# Nanotechnology's Latest Oncolytic Agent: Silver, Cancer & Infection Associations Part III

By John Apsley, DC, Kent Holtorf, MD, Eric Gordon, MD, Wayne Anderson, ND, and Rashid Buttar, DO.



## Introduction

Silver-based drugs have one core common denominator – their active ingredient is their content of "oligodynamic" silver ions (i.e., $Ag^+$). Carl Nageli (1893) first coined the term oligodynamic (from the Greek *oligos* = few, and *dynamis* = power). Nageli discovered that exceedingly small metal ion concentrations demonstrate extraordinary antimicrobial properties.[1] In 2003 Rentz provided a comprehensive retrospective review on the universal antimicrobial effects of oligodynamic $Ag^+$. From the historical authoritative medical literature, he documented hundreds of viral, bacterial/spirochete, fungal and protozoan pathogens that succumb to silver-based drugs containing sufficient amounts of oligodynamic $Ag^+$.[2]

Modern nanoscience is still making new discoveries regarding oligodynamic metals. Nanoscientists appear positioned to develop some of the most complicated strategies for fighting cancer. For example, they are discovering that cancer drugs must be able to easily disrupt and penetrate tumor cell membranes *in situ* to enable the fullest possible oncolytic effects. Picoscalar or near-picoscalar oligodynamic $Ag^+$ hydrosol enjoys the greatest surface presentation (i.e., ~ 6 $km^2$ per gram Ag)[3, 4] for tumor cell membrane adherence and penetration, leading to greater oncolytic effects.

## History

The works of Moyasar et al., (1990),[5] Hamilton-Miller and Shah (1993),[6] Zhao and Stevens (1998),[7] Baker et al., (2004),[8] Sondi and Salopek-Sondi (2004),[9] and Morones et al., (2005)[10] collectively established that the therapeusis of bioactive silver extends well beyond its virotoxicity. It is also a broad-spectrum bactericidal and fungicidal agent. Berger showed that oligodynamic $Ag^+$ is 10 to 100 times superior to silver sulfadiazine for both gram-positive and gram-negative pathogens in terms of achieving the minimal lethal dose (MLD).[11]

It has long been suspected that infectious agents are associated with solid tumor cancers (a notable example is Kaposi's Sarcoma) as well as non-tumor based cancers such as leukemia. Also, cancer patients often undergo immune suppression therapy, allowing for multiple pathogen foci to seed. Oligodynamic $Ag^+$ may have the potential to play a dual role: either destroy the infectious etiological agent of the cancer, and/or destroy the pathogen loads arising within immunocompromised patients.

## Impact

In the U.S., cancer is the second leading cause of death in humans.[12] Virginia Livingston-Wheeler was among the first to propose an infectious etiology for cancer.[13] Cancer rates stemming from an infectious etiology (e.g., HIV,[14, 15] HHV8,[16] HPV16,[17] and EBV[18]), as well as infectious rates from immunocompromised patients (e.g., BK and JC Polyomaviruses,[19, 20] Respiratory Syncytial virus, Influenza viruses, and Parainfluenza viruses,[21] Fungemia,[22, 23] Rotavirus,[24] CMV[25] and Streptococcus pneumoniae[26]) have climbed alarmingly over the past two decades. Rentz documented that many of these cancer associated infections are susceptible to oligodynamic $Ag^+$.[2]

## Discussion

One critical strategic advantage to ~ 1 nm to 10 nm or less (e.g., picoscalar) silver particles is their ability to absorb,[27, 28] interact with, and destroy bacteria,[10] affect abnormal human tissue in situ,[33] or favorably upregulate immune tissues and healing mechanisms.[3] These abilities are augmented by the fact that $Ag^+$ hydrosols comprised of the lowest-sized nanoclusters and even picoclusters enjoy the greatest surface presentation and Particle Diffusion Coefficient ($10^{-5}cm^2/sec$) for bioactivity ever created.[3, 37] At this size range, in vitro studies sponsored by NASA at the University of WI offer a fascinating mathematical probability: by skillfully administering $Ag^+$ hydrosol in vivo in order to saturate target loci or foci, picoscalar $Ag^+$ will impregnate *all* collective atoms within *each* tumor cell or pathogen cell with up to one silver ion.[29] This saturation potential supercharges $Ag^+$'s ability to displace the $K^+$ dependent glucose transport mechanism (the *exclusive* means by which cancerous cells feed themselves as opposed to normal cells that enjoy two other additional means to feed themselves), thereby selectively starving cancer cells without harming normal cells.

