

The Role of Laparoscopic Surgery in the Surgical Treatment of HIV Patients

Vijaykumar Rajaram Naik

Consultant Laparoscopic Surgeon and GI Endoscopist, Bel-air Hospital, Panchgani, Dist- Satara, Maharashtra, India

AIMS OF STUDY

The purpose of present study is to evaluate the role of laparoscopic surgery in the surgical treatment of HIV patients (related or unrelated to HIV illness in whom requiring surgical intervention) by comparing results of open surgeries with the results of review articles on laparoscopic surgeries under following headings as:

1. Universal precautions during surgery
2. Procedure details
3. Operation time
4. Blood loss
5. Occupational exposure risk
6. Postoperative analgesics requirement
7. Postoperative morbidity and mortality
8. Economy

INTRODUCTION

Despite much clinical experience, there are few published accounts of the surgical manifestations of HIV/AIDS and role of laparoscopic surgery in HIV patients. More than 40 million people worldwide are infected with HIV. Surgical treatment of HIV-infected patients is indicated for problems both related and unrelated to HIV infection.³ The laparoscopic surgeon plays an important role in the diagnosis and management of AIDS related conditions in conjunction with physician. As most of the HIV patients are poorly nourished, immunocompromised and final outcome of the open surgeries is not satisfactory. Laparoscopic procedures provide several specific advantages over routine (open) procedures in this population. For the patient, the extent of invasiveness is diminished; incisions are limited,⁶ associated with better preservation of the immune system than open surgery⁷ which decreases healing time and wound complications, pulmonary function is optimized; and the patient rapidly returns to regular activity. Although CO₂ pneumoperitoneum affects the peritoneal response to injury, it seems to have no harmful effect in terms of intra-abdominal infection. For the surgical team, risk of exposure to body fluids is minimized.⁵

REVIEW OF LITERATURE

A computerized Medline Search was conducted from 1966 through the present and turned up only 10 papers concerning HIV positivity and surgery, none of them being in transgendered or transsexual individuals. In 1997, Flum and Wallack¹ conducted a literature search concerning the impact of the human immunodeficiency virus infection and syndrome has had on the practice of surgery. They concluded that the incidence of human immunodeficiency virus infection ranges from 1.3% of patients hospitalized at sentinel hospitals to 1.5/1,000 patients in lower risk environments. The rate of percutaneous injury during an operation is 5 to 6% and human immunodeficiency virus transmission after percutaneous injury with a needle contaminated with the human immunodeficiency virus is 3%. Furthermore, Lowenfels, Mehta, Levi, Montecalvo, Savino and Wormser² reported in 1993 on the incidents of percutaneous injuries in surgeons. They reported that there was a decrease in the frequency of reported percutaneous injuries over the period 1988 to 1993. The number of yearly injuries per surgeon decreased from 5.5 to 2.1. As Flum and Wallack¹ reported, the transmission of human immunodeficiency virus after percutaneous injury with a needle contaminated with HIV is 3%. It would therefore seem not particularly dangerous to the individual surgeon, providing universal precautions are undertaken, to undertake surgery on HIV positive patients. From the first case in 1988 until mid 1995, our index of severity of HIV infection was the CD4 Lymphocyte count. After this time the viral load has been used and this is measured as viral RNA. Before 1995, measurement of viral load was unavailable to us. In 1901, first diagnostic laparoscopy was performed by Kelling on dog. After him in 1910, a Swedish internist, Jacobaeus performed first diagnostic laparoscopy in human. After that an era of minimal access surgery created outbreak in the treatment of HIV patients due its advantages over traditional open surgeries.

INDICATIONS OF LAPAROSCOPY IN HIV PATIENTS

Indications of laparoscopy in surgical patients and HIV patients are almost same as HIV- negative patients.

Laparoscopy in HIV Positive Patients with Acute Abdomen

- Correct diagnosis achieved with least surgical trauma.
- Institution of timely and effective treatment.
- Reduction of risks of transmission of virus to theater personnel's due to small incision and less contact with patient's body fluids.

Diagnostic laparoscopy minimizes unnecessary laparotomies and complications.

