





**1. Patient Selection** IVC 2. Adverse Reactions In Your 3. Mixing/Administration Office 4. Drug Interactions Clinical Implementation 5. Monitoring Outcomes





## 1. Patient Selection



#### The Riordan IVC Protocol Inclusion Criteria and Candidates

 Those who have failed standard treatment regimens
 Those seeking to improve the effectiveness of standard cancer therapies (IVC as an Adjunctive Care Strategy)

- 3. Those seeking to decrease the severity and carcinogenicity of standard cancer therapy side effects and toxicities
- 4. Those attempting to prolong their remission with healthenhancing strategies



#### The Riordan IVC Protocol Inclusion Criteria and Candidates

- 5. Those declining standard treatment, yet wishing to pursue alternative treatment strategies
  - Important NOTE patients in category 5 should be carefully screened for:
  - significant psychiatric disorder
  - end-stage CHF
  - other uncontrolled co-morbid conditions.

ALL IVC PATIENTS (or guardian/legally recognized caregiver) MUST SIGN AN IVC CONSENT FORM PRIOR TO INITIATION OF IVC TREATMENT



#### The Riordan IVC Protocol:

- Baseline and screening laboratory and baseline weight
- Serum chemistry profile with electrolytes
- Complete blood count (CBC) with diff.
- Red blood cell G6PD (must be normal)
- Complete urinalysis
- Patient weight before the first IVC





#### The Riordan IVC Protocol

(recommendations for inclusion in cancer research)

- Complete patient record prior to beginning IVC therapy:
- Tumor type and staging, including operative reports, pathology reports, special procedure reports, and other staging information.
- Re-staging may be necessary if relapse and symptom progression has occurred since diagnosis.
- Tumor markers, CT, MRI, PET scans, bone scans, and x-rays.
- Prior cancer treatments, the patient's response to each treatment type, including side effects.
- The patient's functional status with an ECOG Performance Score.



## 2. Adverse Reactions



#### **IVC** | Adverse Reactions

Riordan Clinic's 40 years of clinical experience

50,000+ onsite IVC treatments Side effects of and adverse reactions to IVC **ARE RARE** 





#### IVC | Adverse Effects - The Padayatty Study

- Vitamin C: Intravenous Use by Complementary and Alternative Medicine Practitioners and Adverse Effects.
  - Padayatty SJ et al. PLoS One. 2010;5(7):e11414.
- Common reasons for treatment included infection, cancer, and fatigue.
- Manufacturers' yearly sales were
  - 750,000 vials (2006)
  - 855,000 vials (2008)





#### **IVC** | Anxiety Reactions

- The practitioner should be mindful that many patients are afraid of IV therapy
- Health-minded people often have never experienced intravenous therapy
- Answer all questions first. Review all aspects of the IVC Consent Form.
- Check on IVC first-timers frequently.
- TLC prevents and/or relieves many common "adverse reactions"





#### IVC | Adverse Effects in 9,328 Patients

• 101 had side effects - mostly minor, including lethargy/fatigue

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- 59 patients had a change in mental status
- 21 patients vein irritation
- 6 patients with phlebitis
- 2 deaths in pts known to be at risk.



#### IVC A Common Adverse Reaction

- IV site irritation may occur at the infusion site when given in a vein and not a port
- Slowing the rate of IVC infusion is always the first action step and it typically helps
  - Infusion rates exceeding 1.0 gram/minute are more likely to cause vein irritation

The Riordan Protocol adds magnesium chloride to every IVC Magnesium reduces the incidence of vein irritation Magnesium reduces the hypoglycemic effects of high dose IVC



#### IVC | Mild Chelation-like Effects

Like EDTA, IVC can cause a slight dip in serum calcium (parathyroid hormone stimulant?)
Low calcium may result in transient shakiness
If severe, push of 10 mL's of IV calcium gluconate, 1.0 mL per minute.





#### IVC | Ascorbate Mimics Glucose

The rapid rise in ascorbate can mimic a glucose surge

This can trigger a pancreatic response of increased insulin secretion

- The resulting low glucose can create hypoglycemic symptoms such as shakiness
  - (Is this hypoglycemic reaction a beneficial IPT effect Insulin Potentiation Therapy?)

