

Chemo Drugs: New Uses, New Exposures, Failure to Protect Consequences



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Global Cancer Facts

- Cancer: abnormal cells (neoplastic cells) that divide without control, can invade nearby tissues and spread throughout body
- 2nd leading cause of death (1st cardiovascular disease)
- 1 in 6 deaths globally due to some form of cancer
- More than 100 forms of cancer



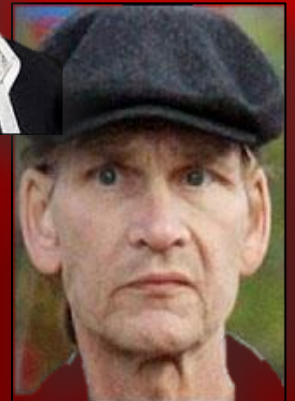
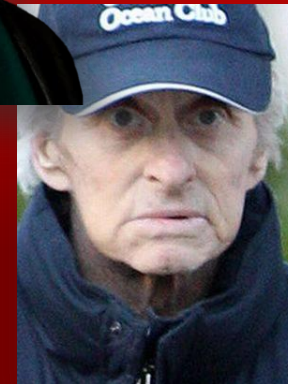
Steve
Jobs



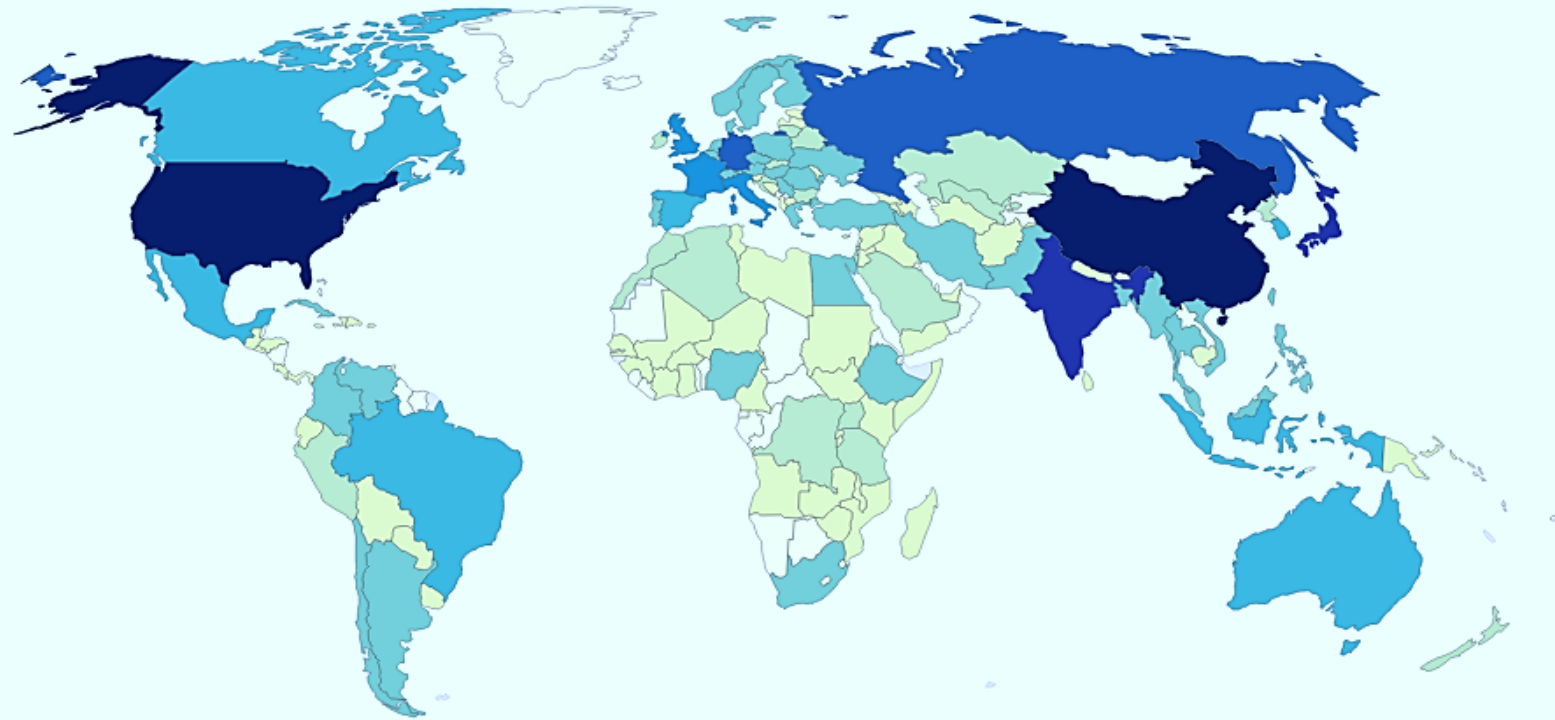
Michael
Douglas



Patrick
Swayze



Number of people living with some kind of Cancer, 2016



Source: IHME, Global Burden of Disease

OurWorldInData.org • CC BY-SA

- Survival all cancers up from 50% to 67% since 1970's due to Earlier Detection + New/Improved Treatments

By Year 2020

- Due to expanding global population, increasing life expectancy, rising percentage of elderly, Cancer will increase:

**By 2020: 16 Million
New Cancer Cases Yearly**

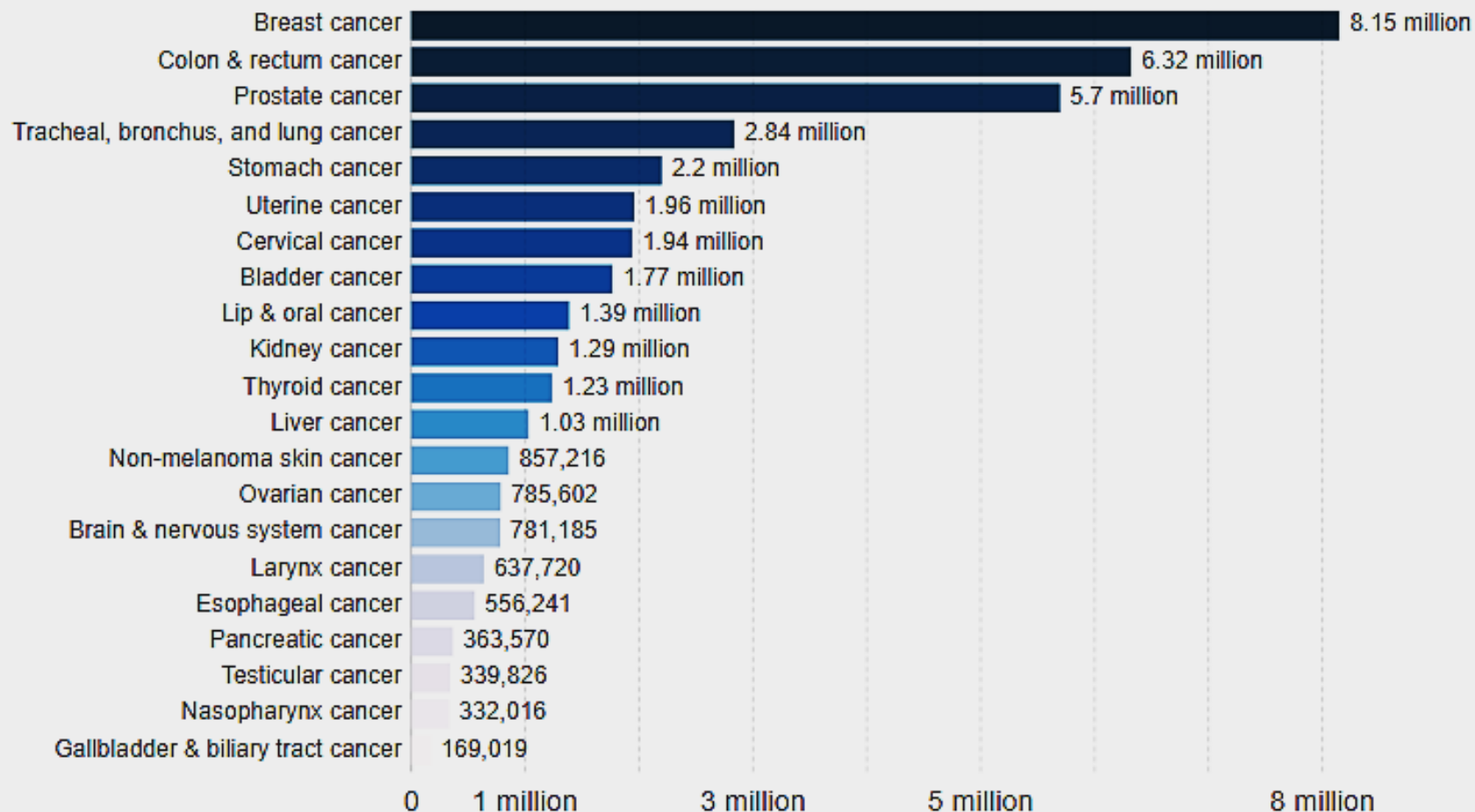


**By 2030: 23.6 Million
New Cancer Cases Yearly**

Number of people with cancer by type, World, 2016

OurWorld
in Data

Total number of people suffering from cancer at any given time, differentiated by cancer type. This is measured across both sexes and all ages.



Source: IHME, Global Burden of Disease

- Max Roser and Hannah Ritchie (2018) - "Cancer". Published online at OurWorldInData.org. Retrieved from: '<https://ourworldindata.org/cancer>'

Cancer Treatments

Protect
the
Wearer

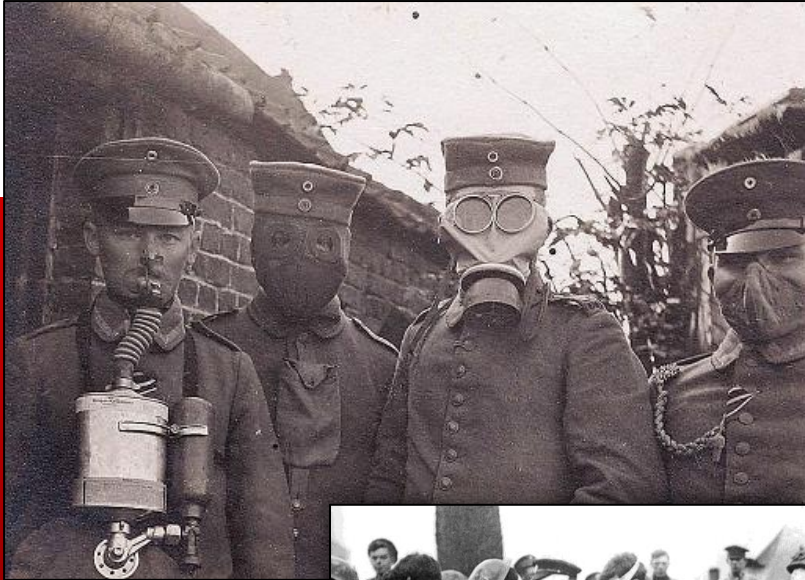
1. Chemotherapy - different chemicals tagged to:
 - kill specific types of cancer cells
 - kill all rapidly reproducing cells of any type
 - prevent specific or general cell organelles or stages of development
2. Surgery: Removal of cancerous tissues, tumors
3. Hot Surgery
4. Hormones (specific): some cancers require or are injured by specific hormones
5. Radiation treatments: Standard and radioactive implants
6. Immunotherapy:
 - monoclonal antibodies (cell target specific)
 - anti-angiogenesis: prevents formation of new blood vessels that feed the rapidly growing/multiplying cancer cells (e.g. tumors)
 - T-cell therapy (remove T-cells [Immune/White Blood cells], alter & train them to fight cancer; multiply them; put them back into patient)
 - cancer vaccines: prevent and/or treat cancer

Protect the Wearer



History of Chemotherapy Drugs

- Mustard Gas: one of three poisonous gasses in WWI



Mustard Gas Poison to Cancer Drug

- Noted some individuals who had excessively high white blood cell counts had much lower counts after mustard gas exposure
- Some with cancer found their tumors reduced in size after gas exposure

Initiated use of poisonous Chemicals to treat Cancer

- >150 different chemo drugs; often used in combinations: “Chemo-Cocktails”