Laparoscopy in Trauma Patients (Blunt and Penetrating)

Trauma patients with equivocal signs are always a dilemma, more so when patients are victims of "Urban violence, car accidents, intoxication by alcohol, spinal cord injury and/or head injury. Commonly used diagnostic peritoneal lavage (DPL) has a sensitivity of > 95% and specificity of 83%. The rate of unnecessary laparotomy is still very high with a morbidity of 20% and mortality of 6%. If diagnostic laparoscopy is combined with diagnostic peritoneal lavage then the sensitivity can be increased up to 100% and specificity up to 90%. Diagnostic laparoscopy is extremely useful in patients with equivocal signs and hemodynamically stable. It is slowly replacing the old belief that, all penetrating abdominal wounds whether stab or gunshot should be explored. Also in cases of subcapsular tears of liver or spleen or minor tears in mesentery or omental injury can now be completely conserved saving the number of non-therapeutic laparotomies (NTL).

Laparoscopy in ICU Patients/Critically Ill

- Acalculus/Calculus cholecystitis.
- Large bowel perforation.
- Duodenal and gastric perforations (e.g. stress ulcers)
- Duodenal and gastric perforations (e.g. stress ulcers)
- Pancreatitis (due to biliary sludge)
- Intra-abdominal hemorrhage.

It is extremely difficult to diagnose above mentioned complications in a patient who is already in MOF (multiple organ failure). There are no symptoms and signs which can be elucidated as patients are on ventilation or gravely ill and delay in surgical treatment may lead to increase in morbidity and mortality.

Laparoscopy in Chronic Abdomen in HIV Patients

Most of patients presenting with chronic abdominal pain after laparotomy found to have mesenteric lymphadenopathy, or drug induced pancreatitis, here diagnostic laparoscopy can take mesenteric lymph node biopsy without much major surgical trauma.

Role of Laparoscopy in Gynecological Emergencies

Laparoscopy is useful in the early recognition of pelvic inflammatory disease and Fitz Hughes Curtis syndrome (Perihepatitis associated with PID). It is also useful in the early recognition of pelvic inflammatory disease and Fitz Hughes Curtis syndrome (Perihepatitis associated with PID).

Role of Laparoscopy in Suspected Acute Appendicitis

Commonest abdominal emergency all round the world is acute appendicitis. An early diagnostic laparoscopy in suspected acute appendicitis reduces the risk of appendiceal perforation, improves diagnostic accuracy and reduces the number of negative laparotomies. It helps the surgeon to rule out concomitant problems but two important groups of patients where it is immensely useful in:

- Premenopausal women when it is difficult to rule out gynecological conditions.
- Obese patients in whom large incisions may be required to remove the appendix.

Laparoscopy in Patients with Perforated Peptic Ulcers

Early diagnosis and treatment of perforated peptic ulcer within 6 hours of the incident can reduce mortality from 90% to about 10%. Diagnostic laparoscopy is much more sensitive than CT as it can determine the type of fluid along with food debris and can accurately localize the site of perforation. Perforations are closed by simple suture, omental patch, fibrinous glue, falciform ligament patch or ligamentum teres patch. The trend is towards suture less closure or ligamentous patches. A larger delay, beyond 6 hours, makes closure difficult and hazardous due to inflammatory changes and phlegmon. Main disadvantage is increased operating time and recent studies have not shown to decrease length of hospital stay, resumption of normal diet, reduction of pain in the first 24 hours, or early return to normal activities. Prospective random trials are needed to clarify these factors.

Laparoscopy and Small Bowel Obstruction (SBO)

Early SBO, with minimal peritonitis, single band adhesions, without obvious gangrenous changes in the bowel can be managed by therapeutic laparoscopy.

The other criteria for selection are:

- Proximal obstruction.
- A partial obstruction.
- Obstruction partially responding to nasogastric suction.

Laparoscopy and Diverticular Disease

Diagnostic laparoscopy is very useful in diagnosing severity of diverticular disease so that management decision can be

taken whether to conserve or proceeded to surgery. Abscesses can be drained under direct vision.

Laparoscopy in Biliary Disorders

Commonest surgical presentation in HIV patients is acalculous cholecystitis where open cholecystectomy is dangerous here laparoscopy is the best option. Also conditions like obstructive jaundice due to ca-pancreas laparoscopic Whipple's operation can be done.

Laparoscopy in Pulmonary Diseases

Laparoscopy is also useful for diagnosis (thoracoscopy) and different therapeutic procedures in HIV patients like closure of bullies, pnuemonectomy, etc.

