSCT for Crohn's

- Phase I trial of 12 patients
- Number completed HSCT--12
- Post HSCT follow-up-- 2: 3.0 years
 - 4: 18 months
 - 4: 6 months
 - 2: 2 months

Toxicity of HSCT

- 48 hours of culture negative fever during hospitalization
- Resolution of pain and diarrhea during hospitalization

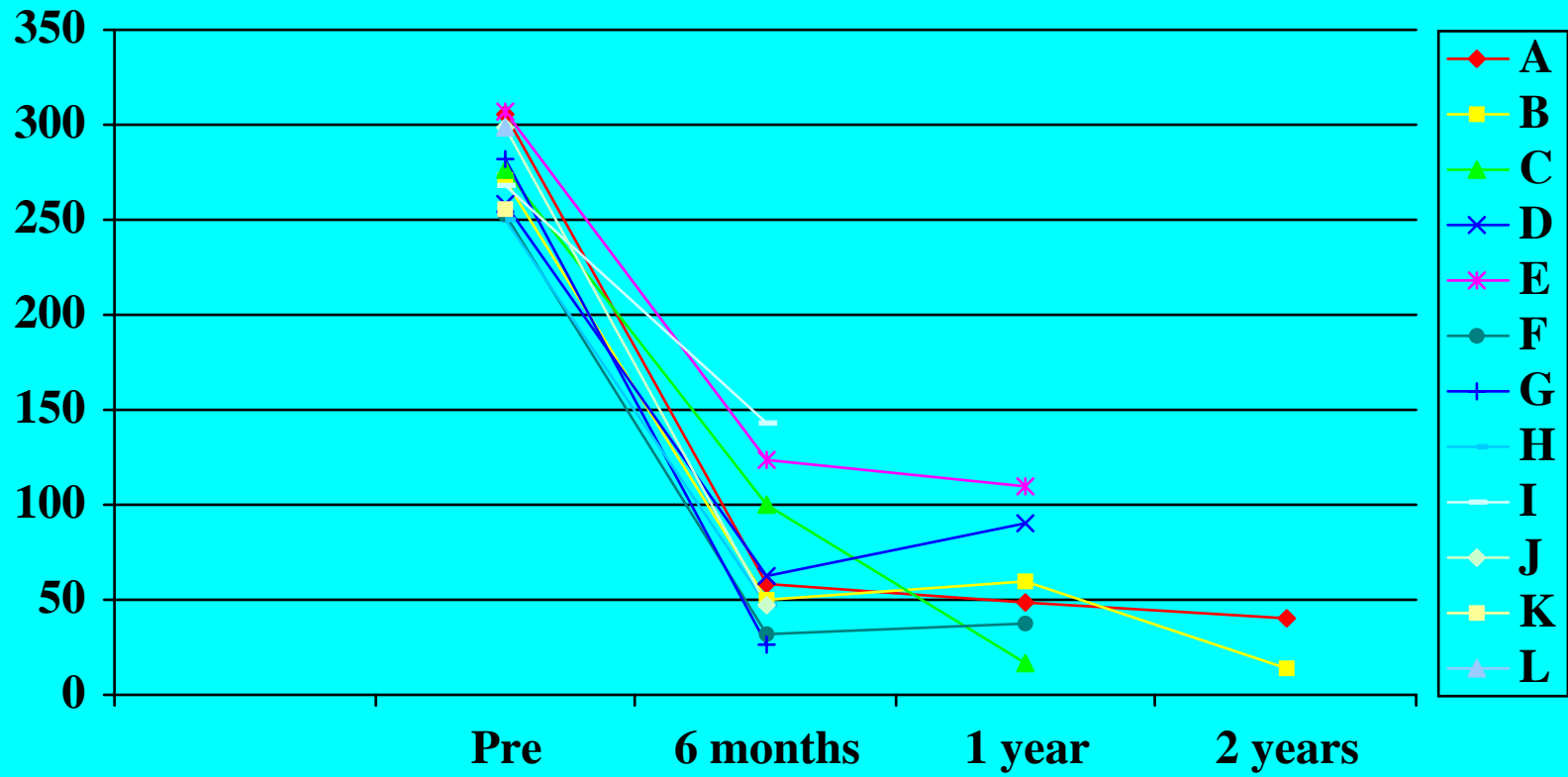
Crohn's HSCT Course

- Each patient markedly improved immediately
- One persistently inflamed vulva
- Three persistently inflamed perianal area, one requiring 5-ASA and Metronidazole
- CD therapy discontinued on all others
- QOL questionnaire, marked improvement

