Clinical Approach to Aging Reversal and Health Span Optimization

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The concept of biological age vs chronological age has been studied now in-depth for quite some time. This focus on epigenetic or the pace of aging has us as practitioners and patients both evaluating our health and longevity from this new perspective. Laboratory values of blood count, liver function and kidney filtration rate can now be augmented with data from programmed multi-tissue epigenetic clocks that enable us to evaluate and assess practical modalities that truly extend lifespan.

We credit the development of the first-generation clocks to Horvath and Hannum. They predicted all-cause mortality using regression models based on CPG methylation status. [1] Second generation clocks such as the Grimm age added blood and health bio markers, calculating time till death. [2] The DunedinPACE clock has created an even more accurate evaluation of the aging rate and mortality risk as it uses CPG sites and blood and health markers within individual patients. [3]

Therapeutic plasma exchange has been shown to remove pathologic inflammatory markers [4] and treat a multitude of diseases including those with an autoimmune and neurological basis. [5-6] Recently published by the Conboy lab was a plasma exchange study illustrating that the "dilution of old blood plasma yields an increase in the determinants of brain maintenance and repair in mice and in people." They quoted…" rapid cognitive improvements of old mice in this study are thought to arise from abrogating (through NBE-Neutral blood exchange) the otherwise age-increased extent of neuroinflammation." [7]

Young plasma benefits as quoted by the Wyss-Coray lab at Stanford:

Intriguingly, we observed an almost universal loss of gene expression with age…aged blood reduces global gene expression, and young blood restores it.

- Immune cell accumulation in adipose depots is a fundamental feature of ageing, and indeed most types, including T cells, B cells, neutrophils, and plasma cells, accrue across diverse organs.

- 1,000 hematopoietic stem cells genes are altered by young blood, perhaps indicating a tight-knit relationship between ageing of the immune system and changes in blood composition.

- Rejuvenation appears to be a much more concerted process: the core network of ageing rescued by rejuvenation consists of mitochondrial electron transport chain genes for multiple cell types.

Young blood both reverses age-related profiles and initiates novel pathways. Systemic rejuvenation of genes encoding components of the electron transport chain is especially striking.

- young blood is a potent instigator of mitochondrial function.

- mitochondrial genes arise even for cell types in which age-related decline is not evident, like marrow monocytes, supporting the notion that young blood may indeed broadly enhance mitochondrial function. [8]

Past young Fresh Frozen Plasma (yFFP®) patients have reported improvements in:

Eczema

Autoimmune Graves' - ophthalmic disease and peripheral neuropathy

Blood glucose and diabetes - meds eliminated or cut in half

Knee pain/degenerative arthritis - that PRP could not help

Lower spine/back pain

Torn rotator cuff and resolution of pain, and muscle pathology

Improvement of erectile dysfunction

Eyesight improvement documented from 20/40 to 20/20

Combining an approach of removing aliquots of plasma and then replacing the same amount with young Fresh Frozen Plasma (yFFP) joins 2 therapies with maximal effect.

Preliminary results of two yFFP exchange case studies that are ongoing:

Patient A:

56 year old male – received a 3 liter albumin/saline Total Plasma Exchange 2 weeks prior to his young Fresh Frozen Plasma Mini Exchange. On the day of his infusion, he received a 1 liter removal of his plasma and then a 1 liter replacement with Spectrum Plasma yFFP.

A baseline test before his receiving the 3 liter albumin/saline exchange is not available. Within 2 weeks of receiving his young fresh frozen plasma he reported:

"First, over the past year I've experienced dry mouth. Doc says it's cuz I'm not metabolizing my depression meds as well since I'm older. For over a week now … very very little dry mouth.

Second, I've been on a diet for the last couple of months and the weight loss has been difficult - until the past week and a bit. Pounds are coming off much easier. Noticeably easier.

Third, when I was intimate with my wife the other day, she said I was much much firmer down there."