Laparoscopy for Lymph Node Biopsy

This is most common indication for diagnosis of different conditions histopathologically, (e.g. cervical lymph nodes) during this risk of needle prick injuries are more during open surgery so laparoscopic approach is best for same. It is also useful for biopsy of mesenteric and pre- and para-aortic lymph nodes avoiding major laparotomy.

Anal Disorders

This is the one of commonest surgical presentation in HIV patients due to loss of perianal fat there develops piles and rectal prolapse which can be treated laparoscopically with minimum complications.

CONTRAINDICATIONS FOR LAPAROSCOPY

Contraindications for laparoscopy are same for both HIV positive and negative patients.

1. Severe COPD and cardiac diseases
2. Grade II and III shock
3. General peritonitis
4. Previous extensive abdominal surgery
5. Bleeding disorder
6. Advanced stages of pregnancy
7. Suspected malignancy
8. Patients with cryptococcal meningitis

MATERIAL AND METHODS

The source of data was open surgeries performed on HIV patients at Bel-Air Hospital, Panchgani, during the period of November 2006 to December 2007. Bel-Air Hospital is one of leading institute for HIV treatment and doctors training center under Indian Red-Cross Society and NACO. The results of open surgeries are compared with the review articles data

collected by reviews of articles laparoscopic surgeries on HIV patients by using search engine Google, Highwire press, Springerlink, PubMed, Yahoo & other linked references. The keywords used are HIV, laparoscopy, universal precautions, immunocompression and complications.

SOURCE OF DATA

Seventy-four patients of HIV operated for various surgical presentations operated at BEL-AIR HOSPITAL, PANCHGANI, MAHARASHTRA forms main source of data for present study. Patients were presented to surgery OPD, referred from HIV wards for surgical problem and from other medical practitioners after diagnosis of HIV.

SELECTION OF PATIENTS

The patients with surgical indication were selected as per their presentation for either emergency or planned open surgeries. For the routine surgeries patients were investigated for basic and anesthesia point. HIV confirmatory test, CD4 count was also done apart from above investigations. Preoperative single dose of antibiotics were given almost every case.

OPERATIVE TECHNIQUE

During surgery strict universal precautions were taken by whole surgical team, like use of eye protective goggles, full rubber shoes, plastic arm guards, foot cover, waterproof surgical gowns, double gloves etc. Also precautions were taken to avoid spillage on floor, needle stick injuries were prevented by avoiding direct transfer of sharp instruments from surgeon to nurse and vice versa, i.e. keeping a kidney tray between. All waste materials were disposed as per CDC guidelines. As much as disposable items were used.

Postoperatively patients were transferred either to SICU or wards as per patient's condition. Usually patients were discharged on 9th or 10th day after removal of sutures.

Post Exposure Prophylaxis (PEP)

Post exposure prophylaxis (PEP) is antiretroviral drug treatment that is started immediately after someone is exposed to HIV. The aim is to allow a person's immune system a chance to provide protection against the virus and to prevent HIV from becoming established in someone's body. In order for PEP to have a chance of working the medication needs to be taken as soon as possible and definitely within 72 hours of exposure to HIV. Left any longer and it is thought that the effectiveness of the treatment is severely diminished³³ PEP usually consists of a month long course of two or three different types of the antiretroviral drugs that are also prescribed as treatment for people with HIV. The commonest used regimen in our hospital

is—Tab. Lazid (Zidovudine 300mg + Lamivudine 150 mg) for 28 days. As with most anti-retrovirals these can cause side effects such as diarrhea, headaches, nausea/vomiting and fatigue. Some of these side effects can be quite severe and it is estimated that 1 in 5 people give up PEP treatment before completion.³³

RESULTS

Total of 74 patients presented with surgical problems, out of them 22 patients treated with conservatively while remaining 52 treated with operative treatment forms basis of study.

Time of Surgery

Out of 52 operated patients, 14 (26.92%) patients operated on an emergency basis and 38 (73.08%) had planned surgeries.

| | <i>No. of patients</i> | <i>Percentage (%)</i> |
|-----------|------------------------|-----------------------|
| Emergency | 14 | 26.92 |
| Planned | 38 | 73.08 |
| Total | 52 | 100 |

Type of Operation

Out of 52 patients 18 (26.92%) patients underwent major and 34 (47.06%) minor surgeries.

| | <i>No. of patients</i> | <i>Percentage (%)</i> |
|-------|------------------------|-----------------------|
| Major | 18 | 52.94 |
| Minor | 34 | 47.06 |
| Total | 52 | 100 |