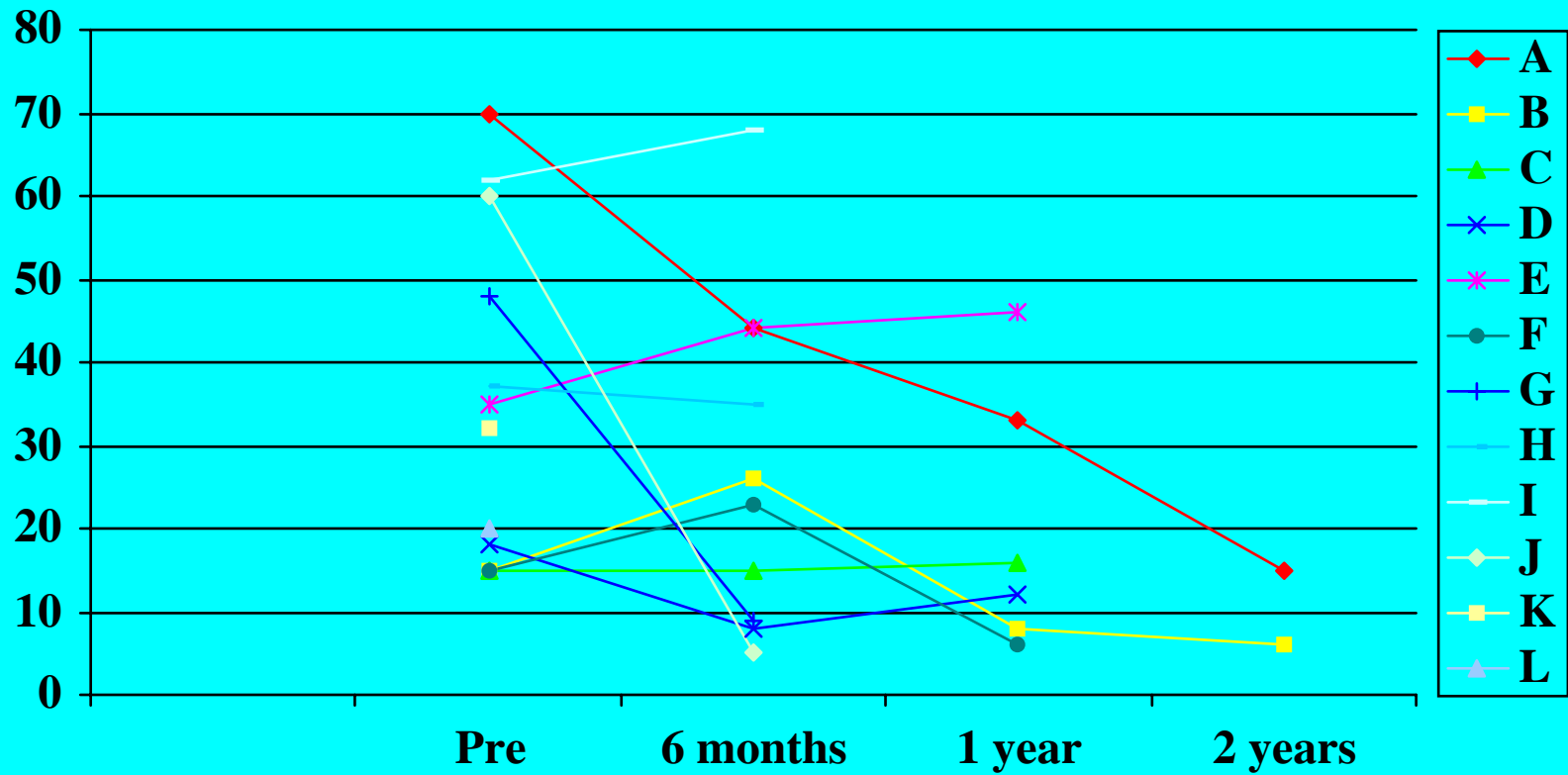
Crohn's HSCT Course II

- One patient developed a central line infection, acute renal failure, secondary to Dilaudid drip
- One patient developed a small intestinal obstruction requiring surgical removal 4 months post HSCT. Known stricture pre HSCT. Two others have persistent obstructive symptoms.
- Most have had some ulceration of colon or small bowel on follow up
- Most have had some persistence of laboratory abnormalities on follow up (sed rate, CRP, anemia, albumin)