Identifying Those at Collateral Risk

- 1970s: Noted rates of certain cancers higher in healthcare professionals who treat cancer patients
- 1980-2009: Found nurses, doctors, pharmacists working with cancer drugs & patients had increased:
 - leukemias
 - breast cancer
 - thyroid cancer
 - nervous-system & brain cancer
 - miscarriages; stillborn births
 - premature births
 - birth defects
 - children with poor motor skills (2.5 – 5X more than normal)
 - children with learning disabilities
- Also causes:
 - decreased fertility
 - ectopic pregnancies
 - highly toxic to certain internal organs
- US Oncology (Cancer) Unit: 3 consecutive head nurses:
 - all 3 sustained severe liver damage



Chemotherapy Drugs

- Studies: Also exposed to Chemo and at increased risk:
 - pharmacy & research lab workers even if not working chemo directly
 - transports/carriers of unopened chemo drugs
 - unit clerks
 - nursing assistants
 - housekeeping staff
 - patient's family members
- Despite national & global acknowledgement, regulations, required safety procedures, still found:
 - chemo drugs in urine plus chromosomal damage in staff who:
 - mixed chemo drugs
 - administered chemo to patients
 - cleaned-up after chemo drugs administered
 - chemo drugs still contaminate work areas
 - many chemo drugs remain hazardous for months long after they dry



Chemotherapy Infusion Staff Exposures

	Staff Failed to Prevent Exposure/Cause Exposure	%
1	Did not double glove	80%
2	Reported leak/spill exposure when attaching, injecting, detaching IV line	70%
3	Performed activities wearing same gloves worn to administer chemo drugs (touched IV pole & pump, bed controls, waste basket, door knobs, cabinets, drawers, used handled computer, calculator, files, charts, pens, pencils)	60%
4	Did not always wear non-absorbable gown w/closed front, tight fitting cuffs	42%
5	Safety training over 12 months previous	36%
6	No gloves worn	15%
7	Spills or leaks during administration	12%
8	Direct skin contact with the drug when administering drug to patients	4%
9	Lacked safe handling training at all	4%
10	Reused gloves	1%
11	Skin punctured by a sharp when administering chemo drug	1.4%
12	Reported spills or leaks were not always cleaned up	1%

Sue Crump: Pharmacist Mixed Chemotherapy Drugs



Secondhand Chemo deaths
within 5 months of Sue's death:

Bruce Harrison,	Pharmacist
Karen Lewis,	Pharmacist
Brett Cordes,	Veterinarian
Sally Giles,	oncology nurse

- Pharmacist for 23 years
- Mother of Chelsea to graduate college
- Sue acquired pancreatic cancer
- Believed from “Secondhand Chemo”
- Informing young pharmacists & nurses to protect themselves
- Died Sept. 2010, age 55, (before Chelsea graduated)



Where are HCWs Getting Contaminated?

“So many people think it’s just a ‘little bit.’ They don’t understand, it’s a little bit of something designed to be toxic, and to be highly absorbed biologically.”

Dr. Melissa McDiarmid, Director, Occupational Health, University of Maryland

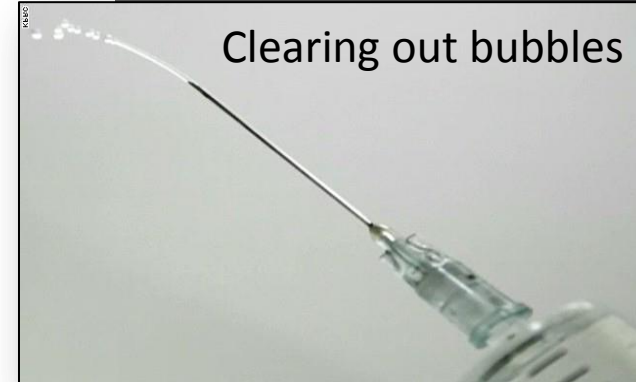
- 1) Shipping cartons
- 2) Reconstituting powdered or lyophilized Chemo drugs
- 3) Mixing reconstituted chemo drugs together
- 4) Touching outside of bottles, vials, ampules, syringes, bags without gloves (from manufacturer; after compounding; during/after infusion)
- 5) Setting up or taking down infusion IV sets
- 6) Clearing air from syringes or tubing
- 7) Transporting chemotherapy agents or patients
- 8) Handling of urine & any other body fluid **(48-72hr still toxic)**
- 9) Cleaning-up vomit of treated patients **(48-72hr still toxic)**



Where are HCWs Getting Contaminated?

- 10) Cleaning up diarrhea of treated patient **(48hrs -72hr still toxic)**
- 11) In heavy dose chemo: sweat from patient
- 12) Leaking intravenous tubing connections
- 13) Improper cleaning of spills
- 14) During removal of contaminated PPE
- 15) Food & drink in chemo prep areas
- 16) Disconnecting during change-outs or session end
- 17) Sprays, spills, IV tubing disconnects
- 18) Recent study: Nurses in outpatient settings reported almost 17% had skin or eye direct exposure to chemo agents & these accidents are significantly under reported

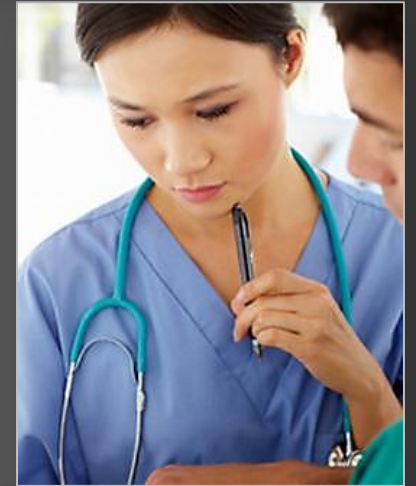
Reports looking at infusion center waiting rooms, wheel chairs, IV poles, etc. found some level of contamination almost everywhere. Need to do a better job of cleaning as **chemo drugs remain hazardous on surfaces for months.**



Recently, Still Found Contaminated

Contaminated items

- Floor/trays of lab refrigerators
- Phone handles
- I.V. solution bags
- Working station for mixing; bio-safety hood
- Working surface for packaging and labeling
- Floor of preparation room surfaces, floors, refrigerators, hoods
- Waste such as pads in treatment area
- Contaminated pens, pencils, papers, food & food trays
- Spills (small dried drips hazardous for months)