Operation Time

Maximum number of patients (40) required 30 minute to one hour time, only some complicated cases (3) required more operative time i.e. 3 to 4 hours.

| <i>Time</i> | <i>No. of patients</i> | <i>Percentage (%)</i> |
|-------------|------------------------|-----------------------|
| 0–1 hour | 40 | 76.52 |
| 1–2 hours | 04 | 07.69 |
| 2–3 hours | 05 | 09.61 |
| 3–4 hours | 03 | 05.76 |

Blood Loss

The approximately blood loss during surgery varies from minimum of 30 ml to maximum of 300 ml depending of type of surgery and findings.

Occupational Exposure

During overall study total 4 assisting nurses subtended with needle prick injury while assisting the surgeries in operation theater. They all received emergency PEP (Post-exposure prophylaxis).

Postoperative Antibiotics

Most of the patients received at least 7-8 day course of postoperative higher antibiotics.

Postoperative Analgesics

Present study on open surgeries analgesics were given as three times a day for 7 to 8 days.

Incidence of Wound Infection

Incidence of wound infection was found in almost 20-25% of cases in the form of stitch abscess. It is found that incidence of wound infection was more in patients having low CD4 count (< 200). One patient developed fecal fistula after resection anastomosis and treated conservatively. Incidence of respiratory complications like pneumonia observed in 12 patients (23.07%).

Hospital Stay

Hospital stay for patients underwent open major surgeries varied from 8 days to 15 days.

Economy

Average total expenses for surgery was 800 to 12000 depending upon type of surgery, hospital stay and complications.

Mortality

Total 4 patients died in present study out of 52 operated patients. So overall mortality rate was 7.69%.

DISCUSSION

The literature on postoperative complications is descriptive and inconsistent and does not support a firm conclusion on the association between rates and HIV serostatus or disease stage. The ultimate outcome of surgery in HIV-infected patients is most likely dependent upon many independent variables and not just the underlying viral infection or disease stage.⁴

Total number of patients with surgical problems was 74, out of that 52 (70.27%) patients required open surgery. The number of patients in the data is less as compared to other studies,^{8,11,12} as HIV is still a social stigmata and most of patients are not exposing themselves. Also most of patients are managed symptomatically by general practitioners. The overall incidence

of postoperative complications during open surgeries was 25% as compared to laparoscopic surgeries.^{2,4,10,26-28} Also respiratory complication rate is also to the higher side as compared to laparoscopic surgeries,^{2,6,9-12,25,29} this is due to most of the patients are suffering from pulmonary TB, also due to poor built and weakness the ambulation is problem as compared to laparoscopy surgery maintains interior milieu.^{7,30,31}

The blood loss during major surgeries was ranged from 30 to 300 ml; it is very much towards higher side as compared to literatures on laparoscopic surgery.^{6,13,18} This is because laparoscopy is an electrosurgery and there is minimal tissue dissection and trauma.⁶ Postoperative analgesics requirements were higher side as compared to laparoscopic surgery. The incidence of needle prick injuries during open surgery was found to be 7.6% is quite a higher than comparative to the standard rate, i.e. 0.3 %.³ The results of laparoscopic surgeries shown negligible risk of occupational transmission. This is because in laparoscopy there is no direct exposure to the blood and secretions, also suturing is done via small wound, also no much sharp instruments used routinely.^{5,23}

The average operative time was 3 hours for major surgery and 30 minutes for minor surgery. Literature study showed laparoscopic surgeries are taking more time than open surgeries,⁵ this is because maximum time is wasted in instrument set up like insufflators adjustment, light adjustment, white balancing, access, etc.

Mortality rate in present series of open surgeries is 7.69%. The comparative study on laparoscopy shown less mortality rate with expertise hands but mortality rate is higher with inexperienced hands due to major vessel bleeding. Hospital stay during open surgeries varied from 2 to 15 days as compared to literatures on laparoscopic surgery, laparoscopic surgeries have very less hospital stay, i.e. only 1-2 days.

Economically, open surgeries costs 2000 to 12000 rupees while laparoscopic surgery cost ranges between 15000 to 50000 rupees. The higher cost is due to cost of staplers, hemostatic instruments.

CONCLUSIONS

Above study revealed following conclusions.

Compared to traditional operations, there are fewer traumas to the skin and muscles and less postoperative pain and disability with a laparoscopic procedure. Also, patients have a shorter hospital stay and a quicker recovery period.