An additional 1.0 mL of 50% MgCl to the IVC solution will usually resolve these issues

Also, a simple snack will often relieve this response



#### IVC | WARNING - IVC Alters Glucometer Readings

- IVC interferes with the accuracy of glucometer finger-stick measurements
- IVC at levels 15 grams and higher will cause a false positive glucometer reading
- This affects MOST glucometers using the electrochemical method
- The hexokinase serum glucose laboratory method is not affected
- Duration of the interference: 8-12 hours
- Oral vitamin C does NOT cause this glucometer interference
  - (Jackson & Hunninghake, 2006)





#### IVC | Infusion Rate and Adverse Reactions

- IVC is typically given by slow intravenous drip at a rate of 500 mg per minute.
- Faster infusions can lead to nausea, shakes, and chills
- IVC infusion rates in the 1000 mg per minute range create a pro-oxidant effect





#### IVC Push

- IVC push is generally not recommended
- The osmolality of high dose|rapid infusion can cause sclerosing of peripheral veins
- A safe Riordan Clinic IVC Push has been developed, tested and approved for use.
- (See IVC Push Video)
- Special instructions are required for intramuscular ascorbate



#### IVC | WARNING - Tumor Lysis Syndrome

- Tumor necrosis or tumor lysis syndrome has been reported in one patient after high-dose IVC (Campbell & Jack, 1979).
- Tumor lysis with IVC is extremely rare. Observed mostly in the early days of IVC therapy.
- Begin with the small 15 gram IVC dose
- Careful observation of all new IVC cancer patients is the best policy



#### IVC | PRECAUTION - Glucose 6 Phosphate Dehydrogenase Deficiency

- G6PD deficiency-caused hemolysis is rare
- Hemolysis has been reported in patients with G6PD deficiency when given high-dose IVC (Campbell, et al., 1975)
- Using the Riordan Protocol of 15, 25, 50 gram IVC infusions on successive days allows for ascorbate induction of higher G6PD levels in potentially susceptible patients
- A baseline G6PD test done early on is a good medical/legal strategy
  - NOTE hemolysis is more likely to be caused by accidental hypotonicity

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#### IVC | Renal Function Issues

- Adequate renal function, hydration, and urine voiding capacity must be documented prior to starting high-dose IVC therapy.
- Patients who show no prior signs or Hx of renal malfunction are unlikely to suffer ill effects to their renal systems as a result of intravenous ascorbate (Riordan, et al., 2005).
- The incidence of renal calcium oxalate stones during or following IVC is negligible (Riordan, et al., 2005).



#### IVC | PRECAUTION - Kidney Stones

- Ascorbate and Renal Stones
  - 6 yrs. study 45,251 men
  - 14 yrs. study 85,557 women
- Routine restriction of vitamin C to prevent stone formation appears unwarranted.
- If preexisting renal problems, caution is advised. (Riordan, et al., 2005), (Wong, et al., 1994).
  - Full blood chemistry and urinalysis work-up is thus recommended prior to the onset of IVC therapy.
  - With a history of kidney disorders --> kidney failure has been reported after ascorbic acid treatment.





#### IVC | More on Kidney Stones

- Oxalic acid excretion is less than 0.5% (80 mg) of the very large intravenous dose of AA (100 gm)
- Robitaille/Hoffer/Levine et al. Metabolism Clin and Exp 2009
- Oxalate nephrocalcinosis develops over months or years; therefore, this exposure poses a minor risk.
- Generally there is no association between a high daily intake of vitamin C and the risk of stone formation, even when consumed in large doses.
- Routine restriction of vitamin C to prevent stone formation appears unwarranted.



#### IVC | Prevention of Kidney Stones

- Magnesium deficiency, excessive intake of calcium supplements, acidosis, and dehydration are major causative factors in kidney stone formation - treat these!
- Large doses of vitamin B6 may reduce the risk of kidney stone formation in women.
  - Curhan et al. J Urol. 1996;15 5(6):1847-51.
  - Curhan et al. J Am Soc Nephrol. 1999;10:840-5.
- IVC patients with a tendency to develop kidney stones should be treated with caution.
  - NOTE conventional practitioners still live in the myth that vitamin C CAUSES kidney stones!