Landmark studies over the past several decades have demonstrated that oligodynamic $Ag^+$ could play a pivotal role in overcoming cancerous processes. This article will review these findings and offer a proposal for future studies and protocol development.

## In vitro Testing

Becker reported in 1985 that his research group had "…studied malignant fibrosarcoma cells (cancerous fibroblasts) and found that electrically injected silver suspended their runaway mitosis."[30, 31] In 2003, a similar in vitro test was conducted utilizing 1.44 ppm, 2.88 ppm, 5.75 ppm, 10 ppm, 11 ppm, 11.5 ppm & ~ 22.5 ppm concentrations of picoscalar or near-picoscalar oligodynamic $Ag^+$ hydrosol against immortal (cancerous) L-929 Murine fibroblast cell lines (ATCC CCL 1, NCTC Clone 929, of strain L, or equivalent source). Respectively, the oncolytic effects upon the cancerous fibroblasts ranged from 55% to 84% and were $Ag^+$ concentration dependent.[32]

## In vivo Testing

Thirty Central American female patients diagnosed with breast cancer by an oncologist utilizing mammograms and biopsies comprised a subject group 32 to 52 years of age. Each received a single intravenous dosage of silver-oxide-hydrosol ($Ag_4O_4$) to achieve a blood plasma concentration of 10 ppm. The 30 subjects were equally divided by three histologic groups: infiltrative canalicular breast carcinoma (Group I), ductile carcinoma, medular breast cancer (Group II), and infiltrative lobular breast cancer (Group III). The dose was administered to 50% of the patients over ten minutes and to the other 50% over four hours within each respective group.[33]

### *Results*

- Group I: At 19 days post-treatment, a re-biopsy of all patients was performed, with a resulting diagnosis of 100% normal mammary tissue.
- Group II: At 23 days post-treatment, re-biopsy of all patients revealed 100% normal mammary tissue.
- Group III: At 29 days post-treatment, re-biopsy showed 100% normal mammary tissue.

### *Conclusions*

Four out of the 30 patients (13%) experienced JHEs (die-off effects) from treatment. These side reactions were minimal, and were confined to self-resolving, self-limiting and uneventful hepatomegaly and mild fever. At 30 days post-treatment, silver-oxide-hydrosol appeared to have cured the breast cancers of the 30 test subjects.

## Case History – Irving Cohen

In November 2001, 81-year-old Irving Cohen[a] from Adventura, Florida, was diagnosed with primary cancer at the head of his pancreas at Mt. Sinai Hospital by both his gastroenterologist (via ERCP) and his attending oncologist via follow-up CAT scan. A needle biopsy was performed, but missed the intended mark. Mr. Cohen decided not to repeat the needle biopsy. Notwithstanding, his oncologist informed him he had five months to live.

Mr. Cohen declined conventional cancer treatment, and instead chose to pursue orthomolecular/nutraceutical support and dietary therapy. He was subsequently treated with a strict macrobiotic-vegetarian diet, and supported by *p.o.* mega-doses of ascorbic acid, lysine, proline, high potency green tea catechin extract (EGCG), Lipoic acid to recycle and reactivate the ascorbic acid, VascuStatin (Convolvulus arvensis), and Imm-Kine® (Muramyl polysaccharide glycan complex).