Handling of Cytotoxic Drugs

- Risk depends on:
 - toxicity of cytotoxic drug
 - time of exposure
 - frequency of exposure (toxic injury is cumulative)
- Staff Exposure can enter through
 1. Skin (primary)
 2. inhalation
 3. ingestion (food or drinks)
 4. accidental injection



Rub in Chemo Lotion


**Chemo-
Ointment**

Metastatic Melanoma



Acute Symptoms Associated With Exposure



Allergic	Cardiac	Gastro-intestinal	General	Immune	Neurological
Allergic reactions	Shortness of breath	Anorexia	Alopecia (hair loss)	Chronic cough; sore throat	Headaches
Eye irritation	Irregular pulse	Nausea	Nail hyperpigmentation	Fever	Dizziness
Rash	Peripheral edema	Vomiting	Dysuria (Painful urination)		Fainting
	Chest pain	Diarrhea	Decreased libido		Insomnia
	Elevated blood pressure	Constipation	Malaise		



Test Methods Chemotherapy Labeled Gloves

	ASTM F739-12 No longer for new 510(k)s	ASTM D6978-05(2013)	EN 16523-1:2015 (formerly 374-3:2003)
Temperature	23°C	35°C (temperature of Hand-glove interface)	23°C
Permeation rate	0.1 µg/cm²/Min	0.01 µg/cm²/Min	1.0 µg/cm²/min
Scope: Resistance against	Chemical in general	Cytotoxic drugs specifically	Chemicals in general
Chemicals used for testing	Chemical and concentration left to Manufacturer	9 cytotoxic drugs - minimum: 7 specified + 2 own choice Concentration dose use specified	12 standard but no Chemotherapy drugs. Left to Manufacturer

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Part tested	Any part	Thinnest part of glove	Palm for gloves of homogenous design
Surface tested	Not specified	Outer surface	Outer surface
Test time		240 minutes	480 minutes
Listed to also consider	ASTM: D471, D543, D 751, E105, E171, E177, E691, F903, F1001, F1194, F1383	ASTM: D471, D3577, D3578, D3767, D5250, D6319, D6977, F739	EN420;
Min. requirements	Not stated	Length (30cm per D3577 / D3578, No powder, Syn/Low Protein if NRL)	26cm per EN420

Chemo Gloves - Test Penetration Potential: 7 Specific Chemo Drugs Using ASTM D6978

- Cyclophosphamide 20.0 mg/mL
- Doxorubicin HCl (Adriamycin) 2.0 mg/mL
- Etoposide 20.0 mg/mL
- Fluorouracil (Acrucil) 50.0 mg/mL
- Paclitaxel (Taxol) 6.0 mg/mL
- ThioTEPA 10.0 mg/mL
- Carmustine 3.3 mg/mL (plus 10% ethanol)

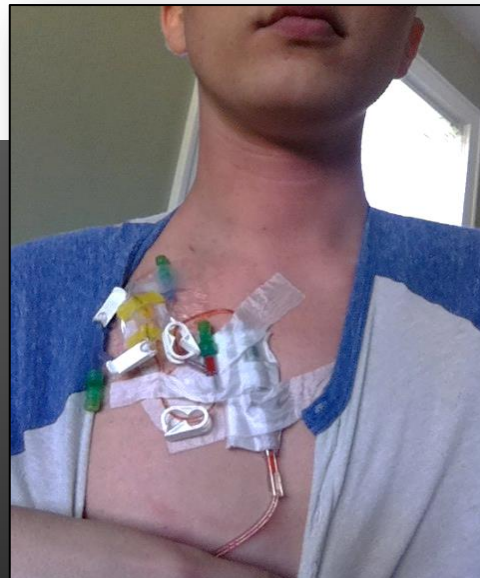
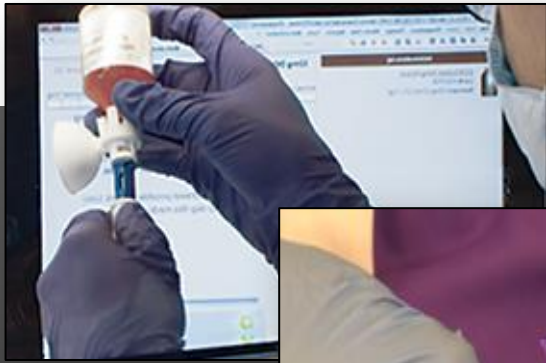
Each represents a different drug family: penetrate differently

Now more than 150 approved chemotherapeutic drugs!!



A Personal Plea

- Companies that are FDA “grandfathered” into older versions (e.g. ASTM F739), please re-submit with the more stringent Chemotherapy Drug specific ASTM D6978-05(2013) Customers have no clue there is a difference testing stringency.
- It is not required by FDA for gloves cleared through the 510k process before the new ASTM test was developed to be retested
- However, it is ethically the right thing to do to protect your customers



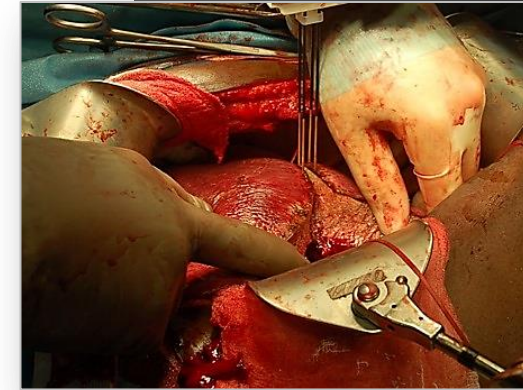
Clarifying a Misconception; Encouraging New Technologies

- “Chemo glove penetration **WRONG!!!** on the glove thickness”
- **SHOULD Say**: “Chemo drug penetration rate will change if the thickness of a glove made specific material and formulation is altered”

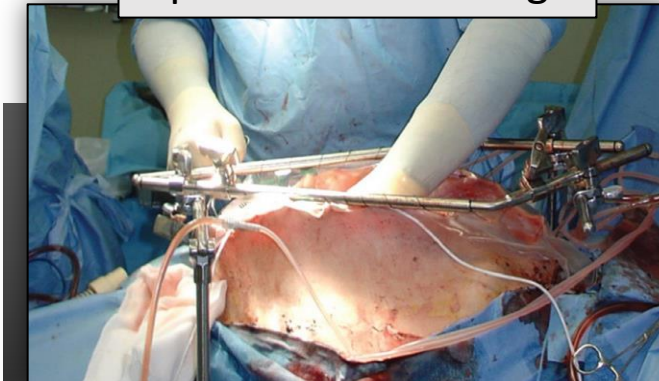
“Hot” Concentrated Chemo Surgery!!