#### IVC | PRECAUTION - Fluid Overload

- IVC fluids could adversely affect ANY CONDITION that is complicated by fluid or sodium overload
  - Congestive heart failure,
  - edema,
  - ascites,
  - chronic hemodialysis,
  - unusual iron overload,
  - inadequate hydration or urine void volume (Rivers, 1987)





## IVC | WARNING - Ascorbate Extravasation is Painful!

- As with any I.V. infusion, infiltration at the site is possible.
- #23 Butterfly needles with a shallow insertion is very reliable with rare infiltrations NOTE: see my powerpoint on Butterflies
- Angio cath 22-24 are even better





## 3. Mixing Administration



# IVCa. Basic ConceptsMixingb. Osmolarity | Tonicityc. Which IVC Solution?

#### Administration





#### Why Do We Use Intravenous Nutrients?

- All life is composed of cells and cellular products
- If our cells are not healthy, our goal is
- to provide nutrients and fuel
- to facilitate detoxification
- Cellular transport/absorption/detoxification are crucial





#### **Concentration: The Membrane Gradient**

- Cell wall transporters
- Depend on healthy enzymes and a functional semi-permeable membrane
- With severe disease and membrane dysfunction, supplemental nutrients are often difficult to absorb in adequate amounts
- In particular, not enough vitamin C can be absorbed through the gut to obtain levels required for the anti-oxidant/oxidative effect.





#### "It's the Dose, Silly!"

- Curing the Incurable Dr. Thomas Levy (ala Dr. Fred Klenner)
- When we have the sick cell syndrome as in cancer
- The cell membrane transport mechanisms are not working well
- Generating a higher concentration on the external cell gradient can increase nutrient transport across the membrane
- Malignant cells have notably upregulate GLUT transporters
- Dehydroascorbate is more readily transported due to its similarity to glucose

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#### **KEY CONCEPT**

- Osmolarity is another way of saying CONCENTRATION
- Concentration is really "Cellular Membrane DOSAGE"
- Higher osmolarity often equals better membrane transport
- The limiting factor here is "Excessive osmolarity damages vascular endothelial cells"





#### Who Needs IV Fluids? (in general)

- Failing Patients...Serious Illness
- Chronic Fatigue, Fibromyalgia
- Infectious conditions such as Lyme or EBV
- Flu or flu-like symptoms
- Toxic conditions
- Cancer / Malignancies





## Who Should NOT get IV's (or with extreme caution)

- Kidney failure
- Advanced Congestive Heart Failure
- Any fluid overload situation i.e. anasarca
- IVC Infusion Excess Hypertonicity





#### a. Basic Concepts IVC b. Osmolarity | Tonicity Mixing c. Which IVC Solution?

#### Administration





#### **Isotonic Solutions**

- •240-375 mOsm/L
- This is the range of NORMAL plasma osmolarity
- •Examples:
- •0.9% saline
- •5% dextrose (D5W)
- Lactated Ringers





#### Hypotonic Solutions (by definition)

- Below 240 mOsm/L
- lower osmolarity than isotonic plasma
- Half norma saline = 0.45% NaCl = 160 mOsm/L
- Fluid tends to shift from blood into cells and interstitial spaces
- Useful in dehydration
- Use with caution in hypotension





#### Hypertonic Solutions

- Above 375 mOsm/L = higher osmolarity than plasma
  - Ex: 0.9% saline, 5% dextrose (D5W) and lactated ringers solution
- Shifts extracellular fluid from interstitial to the plasma
- Useful in hypotensive patients
- Could be harmful in hypertensive patients
- Electrolyte replacement solutions are hypertonic
- Most IV vitamin and mineral solutions are hypertonic





## Where Does Cellular Water Flow (with Hypertonic Solutions)

- When a cell is immersed into a hypertonic solution,
- The tendency is for water to flow OUT OF THE CELL
- in order to balance the concentration of the solutes.
- The cell "dehydrates"
- Patients receiving hypertonic solutions get very THIRSTY





#### IVC Infusions are Typically Hypertonic

- Examples: 10% dextrose in water (D10W)
- IVC Push
- Meyers Cocktails: 600 1200+ mOsm/L





#### **IVC Infusion - Tonicity**

- Isotonic Fluids
- 240-375 mOsm/L = normal plasma osmolarity
- Expands the extracellular fluid compartment





## a. Basic Concepts b. Osmolarity | Tonicity Mixing

c. Which IVC Solution?

