Terrestrial Spaceflight Analogs:

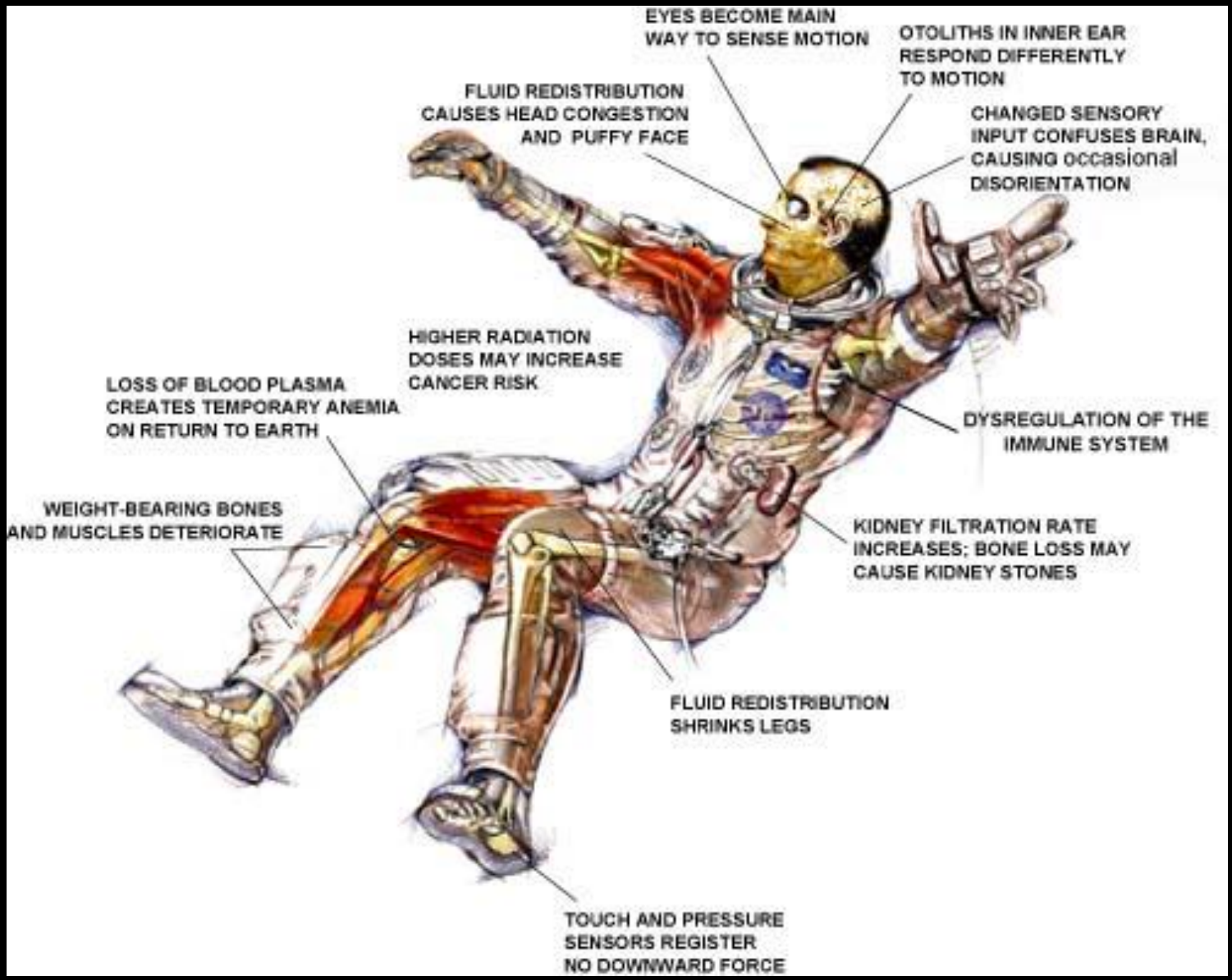
Antarctica

Brian Crucian
September 17, 2013

Photo: ESA/Alex Salam

Spaceflight Physiology

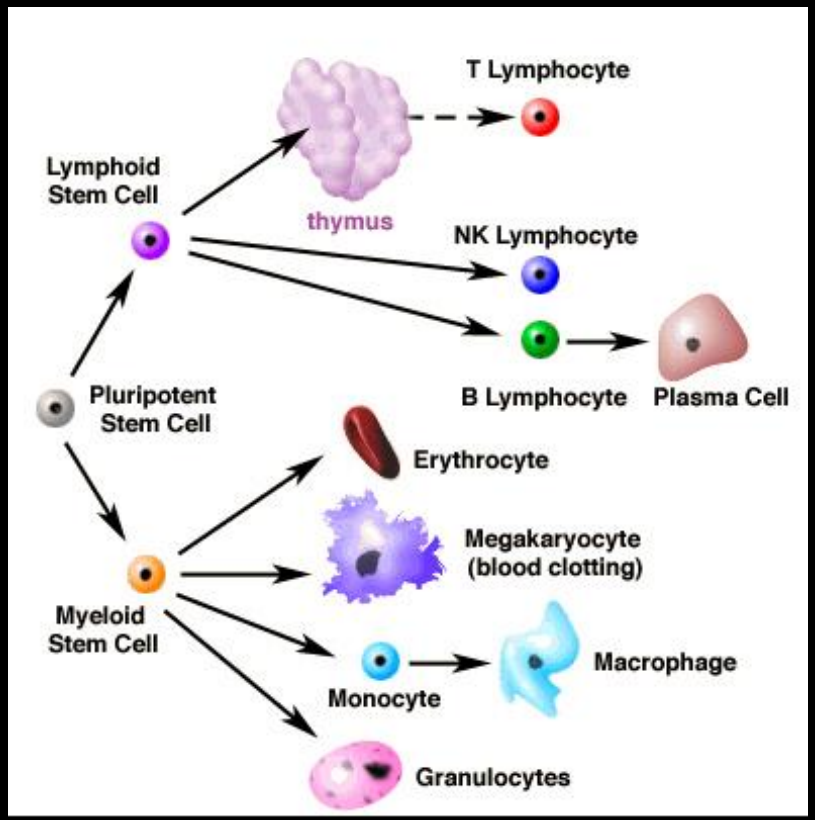
Microgravity Effects on the Human Body

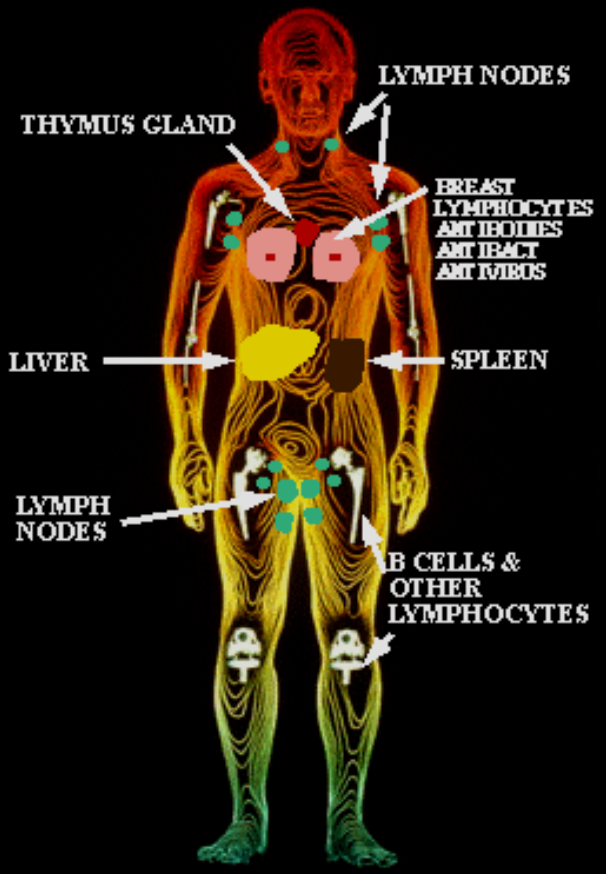


THE IMMUNE SYSTEM

•One of largest tissues in the human body, although largely in fluid state.

•Consists primarily of white blood cells (WBCs) located in lymph nodes and the peripheral blood.

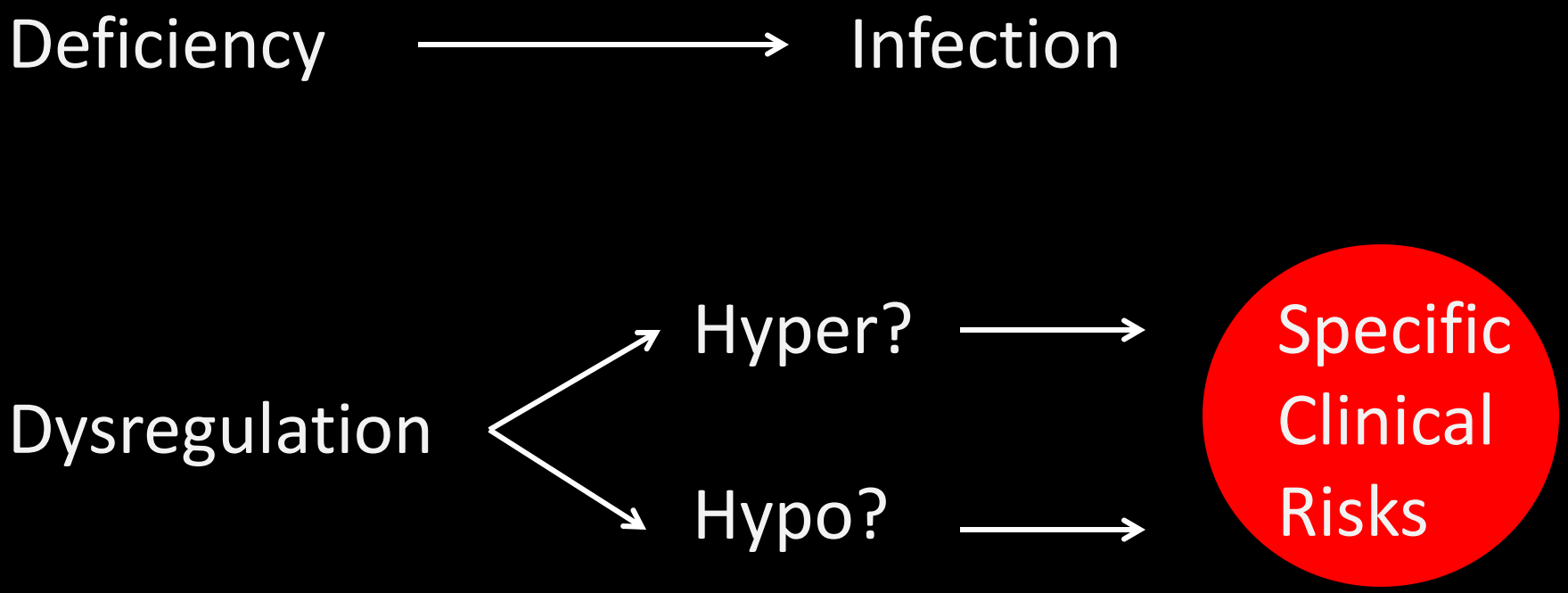




•Responsible for protection against viral and bacterial infection, latent viral reactivation, tumor surveillance, wound healing, etc.

•Dysregulation can result in increased infection rate, malignancy, autoimmunity, allergy, etc.

Immune System Disease

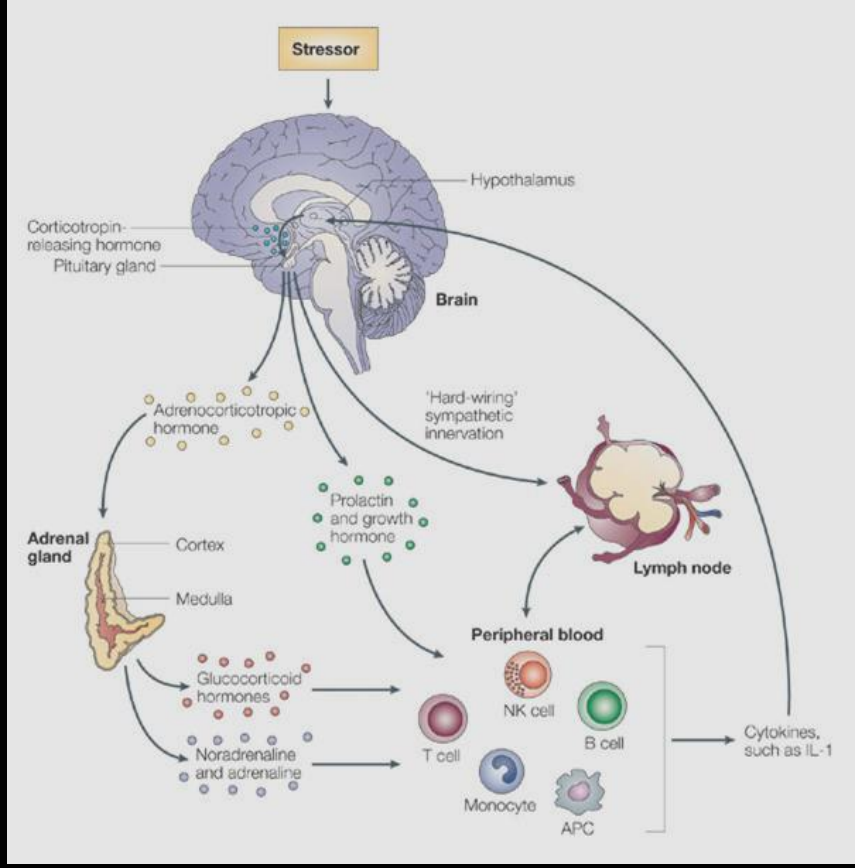


Stress

Acute

Fight or Flight
ANS/Sympathetic NS
Catecholamines
Shorter space flight?

↑NK cytotoxicity
↓ T regulatory cells



Chronic

Anxiety, worry (rest/digest)
HPA
Corticosteroids
Longer space flight?

↓NK, CTL function
↓ IL-2, IFN
↓ DTH
↑ IL-4
↑Ab levels
↑ Illness severity

CYTOKINE NETWORK and DISEASE

Th1 - Immunity to intracellular pathogens, viruses

Normal Function

- Cell Mediated 'Inflammatory' Response
- Fight intracellular pathogens (viruses)
- Control DTH response to skin viral/bacterial antigens
- Fight tumor formation
- Phagocyte dependent inflammation

Disease correlations:

Rheumatoid arthritis
organ specific immune disorders
Chohn's disease
Sarcoidosis
Acute allograft rejection
Unexplained recurrent abortions
Multiple sclerosis

Th2 - Antibody response to extracellular pathogens, parasites

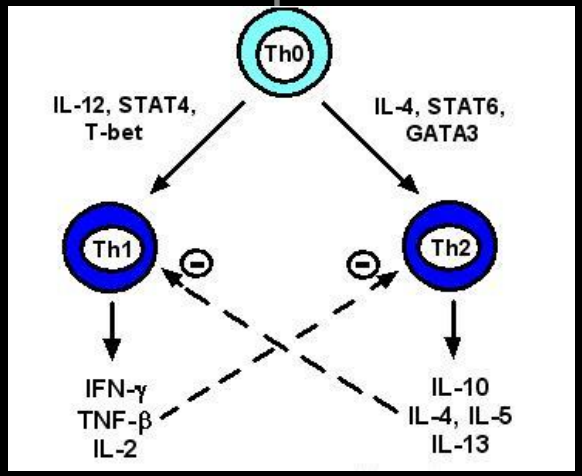
Normal Function

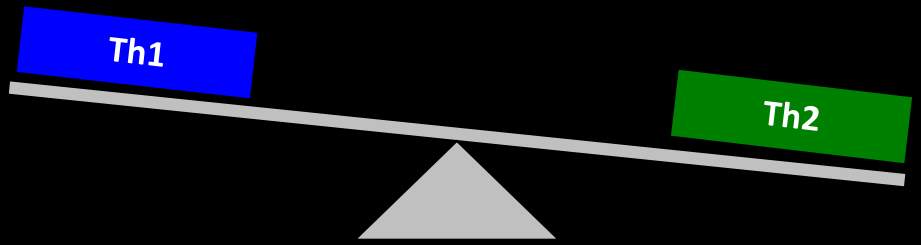
- Humoral (Antibody) Responses
- 'Anti-Inflammatory Response

Disease correlations:

Rapid progression of HIV to AIDS
Chronic graft vs. host disease
Systemic autoimmune diseases
Atopic asthma
Scleroderma
Serum lupus erythematosus
Chronic allergies/sensitization
Atopic dermatitis

- Genetics
- Pathogen
- Local APC Ck environment (NK=IFN;, DC:IL-10, Mast:IL-4)
- Antigen dose/route





NUTRITION

Proper nutrition is a requirement for a normal immune response. Deficiencies in any of several dietary requirements have been linked to diminished immune function and/or clinical illness

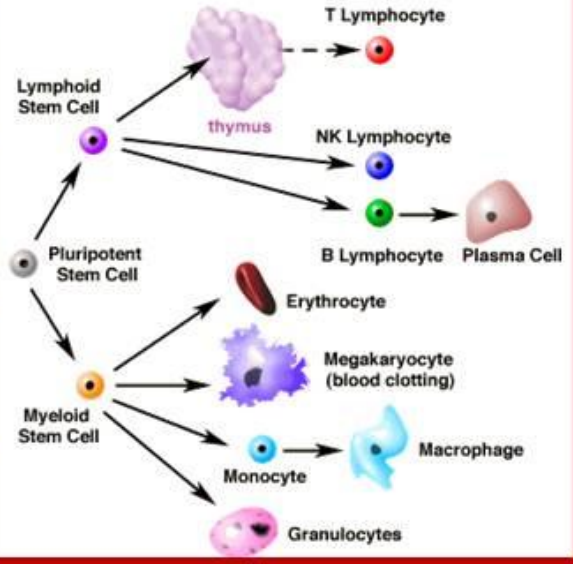
RADIATION

Immune cells generally susceptible to radiation damage. Peripheral T and B cells via apoptosis induction; and via lethal damage to marrow stem cells

BONE

Within the bone marrow cavity, cytokines produced by immune cells also have important effects on regulating bone homeostasis. RANKL, M-CSF, TNF, ILs, and IFNs, affect the differentiation and activity of osteoclasts and bone resorption. During chronic inflammation, the balance of bone modeling and remodeling can be greatly affected.