- Concentrated chemo drug mixture is made
- Then heated to about 107°F (42°C) – (recirculated to maintain temperature)
- Surgeon massages warmed concentrated chemo into cancerous organ
 - highly concentrated hot dose delivered directly where needed
 - same concentration would kill patient if into bloodstream
- Will their surgical gloves hold up to:
 - concentration of the chemo?
 - heated chemo agent?
 - rubbing chemo into cancerous organs
 - length: protect arm

Specialty glove in your Chemo-glove line; also good for many Veterinary uses!



Open Chemo massage



Closed Chemo Flushing



Hormone Therapy

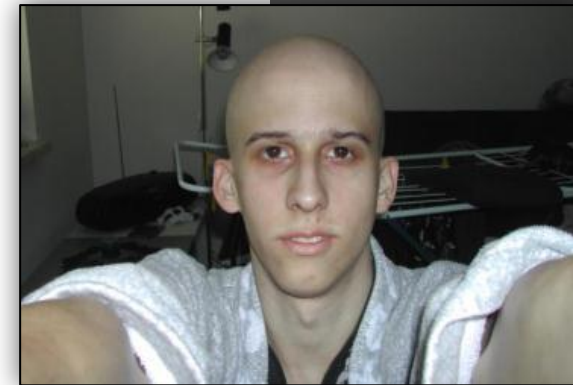
- Used most often when cancer in tissues of:
 - breast
 - prostate
 - endometrium
 - adrenal cortex
- Using forms in the categories:
 - progestogens
 - androgens
 - estrogens
 - somatostatins
- Also hormonal immunotherapy (to stimulate the immune system)



- Induce receptor expression on cancer cell to:
 - target cancer cells
 - bind toxin to hormone taken into cell (Trojan Horse)
- Shut down receptors on cancer cells:
 - starve cancer (hormone disruptors)
- Activate/Deactivate systems:
 - immune cells activate/multiply
 - antibody production
 - anti-angiogenesis (prevent new blood vessels-suffocate/starve tumor)

Future: Expanding Chemo Use

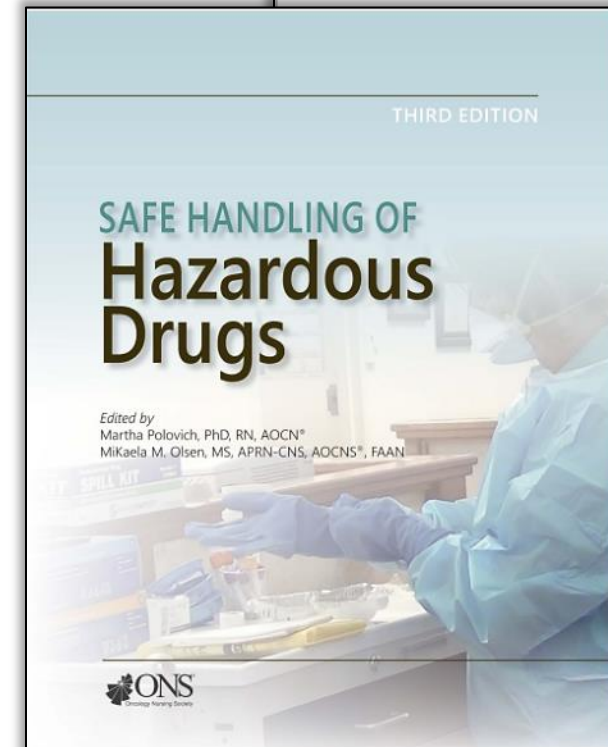
- Millions HCW exposed to chemo agent annually: nursing, pharmacy, transport, cleanup
 - about 1/2 of those mix or dispense chemo drugs
 - recently in a country lecturing; demonstration outside young nurses required to mix chemo drugs with no hoods, or hood that do not work
- Those numbers will grow
 - cancer patients to climb as population ages and more receive treatment
 - more HCW & staff required & exposed
 - more likely patients will be treated in less controlled
 - outpatient clinics; private homes



References

- About 280 drugs used widely in healthcare settings are listed that should be handled as hazardous. Good discussions Department of Health and Human Services: CDC & NIOSH
- Safe Handling of Hazardous Drugs (Book). Oncology Nurses Society; Edited by M. Polovich & M.M. Olsen, 2017

NIOSH List of Antineoplastic
and Other Hazardous Drugs
in Healthcare Settings 2010



Expanding Chemo Drug Applications; Increasing Rates of Autoimmune Diseases Globally

Non-Cancer Disorders Now Reported to be Improved When Treated with Chemo Drugs

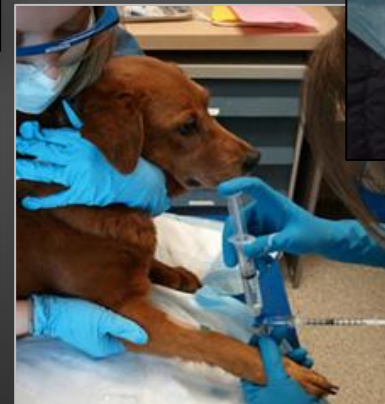
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|---|---|
| <ul style="list-style-type: none">• Inflammatory bowel disease<ul style="list-style-type: none">– Crohn's disease– ulcerative colitis• Lupus• Multiple sclerosis (MS)• Myasthenia gravis• Psoriasis• Rheumatoid arthritis | <ul style="list-style-type: none">• Sarcoidosis• Sclerosis (scleroderma)• Solid organ transplant<ul style="list-style-type: none">– rejection treatment– prophylactic preventative• Ectopic pregnancy• Vasculitis• Treat bone prior to bone marrow transplant |
|---|---|