### & Administration



IVC



#### IVC: Why Not Add Ascorbic Acid to Water





#### IVC: Which Solution? Normal Saline

- Normal Saline SODIUM CHLORIDE
- 0.9% sodium chloride
- Isotonic Solutions
- Uses
- fluid replacement
- alkalosis with fluid loss (emesis)





#### IVC: Which Solution? Sterile Water

- Sterile Water
- Hypotonic Solution ( !! )
- Extreme caution
- Do not forget to add the Sodium Ascorbate!
- An infusion of sterile water can cause hemolysis and death.





IVC | How is IVC Different from Normal Saline | Sterile Water?

HypertonicNo chloride





#### IVC: Which Solution? Ringer's Lactate

- Lactated Ringers/LR
- Isotonic Solution (similar to Normal Saline)
- Contains potassium and calcium
- (exchanged for Na ions = to blood plasma)
- Sodium, chloride, potassium and lactate come from NaCl (sodium chloride), NaC3H5O3 (sodium lactate), CaCl2 (calcium chloride), and KCl (potassium chloride)

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• Bicarbonate precursor (helpful for acidosis)



## IVC | Why Not Add Ascorbate to Ringer's Lactate?





#### **IVC:** Which Solution?

- Half-normal saline
- 0.45% sodium chloride
- Hypotonic Solution
- Lower osmolality
- Sodium Ascorbate could be safely added to Half-normal saline





#### IVC Osmolarity Made Simple

• Riordan IVC Standard Typically Used at Center





## 4. Drug Interactions



#### IVC | Efficacy of Chemotherapeutic Agents

- MOUSE MODELS of human lymphoma and multiple myeloma
- Mice treated with combination of
- Vitamin C and the drug bortezomib \*Velcade"
- More tumor growth than mice treated with bortezomib alone





#### IVC | Efficacy of Chemotherapeutic Agents

• Slide One Chart





## IVC | Efficacy of Chemotherapeutic Agents (copy)

- Slide Two Chart
- Note decreased efficacy "in vitro" of methotrexate and TRAIL Ligand with vitamin C





## 5. Monitoring Outcomes



#### **5. MONITORING OUTCOMES**





#### IVC Protocol: 15, 25, 50 gr

- Begin with a series of three consecutive IVC infusions at the 15, 25, and 50 gram dosages
- Follow each infusion with a "post IVC saturation level" (a plasma C level after !VC)
- This will help the administering physician to determine the patient's oxidative burden

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• These three levels will help to determine the optimal dosage for subsequent IVC's



#### **Post-IVC Saturation Levels**

- Therapeutic goal of reaching a peak-plasma concentration of ~20 mM (350- 400 mg/dL) is most efficacious.
- The first post IVC plasma level following the 15 gram IVC has been shown to be clinically instructive:





## Levels below 100 mg/dL correlate with higher levels of existent oxidative stress:

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- Higher tumor burden,
- Chemo/radiation damage,
- Hidden infection,
- Root canals
- Chronic Apical Periodontitis
- Tonsillitis
- Methylation disorders
- Other oxidative insults
- Smoking
- Stress



#### **Co-morbidities**

- If after four infusions the post IVC dosage remains sub-therapeutic:
- Investigate and treat (as best you can) co-morbidities (some examples follow)

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- infection
- diabetes
- smoking
- tumor progression
- increase the 100 gram IVC frequency to three times per week.



#### **IVC** Infusion

• Higher infusion doses beyond 100 grams are not recommended without serum osmolality testing





## Post 15 gram IVC Serum Ascorbate Levels in Healthy vs. Cancer Patients by Stage

• See chart





#### Quick Recap of Osmolarity/Tonicity

- Isotonic solution = 290 (240-375) mOsm/L
- Hypertonic solution = > 375 mOsm/L
- < 600 mOsm/L guarantees maximum safety
- 600 -1200 mOsm/L is generally well tolerated
- Hypotonic solution = < 240 mOsm/L
- Fluid invades the cells
- Water intoxication (the bloated cell)
- Minimum osmolarity for solution that can be infuse to prevent hemolysis of RBC's is 145 mOsm/L





#### Conclusions

- Vitamin C can be safely administered by intravenous infusion at maximum doses of one-hundred grams or less,
- provided the precautions outlined in this report are taken.
- At these doses, peak plasma ascorbate concentrations generally exceed 20 mM or 400 mg/dl

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• High concentrations of IV ascorbate is preferentially toxic to tumor cells

