ANTI-ADHESION

Prevention of Post-Surgical Adhesions
Adhesions are a natural body process where the body tries to repair itself in response to any tissue disturbance. Adhesions are scar tissue formation which occur anywhere there is repair going on in the body.

**PROBLEM:**
**POST SURGERY ADHESIONS**

POST SURGERY ADHESIONS ARE INEVITABLE!
An adhesion is a band of scar tissue that binds together anatomic surfaces which are normally separated from each other.

- Scar tissue & adhesion are a normal, even necessary part of the wound healing process. But,
- Adhesions are a serious & frequent complication of surgical interventions and can require further
- Adhesions are fibrotic tissue bands that connect tissue plains that are normally not connected
- Adhesions normally occur at the site of the surgical procedure and frequently develop during first 3~5d
"Subj: adhesions  
Date: 88-04-14

I have come back from the Cedar Sinai, the GI specialist said that they were 10 - 12 years from knowing how to treat this problem. I still run into alot of MD's who say adhesions don't cause pain, but since I have had 7 surgeries and each time adhesions are "taken down" I get about 1 years worth of pain relief. I have even showed them research studies that show a decrease in pain s/s after surgery and they still are skeptical. Anyway, they are sending me to a Dr. Kaizer who supposedly specializes in this kind of pain. I hope to have an appointment at the end of April. I'll let you know how it turns out. Keep me informed of any developments that might be helpful with my case. Thanks"
Types of Surgery

- Abdominal surgery
- Laparoscopy
- Gynecology
- Abdominal Surgery
- Orthopedic Surgery
- Spine Surgery
- Heart Surgery
- ANY SURGERY WHERE SOFT TISSUES ARE INVOLVED

Post surgery implications

- Impaired organ function
- Decreased fertility
- Life-long pain
- Bowel obstruction
- Repeated operations to remove scar tissue
Incidence of adhesions:

- After minor surgery = 51%
- After major surgery = 72%
- After multiple surgeries = 93%

- 1% of all laparotomies developed obstruction due to adhesions within one year of surgery

- All cases of small bowel obstruction in the US, 60-70% of cases involve adhesions

- Postoperative adhesions occur in 60% to 90% of patients undergoing major gynecologic surgery

ECONOMIC IMPLICATIONS

Economic Costs

Y1988, United States, Cost of Adhesional complication : 12 Bil USD

- Cost gradually grow
- Found new complication
POSSIBLE SOLUTIONS

Treatment
• Cutting the adhesion scar tissue (*adhesiolysis*)
• Not very effective as in many cases the adhesion recur

Prevention
• Change in surgery technique → still adhesions are possible but chances are reduced
• Anti-clotting/anti-inflammatory drugs (DHA, warfarin, TPA, steroids) → have their own issues of monitoring and side-effects
• Barrier method → by far the safest and most effective at prevention

www.adhesions.org
TYPES OF BARRIER AGENTS

- Films
- Sprays/Solutions
- Gels
## BRANDS OF BARRIER AGENTS

<table>
<thead>
<tr>
<th>Adhesion prevention barrier</th>
<th>Type</th>
<th>Product</th>
<th>Chemical composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraperitoneal instillator</td>
<td>solution</td>
<td>Adept</td>
<td>4% icodextrin solution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ringer's lactate solution</td>
<td>Compound sodium lactate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyskon (Dextran 70)</td>
<td>32% dextran 70 solution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CMC solution</td>
<td>Carboxymethylcellulose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sepracoat</td>
<td>Sodium hyaluronate solution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Saline</td>
<td>0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>gel</td>
<td>Intergel</td>
<td>Ferric hyaluronate gel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spraygel</td>
<td>In situ crosslinkable polyethylene glycol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intercoat</td>
<td>CMC + hyaluronate gel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gardix-sol</td>
<td>Gel of Hyaluronic acid + sodium carboxymethyl cellulose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adcon</td>
<td>Gelatin/proteoglycan</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Incert</td>
<td>Chemically crosslinked hyaluronic acid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sepragel</td>
<td>Hyaluronic acid-carboxymethylcellulose gel</td>
</tr>
</tbody>
</table>