IMMUNE SYSTEM



NEUROLOGY

A reciprocal flow of information and functional connection exists between the nervous and immune systems. Communication occurs via soluble mediators and cell-cell contacts.

MICROBIOLOGY

Host-pathogen interactions determine susceptibility to disease. Microbial virulence in conjunction with immune status determines the magnitude and outcome of infection

EXERCISE

Research is uncovering a link between moderate, regular exercise and a strong immune system. However, there is also evidence that too much intense exercise can reduce immunity and may even make you sick

MICROBES INCREASE VIRULENCE

STRESS

MICROGRAVITY

DISRUPTED CIRCADIAN RHYTHMS

RADIATION

ISOLATION

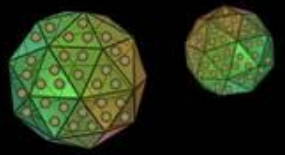
REDUCED IMMUNE CELL FUNCTION

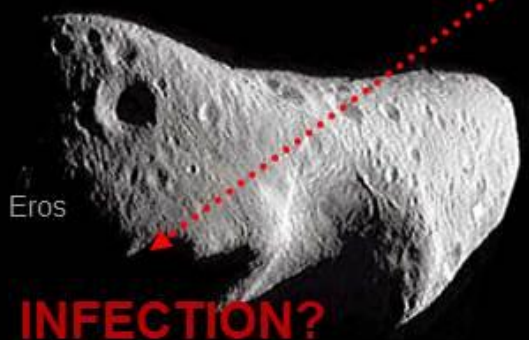
ALTERED CYTOKINE BALANCE

Th1/ Th2

LATENT VIRUS REACTIVATION

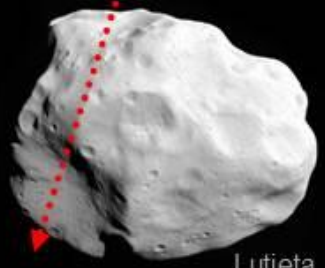
INCIDENCE?





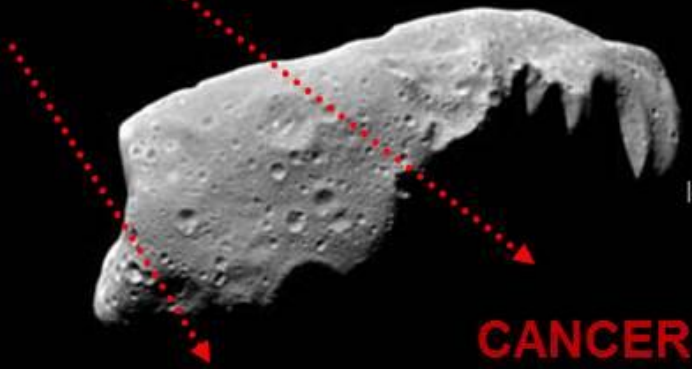
Eros

INFECTION?



Lutieta

HYPERSENSITIVITY?



Ida

CANCER?

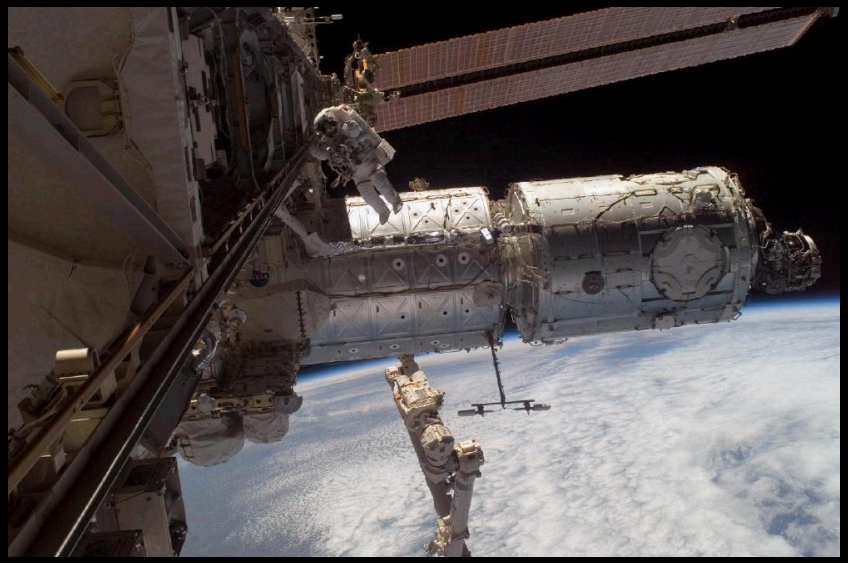
AUTOIMMUNITY?

Spaceflight Analogs

SPACEFLIGHT GROUND ANALOGS

- Validation of monitoring strategy, countermeasures
- Determination of mechanism
- Validation of flight hardware

WHAT CAUSES IMMUNE CHANGES DURING SPACEFLIGHT?



FLIGHT-RELATED

-Radiation

-Microgravity

MISSION-ASSOCIATED

-Physiological stress

-Confinement

-Prolonged isolation

-Altered microbial environment

-Altered nutrition

-Disrupted circadian rhythms

What are GROUND BASED SPACEFLIGHT ANALOGS?

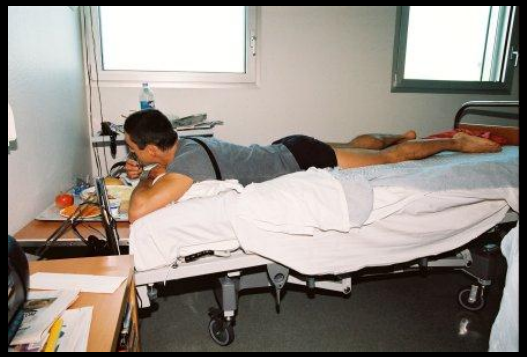
-Simulate some aspects of spaceflight on Earth for research purposes.

-Routinely used for human physiology research, development of a monitoring strategy, investigation of mechanism, countermeasures development/validation.

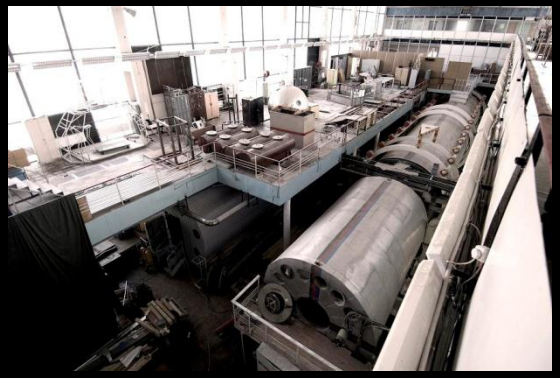
-Useful considering the microgravity restrictions on flight hardware.

(Human) Ground-based Space Flight Analogs

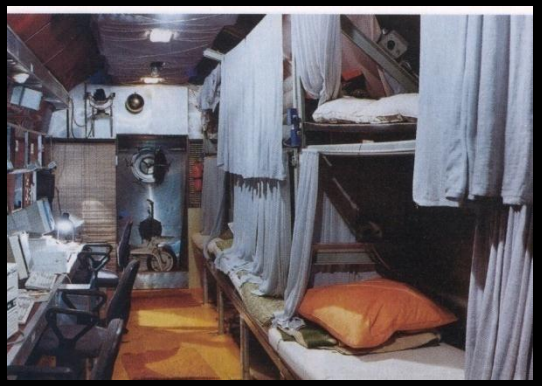
Extended head-down bed rest



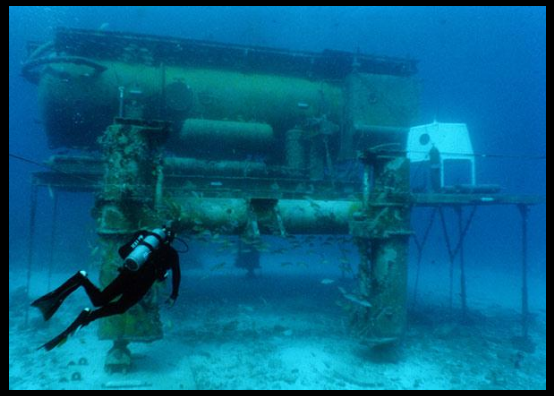
MARS-500 (IBMP – Moscow)



Closed Chamber Confinement



NEEMO Aquarius Station



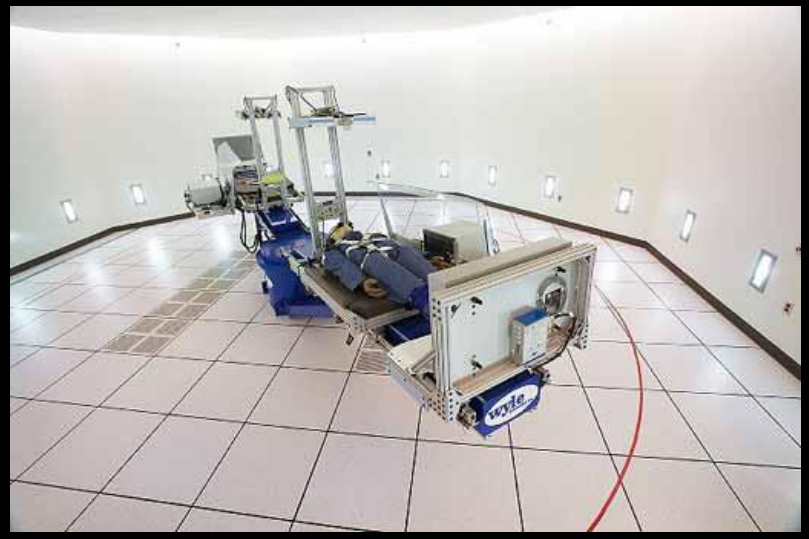
Haughton-Mars Project

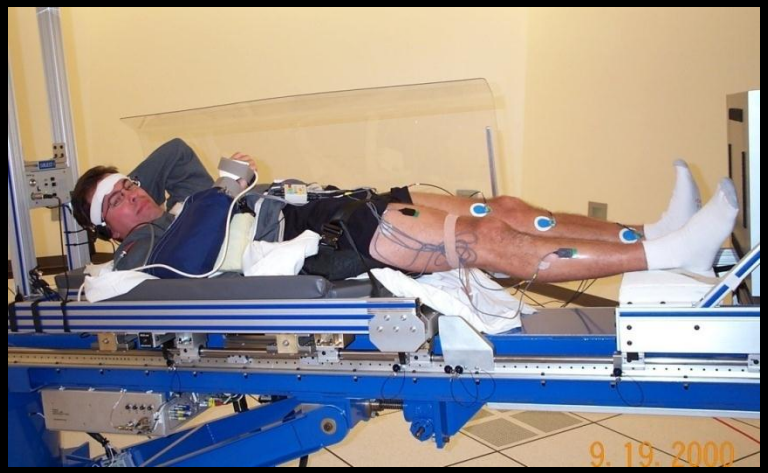
Antarctica winter over

Best Analogs for SAID

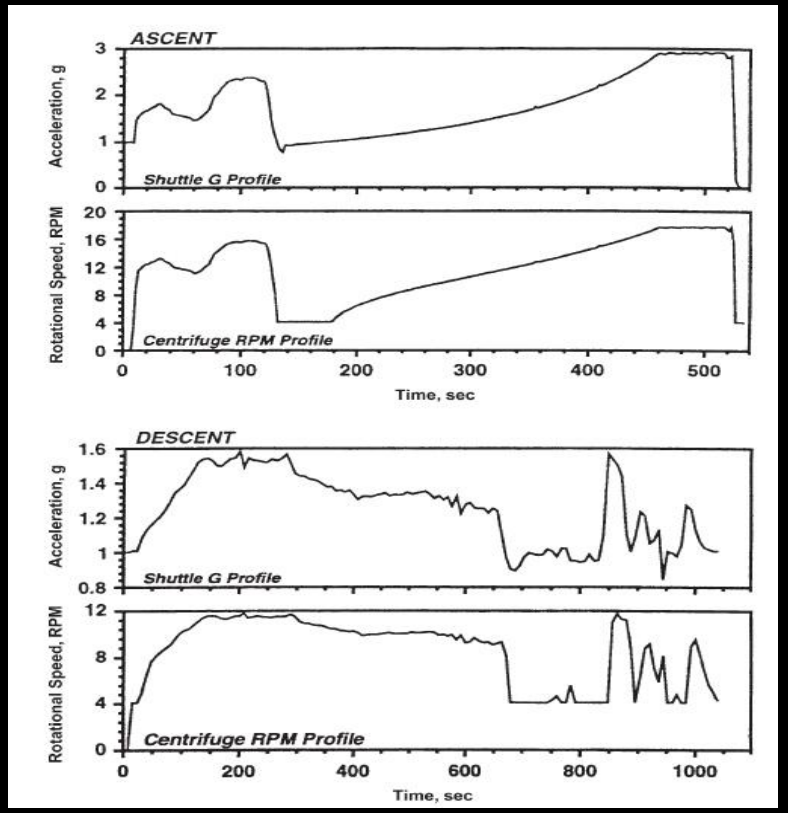
An analog which simulates (or actual) mission-deployment, associated risk, adverse environment, isolation, psychological/physiological stress, disrupted circadian rhythms, etc.

Bed Rest + Artificial Gravity





Bed Rest + Artificial Launch/Landing Stress



1xG CONTROL

MODELED MICROGRAVITY

Red: Actin localization

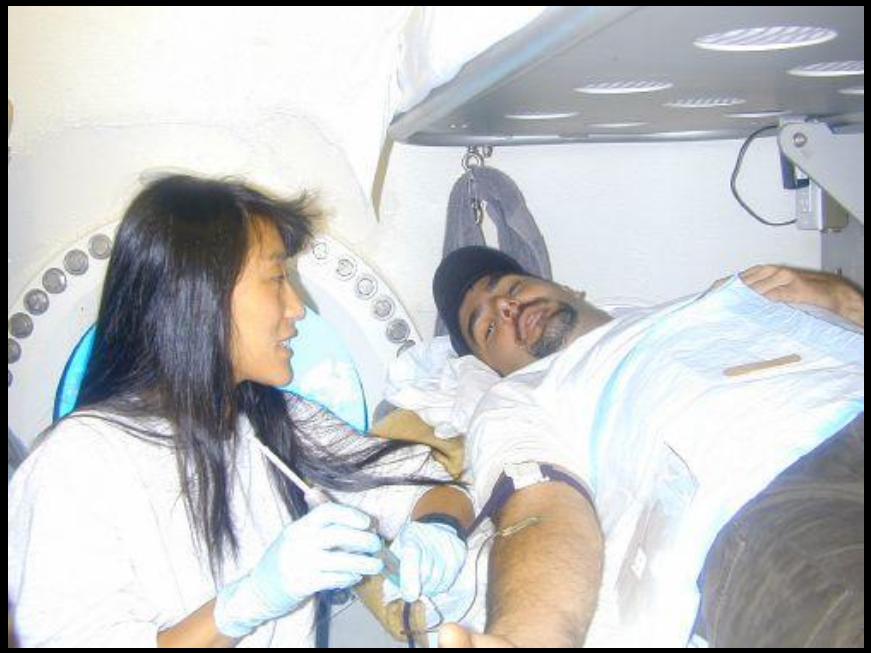
Green: Microtubules/MTOC

-Mayra Nelman-Gonzalez/JSC

NEEMO Aquarius Station
(Key Largo - Florida)


AQUARIUS
6. 30. 2003

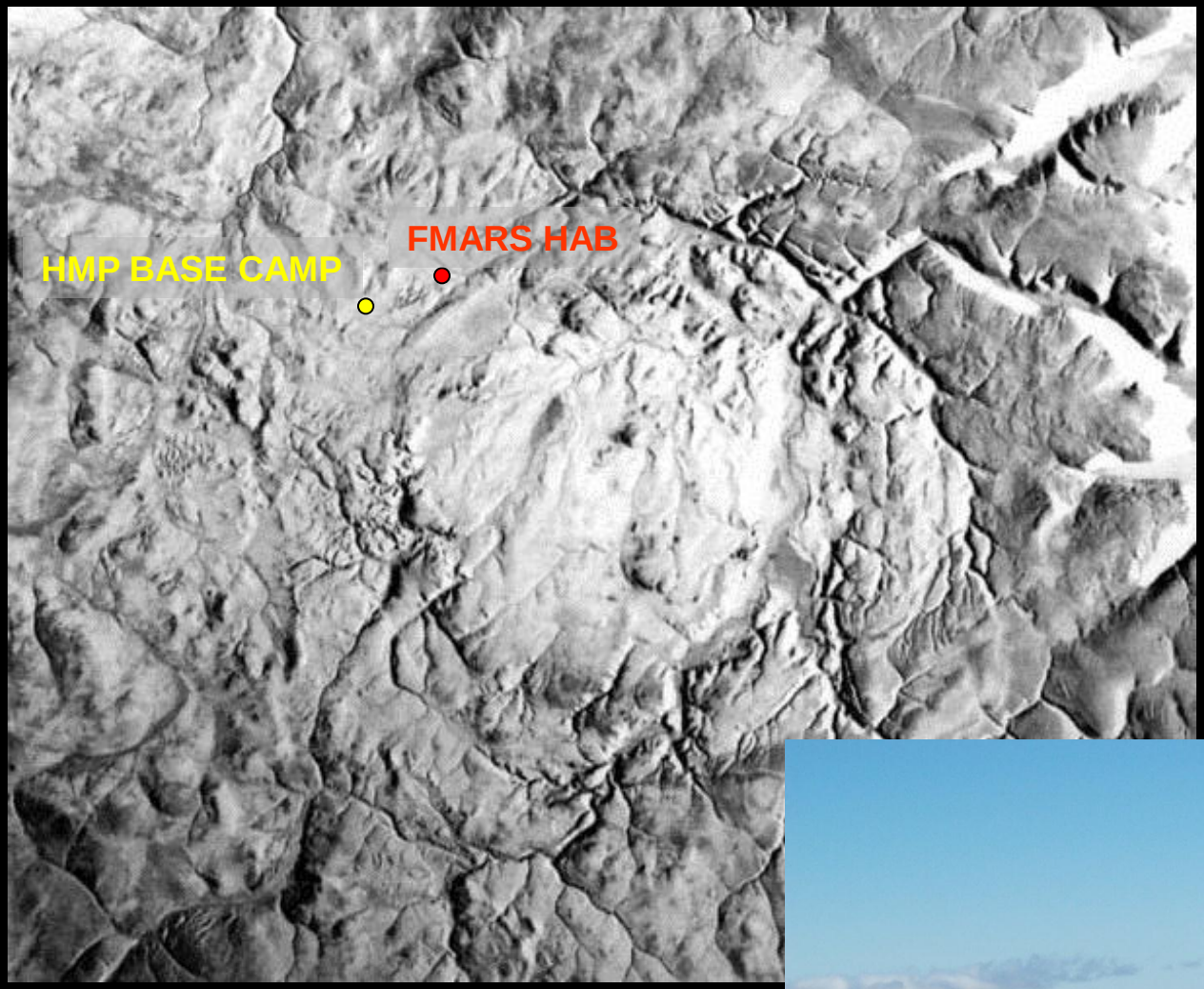

RV RESEARCH
DIVER
6. 23. 2003




6. 22. 2003

Haughton-Mars Project
(High Canadian Arctic – Devon Island)

Haughton Crater



Antarctica

Antarctica is the highest, driest, windiest, emptiest, coldest place on earth. An ice sheet covers all but 2.4 percent of Antarctica's 14 million square kilometers.