After four months on his nutritional program, he remained fairly stable. He traveled to Sloan-Kettering, where his original diagnosis was re-confirmed. At that time, the Sloan-Kettering oncologist (who restricted her practice to pancreatic cancer) was asked if the pancreatic tumor could be lymphoma. The oncologist stated clearly that it could not, but added that without pathology no one could say 100%.

During Mr. Cohen's trip home he began to feel weak, lost his appetite, and developed jaundice. A pancreatic bilary stent was installed by his surgeon, but this procedure gave rise to a highly resistant nosocomial infection in and around his pancreatic duct. He was given Cipro® and Flagyl®, but he continued to rapidly decline. We then modified his CAM treatment to include picoscalar oligodynamic $Ag^+$ hydrosol, both p.o. and administered as a rectal implant. His p.o. dosage was 5cc every 20 minutes on an empty stomach, and his rectal implant using a bulb syringe consisted of 15cc to be retained at bedtime.

After five days, Mr. Cohen regained his strength and appetite. However, on day six, he broke out with two $6cm^2$ herpetic lesions, one anterior and one posterior to his mid-upper right abdominal/flank quadrant, with a single connecting red lesion tracking along the associated intercostal nerve. The patient reported no prior history of shingles. His lesions were subsequently diagnosed as a die-off event from an unsuspected Herpes zoster foci in or near his pancreas. With dermal laser treatment, his painful lesions healed completely after several days. His nosocomial infection also completely resolved.

As his CAM treatment continued, the patient regained greater health than he had previously experienced well before his cancer diagnosis. A $2^{nd}$ CAT scan confirmed no subsequent growth in the pancreatic cancer. Late into 2002, his primary oncologist reported to Mr. Cohen that he had now concluded Mr. Cohen did not have pancreatic cancer, since he should now be dead!

Sometime thereafter, Mr. Cohen discontinued his CAM treatments. Approximately a year later, he discovered he had developed non-Hodgkins lymphoma, which was treated with chemotherapy. At the time of this writing, Mr. Cohen who is now 85 and his wife Audrey are celebrating their $60^{th}$ wedding anniversary. He remains fairly stable with Retuxin® immunotherapy as his sole treatment administered once quarterly.

## Investigational Protocol Proposal

### *Nutritional loading*

Nutritional loading concerns itself with providing an optimal biochemical state to maximize $Ag^+$'s effectiveness while mitigating potential problems. For example, if an unsuspected or underlying hypokalemia is present (i.e., adrenal insufficiency), this should be carefully monitored and treated

[a] Mr. Cohen kindly granted Dr. Apsley permission to use his name and medical history.

since $Ag^+$ can displace $K^+$ to a degree in host cells. Normally, $K^+$ is protected from this effect by adequate levels of N-acetyl-cysteine, as recommended below. [34] Fortunately, cancer cells appear to lack antioxidants to defend against this $K^+$ displacement by $Ag^+$.[35]

Along related lines of reasoning, ARG antioxidants 30 days pre-treatment are recommended to help lessen or eliminate JHEs and a down-regulated liver antioxidant profile. The following doses are for a 75 kilo patient. Reduce by body weight accordingly:

- Buffered Vitamin C Powder – 10 to 20 grams daily according to bowel tolerance
- L-lysine – 3 t.i.d.
- Chemogen™ – 1 t.i.d.
- VascuStatin – 2 t.i.d.
- Imm-Kine® – 1 t.i.d.
- ThioDox® – 1 t.i.d.
- Phosphatidyl Choline – 2 t.i.d.
- Aller Aid Formula II – 1 t.i.d.
- Natural Source E – 800iu daily
- Fibrenase III – 3 before bed

All supplements are discontinued 72 hours prior to administering the silver hydrosol treatment protocol, and are resumed again 72 hours post treatment for the next 30 days at which time both the patient as well as the protocol should be completely re-evaluated.