### Adhesion barrier (membrane)

<table>
<thead>
<tr>
<th>Film</th>
<th>Product</th>
<th>Chemical composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poloxamer 407</td>
<td>Polypropylene glycol + polyethylene glycol</td>
<td></td>
</tr>
<tr>
<td>Cardix MB</td>
<td>Hyaluronic acid + sodium carboxymethyl cellulose</td>
<td></td>
</tr>
<tr>
<td>Hyaluronate gel</td>
<td>Hyaluronic acid</td>
<td></td>
</tr>
<tr>
<td>Seprafilm</td>
<td>Hyaluronic acid + carboxymethylcellulose membrane</td>
<td></td>
</tr>
<tr>
<td>Surgiwrap</td>
<td>70:30 poly(L-lactide-co-D-L-lactide)</td>
<td></td>
</tr>
<tr>
<td>Repel</td>
<td>Polyethylene glycol and polyactic acid block copolymer membrane</td>
<td></td>
</tr>
<tr>
<td>Gore-tex</td>
<td>Polytetrafluorethylene</td>
<td></td>
</tr>
<tr>
<td>Interceed</td>
<td>Oxidezed regenerated cellulose</td>
<td></td>
</tr>
<tr>
<td>Prelude</td>
<td>Expanded Polytetrafluoroethylene membrane</td>
<td></td>
</tr>
<tr>
<td>Collagen membrane</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVA</td>
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</tbody>
</table>
ADVANTAGES & DISADVANTAGES OF BARRIER AGENTS

- **Adept** – icodextrin solution – first FDA solution production, biocompatible, but dangerous for starch and maltose intolerant patients

- **Hyskon** - dextran solution – not much used due to edema and decreased thrombocyte function, allergic reaction

- **Surgiwrap** – polylactide film – biodegradable, but inflexible and needs suturing to keep it in place

- **Interceed** – cellulose – light, biodegradable barrier but low effectiveness

- **Seprafilm** – hyaluronic acid/cellulose film – biodegradable, flexible and good protection but need to roll out and fragile, unpredictable outcome
HOW GEL BARRIERS WORK

1 day
The functional element have a functional surface has an anti-adhesion layer during for wound healing

2 days
The most of macrophage are laid on scar tissue. Mesothelial cells are not exist yet

5 days
Mesothelial cell has been shown to play a role in anti-adhesion

7 days
The mesothelial cell layer serves as an anti-adhesion barrier. It’s prevent the newly formed adhesion

- The use of barrier gels is most common. Latest technology.
- They separate opposing tissue plains
**HI-BARRY™ ANTI-ADHESION GEL**

**Pure Hyaluronic acid**
- Excellent biocompatibility and biodegradability

**Cross-linked HA**
- Adjustable anti-adhesion retention time

**High viscosity · High molecular weight**
- Flow prevention when applied & catch the target correctly.

**Endotoxin-free / Protein-free**
- Safety, Minimize adverse

- Using the Cross-linked Hyaluronic acid; Maintenance a certain period in the body.

- Using the high molecular weight and high viscosity undiluted solution; Optimal role of physical barriers.

- Dose not contain synthetic substances; CMC (Carboxymethyl cellulose), HES (Hydroxyethylstarch), Alginate Excellent biocompatibility.