At its thickest point the ice sheet is 4,776 meters deep and averages 2, 160 meters thick. This is 90 percent of all the world's ice and it is 70 percent of all the world's fresh water.

The mean annual temperature at the South Pole is minus 56 degrees F. During the Austral Summer, temperatures at McMurdo base, on the Ross Sea, may get as high as 40 degrees F, while at the South Pole, at the Amundsen- Scott station, temperatures may reach 0 degrees F.

The area below 60 degrees south enjoys one long day and one long night each year. The sun sets in March and rises in October.

At the dawn of the 1900s, Antarctica remained the only continent untouched by humans. In 1895, the 6th International Geographical Congress declared that Antarctica's ice-choked seas and frozen peaks were the next frontier for scientific discovery, ushering in what has come to be known as the Heroic Age of Antarctic Exploration.

The Antarctic continent wasn't even actually seen until 1820.

No man set foot in Antarctica until 1895. The first human landing there is claimed by Henryk Bull, with a party from a whaling ship. They landed at Cape Adare . It was 1935 before the first woman set foot there. Her name was Catherine Mikkelson, and she was the wife of a Norwegian whaling captain.

The South Pole was first reached by a Norwegian named Roald Amundsen in 1911, and shortly after by British explorer Robert Scott.

Amundsen and crew at the South Pole, December 14, 1911

Eskimos and polar bears are found in the ARCTIC, not the Antarctic.

All warm-blooded animals living on and around Antarctica--whales, seals, sea birds, penguins--rely on thick layers of blubber to insulate them from the cold.

Plants grow in Antarctica in ice-free regions (only about 2 percent of the continent is ice-free). Lichens and moss grow in any favorable niche.

There are 21 species of penguins in Antarctica, including Emperor, Rockhopper and Adelie.

There are actually more petrels than there are penguins! Petrels include albatrosses, fulmars, prions, shearwaters, storm petrels, diving petrels and Gadfly petrels. Other birds that live in or breed in Antarctica include cormorants, gulls, and skuas

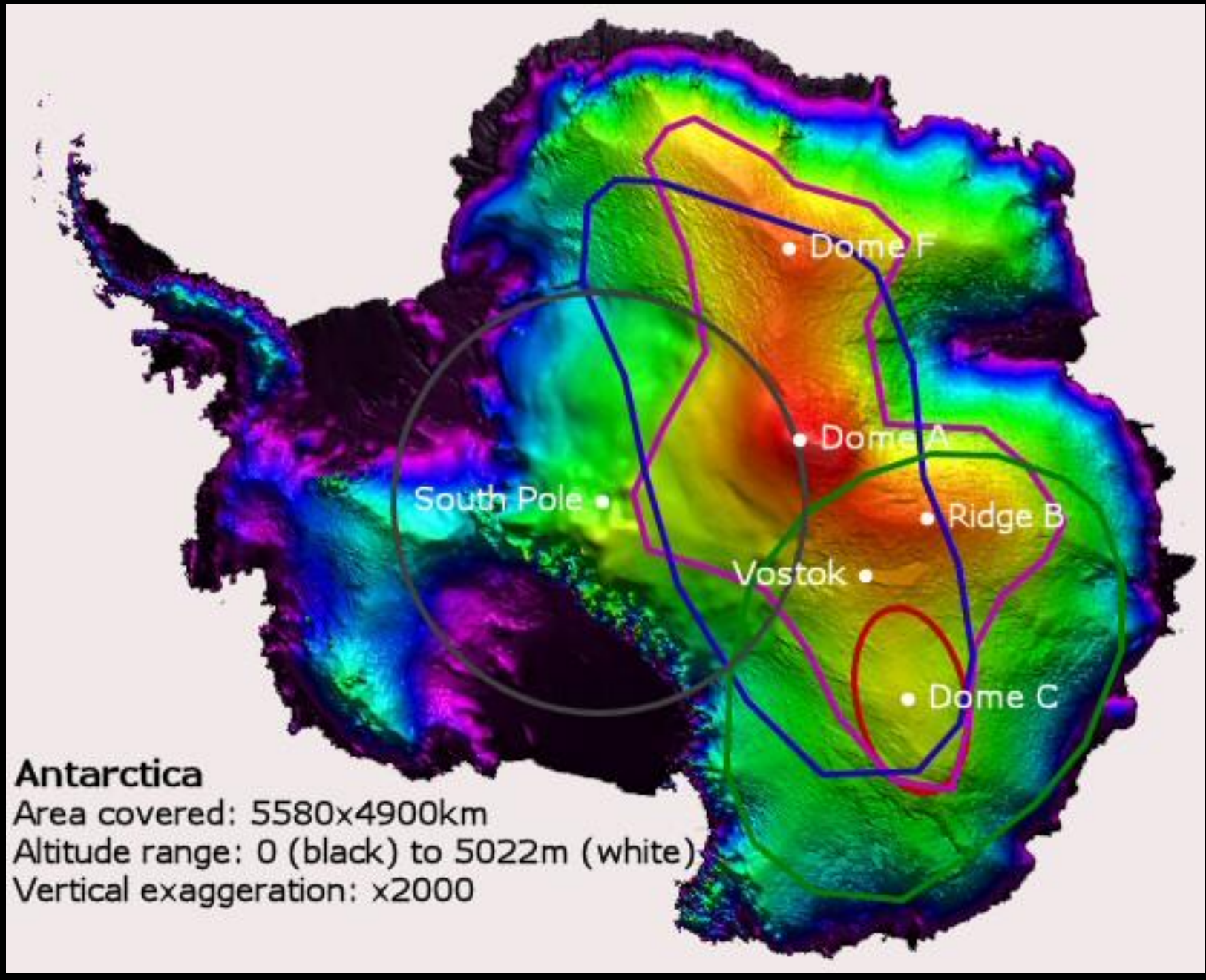
Ernest Shackleton

Nimrod Expedition 1907-1909: 112 miles from Pole, first ascent of Mt. Erebus, first plot of magnetic pole

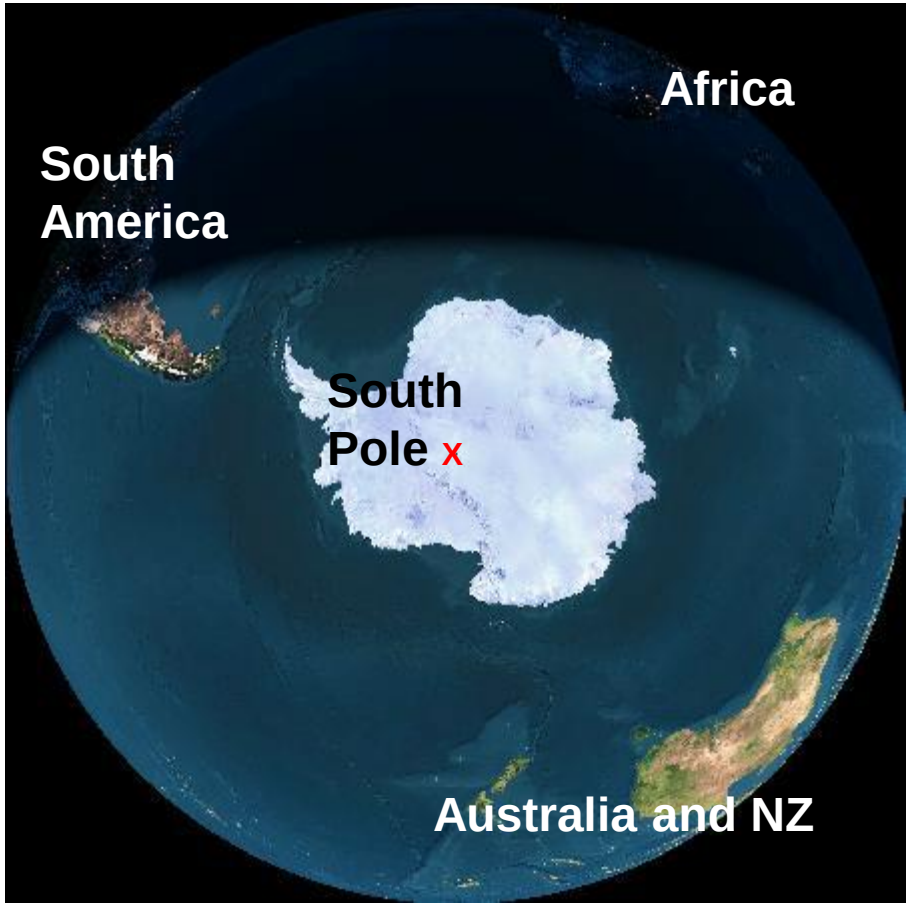
Endurance Expedition 1914-1916: Planned trans Antarctic traverse.


SOUTH AMERICA
PUNTA ARENAS
SOUTH GEORGIA
750 MILES
ELEPHANT ISLAND
GRAHAM LAND
WEDDELL SEA
COATS LAND
1 - Depart Grytviken, South Georgia, Dec 5 1914
2 - Entered Pack-ice, Dec 7 1914
3 - Endurance trapped, Jan 18 1915
4 - Endurance crushed, Oct 27 1915
5 - Endurance sunk, Nov 21 1915
6 - Launched boats for Elephant Island, Apr 9 1916
7 - Boat journey to South Georgia, Apr 24-May 10 1916
8 - Shackleton and 3 others reach Stromness whaling station, May 20 1916
9 - Three crew from small boat rescued from beach on South Georgia, May 21 1916
10 - Crew rescued from Elephant Island, Aug 30 1916


British Claim
Norwegian Claim
Indian Ocean
Scotia Sea
South Orkney Islands
Orcadas (Argentina)
Argentine Claim
Brazilian Zone of Interest
Weddell Sea
Bellingshausen Sea
Peter I Island
Ronne Ice Shelf
Fossil Bluff (U. K.)
Filchner (Germany)
Halley (U. K.)
Belgrano II (Argentina)
Druzhnaya-3 (Soviet Union)
Dresdner (Germany)
Georg von Neumayer (Germany)
Sanae (South Africa)
Maitri (India)
Dakshin Gangotri (India)
Georg Forster (Germany)
Novolazarevskaya (Soviet Union)
Troll (Norway)
Aboa (Finland)
Serie Marais (South Africa)
Wasa (Sweden)
Asuka (Japan)
Syowa (Japan)
Molodezhnaya (Soviet Union)
Mizuho (Japan)
Mawson (Australia)
Dovers (Australia)
Soyuz (Soviet Union)
Progress (Soviet Union)
Zhongshan (China)
Davis (Australia)
Law (Australia)
Mirnyy (Soviet Union)
Edgeworth David (Australia)
Oasis II (Soviet Union)
Vostok (Soviet Union)
Dome C
Casey (Australia)
Amundsen-Scott (U. S.)
South Pole
Byrd (U. S.)
Ross Ice Shelf
McMurdo (U. S.)
Vanda (New Zealand)
Scott (New Zealand)
Cape Bird (New Zealand)
World Park (Greenpeace)
Terra Nova Bay (Italy)
Gondwana (Germany)
Dumont d'Urville (France)
Leningradskaya (Soviet Union)
Lillie Marleen Hütte (Germany)
Commonwealth Bay (Australia)
Russkaya (Soviet Union)
Ross Sea
Balleny Islands
Antarctic Circle
New Zealand Claim
Australian Claim
Australian Claim
limit not defined
limit not defined
limit not defined
20° W
25° W
53° W
74° W
80° W
150° W
45° E
136° E
142° E
60°
70°
80°
90°


Dome F
Dome A
South Pole
Ridge B
Vostok
Dome C
Antarctica
Area covered: 5580x4900km
Altitude range: 0 (black) to 5022m (white)
Vertical exaggeration: x2000

Antarctica covers the South Pole



Midnight at the pole 21st December

Midday at the pole 21st June

The commonest way to get to Antarctica is still by ship. This means crossing the “Drake’s Passage”, the narrow band of sea between Cape Horn and the Antarctic Peninsula. It is the roughest sea on Earth.

Increasing numbers of people now arrive in Antarctica by air. Ice runways are becoming more and more common and this is an increasingly common form of transport for those on scientific bases. The passengers can be dropped off in South America or Australia for onward transport rather than spending weeks on board ships as was the case until relatively recently.

As the winter approaches, the only people left behind in Antarctica are scientists and support staff on research stations. About 1000 people in an area 1.5 times larger than the USA. Sea-ice doubles the area of Antarctica at this time and flights are very rarely attempted due to the darkness and weather conditions. This is Signy station (UK).

Antarctic bases old and new. In the foreground on Hut-Point McMurdo Sound is Scott's 1904 hut from the Discovery expedition that housed 25 men, in the background is the modern McMurdo base that houses about 250 people in the winter and around 1000 in the summer – it is far and away the largest Antarctic Base.

The interior of Scott's hut is preserved like a time capsule. A combination of lack of visitors, cold temperatures and great respect shown by the few visitors there have been means that many items are exactly as they were when left over 100 years ago.

Amundsen-Scott Base at the South Pole. This base houses 75 over the winter and 250 in the summer. It is the third base in this location, the previous two were buried by accumulating snow and ice. Like other modern base designs built on ice, this is elevated on legs and can be raised to stay clear when the accumulation threatens to take over.