### *Safety*

Marino (1974)[36] and Berger et al. (1976)[11] confirmed that the effective dosage level of pure oligodynamic $Ag^+$ is safe for mammalian tissues. The *CRC Handbook to Chemistry and Physics* stated that, "While silver itself is not considered to be toxic, most of its salts are poisonous."[37] Picoscalar oligodynamic $Ag^+$ hydrosol containing only $Ag^+$ and ultra-pure water is virtually devoid of toxicity. The EPA's lowest observed adverse event level (LOAEL) for silver exposure relates purely to argyria, as it is the only established adverse event known for silver exposure.[38, 39] For intravenous administration, the EPA has determined that over any given two to nine year period, administering under 1 gram total elemental silver presents no risk for developing argyria.

Therefore, based on the studies and from a purely mathematical perspective, 100cc isotonic[b] $Ag^+$ hydrosol with a 25 ppm concentration or less, could be administered as an I.V. drip every day for *a year* without risking the development of argyria. Likewise, a dose of 500cc (isotonic) of oligodynamic $Ag^+$ administered daily for up to 79 consecutive days or 1000cc (isotonic) of oligodynamic $Ag^+$ administered daily for up to 39 consecutive days still falls short of the risk threshold for developing argyria.

### *I.V. Protocol*

Physicians interested but not experienced in pursuing CAM I.V. protocols should first become certified to do so before incorporating them into clinical practice to mitigate possible liability issues. For further information the reader is advised to contact the Advanced Medical Education & Services Physician Association at - http://www.amespa.org.

According to patient tolerance, dosage levels should aim to deliver a 10 ppm $Ag^+$ blood plasma concentration over a two to four day period. In theory, this would require 633cc of isotonic picoscalar

[b] Consulting with a compound pharmacist would reveal that by mixing 5.3875 grams of injectible-grade sorbitol into each 100cc of injectible-grade hypotonic $Ag^+$ hydrosol would render the mix isotonic (i.e., ~300mOSM). To avoid any loss of potency of the oligodynamic content within the $Ag^+$ hydrosol, the sorbitol should be mixed in to render the $Ag^+$ hydrosol isotonic 5 to 10 minutes prior to I.V. administration.

or near-picoscalar oligodynamic $Ag^+$ hydrosol administered via I.V. drip over 4 hours daily for 4 consecutive days, with each $Ag^+$ drip followed up exactly 90 minutes later with 125cc 0.0375% $H_2O_2$ with standard amounts of DMSO, Mg, and Mn, and bicarbonate administered via I.V. drip over 90 minutes.

For further information see Parts I & II. Part II previously outlined the extension of the oligodynamic therapeusis by way of synergism with $H_2O_2$; mitigation and management of possible Jarisch-Herxheimer Events; adjunctive CAM supplements for treating influenza; plus the issues surrounding jurisprudence.

## Conclusion

More research needs to confirm the oncolytic role of $Ag^+$. Today's nanotechnology has rendered commercially available, high quality, and cost-effective picoscalar or near-picoscalar oligodynamic $Ag^+$ hydrosol. In the near future, the promise of synergistic effects with *mildly hypotonic* picoscalar oligodynamic Pt,[40] Ag, Au,[41, 42] Co and Cu[33] should prove most fruitful for follow-up investigational cancer research.

## Correspondence

The authors have extensive clinical experience using picoscalar oligodynamic $Ag^+$ hydrosol. With the exception of Dr. Apsley, Executive Director of Immunogenic Research Foundation, which accepts endowments and grants from the silver industry at large, none of the remaining authors have any financial ties to commercial or proprietary silver hydrosol products. Dr. Apsley may be contacted at japsley@msn.com. Dr. Holtorf is Medical Director for the Hormone and Longevity Medical Center, Inc. at 23441 Madison Street, #215, Torrance, California 90505; 310-375-2705. He may be reached at www.hormoneandlongevitycenter.com. Dr. Gordon is Medical Director for Gordon Medical Associates in Santa Rosa, California. Drs. Gordon and Anderson may be contacted at gordonmd@sonic.net. And finally, Dr. Buttar is the Medical Director for The Center for Advanced Medicine at 20721 Torrence Chapel Road, # 101-103, Cornelius, NC 28031; 704-895- 9355. He may be reached at www.drbuttar.com.