- **9 million** Americans suffer from cancer
- **50 million** Americans have autoimmune disease (AARDA) (NIH: 23.5 million if only accept studies)
- There are 100-150 different autoimmune diseases
- Globally: Autoimmune diseases just below 20% of the population and are increasing

Clientele Is Increasing

- In the US: 6 million new cases cancer diagnosed each year
- Veterinarians increasingly using chemo for cancer
- Tufts University Veterinary Medicine alone treats >26,000 cancer cases a year
- Many staff no idea protection needed 48hr active chemo urine, stools, vomit
- UK and France have the only strict chemo compliance for veterinary



Job Titles of those Exposed: Depends on Assignments

- Pharmacists & pharmacy technicians (note: often use alcohol to wipe gloves first)
- Nurses, Nurses aids, volunteer
- Physicians & Physician's assistants
- Dietitians
- Surgical personnel
- Home healthcare workers
- Veterinary & veterinary technicians
- Environmental services
 - custodial staff, laundry personnel, maintenance workers
- Individuals who ship, transport, receive, unpack hazardous drugs
- Researchers & their assistance & custodians

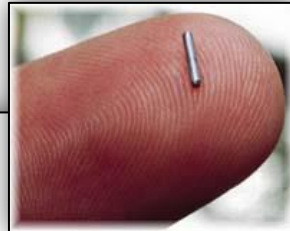
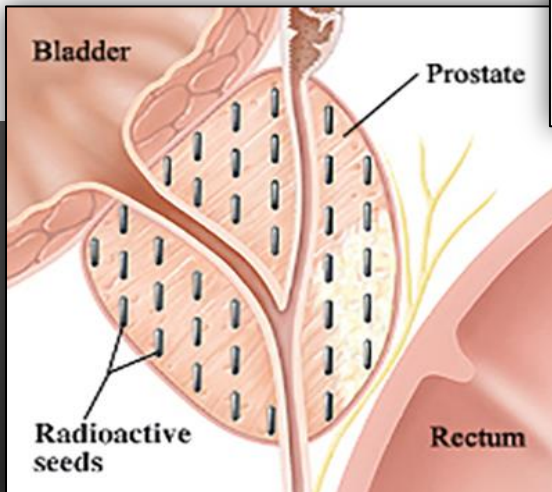
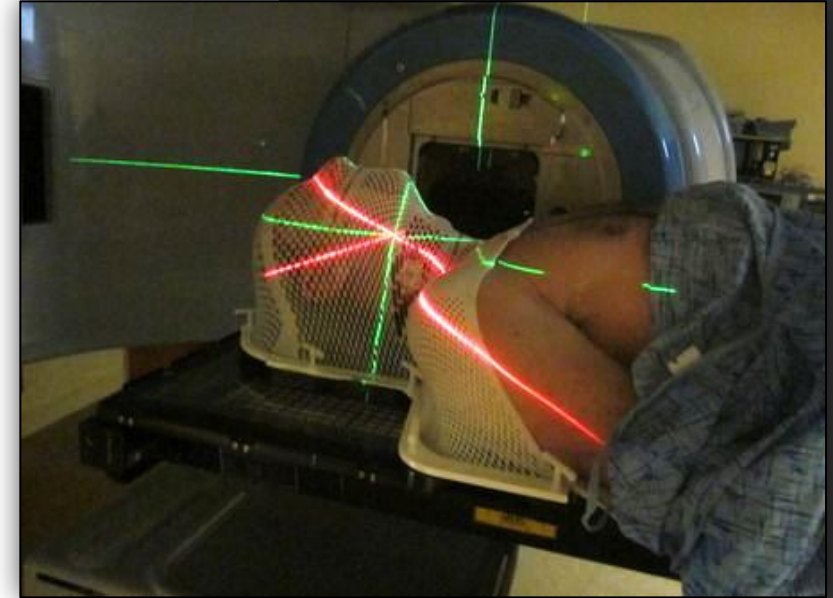


Hon CY, 2014

2-fold increase in spontaneous abortions among those exposed to antineoplastic (anticancer) drugs for more than one hour a day in first trimester

Radiation Cancer Treatment

- Hands of medical attendants can be exposed to radiation during cancer targeted
 - directed radiation sessions
 - surgical implantation of radioactive “seeds”
- Radiation attenuation gloves primarily
 - lead containing, or
 - barium containing



Cancer Treatments

1. Chemotherapy - different chemicals tagged to:
 - kill specific types of cancer cells
 - kill all rapidly reproducing cells of any type
 - prevent specific or general cell organelles or stages of development
2. Surgery: Removal of cancerous tissues, tumors
3. Hot Surgery
4. Hormones (specific): some cancers require or are injured by specific hormones
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 - T-cell therapy (remove T-cells [Immune/White Blood cells], alter & train them to fight cancer; multiply them; put them back into patient)
 - cancer vaccines: prevent and/or treat cancer