Dumont d'Urville (France)

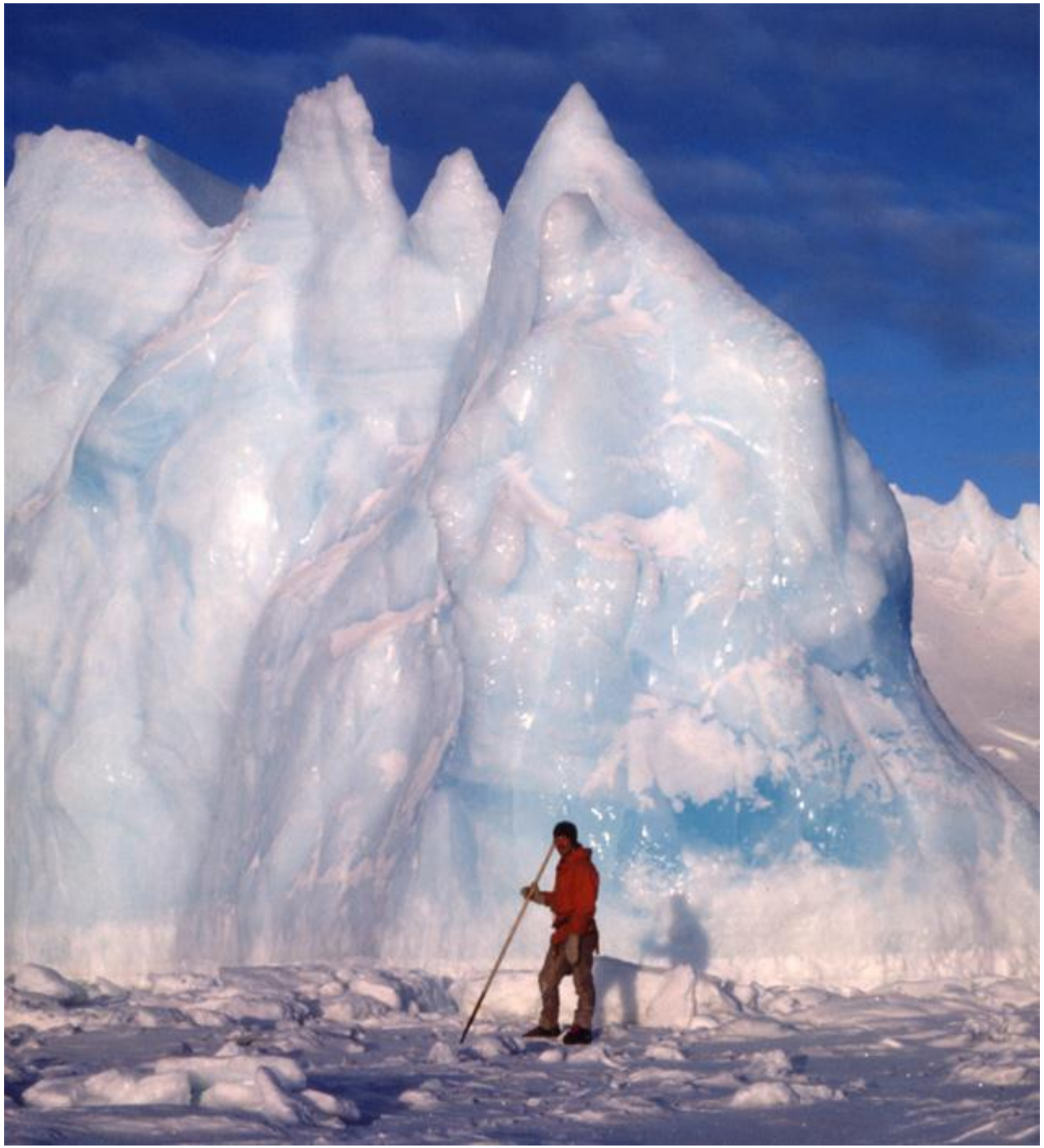
Mario Zucchelli Station at Terra Nova Bay (Italy)

Neymayer III Station (Germany)

Casey Base(Australia)

Science in Antarctica. Bases in Antarctica exist so that science can take place, there are a great number of different projects from the small to the large. This is a 10m telescope and laboratory at the South Pole.

A huge silence. As the temperature falls, so any water vapour in the air freezes and falls out. You can see as far as there's anything to see. From this point it is possible to see over 100 miles (160km) in all directions. With no wind, the entire area is motionless and totally silent.



Standing next to even a small berg can be an un-nerving experience.

If the sun is out, the different colours warm up at different rates, clear regions can act like a lens warming up the interior.

The result is all kinds of creaks and bangs.

Add to this the sea-ice around it creaking as the tide rises or falls and it becomes an uncomfortable place to be.

There’s also the fact that you’re on ice not very thick and there’s 8-10 times more ice below your feet than you can see.

Antarctic land transport. Many vehicles are tracked including all that go away from the bases, wheeled transport is used in and around bases where conditions are predictable.

A pair of adélies all clean and glistening after being freshly laundered by the sea take a short break on their way to the breeding colony. These only had a few miles to walk across the frozen sea. Sometimes if the ice persists, they can have 10’s of miles to go. Must be so much worse when you only have such little legs.

The large icy step is called an “ice foot” it completely surrounds coasts at the end of winter. As the tide rises and falls, so it leaves a layer of ice each time which builds up to be left as a large step when the attached sea-ice breaks up and floats away.

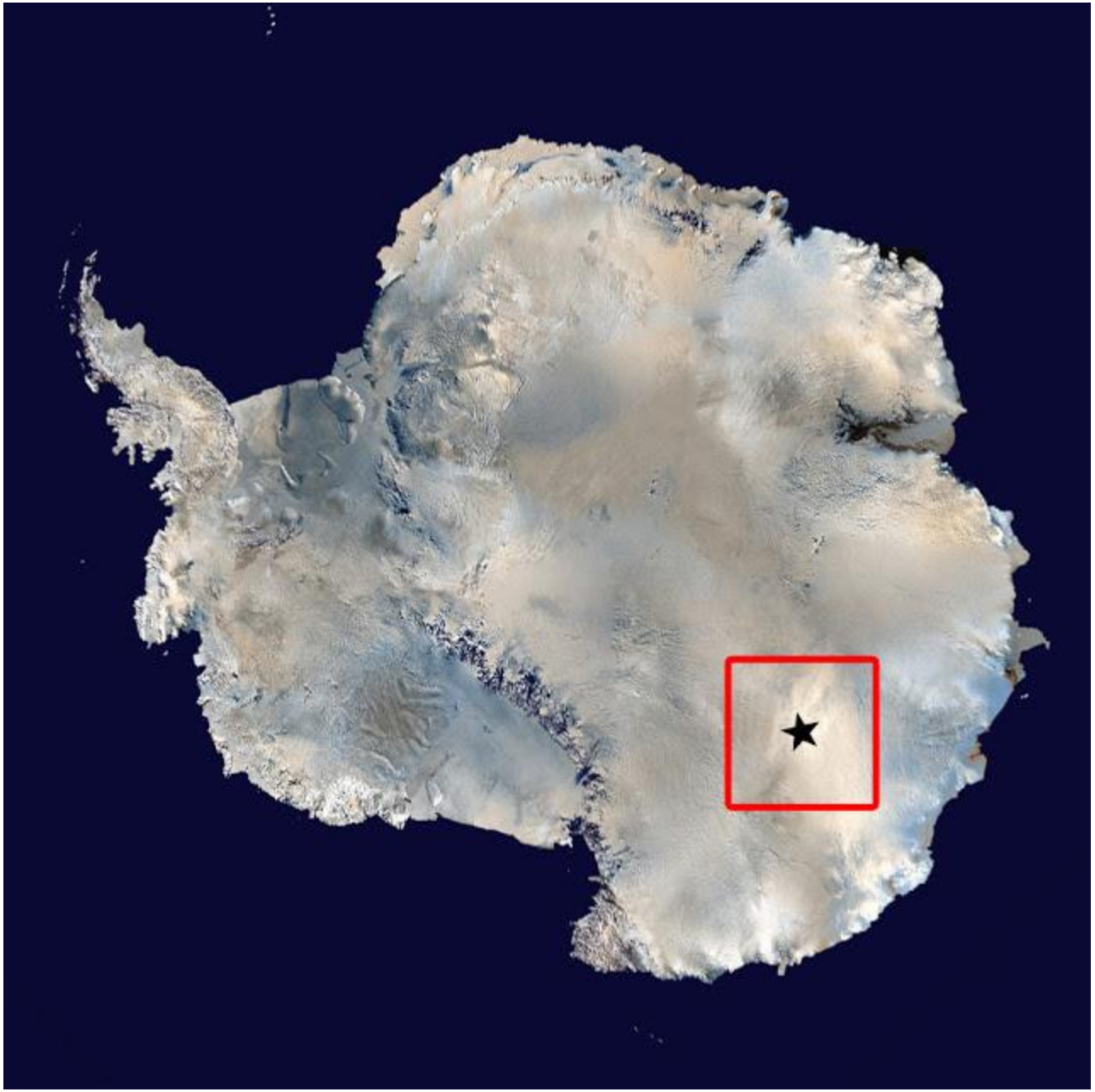
These penguins are returning from a fishing trip to find the tide has gone out and they can’t get back to the shore, so they wander up and down the bottom of the ice foot until the tide comes back in and can float them back up to the right level.

Despite their small size and apparent fragility, snow petrels are quite capable of toughing it out on the ice with no other shelter than putting their head under their wing. Here at -20°C and 15-20 knot winds.

Displaying skua. Display is to, or for a mate or other skuas to establish a territory. Sometimes the birds do this as a pair, it is quite an impressive sight and the squawking can be heard some considerable distance away. Skuas will also do this if their nest is being approached by an unwanted visitor.

Southern Elephant Seals were one of the main targets for Antarctic sealers. They were hunted for their blubber. Blubber is a “blanket” of fat just beneath the skin. They need this as they are warm blooded mammals and need to keep a normal body temperature despite hours in seas below freezing that would kill most mammals within minutes.

Concordia Station



Environmental Factors

Difficult travel in/out

Extreme isolation, even greater than ISS

Altitude 3200m (10,500 ft)

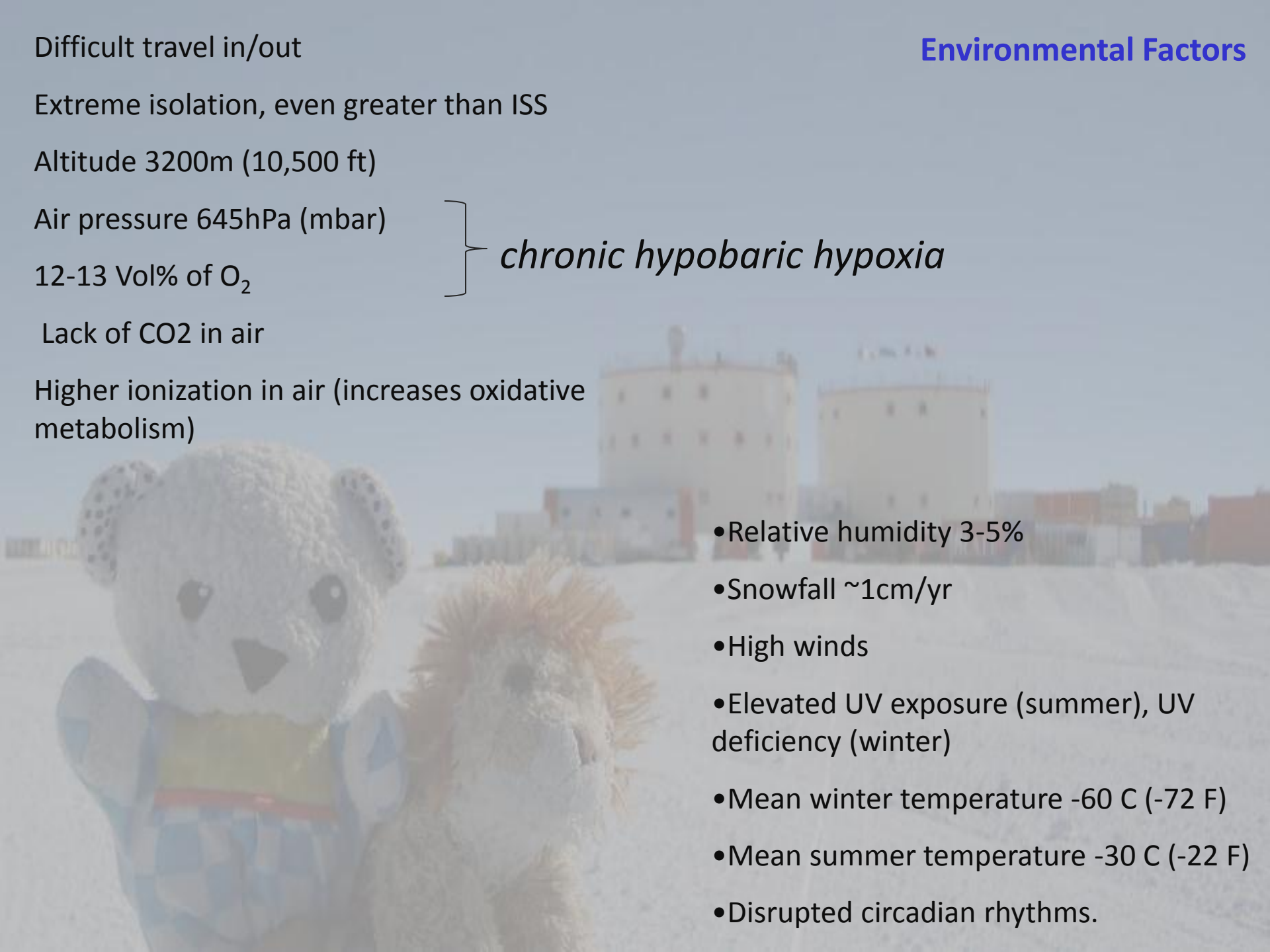
Air pressure 645hPa (mbar)

12-13 Vol% of O_2

} *chronic hypobaric hypoxia*

Lack of CO2 in air

Higher ionization in air (increases oxidative metabolism)



- Relative humidity 3-5%
- Snowfall ~1cm/yr
- High winds
- Elevated UV exposure (summer), UV deficiency (winter)
- Mean winter temperature -60 C (-72 F)
- Mean summer temperature -30 C (-22 F)
- Disrupted circadian rhythms.

Human Factors

- Isolation, confinement for prolonged duration
- Limited communication capability with outside world (more isolated than ISS!)
- International crew, multiple languages
- Realistic station lifestyle
- Sleep/wake cycles disrupted
- Actual extreme environment deployment w/ associated risks (not a mission analog!)
- Winter over crew: 12
- Summer crew: ~50

CHOICE Study

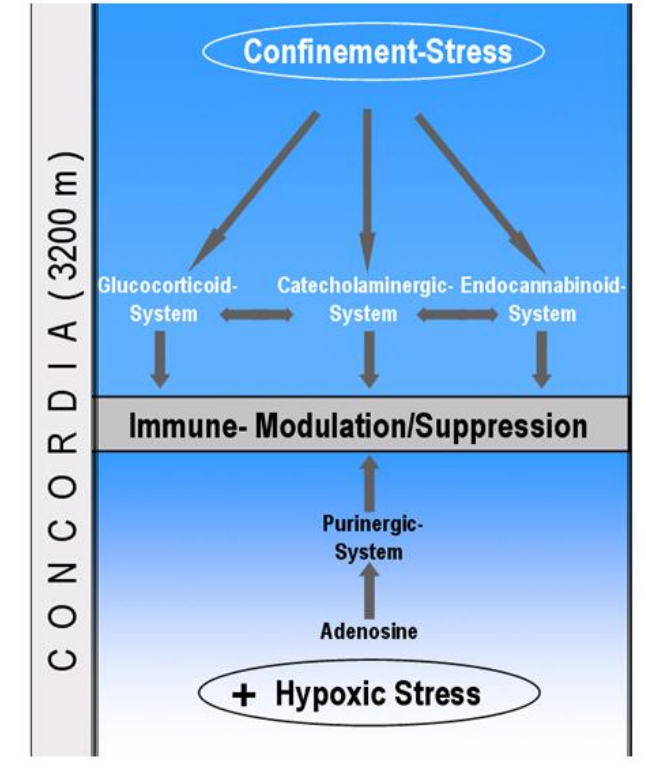
CONCORDIA STATION, DOME C, ANTARCTICA AS A GROUND-BASED ANALOG FOR SPACEFLIGHT/PLANETARY EXPLORATION:

The *CHOICE** Immunology Study

Final Data; NASA Assays - February, 2012

**Consequences of both long-term confinement ("Confinement Stress") and hypobaric hypoxia ("Hypoxic Stress") on Immunity ("Immune-Modulation/Suppression") in the Antarctic CONCORDIA Environment.*

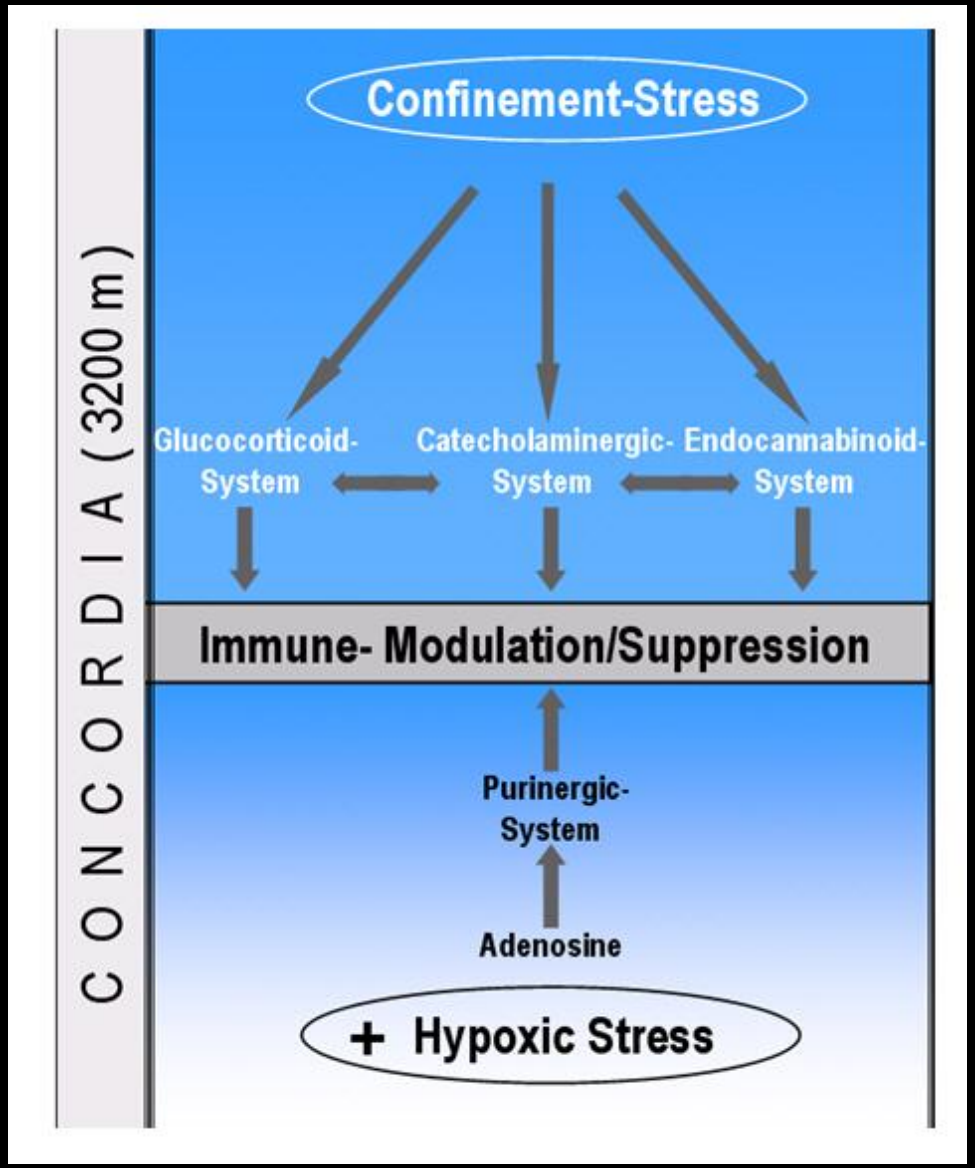
NASA Paradigm



Effects of Space Flight

Immune System Changes
(Status and Function)

Adverse clinical outcomes
(Latent Viral Reactivation)



CHOICE-Study: Consequences of both long-term confinement ("Confinement Stress") and hypobaric hypoxia ("Hypoxic Stress") on Immunity ("Immune-Modulation/Suppression") in the Antarctic CONCORDIA Environment.