# References


[1] Von Nageli C. On the oligodynamic phenomenon in living cells. *Naturforsch Ges, Denkschriften der Schweiz.*1893;33:1.
[2] Rentz E. The Broad-Spectrum Antimicrobial Properties of Oligodynamic $Ag^+$ As Silver Hydrosol. Featured lecture presentation of the American Academy of Environmental Medicine (AAEM). 2003 Summer Conference. The comprehensive medical library of the Natural-Immunogenics Corp., located in Pompano Beach, Florida, provided complimentary medical references for Dr. Rentz's AAEM presentation.
[3] Gordon E, Holtorf K. Promising cure to URTI pandemics including the avian flu (H5N1): Has the final solution to the coming plagues been discovered? Part II. *Townsend Letter.* 2006 April;#273.
[4] Russell AD, Path FR, Hugo WB. Antimicrobial activity and action of silver. *Prog Med Chem.* 1994;31:354.
[5] Moyasar TY, et al. Disinfection of bacteria in water systems by using electrolytically generated copper, silver and reduced levels of free chlorine. *Canadian Journal of Microbiology*. The National Research Council of Canada, Ottawa, Ont., Canada. 1990;109-16.
[6] Hamilton-Miller JM, Shah S, Smith C. Silver Sulphadiazine: A comprehensive in vitro reassessment. *Chemotherapy*. 1993;39:406.
[7] Zhao G, Stevens SE. Multiple parameters for the comprehensive evaluation of the susceptibility of Escherichia coli to the silver ion. *Bio Metals*. 1998;11:27.
[8] Baker C, et al. Synthesis and antibacterial properties of silver nanoparticles. *J Nanosci Nanotechnol.* 2005 Feb;5(2):244-9.
[9] Sondi I, Salopek-Sondi B. Silver nanoparticles as antimicrobial agent: A case study on E. coli as a model for Gram-negative bacteria. *J Colloid Interface Sci*. 2004;275:177–182
[10] Morones JR, et al. The bacteriocidal effects of silver nanoparticles. *Nanotechnology.* 2005;16:2346-53.
[11] Berger TJ, et al. Electrically generated silver ions: Quantitative effects on bacterial and mammalian cells. *Anti Microb Agents*. 1976;9(2):357-8.
[12] See: http://www.cdc.gov/nchs/fastats/lcod.htm
[13] Livingston-Wheeler V, Wheeler OW. The Microbiology of Cancer: Physician's Handbook, A Livingston-Wheeler Medical Clinic Publication. Spring Valley, CA, 1977.
[14] Spano JP, et al. Non-AIDS-defining malignancies in HIV patients: clinical features and perspectives. *Bull Cancer*. 2006 Jan 1;93(1):37-42.
[15] Fields CB, et al. Method for treating blood borne viral pathogens such as immunodeficiency virus. *United States Patent No. 6,066,489*. 2000 May 23.
[16] Sola P, et al. New insights into the viral theory of amyotrophic lateral sclerosis: study on the possible role of Kaposi's sarcoma-associated virus/human herpesvirus 8. *Eur Neurol*. 2002;47:108-12.
[17] Kuck D, et al. Intranasal vaccination with recombinant Adeno-associated virus Type 5 against Human Papillomavirus Type 16 L1. *J Virol.* 2006 Mar;80(6):2621-30.
[18] Serraino D. Infection with Epstein-Barr virus and cancer: an epidemiological review. *J Biol Regul Homeost Agents*. 2005 Jan-Jun;19(1-2):63-70.
[19] Eash S, et al. The Human Polyomaviruses. Reviewed by Cellular and Molecular Life Sciences (CMLS). Publisher: Birkhäuser Basel, ISSN: 1420-682X, 2006 Feb 23.
[20] Weinreb DB, et al. Polyoma virus infection is a prominent risk factor for bladder carcinoma in immunocompetent individuals. *Diagn Cytopathol*. 2006 Feb 9;34(3):201-203