There is a reduced infection rate. This is because delicate tissues are not exposed to the air of the operating room over long periods of time.

Video magnification also offers surgeons better exposure of the diseased organ and its surrounding vessels and nerves. As a result, delicate maneuvers can better be performed.

Laparoscopy reduces risk of occupational transmission in surgical team.

The disadvantages of laparoscopy include the expensive equipment involved in performing it. Not all hospitals may be able to afford certain procedures.

Another issue is the need for surgeons to take special training in performing the minimally invasive operations. The need for additional training is because laparoscopic surgeons leave the familiar territory of a three-dimensional operating field to working on a two-dimensional flat video display. Learning the procedures requires some degree of practice moving the long laparoscopic instruments while handling delicate tissues.

Finally, laparoscopy cannot always be performed on everyone. For example, some patients with many prior operations may have so much scar tissue within the body that a safe laparoscopic operation cannot be done.

Thus, in modern era of minimal access surgery laparoscopy is an asset to the HIV patients by reducing mobility and increasing their life expectancy.

REFERENCES

1. Flum DR, Wallack MK. The surgeon's database for AIDS: a collective review. *Journal of the American College of Surgeons* 1997;184(4):403-12.
2. Lowenfels AB, Mehta V, Levi DA, Montecalvo MA, Savino JA, November 1998, 12:17 > Complications of surgery in HIV-infected...
3. Surgery in patients with HIV-HIV InSite Knowledge Base Chapter, February 2003-William P. Schechter, MD, University of California San Francisco Peter Stock, MD, University of California San Francisco.
4. Empanan C, Iturburu IM, Portugal V, Apecechea A, Bilbao JE, Mendez JJ: Infective complications after minor operations in patients infected with HIV: role of CD4 lymphocytes in prognosis. *Eur J Surg* 1995; 161:721-723.
5. Wormer GP. Reduced frequency of percutaneous injuries in surgeons. *AIDS*. 1933;9(2):199-202ZZ.
6. Laparoscopic surgery for HIV- infected patients: minimizing dangers for all concerned. *J Laparoendosc Surg*. 1991 Oct; 1(5):295-8.
7. Luigi Boni, Angelo Benevento, Francesca Rovera, Gianlorenzo Dionigi, Matteo Di Giuseppe, Camillo Bertoglio, Renzo Dionigi. *Surgical Infections*. July 1, 2006, 7(supplement 2): s-109-s-111. doi:10.1089/sur.2006.7.s2-109.
8. Aids and surgery – G Morino, N Laldal, etc. – *East African central journal of surgery*, vol.-9, December 2004.
9. Laparoscopically Assisted Sigmoid Colectomy in Human Immunodeficiency Virus (HIV) Patients: A Good Indication for Laparoscopic Surgery. *Brief Clinical Report -Surgical Laparoscopy and Endoscopy*. 6(5):414-416, October 1996.Oliveira, Lucia M.D.; Wexner, Steven D. M.D.
10. Complications of laparoscopic cholecystectomy in HIV and AIDS patients, *surgical endoscopy*, volume 9, Aug. 1995.
11. Effect of Human Immunodeficiency Virus-1 Infection on Treatment Outcome - of Acute Salpingitis -Nelly R. Mugo, MB