Assays

BLOOD ASSAYS

Comprehensive immunophenotype

Intracellular cytokine profiles (T cell)

T cell function

Secreted cytokine profiles

Viral DNA - PBMC

Circulating viral-specific T cells

Viral-specific T cell function

Viral antibodies titers

Viral antibodies titers

Plasma stress hormones

SALIVA ASSAYS

Saliva stress hormones, Diurnal

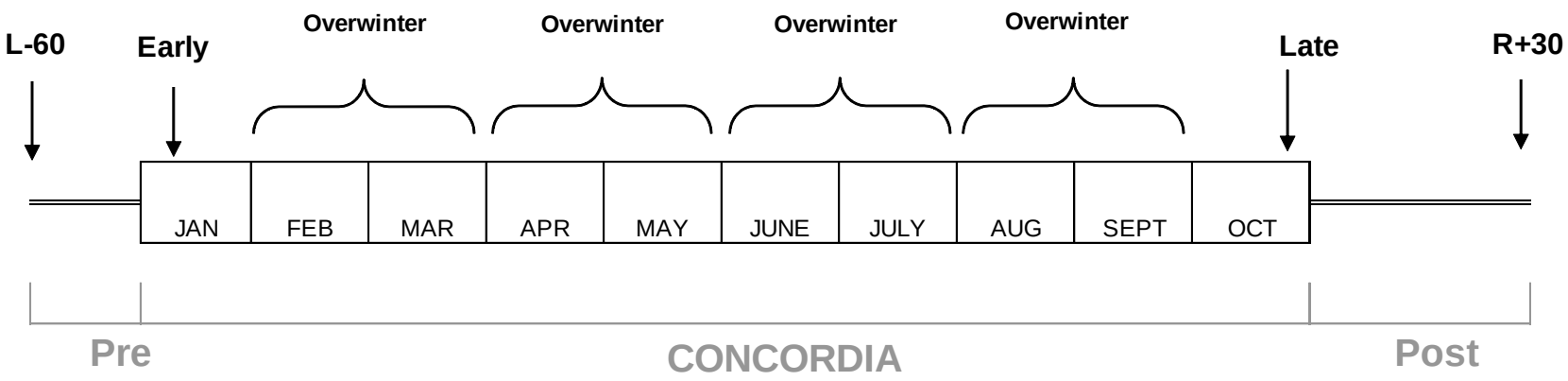
Viral DNA by PCR

URINE ASSAYS

Viral DNA by PCR

Urine stress hormones

Sampling

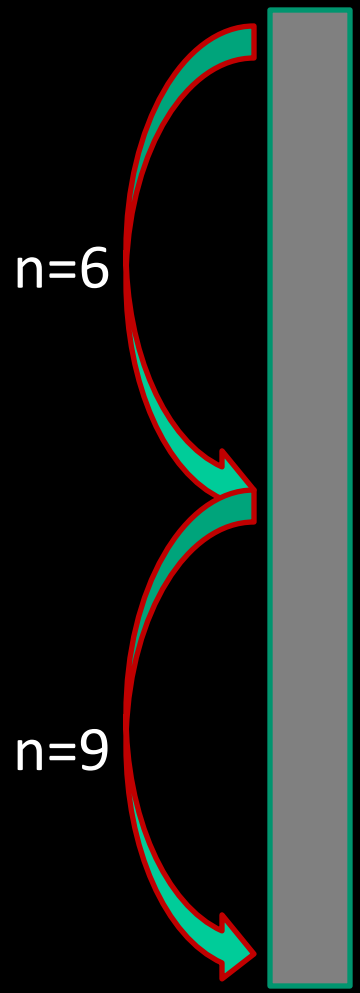


ASSAY	SAMPLE*	Pre/Post	Overwinter	Mitogen/ Specific Analyte	NASA Lab
Comprehensive immunophenotype	Whole blood	X		(see panel)	Immune
T cell intracellular cytokine profiles	Whole blood	X		PMA+ION, LPS	Immune
T cell function/24hr early blastogenesis	Whole blood	X		CD3/CD28, A+B	Immune
Secreted cytokine profiles/48h stimulation	Whole blood	X		Th1/Th2, Inflam.	Immune
Viral DNA - PBMC	Whole blood	X		EBV	Mcgn
Circulating viral-specific T cells	Whole blood	X		EBV, CMV	Mcgn
Viral-specific T cell function	Whole blood	X		EBV, CMV	Mcgn
Viral antibodies titers	Plasma	X	X	EBV, CMV	Mcgn
Viral antibodies titers	Plasma	X	X	VZV	Micro
Plasma stress hormones	Plasma	X	X	cortisol	Mcgn
Saliva stress hormones, Diurnal	Dry saliva	X	X	cortisol, DHEA	Micro
Viral DNA by PCR	Liquid saliva	X	X	CMV*, EBV, VZV	Micro
Viral DNA by PCR	24h Urine	X	X	CMV	Micro
Urine stress hormones	24h Urine	X	X	cortisol*, cat.*	Micro

**Pre, post:* 5.0 ml heparin whole blood, 1.0 ml saliva, dry saliva book, 10 ml of 24 hr. urine

Overwinter: 0.5 to 1.0 ml frozen plasma, 1.0 ml frozen saliva, dry saliva book, 10 ml of frozen 24 hr. urine

Subjects/Logistics



2008/2009 Summer Transition

2009 Overwinter

2009/2010 Summer Transition

2010 Overwinter

2010/2011 Summer Transition

Table: Sampling schedule for CHOICE study. Baseline samples (L-60 and R+30) were collected and processed in Europe before/after deployment. Summer transition samples (+2wk, +9mo) were processed at Concordia Station during the high-habitation summer transition period. All other samples were were processed during the high isolation overwinter period. Not all assays were performed at each timepoint, due to technical or sampling constraints.

			Deployed to Concordia Station													
					Overwinter Isolation											
		L-60	+2Wk	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	+9Mo	R+30
WO 2009	A	X	X			X		X		X					X	X
	B	X	X			X		X		X					X	X
	C	X	X			X		X		X					X	X
	D	X	X			X		X		X					X	X
	E	X	X			X		X		X					X	X
	F	X	X			X		X		X					X	
WO 2010	G	X	X		C, V		X			C, V		X			X	
	~~H~~	X	*Subject withdrawn*													
	~~J~~	X	*Subject withdrawn*													
	K	X	X		C, V		X			C, V		X			X	
	L	X	X		C, V		X			C, V		X			X	
	M	X	X		C, V		X			C, V		X			X	
	N	X	X		C, V		X			C, V		X			X	
	O	X	X		C, V		X			C, V		X			X	
	P	X	X		C, V		X			C, V		X			X	
	J*		X		C, V		X			C, V		X			X	

**Subject added after deployment; no baseline*

X Primary sampling: Phenotype, T cell function, cytokine profiles, viral immunity, viral reactivation.

C Cytokine profiles (culture supernatant)

V Latent viral reactivation (saliva sample)

Unplanned ‘bonus’ mid-winter testing

•Partec cytometer plan: bring in/out for support of each early/late timepoint.

•Revised to leave during winter over, with Dr. Salam to process samples.

•Reagents issues

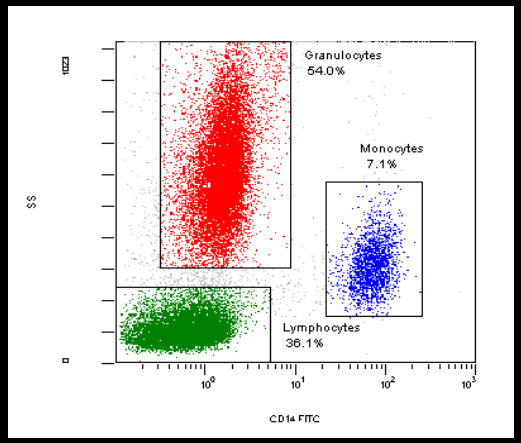
•Consumable supply issues

•Data/training issues

•Additional assays as training/reagents/consumables allowed, phenotype, cell cultures.

•First run: deployment month #2. Samples collected at DC, data acquired at DC, data emailed to JSC, analysis performed at JSC.

Overwinter Data: Phenotype



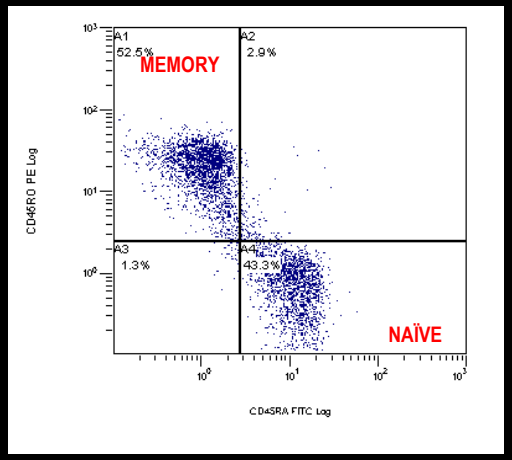
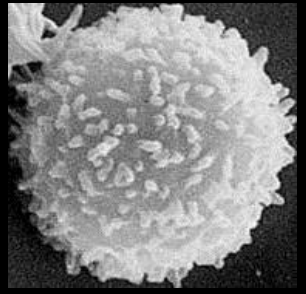


Table 1: Mean peripheral leukocyte distribution for Concordia overwinter subjects. Data are expressed as mean percentage ± SEM. * indicates statistically significant difference p≤0.05. For this assay n=14, except +2wk and R+60 timepoints (n=6 and 5, respectively).

		Deployment Phase					
	Baseline	**+2 Wk**	**+2 Mo**	**+4 Mo**	**+6 Mo**	**+9 Mo**	**R+60**
Granulocytes	52 ± 1.7	**44** ± 1.6*	**31** ± 3.3*	**37** ± 2.3*	**44** ± 2.1*	**46** ± 3.0*	63 ± 2.1
Lymphocytes	40 ± 1.8	**47** ± 2.2*	**49** ± 3.3*	**50** ± 3.0*	45 ± 2.6	44 ± 2.8	32 ± 3.4
Monocytes	5.0 ± 0.4	5.0 ± 0.4	**10** ± 0.8*	**7.0** ± 0.6*	5.0 ± 0.8	5.0 ± 0.5	3.0 ± 0.4
T Cells	67 ± 1.9	**60** ± 1.9*	65 ± 1.3	**55** ± 2.6*	**54** ± 2.0*	**56** ± 2.2*	77 ± 2.2
B Cells	7 ± 1.9	**13** ± 1.8*	**12** ± 3.4*	**11** ± 1.3*	**19** ± 3.2*	**13** ± 1.2*	12 ± 1.6
NK Cells	6 ± 1.6	9 ± 2.2	**10** ± 2.2*	12 ± 2.4	5 ± 1.2	**11** ± 1.2	18 ± 2.2
CD4+ T Cells	59 ± 2.4	**55** ± 3.0*	**50** ± 5.4*	**51** ± 3.0*	**50** ± 2.9*	**53** ± 1.7*	61 ± 2.8
CD8+ T Cells	33 ± 2.1	32 ± 1.4	29 ± 2.2	**26** ± 1.3*	**25** ± 1.9*	30 ± 1.6	27 ± 2.2
Bulk Memory CD4+	54 ± 3.7	59 ± 3.2	56 ± 7.9	59 ± 4.3	**62** ± 2.7*	**68** ± 3.4*	49 ± 6.1
Bulk Memory CD8+	37 ± 2.8	**59** ± 5.2*	41 ± 7.5	**58** ± 5.9*	**59** ± 5.3*	**74** ± 2*	32 ± 5.2
CD8: Naïve/ctx	85 ± 2.8	**49** ± 5.5*	**65** ± 4.3*	**57** ± 4.4*	**62** ± 4.4*	**53** ± 5.5*	92 ± 2.5
CD8: Senescent	12 ± 2.7	**35** ± 4.3*	**24** ± 4.4*	**26** ± 3.7*	21 ± 4.2	**27** ± 4.7*	7 ± 2.1
CD8: True Naïve	38 ± 7.0	35 ± 4.1	27 ± 5.6	31 ± 2.5	35 ± 3.8	28 ± 2.1	21 ± 5.5
Central memory	6 ± 1.5	10 ± 0.9	5 ± 1.7	13 ± 3.0	10 ± 1.3	13 ± 1.6	34 ± 6.0
Effector Memory	39 ± 5.1	**32** ± 3.8*	37 ± 6.5	33 ± 3.9	**32** ± 3.1*	35 ± 2.9	38 ± 5.2
Term. Differentiated	17 ± 2.4	23 ± 1.9	31 ± 6.7	22 ± 2.0	**24** ± 1.4*	25 ± 1.4	7 ± 1.6
CD4/CD69	1 ± 0.2	**6** ± 0.8*	1 ± 0.4	2 ± 0.3	2 ± 0.5	2 ± 0.3	0 ± 0.1
CD8/CD69	2 ± 0.3	**9** ± 1.5*	3 ± 0.3	3 ± 0.5	3 ± 0.7	3 ± 0.8	2 ± 0.4
CD4/HLA-DR	2 ± 0.5	3 ± 0.7	3 ± 0.3	2 ± 0.4	1 ± 0.2	1 ± 0.2	2 ± 0.2
CD8/HLA-DR	3 ± 1.0	**5** ± 1.1*	2 ± 0.7	2 ± 0.5	1 ± 0.2	1 ± 0.3	3 ± 0.8

FUNCTIONAL IMMUNE ASSAYS



Remove cells from body

Stimulate cells during culture, mimicking a natural immune response

Observe characteristics of normal immune activation:

- Signal transduction
- Morphological changes
- Expression of cellular activation markers
- Production of cytokines
- Chemotaxis
- Cytotoxicity
- Proliferation

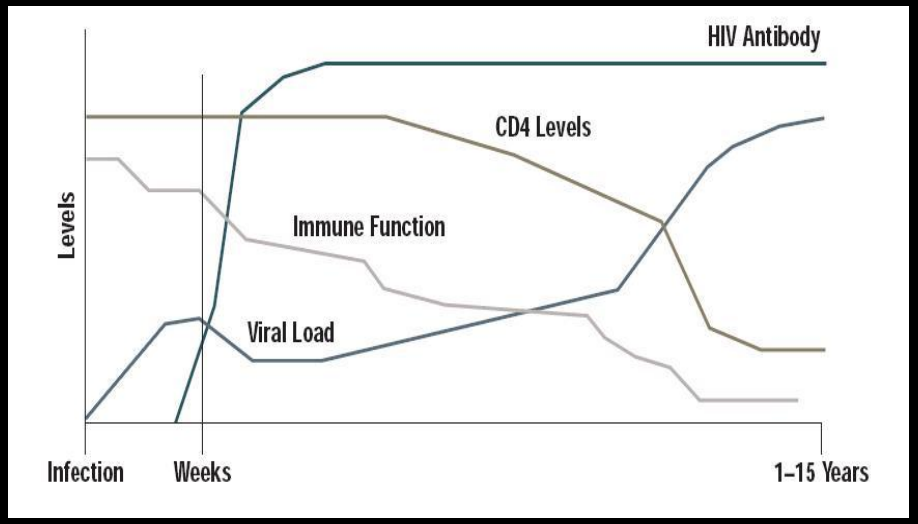
KINETICS OF T CELL ACTIVATION

T 0:00	Ligand-receptor binding
0-5 sec	Membranes increase permeablity to ions Shifts in ions from one intracellular compartment to another Changes in membrane potential Changes in intracellular pH
0-5 min	Changes of state in membrane lipids and proteins Activation of adenylate cyclase, ATPase, and other membrane-associated enzymes Changes in cyclic nucleotide concentractions Changes in receptor distribution and mobity occur Adhension molecule conformational changes
T +30 min	Coalescence of patched receptors into cap at one pole of the cell (dependant on contractioin of cytoskeletal microfilaments, ATP energy source)
T +6-12hr	Expression of CD69 on T cell surface
T +24 hr	Secretion of IL-2, cell surface epxression of IL-2 receptor (CD25) Upregulation of CD40L IL-2 binds to IL-2r (autocrine activation) CD40L binds to CD40 on APC, upregulating CD86/CD80 APC CD86/80 binds to CD28 on T cell surface, results in additional cytokine expression, expression of BCL-x (anti-apoptosis, proliferation
36-72 hr	DNA synthetic activity Epression of HLA-DR
3-4 days	Blast transformation
	Differentiation into Th1/Th2/Th17 cell based on factors such as antigen dosage, local cytokine environment, other costimulatory molecules, APC involvement