[21] Englund JA. Diagnosis and epidemiology of community-acquired respiratory virus infections in the immunocompromised host. *Biol Blood Marrow Transplant.* 2001;7 Suppl:2S-4S.
[22] Abelson JA. Frequency of fungemia in hospitalized pediatric inpatients over 11 years at a tertiary care institution. *Pediatrics.* 2005 Jul;116(1):61-7.
[23] Knapp KM, Flynn PM. Newer treatments for fungal infections. *J Support Oncol.* 2005 Jul-Aug;3(4):290-8.
[24] Liakopoulou E, et al. Rotavirus as a significant cause of prolonged diarrhoeal illness and morbidity following allogeneic bone marrow transplantation. *Bone Marrow Transplant.* 2005 Oct;36(8):691-4.
[25] Chemaly RF, et al. Cytomegalovirus pneumonia in patients with lymphoma. *Cancer*. 2005 Sep 15;104(6):1213-20.
[26] Kumashi P, et al. Streptococcus pneumoniae bacteremia in patients with cancer: disease characteristics and outcomes in the era of escalating drug resistance (1998-2002). *Medicine* (Baltimore). 2005 Sep;84(5):303-12.
[27] Kerker M. The optics of colloidal silver: something old and something new. *Journal of Colloid and Interface Science.* 1985;105:297–314.
[28] Sosa IO, Noguez C, Barrera RG. Optical Properties of Metal Nanoparticles with Arbitrary Shapes. *Journal of Physical Chemistry B.* 2003;107:6269–6275.
[29] Cliver DO, et al. Biocidal effects of silver: Contract NAS 9-9300 Final Technical Report. University of Wisconsin, Accession No. N71-24436, NASA CR-114978, Code G3, Category 04. 1971 Feb;5-2.
[30] Becker RO, and Shelden G, The Body Electric: Electromagnetism And The Foundation of Life. William Morrow and Company, Inc., NY, NY, 1985; p. 175.
[31] Becker RO. Processes and products involving cell modification. *United States Patent 4,528,265*. 1985 July 9.
[32] Weingates-Furiate M, McCoy CM. In vitro cytotoxicity sample. NAMSA. Northwood, OH, Lab No. 03T 01251 01. 2003 July 17.
[33] Antelman MS. Methods of using electron active compounds for managing cancer. *United States Patent No. 692488.* 2000 October 20.
[34] Hussain S, et al. Cysteine protects Na, K-ATPase and isolated human lymphocytes from silver toxicity. *Biochem Biophys Res Comm.* 1992; 189:1444-1449.
[35] Garcia-Giralt E, et al. Preliminary study of GSH L-cysteine anthocyane (Recancostat Compositum™) in metastatic colorectal carcinoma with relative denutrition. *Eur J Cancer* [Part A] 1997;33(Suppl. 8):S17.

[36] Marino AA, et al. The effects of selected metals on marrow cells in culture. *Chem. Biol. Interactions*. 1974;9:217.
[37] Handbook of Chemistry and Physics, ed. David R. Lide, CRC Press, Boca Raton, FL. 2000; Section 4, p. 27 and Section 15, p. 28..
[38] Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Silver – CAS# 7440-22-4. 1990 Dec.
[39] U.S. Environmental Protection Agency – Silver; CASRN 7440-22-4. Last revised – 1996 Dec 1.
[40] Tsujitani S, et al. Administration in a hypotonic solution is preferable to dose escalation in intraperitoneal cisplatin chemotherapy for peritoneal carcinomatosis in rats. *Oncology* 1999 Jul;57:77-82
[41] Ocshner DH. The use of colloidal gold in inoperable cancer. *J Med & Surg*. 1927 Mar.
[42] Ocshner DH. Colloidal gold in inoperable cancer. *Clinical Medicine and Surgery*. 1935 July.