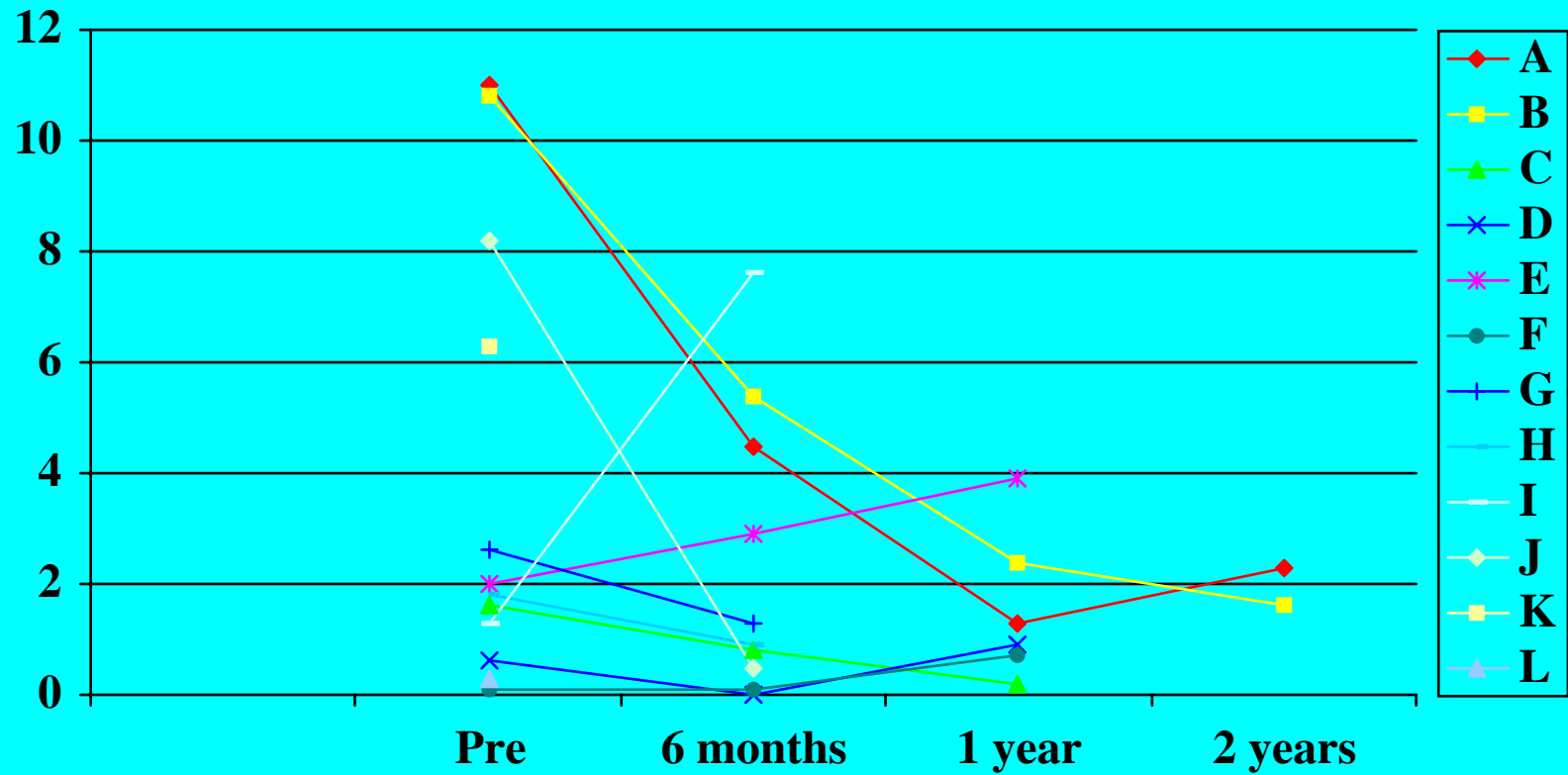
C. D. A. I.