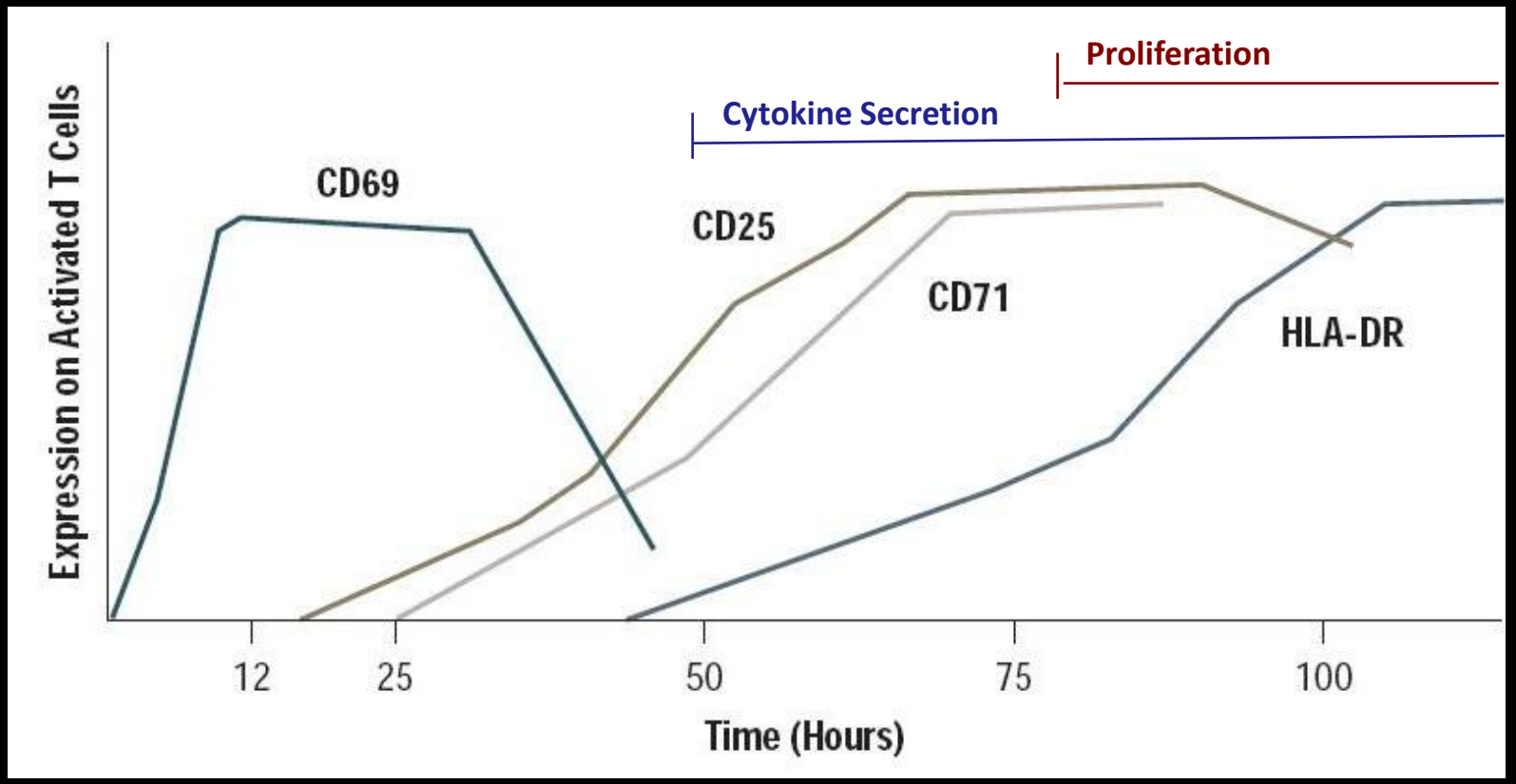
T cell function

- Remove cells from body
- Stimulate cells with mitogens during culture, mimics an in-vivo immune response

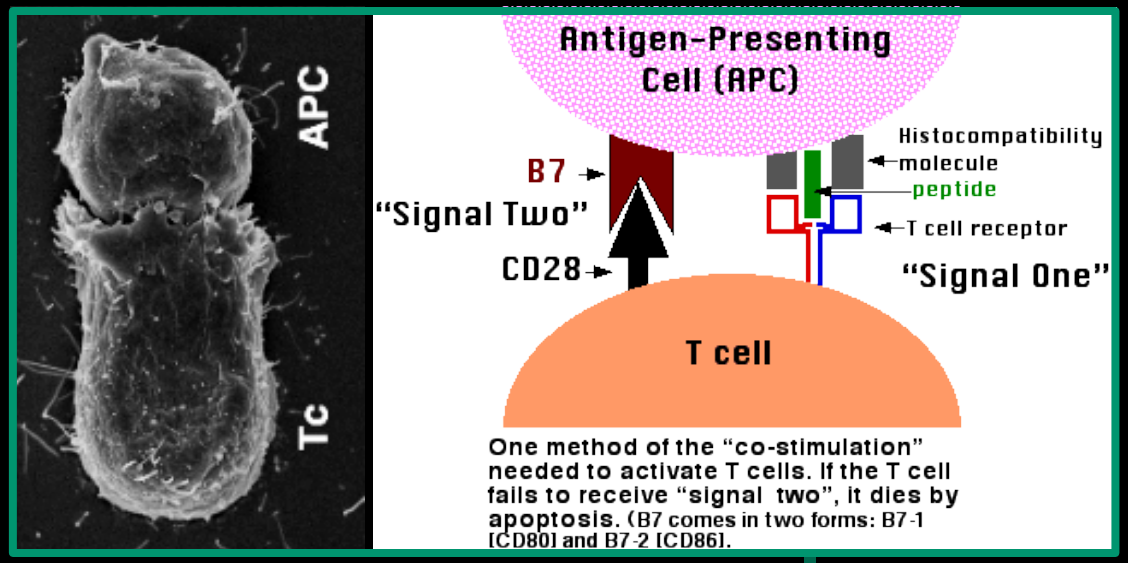
T Cell Function vs. Disease

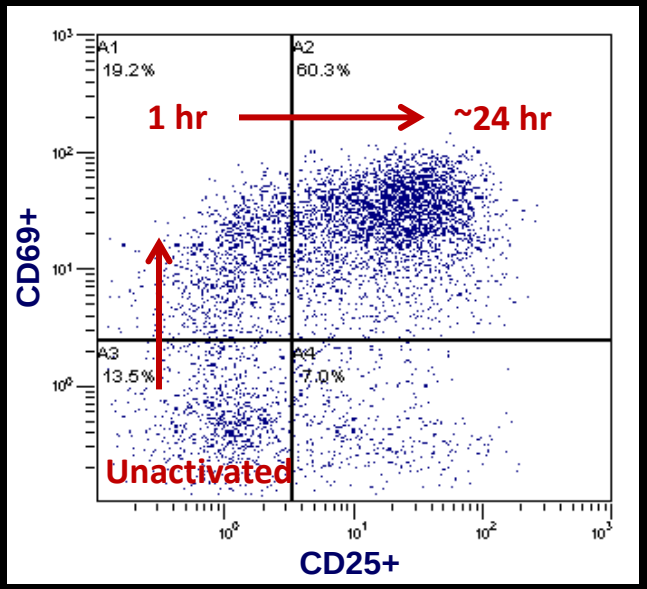


Kinetics of T Cell Activation

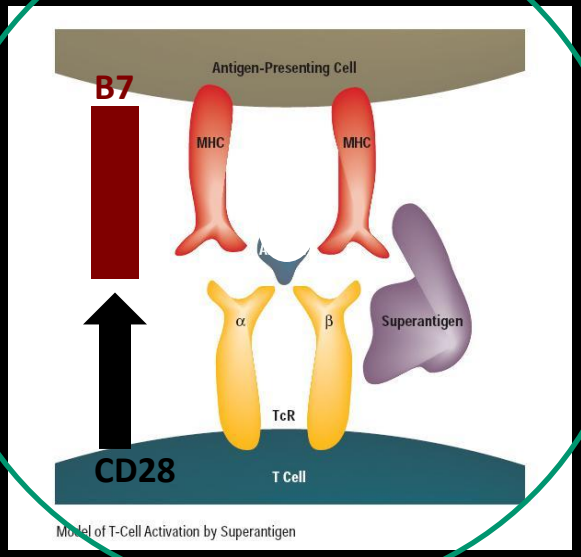


T Cell Mitogen – Mechanism of Action

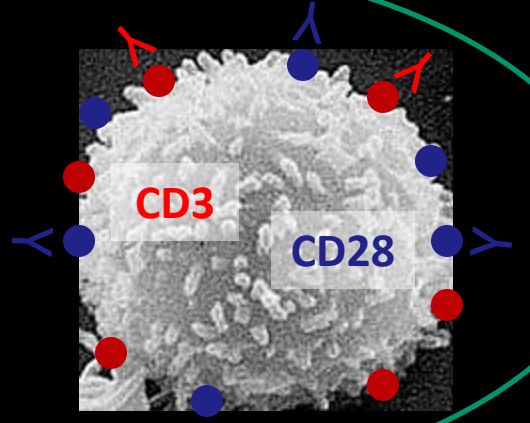




SEA+SEB



Anti-CD3/CD28



EM image obtained from Institute Pasteur website

Overwinter Data – T cell Function

Table 2: Mean T cell function/early blastogenesis for Concordia overwinter subjects following mitogenic stimulation for 24 hours with the indicated mitogen. Data are expressed as mean percent cells stimulated to produce the indicated activation markers (CD69 and/or CD25) ± SEM. * indicates statistically significant difference p≤0.05. For the SEA/SEB assay n=6, for the CD3/28 assay, n=4.

			Deployment Phase		
Mitogen		**Baseline**	**+2 Wk**	**+9 Mo**	**R+60**
SEA+SEB	**CD4/69+**	10 ± 1.2	**21** ± 3.6*	**19** ± 2.4	10 ± 2.7
	CD4/69/25+	2 ± 0.3	**14** ± 3.8	**7** ± 1.2	6 ± 1.3
	CD8/69+	9 ± 1.4	**25** ± 5.3	**30** ± 3.9	15 ± 3.8
	CD8/69/25+	2 ± 0.5	12 ± 4.1	**7** ± 1.4	6 ± 1.5
anti-CD3/CD28	**CD4/69+**	48 ± 1.1	**70** ± 0.6	52 ± 13.7	43 ± 10.5
	CD4/69/25+	37 ± 1.2	**49** ± 3.7	30 ± 11.6	26 ± 6.7
	CD8/69+	51 ± 2.3	**72** ± 5.9	42 ± 11.9	46 ± 10.2
	CD8/69/25+	29 ± 2.7	40 ± 4.9	23 ± 11.1	19 ± 4.8

2009/10 Summer Transition period – Incidence Rates

(mid-November to mid-January)

- Approx. 50% of summer participants contacted infectious disease

- Historically, extremely high incidence rate

- Three periods of epidemic viral infections:

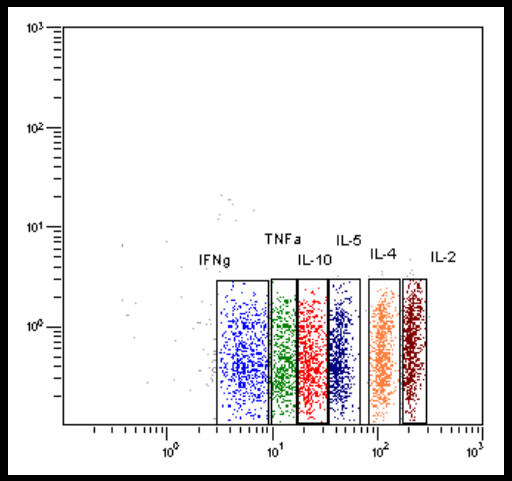
  Period 1: Flu-like (mid-Nov. to mid-Dec.)

  Period 2: Rhinoparyngitis (mid-Dec. to early Jan.)

  Period 3: Gastro-enteritis (late-Dec. to early Jan.)

-Data from Concordia Station, Chief Medical Officer

Overwinter Data: Secreted Cytokine Profiles



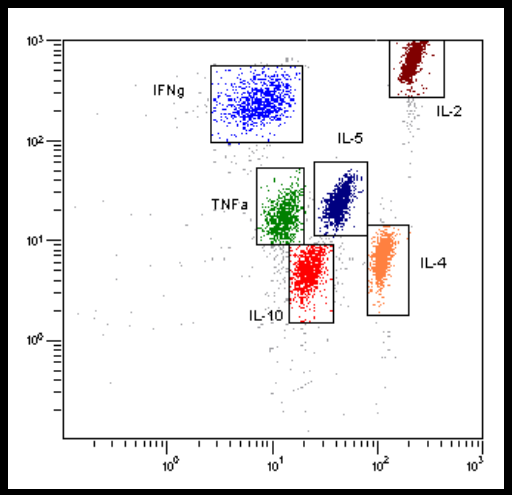
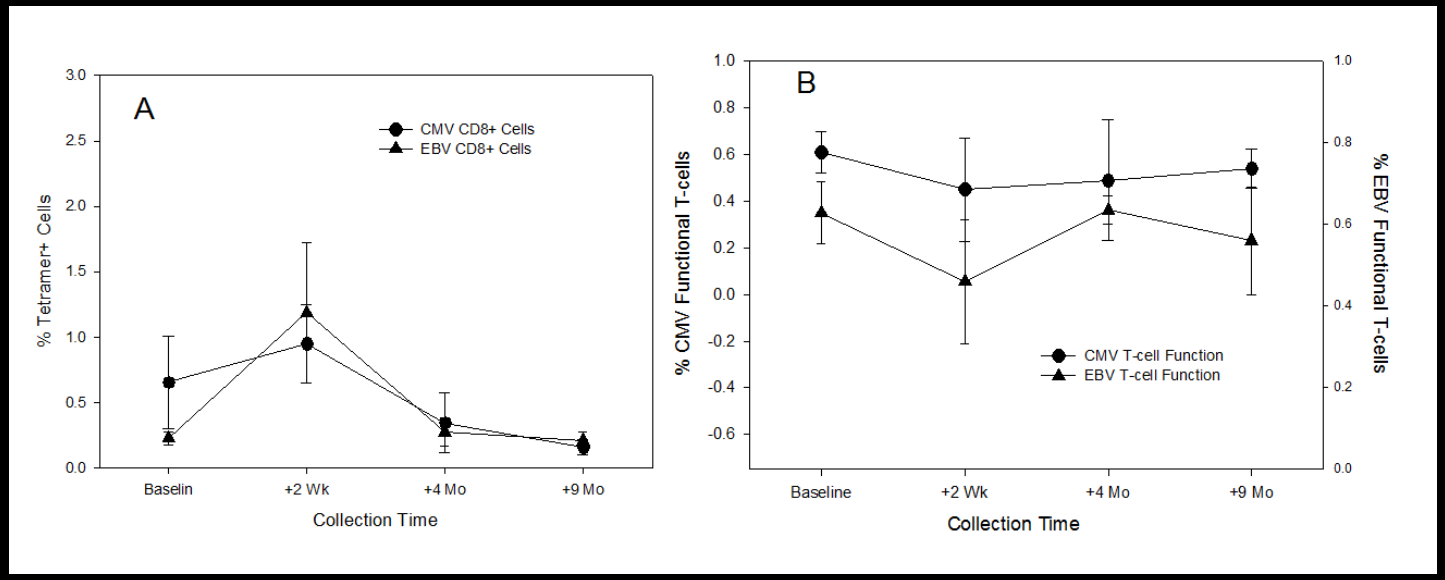


Table 3: Mean intracellular and secreted cytokine levels for Concordia overwinter subjects following mitogenic stimulation for 48 hours with the indicated mitogen. Data are expressed as mean fluorescence intensity (correlates with concentration) ± SEM. * indicates statistically significant difference p≤0.05. For the CD3/28 assay n=4, for the PMA/I assay n=14 except the Aug-Sept and R+60 timepoints (n=8 and 5, respectively), for the LPS assay n=14 except the R+60 timepoint (n=5).