- ChB, M Med1,6, Julia A. Kiehlbauch, PhD2,3, Rosemary Nguti, PhD5, Amalia Meier, PhD3, Joseph W. Gichuhi, MB ChB, M Med1,6, Walter E. Stamm, MD4 and Craig R. Cohen, MD, MPH
12. Laparoscopic surgery in patients with human immunodeficiency virus Tanner AG, Hartley JE, Darzi A, Rosin RD, Professor J. RT Monson *British journal of surgery* Dec. 2005.
 13. Laparoscopy in the evaluation and treatment of patients with AIDS and acute abdominal complaints -J. C. Box1, T. Duncan1, B. Ramshaw1, J. G.Tucker1, E. M. Mason1, J. P. Wilson1, D. Melton2 and G. W. Lucas1 *Surgical endoscopy* Oct 1997.
 14. Indications of laparoscopy in HIV patients, in Pub Med will retrieve citations1: *Med Clin (Barc)*. 2005 Mar 5; 124(8):314-15.
 15. Long-term outcome after laparoscopic splenectomy related to hematologic diagnosis -C. Balagué, E. M. Targarona, etc. *Surgical endoscopy* Aug 2004.
 16. Surgical Outcomes in Human Immunodeficiency Virus–Infected Patients in the Era of Highly Active Antiretroviral Therapy- *Arch Surg*. 2006; 141:1238-45.
 17. Effect of Human Immunodeficiency Virus-1 Infection on Treatment Outcome of Acute Salpingitis Nelly R. Mugo, MB ChB, *Obstetrics & Gynecology* 2006;107:807-812 -© 2006 by The American College of Obstetricians and Gynecologists.
 18. Laparoscopic splenectomy: outcome and efficacy in 103 consecutive patients.-N Katkhouda, M B Hurwitz, R T Rivera, M Chandra, D J Waldrep, J Gugenheim, and J Mouiel *Ann Surg*. 1998 October; 228(4): 568–78.
 19. Laparoscopic Mesenteric Lymph Node Biopsy in the Diagnosis of Mycobacterium avium Complex-Todd A. Ponsky, Chris Coppola, Gary E.Hartman, David M. Powell. *Pediatric Endosurgery & Innovative Techniques*. June 1, 2004, 8(2): 131-35. Doi: 10.1089/1092641041360887.
 20. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques. 12(6):412- 419, December 2002.-Delaitre, Bernard MD; Blezel, Eric MD; Samama, Guy MD; Barrat, Christophe MD; Gossot, Dominique MD; Bresler, Laurent MD; Meyer, Christian MD; Heyd, Bernard MD; Collet, Denis MD; Champault, Gerard MD.
 21. Complications of laparoscopic cholecystectomy in HIV and AIDS patient-*Surg Endosc*. 1995 Aug; 9(8):874-8. Unique Identifier: AIDSLINE MED/96016676 Carroll BJ; Rosenthal RJ; Phillips EH; Bonet H.
 22. Outcome of laparoscopic surgeries in ITP patients Minimally Invasive Surgery, 2004 – 2005 M. J. Rosen, J. L. Ponsky.
 23. Scalpel-free surgery could reduce risk of HIV and hepatitis exposure for health care workers *science daily* (May 4, 2005).
 24. Laparoscopic colectomy for primary colonic lymphoma -D. Martínez-Ramos, J. Gibert-Gerez, J. M. Miralles-Tena, M. Martínez-Banaclocha, J. Escrig-Sos and J. L. Salvador-Sanchís, *Madrid* Oct. 2005.
 25. Effect of Human Immunodeficiency Virus Type 1 Infection upon Acute Salpingitis: A Laparoscopic Study Craig R. Cohen, Samuel Sinei, etc. *The Journal of Infectious Diseases* 1998; 178:1352–58.
 26. Complications of surgery in HIV-infected patients. *AIDS*. 12(17):2243-51, November 1998. Rose, David N. 1, 4; Collins, Megan 2; Kleban, Rebecca 3
 27. Laparoscopic surgery and surgical infection-*British Journal of Surgery*-Volume 87 Issue 5 Page 536-544, May 2000.
 28. The efficacy of laparoscopic surgery in the diagnosis and treatment of peritonitis – surgical endoscopy April 1997 J. Cueto O. Díaz, D. Garteiz, M. Rodríguez and A. Weber.
 29. Laparoscopy may reduce hospital acquired infection rates- *medscape today*- Laurie Barkley, April 2008.
 30. Open Surgery vs. Laparoscopic Surgery for Colorectal Cancer by Donna Myers, *About.com* Updated: May 29, 2007.
 31. Infective Complications in Laparoscopic Surgery- Luigi Boni, Angelo Benevento, Francesca Rovera, Gianlorenzo Dionigi, Matteo Di Giuseppe, Camillo Bertoglio, Renzo Dionigi. *Surgical Infections*. July 1, 2006, 7(supplement 2): s-109-s-111. doi:10.1089/sur.2006.7.s2-109.
 32. Antiretroviral post-exposure prophylaxis (PEP) for occupational HIV exposure Young TN, Arens FJ, Kennedy GE, Laurie JW, Rutherford GW –*Cochrane Database of Systematic Reviews* 2007, Issue 1. Art. No.: CD002835. DOI: 10.1002/14651858.CD002835.pub3.
 33. CDC (2007, April) ‘CDC trials of pre-exposure prophylaxis for HIV prevention’. Accessed 30th January 2008.