TruDiagnostic Testing: https://trudiagnostic.com/

Test 1 – Baseline

Test 2 – 4 weeks post treatment with 1 liter of yFFP

	Test 1	Test 2	Output.Details
Age	56.84	56.92	Chronological Age
PCHorvath1	58.93826	56.98489	PC Clock (Intrinsic - Multitissue)
PCHorvath2	58.6914	57.35199	PC Clock (Intrinsic - Blood and Skin)
PCHannum	61.78434	60.58957	PC Clock (Extrinsic)
PCPhenoAge	56.49739	54.08244	PC Clock (PhenoAge)
PCDNAmTL	6.76875	6.825804	PC Clock (Telomere Length)
PCPACKYRS	3.338655	4.139319	PC Clock (Smoking Pack Years estimate)
PCADM	380.6505	378.7099	PC Clock (ADM protein level estimate)
PCB2M	2802919	2796946	PC Clock (B2M protein level estimate)
PCCystatinC	644339.2	644120.1	PC Clock (CystatinC protein level estimate)
PCGDF15	615.5532	608.3828	PC Clock (GDF15 protein level estimate)
PCLeptin	2949.7233	2922.2506	PC Clock (Leptin protein level estimate)
PCPAI1	31632.02	31517.74	PC Clock (PAI1 protein level estimate)
PCTIMP1	33611.31	33626.09	PC Clock (TIMP1 protein level estimate)
PCGrimAge	68.01181	67.9682	PC Clock (GrimAge)
DunedinPACE	1.1367605	1.1074413	DunedinPACE

Comparing Baseline to 1 month:

PCGrimmAge - decrease of .04 years

PCPhenoAge - decrease of 2 years

DunedinPACE - rate of aging decrease of 3.6%

(2 month results pending)

Patient B:

70 year old male - received a 1 liter removal of his plasma and then a 1 liter replacement with Spectrum Plasma yFFP.

Skin color and energy significantly improved.

Weight loss of 10 pounds within one week with minimal to no effort.

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Test 1 - Baseline

Test 2 - 2 weeks post treatment with 1 liter of yFFP

Test 3 - 4 weeks post treatment with 1 liter of yFFP

	Test 1	Test 2	Test 3	Output.Details
Age	70.2	70.25	70.32	Chronological Age
PCHorvath1	83.04473	87.32947	85.73588	PC Clock (Intrinsic - Multitissue)
PCHorvath2	82.39023	86.62639	82.8635	PC Clock (Intrinsic - Blood and Skin)
PCHannum	79.4805	84.02411	75.72321	PC Clock (Extrinsic)
PCPhenoAge	73.28941	77.31429	71.46241	PC Clock (PhenoAge)
PCDNAmTL	6.551729	6.51663	6.703349	PC Clock (Telomere Length)
PCPACKYRS	5.064994	6.557692	-0.3837024	PC Clock (Smoking Pack Years estimate)
PCADM	402.2327	408.6681	395.2066	PC Clock (ADM protein level estimate)
PCB2M	3021418	3025546	2990643	PC Clock (B2M protein level estimate)
PCCystatinC	692698.2	693703.2	694864.8	PC Clock (CystatinC protein level estimate)
PCGDF15	754.6231	767.8981	748.6947	PC Clock (GDF15 protein level estimate)
PCLeptin	2655.776	2300.257	2453.158	PC Clock (Leptin protein level estimate)
PCPAI1	29785.81	30193.4	25544.22	PC Clock (PAI1 protein level estimate)
PCTIMP1	34382.02	34491.37	33166.33	PC Clock (TIMP1 protein level estimate)
PCGrimAge	76.43525	77.7389	71.31552	PC Clock (GrimAge)
DunedinPACE	0.9738137	1.1037873	1.0071406	DunedinPACE

In this case, we see a type of hormesis reaction evident at the 2 week point where the system is strained and the parameters worsen.

Comparing Baseline to 2 weeks:

PCGrimmAge - increase of 1.3 years

PCPhenoAge - increase of 4 years

DunedinPACE - increase of .1%

Comparing Baseline to 1 month:

PCGrimmAge - decrease of 5.1 years

PCPhenoAge - decrease of 1.8 years

DunedinPACE - increase of .03%

(2 month results pending)

References:

[1] DNA Methylation Clocks and Their Predictive Capacity for Aging Phenotypes and Healthspan https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7376380/#:~:text=Both%20Hannum%20and%20Horvath%20clocks,they%20share%20only%206%20CpGs.

[2] GrimAge Outperforms Other Epigenetic Clocks in the Prediction of Age-Related Clinical Phenotypes and All-Cause Mortality https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8087266/

[3] DunedinPACE, a DNA methylation biomarker of the pace of aging https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8853656/

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4588244/

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7415086/

[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7984263/

[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8050203/

[8] https://www.nature.com/articles/s41586-022-04461-2

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