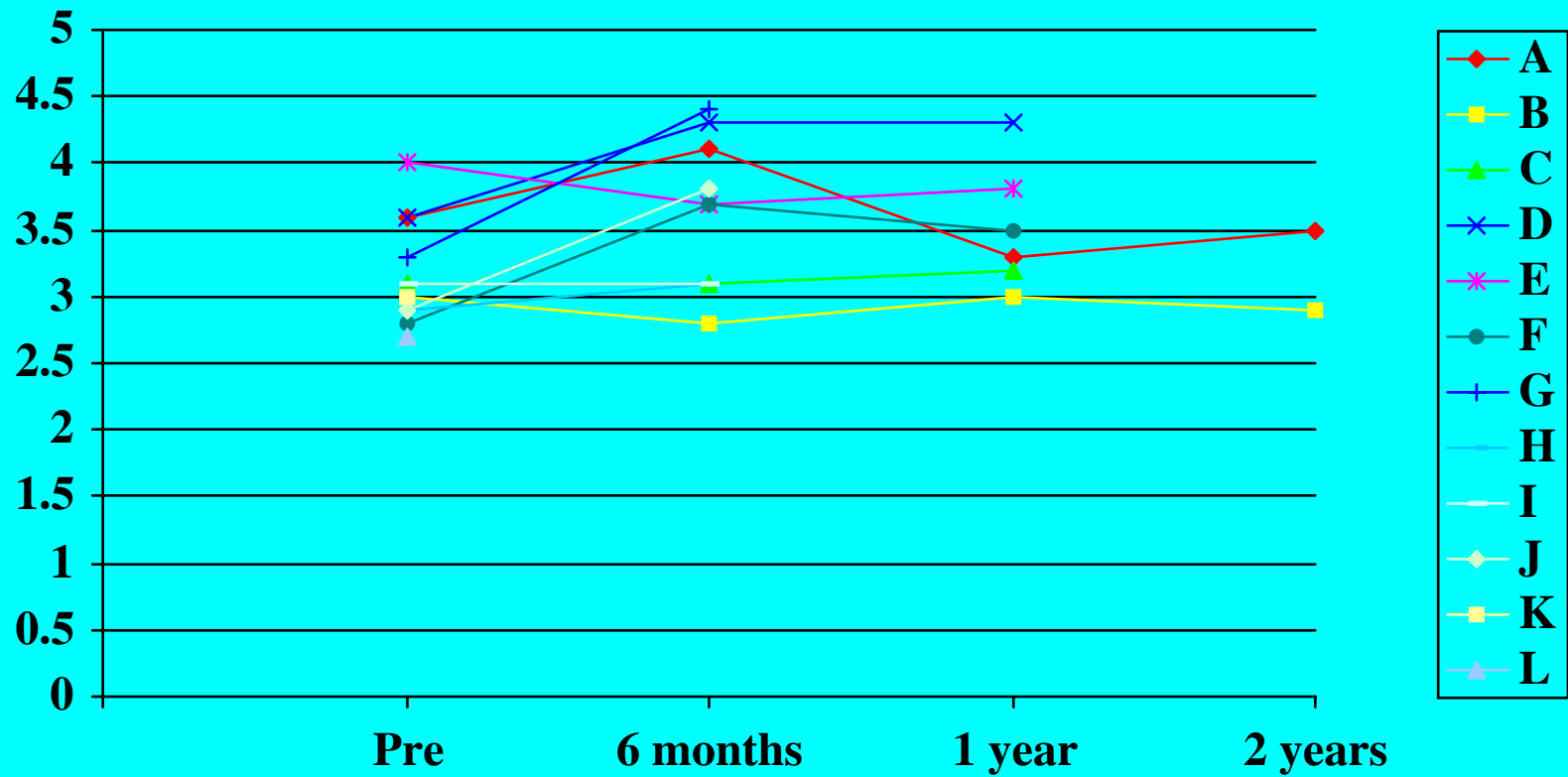
Sedimentation Rate



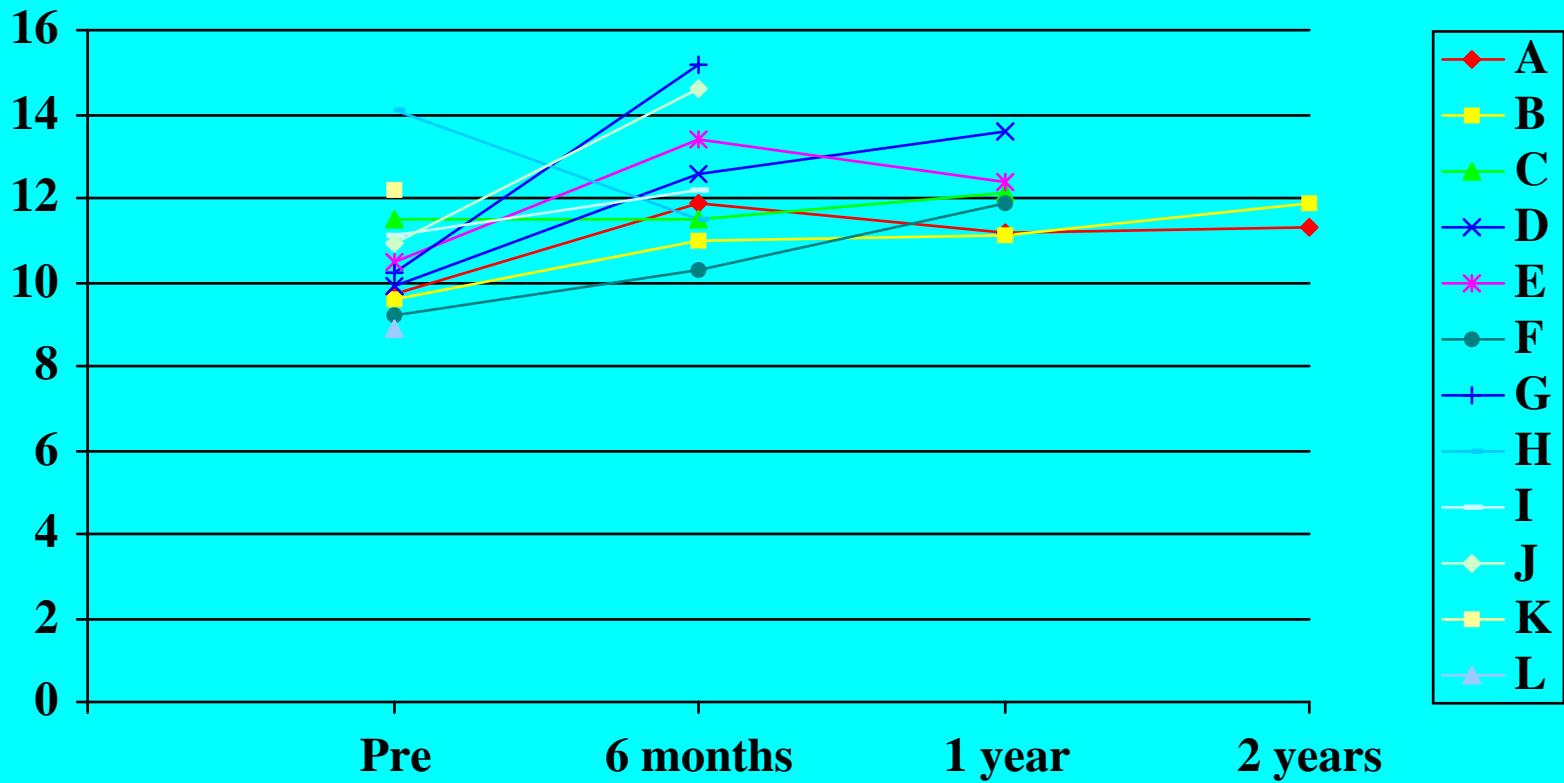
C Reactive Protein



Serum Albumin



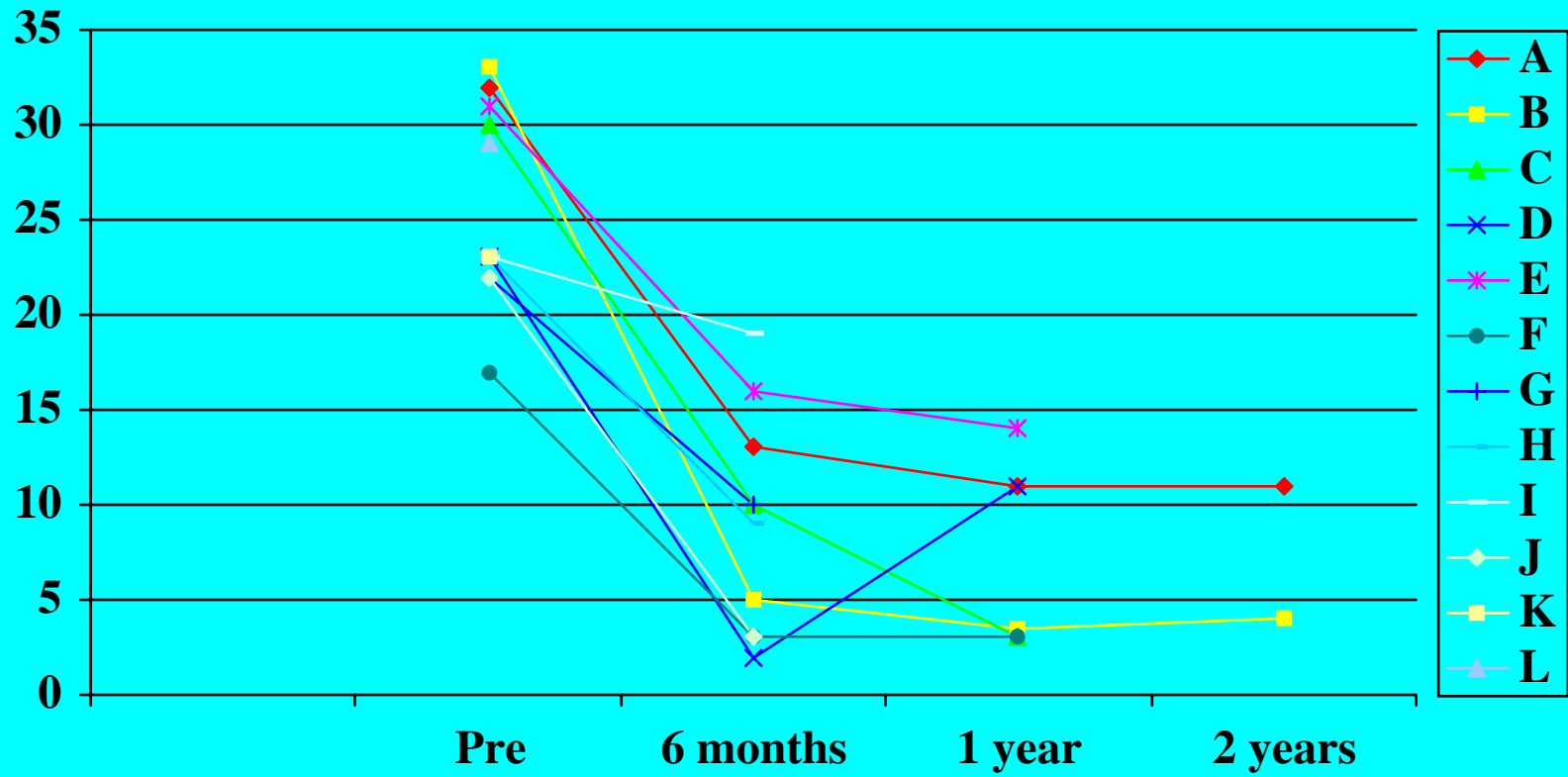
Hemoglobin



Severity Index

Feature Score	Score	Feature
Diarrhea 1		Perianal fissure
3-10/day 1	1	Vulvar inflammation
> 10/day 2	2	Intestinal obstruction
Pain 2		Abdominal mass
Intermittent cramping 1	1	Erythema nodosum
Steady, mild to mod. gangrenosum 3	2	Pyoderma
Steady, severe 1	3	Aphthous stomatitis
Chronic narcotic use 2	2	Iritis
Well being, Fair 2	1	Fever > 1 week
Poor 1	2	Weight loss 10% usual
Terrible 2	3	20% usual
Corticosteroid use normal 1	2	Hematocrit 1-5 <
Immunosuppressives 2	2	6 or more < normal
5-ASA or antibiotics 1	1	CRP abnormal
Enteropathic arthritis G% 1	1	Serum albumin 2.5-3.5
Hepatobiliary complications 2	2	<2,5 G%
Perianal fistula or abscess 1	2	Sedimentation rate >20

Severity Index



HSCT Crohn's, Conclusions

- Can be performed safely in qualified BMT program
- Immune ablation with repopulation with primitive stem cells
- May produce prolonged remission
- Response variable
- Perianal disease may persist and require surgical management
- Fibrosing obstruction might worsen
- Objective indices important
 - Subjective investment in procedure
 - Need for controlled study

Recommendations

1. Importance of objective data; patients and doctors deeply invested in procedure
2. Controlled series advisable
3. For uncontrolled series, insist upon a severity index > 18 .