Protect the Cells

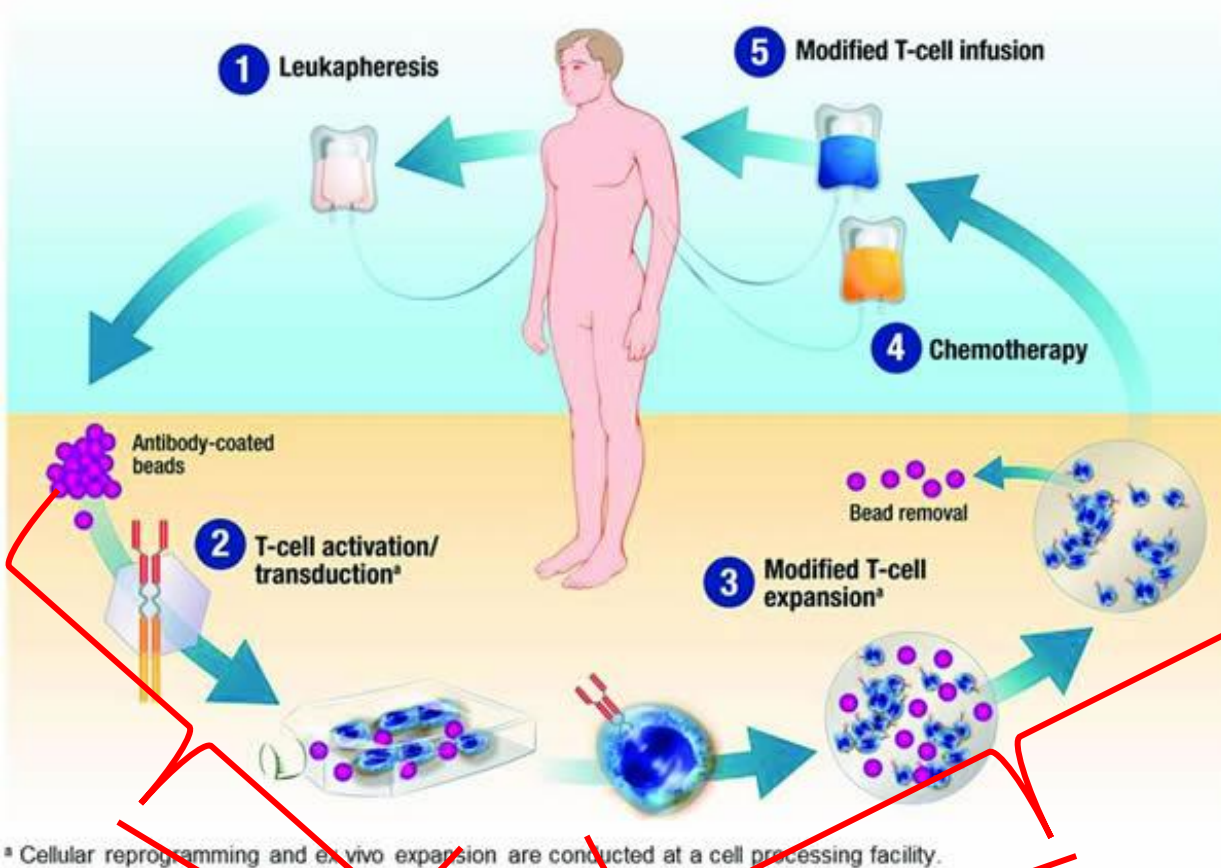


5. Immunotherapy:

- T-cell therapy (remove T-cells [Immune/White Blood cells], alter & train them to fight cancer; multiply them; put them back into patient)
- Monoclonal antibodies (target specific cancer cell receptors)
- Stem cells to replace damaged by radiation or chemotherapy: ex. bone marrow with blood stem cells
- Cancer vaccines: prevent and/or treat cancer
- Anti-angiogenesis: prevents formation of new blood vessels =“strangles cancer tumors”

These Targeted Treatments Primarily require BIOCOMPATIBLE Gloves that protect the Cells and cell media (nutritious fluid cells thrive in) rather than protect glove wearers from hazardous chemo or radiation