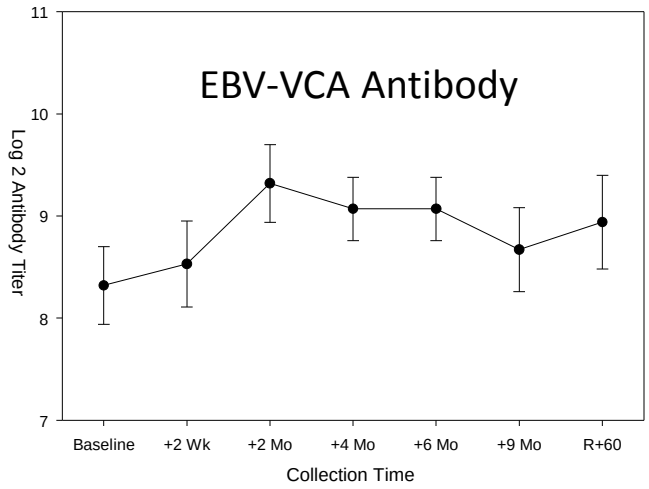
			Deployment Phase					
Mitogen		**Baseline**	**+2 Wk**	**Feb-Mar**	**Apr-May**	**Jun-Jul**	**Aug-Sep**	**+9 Mo**
CD3/CD28	**IFNg**	74 ± 22.1	58 ± 21.1	100 ± 55.6	104 ± 27.9	116 ± 23.3	138 ± 24.7	59 ± 40.4
	TNFa	20 ± 6.2	24 ± 8.9	24 ± 12.5	13 ± 2.0	15 ± 3.7	21 ± 4.3	9 ± 5.9
	IL-10	6 ± 0.3	16 ± 3.7	5 ± 1.8	8 ± 1.0	8 ± 2.1	9 ± 3.3	3 ± 0.7
	IL-4	0 ± 0.1	0 ± 0.0	0 ± 0.1	0 ± 0.1	0 ± 0.2	0 ± 0.1	0 ± 0.1
	IL-5	4 ± 1.7	2 ± 1.2	7 ± 5.9	8 ± 3.3	9 ± 5.9	5 ± 2.5	3 ± 2.9
	IL-2	32 ± 12.2	4 ± 1.3	64 ± 33.7	33 ± 11.3	33 ± 19.2	43 ± 10.8	12 ± 8.0
PMA/ Ionomycin	**IFNg**	287 ± 12.0	281 ± 16.2	251 ± 17.3	247 ± 11.6	248 ± 17.6	**238** ± 12.9ϟ	**220** ± 16.2*
	TNFa	51 ± 6.4	**82** ± 12.7ϟ	**105** ± 15.7ϟ	**127** ± 18.7ϟ	**98** ± 12.3ϟ	**111** ± 16.2ϟ	**35** ± 6.8*
	IL-10	7 ± 1.5	19 ± 2.7	16 ± 2.7	21 ± 2.4	19 ± 4.0	20 ± 2.9	5 ± 1.1
	IL-4	3 ± 0.7	**5** ± 1.1*	**4** ± 0.7*	**5** ± 1.1*	**5** ± 0.9*	**6** ± 1.1*	2 ± 0.3
	IL-5	15 ± 2.8	19 ± 3.4	17 ± 2.9	**19** ± 3.2*	18 ± 3.3	20 ± 2.8	11 ± 2.6
	IL-2	689 ± 26.7	701 ± 44.6	725 ± 34.7	**764** ± 11.2ϟ	**764** ± 13.1ϟ	**736** ± 9.3*	**526** ± 52.7*
LPS	**TNFa**	9 ± 1.6	**20** ± 4.1*	**17** ± 3.8*	**18** ± 3.6*	**21** ± 4.6*	**17** ± 4.0*	12 ± 2.2
	IL-10	14 ± 1.2	**27** ± 4.7*	**43** ± 7.3*	**37** ± 3.4*	**37** ± 3.2*	**42** ± 7.6*	6 ± 2.1
	IL-6	432 ± 25.9	431 ± 34.8	498 ± 32.6	494 ± 25.8	506 ± 29.2	477 ± 24.8	232 ± 41.5
	IL-1b	51 ± 4.8	**95** ± 18.3ϟ	50 ± 6.7	54 ± 8.4	57 ± 6.7	39 ± 7.5	110 ± 16.3
	IL-8	610 ± 16.2	583 ± 37.8	529 ± 40.3	591 ± 21.8	600 ± 30.3	577 ± 29.0	408 ± 68.2

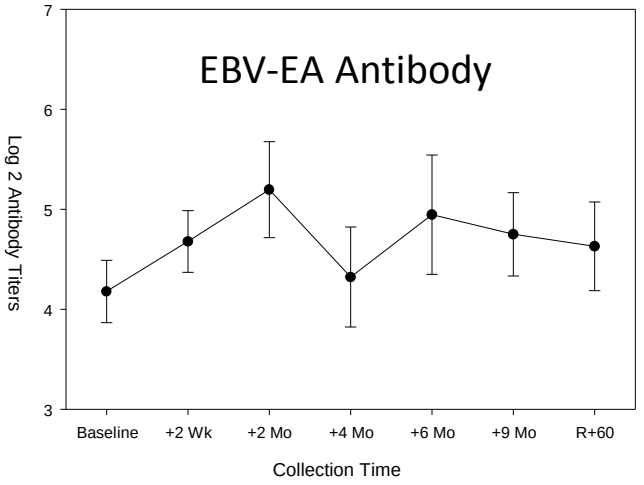
Overwinter Data: Viral Immunity

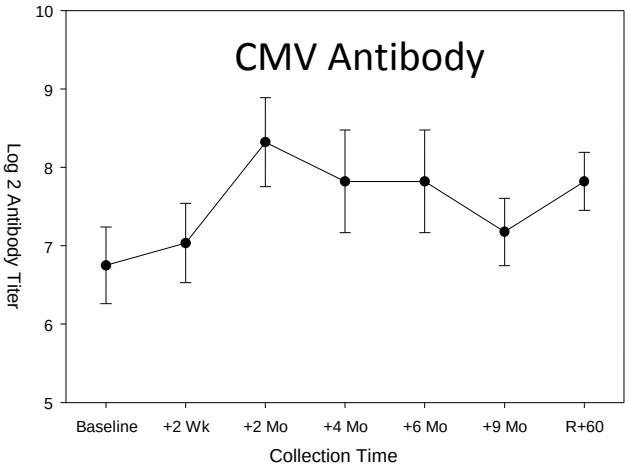


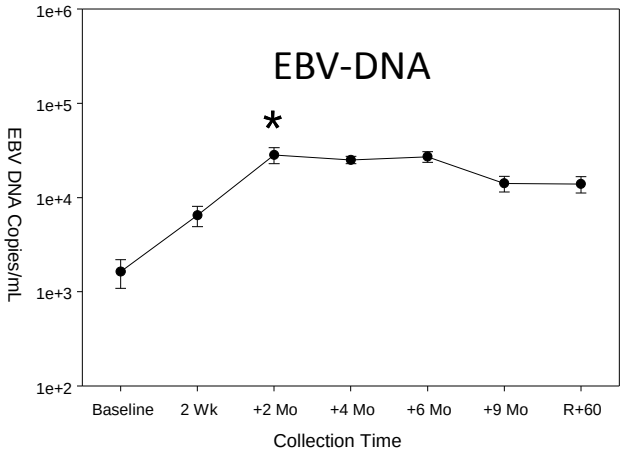
(A) Levels of virus-specific (EBV, CMV) CD8+ T-cells before and during the winter-over period, and (B) Percentage of functional virus-specific T-cells before and during the winter-over period.

Overwinter Data: Viral Immunity





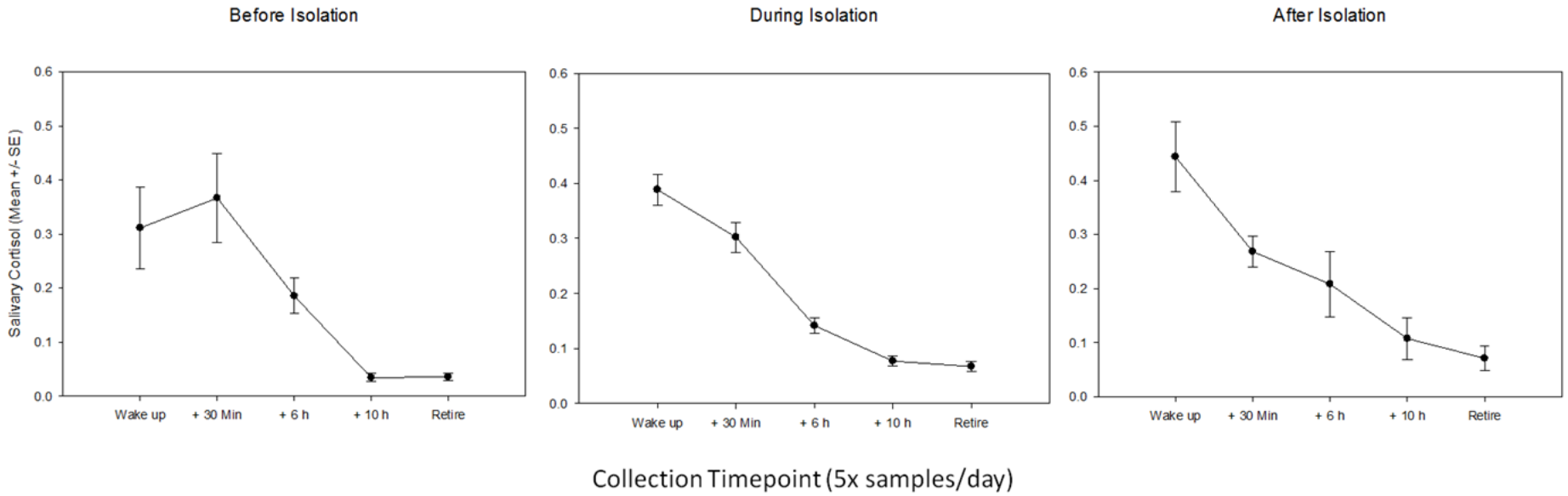




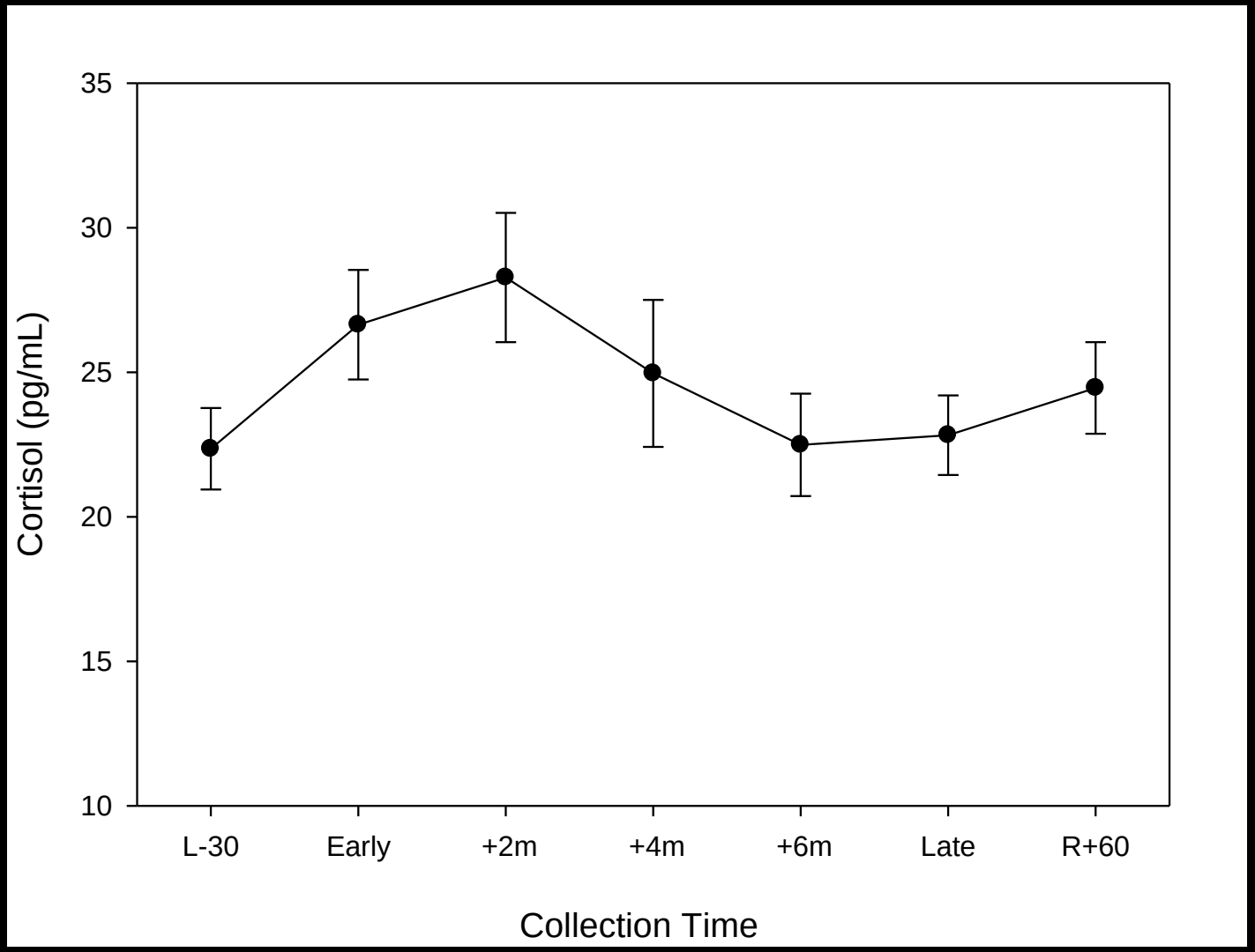
Levels of antiviral antibodies [EBV-VCA (A), EBV-EA (B), and CMV (C)] and EBV DNA in peripheral blood (D) before and during the winter-over period.

Stress Hormone Levels

Salivary cortisol levels before, during, and after the Concordia winter-over period.