→ No long-term residue in the body.
# COMPARISON OF ANTI-ADHESION GELS

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>HIBARRY</th>
<th>GUDIEX-SOL</th>
<th>OXIPLEX</th>
<th>MEDICURTAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>Class III</td>
<td>Class III</td>
<td>Class III</td>
<td>Class III</td>
</tr>
<tr>
<td>Ingredient</td>
<td>Hyaluronic acid + Cross-Linked Hyaluronic Acid</td>
<td>Hyaluronic acid + carboxymethyl cellulose (CMC)</td>
<td>Ethyleneoxide + carboxymethyl cellulose (CMC)</td>
<td>Hyaluronic acid + Hydroxyethylstarch</td>
</tr>
<tr>
<td>Viscosity</td>
<td>3733 cPs (63% high viscosity)</td>
<td>2340 cPs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feature</td>
<td>√ Pure Hyaluronic acid</td>
<td>√ Synthetic substances (CMC)</td>
<td>√ Synthetic substances</td>
<td>√ Synthetic substances (HES Contain)</td>
</tr>
<tr>
<td></td>
<td>√ Excellent viscosity</td>
<td>√ Polymer + simple mixed solution</td>
<td>√ Instability</td>
<td>√ Instability</td>
</tr>
<tr>
<td></td>
<td>√ Excellent biocompatibility</td>
<td>√ low viscosity</td>
<td>√ High viscosity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>√ High Price</td>
<td></td>
</tr>
</tbody>
</table>
# Possible Applications

<table>
<thead>
<tr>
<th>Medical Speciality</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neuro surgery</strong></td>
<td>Spine-related surgery / Larminectomy &amp; Discectomy</td>
</tr>
<tr>
<td><strong>General surgery</strong></td>
<td>Thyroid surgery / Breast-related surgery</td>
</tr>
<tr>
<td><strong>Plastic surgery</strong></td>
<td>Hand, foot micro-surgery / Tissue reconstructive surgery</td>
</tr>
<tr>
<td><strong>Orthopedic surgery</strong></td>
<td>Spine-related surgery / Hand, foot, shoulder and trauma disease surgery</td>
</tr>
<tr>
<td><strong>Obstetrics &amp; Gynecology</strong></td>
<td>Endoscopic and open surgery of the Uterus and attached to the uterine disease / Cesarean/ Curettage (Incomplete missed abortion)</td>
</tr>
<tr>
<td><strong>Thoracic surgery</strong></td>
<td>Cardiac surgery</td>
</tr>
<tr>
<td><strong>ENT</strong></td>
<td>Sinusitis, Otitis media</td>
</tr>
<tr>
<td><strong>Dentistry</strong></td>
<td>Neck dissection / Washing liquor jaw joint</td>
</tr>
<tr>
<td><strong>Urology</strong></td>
<td>Incision of prostate / Urinary tract surgery / Urethral stricture repair</td>
</tr>
</tbody>
</table>

“Focus on minimizing post-surgical adhesion complications drives demand for anti-adhesion products.”
Global market for Anti-Adhesion Products is projected to reach US$2.1 billion by 2020, driven by the growing focus on reducing the economic cost and healthcare burden caused by post-surgical adhesion complications. High prevalence of cardiovascular diseases and the ensuing rise in cardiac surgeries performed annually is driving demand for adhesion prevention products, given its ability to prevent post-surgical sternum adhesion. General/abdominal surgery represents the largest application area, while pelvic/gynecological surgery is forecast to emerge as the fastest growing therapeutic area.

**Major Players...**

- Anika Therapeutics Inc.
- Baxter Healthcare Ltd.
- Covidien
- Ethicon Inc.
- FzioMed Inc.
- Integra LifeSciences Corporation
- Magen OrthoMed Ltd.
- MAST Biosurgery AG
- Sanofi UK
Snapshot Summary of Trends & Drivers

- The United States represents the largest regional market worldwide, while Asia-Pacific ranks as the fastest growing market with a CAGR of 10.4% over the analysis period.

- Focus on Minimizing Post-Surgical Adhesion Complications Drives Demand

- High Costs Associated With Surgeries Undertaken to Lyse Adhesions Spurs Growth

- Rise in Joint Replacement Surgeries Benefits Demand for Joint Adhesion Prevention Products

- Veterinary Healthcare Offers Lucrative Opportunities for Growth

- Effervescent Product Development Keeps Demand Momentum Alive

- Rise in the Popularity of Minimally Invasive Surgeries: A Key Challenge
Thank you for your attention

For more information please contact Althea Global at

www.altheaglobal.com