Activate/Modify Patient's Own Immune Cells (T-Cells) to Kill Cancer Cells

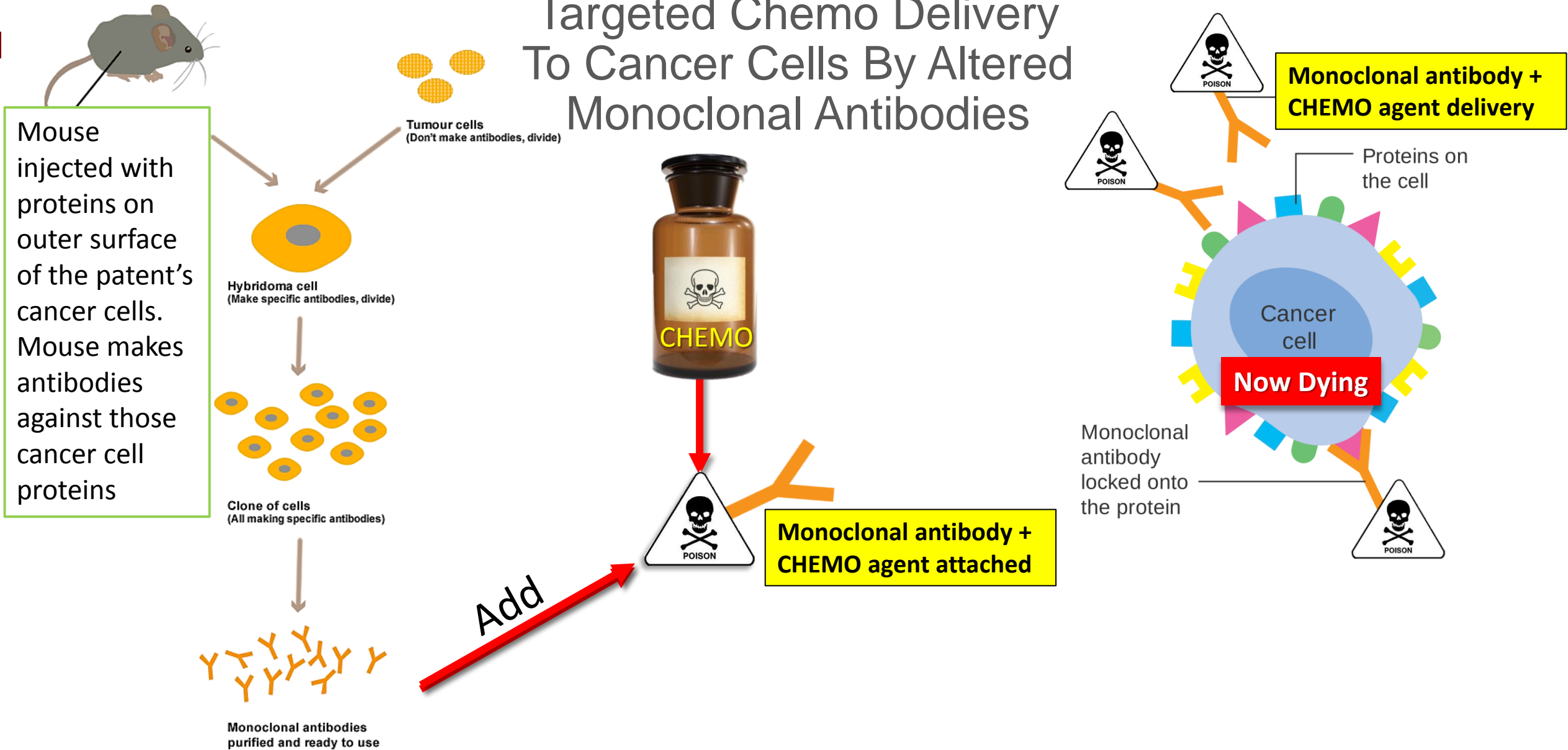


Gloves Must Be Biocompatible

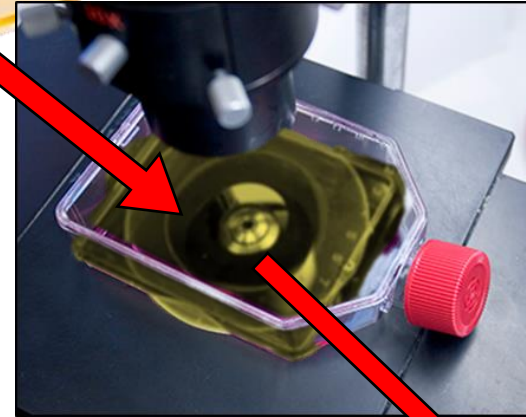
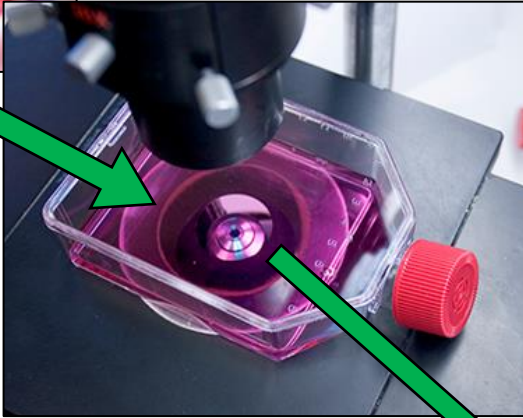
- Biocompatible: Glove to protect the Immune Cells while they are harvested, “trained”, multiplied and placed back into patient to Kill their Cancer Cells:

- 1) Gloves must be sterile
- 2) Non-cytotoxic (won't kill the cells)
- 3) Non-pyrogenic (very low endotoxin)
- 4) Non-hemolytic

Targeted Chemo Delivery To Cancer Cells By Altered Monoclonal Antibodies



Inverted Microscope views from under flask

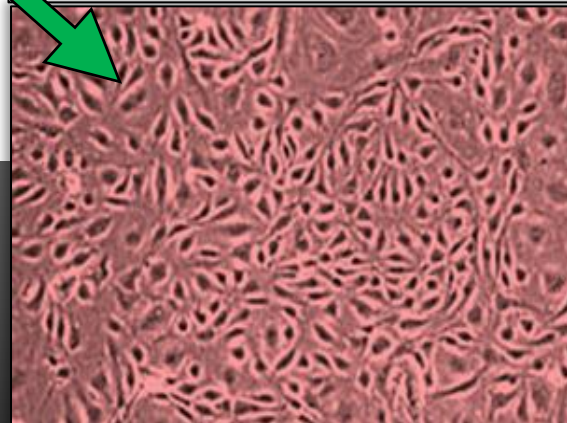


Unfortunately, Must start all over losing precious time for patient incurring expense

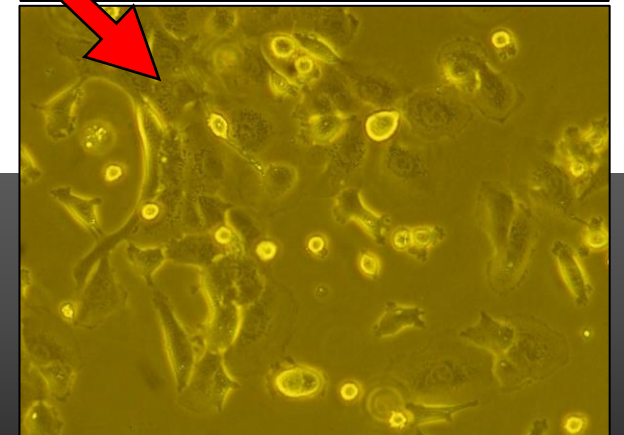
Gloves: Biocompatible:

- Non-cytotoxic
 - Non-hemolytic
 - Non-pyrogenic (low endotoxin)
- (As well as non-irritating, non-sensitizing as already required)

Heathy Cells attached to bottom of flask bathed in nutritious media



Dead & dying Cells due to cytotoxic gloves: losing grasp to flask surface



FDA: “Chemo Glove Quality Has Decreased”

- Mfg started with a cleared Chemo Gloves above specification
- Consistently hitting target above minimum for production thickness
- Then cost increases, operating profits down, hospital pressure for lower costs, FDA seeing:
 - glove thinning (same formulation: decreases time to break-through)
 - adding fillers can increase breakthrough--- it depends (must retest with same chemo drugs)
 - shorter cuffs (reduces splash protection, could pool, can cause slippage or sloppy cuff)
 - reducing chlorination to one side:
 - increased concentration of hypochlorite solution can push cross-linking of surface from beneficial to earlier breakdown (usually during transport –shipping, trucking, hot warehouses) and the less crosslinked non-chlorinated side to earlier permeation/penetration



Manufacturers/Distributors

- Educate own staff in different Business disciplines that impact glove R&D, production, packaging, quality, labeling, marketing, sales, customer inquiry staff
- Do you know:
 - Gloves often placed in hood under UV light upwards of 72 hrs? Are your gloves OK?
 - Lab staff instructions often include 70% alcohol to wipe gloves before compounding mixtures. Are your gloves still OK for chemo protection? Penetration rates change?
 - Do your labels & Education pieces address practices that damage your gloves
- Educate users. Provide:
 - Guidelines
 - occupational exposure watch-outs, known contamination sites
 - potential exposure health consequences for self and family
 - educational courses, brochures, handouts, posters, FAQs,
- Protect your customers; protect their patients; protect your company

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Thank You!!



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