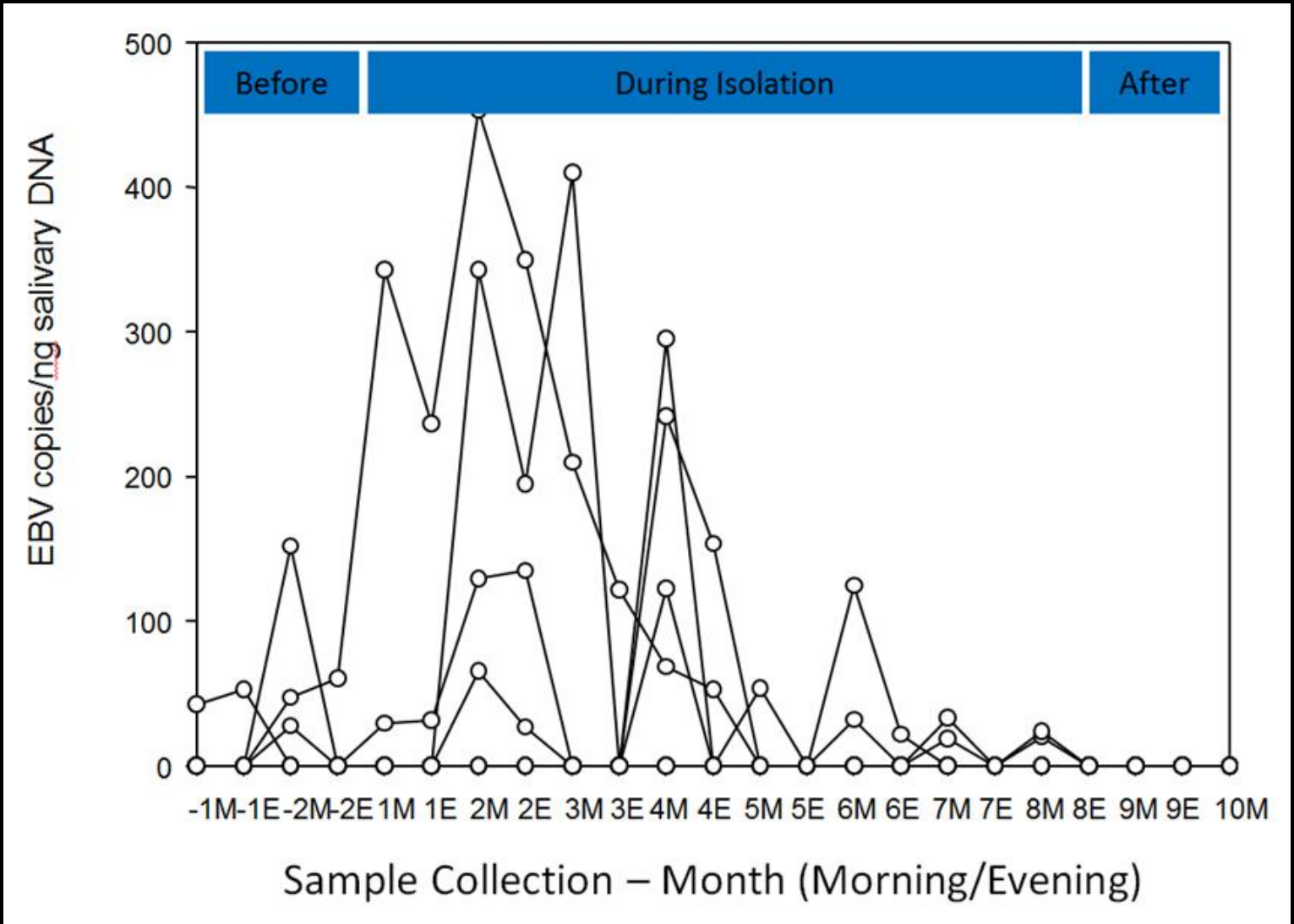
Stress Hormone Levels



EBV and VZV shedding in saliva during Concordia Study

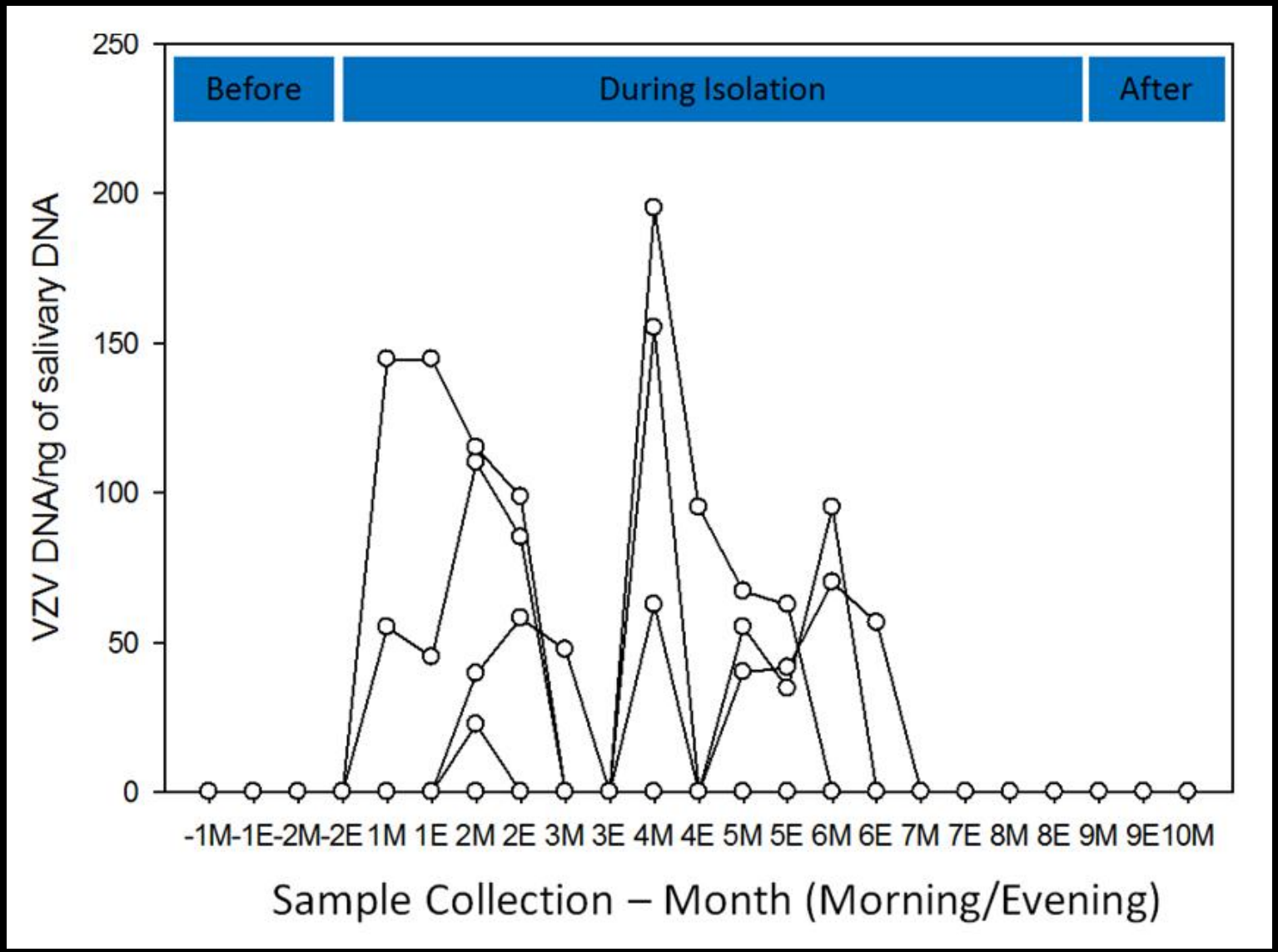
# of Subjects	# of samples from 8 subjects	Samples + for EBV	Samples + for VZV
8	184	35 (6)	25 (5)
		19.20%	13.60%
	() denote number of subject shed virus		
Before	32	6; 19%	0
After	16	2; 13%	0
During	136	27; 20%	25; 18.4%

Overwinter Data: Viral Reactivation



EBV DNA in the saliva of Concordia subjects before, during and after isolation (n=8). 6 of 8 subjects shed EBV at some point during the overwinter period.

Overwinter Data: Viral Reactivation



VZV DNA in the saliva of Concordia subjects before, during and after isolation (n=8). 4 of 8 subjects shed VZV at some point during the overwinter period.

Concordia Station – Clinical Incidence

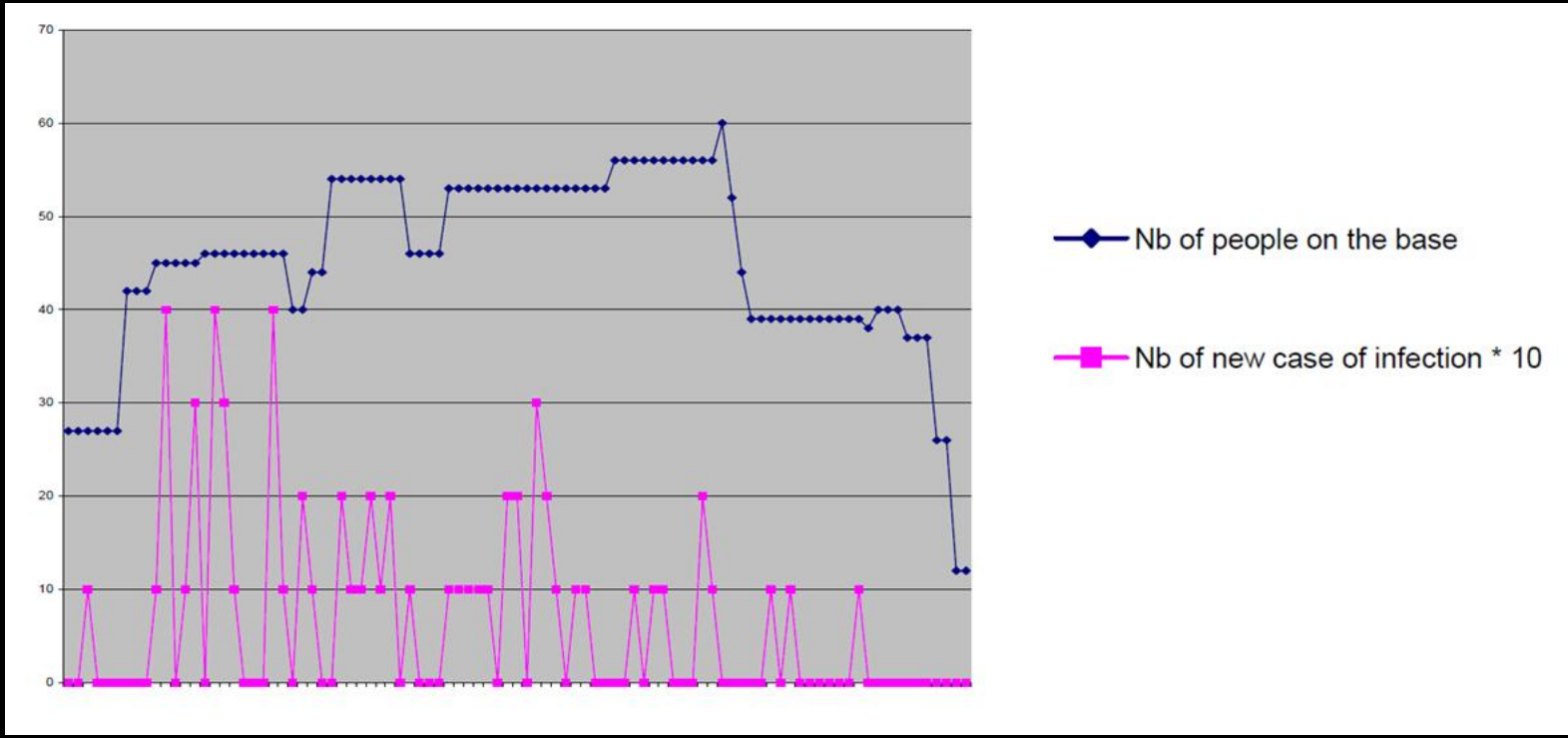
During the early adaptation phase for the 2009 deployment (November the 8th 2008 to February the 8th 2009, 93 days), 85 participants were at Concordia Station (excluding pilots and visits of <48hr). During this period, approximately 50% of summer participants contacted infectious disease. There were 62 new cases of infectious disease, concerning 44 persons (51.76%). 30 persons were infected once, 11 were infected twice, 2 were infected three times and one was infected four times. Historically, these are extremely high incidence rates. Three distinct periods of epidemic viral infections were observed:

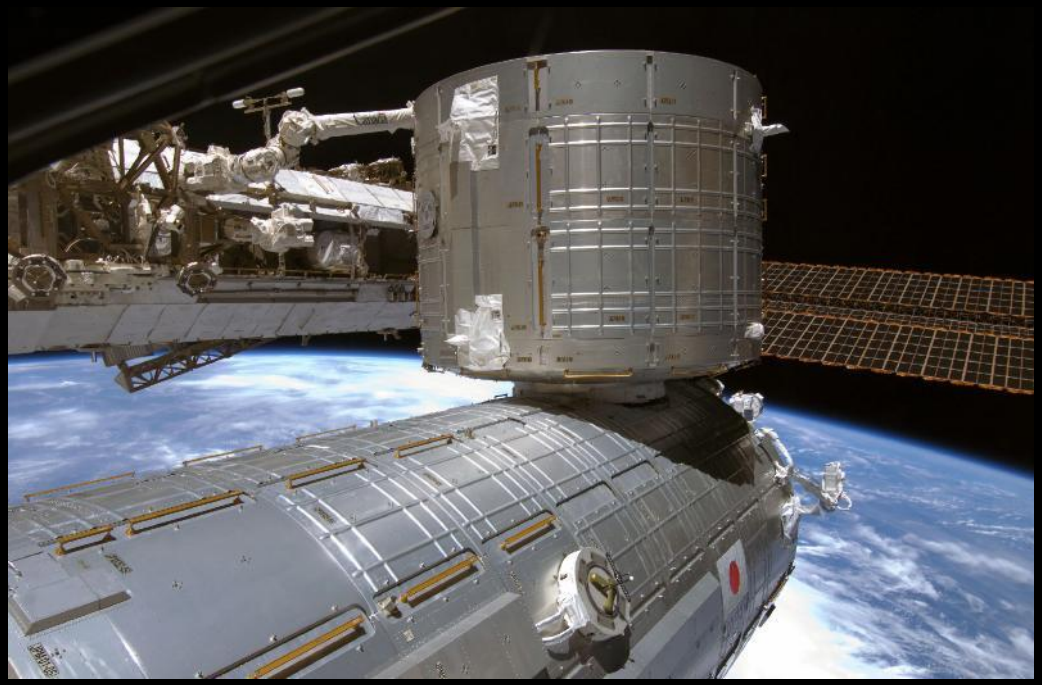
-Period 1: Flu-like (mid-Nov. to mid-Dec.)
-Period 2: Rhinoparyngitis (mid-Dec. to early Jan.)
-Period 3: Gastro-enteritis (late-Dec. to early Jan.)

Specific diagnoses during this period included:

-influenzae : 29 cases
-upper respiratory tract viral infection : 18 cases
-gastro-enteritis : 10 cases
-otitis : 2 cases
-bladder infection : 2 cases
-vaginal infection : 1 case

Concordia Station – Clinical Incidence





‘CHOICE’ Conclusions

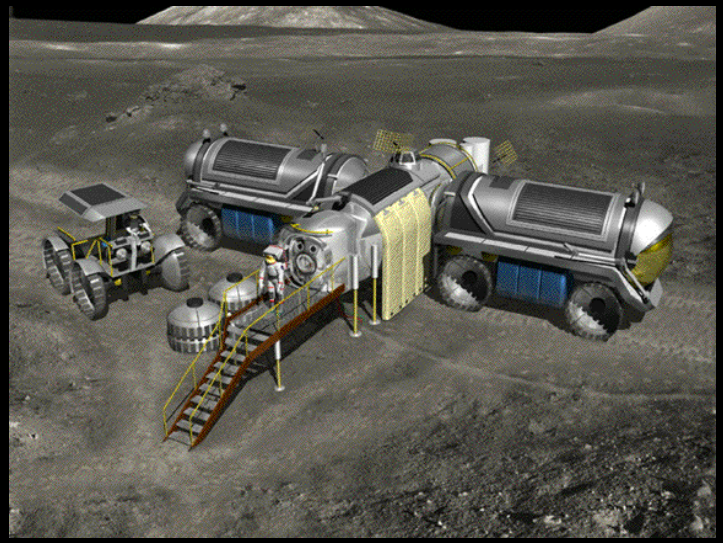
Alterations in immune cell distribution and function, circadian misalignment, stress and latent viral reactivation appear to persist during Antarctic winterover at Concordia Station.

Some of these changes are similar to those observed in Astronauts, either during or immediately following spaceflight. Others are unique to the Concordia analog.

Based on some initial immune data and environmental conditions, Concordia winterover may be an appropriate analog for some flight-associated immune system changes and mission stress effects.

An ongoing smaller control study at Neumayer III will address the influence of the hypoxic variable.

Analogous?

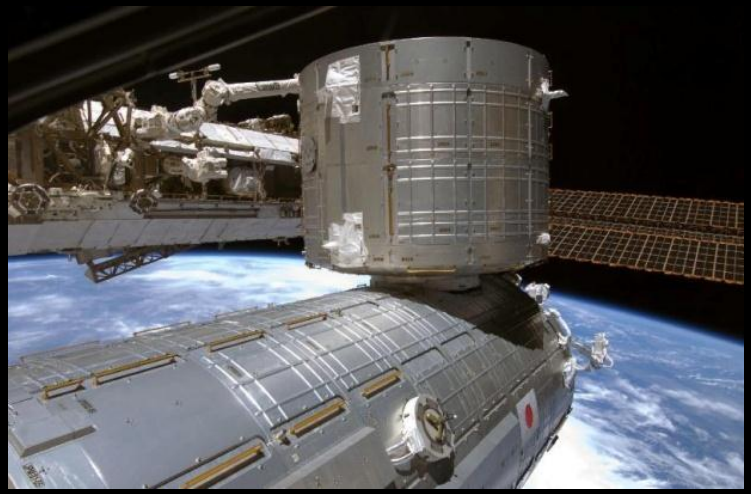


During overwinter

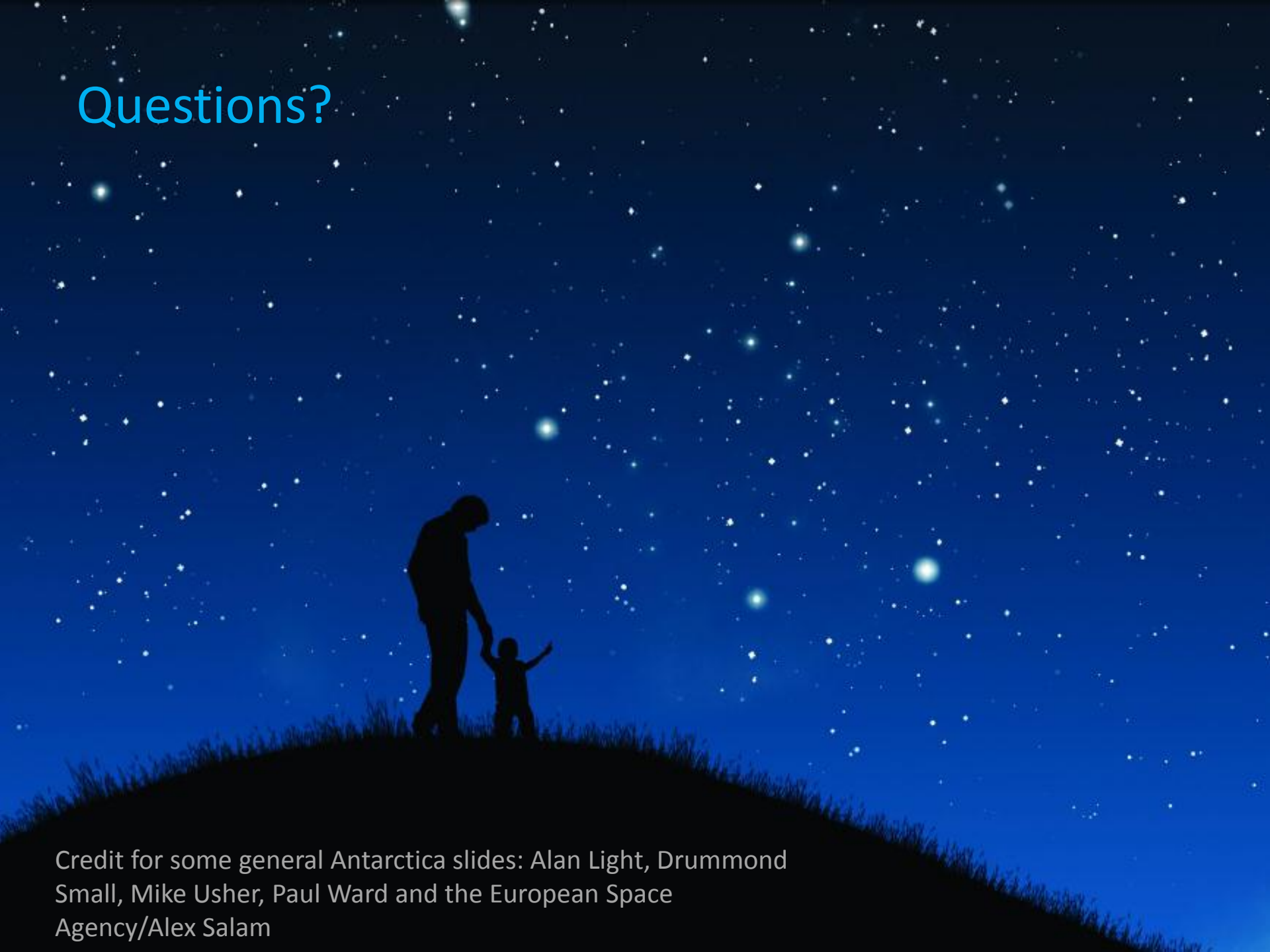
•Changes were observed in the peripheral blood leukocyte distribution consistent with immune mobilization, and similar to those observed during spaceflight.

•Alterations in cytokine production profiles were observed during winterover that are distinct from those observed during spaceflight, but potentially consistent with those observed during persistent hypobaric hypoxia.

•The reactivation of latent herpesviruses was observed during overwinter/isolation, that is consistently associated with dysregulation in immune function.



Questions?



Credit for some general Antarctica slides: Alan Light, Drummond Small, Mike Usher, Paul Ward and the European Space Agency/Alex Salam