1
00:00:01,000 --> 00:00:04,000
[music playing]

2
00:00:16,266 --> 00:00:18,100
- I'M REALLY HAPPY AGAIN HERE

3
00:00:18,100 --> 00:00:22,400
TO WELCOME ALL OF YOU
TO THIS INSTALLMENT

4
00:00:22,400 --> 00:00:24,866
OF THE 75TH ANNIVERSARY
CELEBRATION

5
00:00:24,866 --> 00:00:26,266
OF NASA AMES RESEARCH CENTER

6
00:00:26,266 --> 00:00:29,466
AND THE DIRECTOR'S COLLOQUIUM
SUMMER SERIES.

7
00:00:31,266 --> 00:00:33,700
THE--NOW, THIS IS PARTICULARLY,
AS A LOT OF YOU KNOW,

8
00:00:33,700 --> 00:00:35,666
IS FOCUSED ON, YOU KNOW,

9
00:00:35,666 --> 00:00:37,433
OUR STUDENTS THAT ARE HERE
DURING THE SUMMER,

10
00:00:37,433 --> 00:00:38,866
BUT IT'S ALSO FOCUSED
ON THE REST OF US

11
00:00:38,866 --> 00:00:40,766
WHO, YOU KNOW, LIKE ME,
I'M A BUREAUCRAT.

12
00:00:40,766 --> 00:00:43,400
I DON'T REALLY GET A CHANCE
TO HEAR COOL STUFF.

13
00:00:43,400 --> 00:00:46,100
SO I'M LOOKING FORWARD TO THIS.

14
00:00:46,100 --> 00:00:48,133
TODAY, WE HAVE
DR. JOSH ALWOOD.

15
00:00:48,133 --> 00:00:50,800
HE'S A RESEARCH SCIENTIST IN
THE SPACE BIOSCIENCES DIVISION

16
00:00:50,800 --> 00:00:52,700
HERE AT
NASA AMES RESEARCH CENTER.

17
00:00:52,700 --> 00:00:54,566
AND AS I'LL TELL YOU
IN A MOMENT,

18
00:00:54,566 --> 00:00:56,300
YOU KNOW, I'M KIND OF ENVIOUS,

19
00:00:56,300 --> 00:00:58,466
BECAUSE HE HAS A BACKGROUND
KIND OF SIMILAR TO MINE.

20
00:00:58,466 --> 00:01:00,133
HE STUDIED PHYSICS
AND ASTRONOMY

21
00:01:00,133 --> 00:01:02,266
AND, YOU KNOW, THEN WENT AND DID
SOME ENGINEERING STUFF

22

00:01:02,266 --> 00:01:05,333
AND--AND HE SORT OF TRANSITIONED
TO, YOU KNOW, BIOLOGY,

23
00:01:05,333 --> 00:01:07,033
WHICH I THINK
IS REALLY IMPORTANT.

24
00:01:07,033 --> 00:01:08,633
WHEREAS I'M TOO OLD
TO UNDERSTAND

25
00:01:08,633 --> 00:01:10,033
ALL THE BIOLOGY STUFF.

26
00:01:10,033 --> 00:01:11,766
SOMEBODY TRIED TO TELL ME
ABOUT CELLS,

27
00:01:11,766 --> 00:01:15,333
AND SAID, YOU KNOW--YOU KNOW,
THE ONLY CELLS I KNOW

28
00:01:15,333 --> 00:01:17,633
IS WHEN I WENT
AND VISITED SAN QUENTIN.

29
00:01:17,633 --> 00:01:19,166
[laughter]

30
00:01:19,166 --> 00:01:21,666
BUT, YOU KNOW, JUST TO KIND OF
REVIEW A LITTLE BIT,

31
00:01:21,666 --> 00:01:23,800
THE MISSION OF
THE BIOSCIENCES RESEARCH BRANCH

32
00:01:23,800 --> 00:01:26,533
IS TO ADVANCE

SPACE EXPLORATION

33
00:01:26,533 --> 00:01:29,500
BY NEW SCIENTIFIC DISCOVERIES

34
00:01:29,500 --> 00:01:32,533
IN--IN TECHNOLOGICAL
DEVELOPMENTS IN BIOLOGY.

35
00:01:32,533 --> 00:01:35,000
AND THIS--THIS PARTICULAR
RESEARCH

36
00:01:35,000 --> 00:01:37,166
IS GOING TO REVEAL
REALLY IMPORTANT CLUES

37
00:01:37,166 --> 00:01:40,766
ABOUT WHAT CAUSES OSTEOPOROSIS
AND OTHER BONE DISORDERS.

38
00:01:40,766 --> 00:01:42,766
WHEN YOU GET MY AGE,
IT'S REALLY INTERESTING

39
00:01:42,766 --> 00:01:44,700
TO HEAR ABOUT THOSE.

40
00:01:44,700 --> 00:01:47,466
AND HIS PRIMARY FOCUS IS UNDER--
EXAMINING HOW SPACEFLIGHT

41
00:01:47,466 --> 00:01:50,800
AND MECHANICAL LOADING TRIGGERS
COMPLEX CHANGES IN ORGANISMS,

42
00:01:50,800 --> 00:01:52,966
PARTICULARLY
THE MAMMALIAN SKELETON.

43
00:01:52,966 --> 00:01:55,533
HE RECEIVED HIS PhD
FROM STANFORD UNIVERSITY--

44
00:01:55,533 --> 00:01:57,133
IT'S A JUNIOR COLLEGE
UP THE ROAD HERE,

45
00:01:57,133 --> 00:01:58,166
FOR THOSE THAT DON'T KNOW--
[laughter]

46
00:01:58,166 --> 00:01:59,766
IN AERONAUTICS AND ASTRONAUTICS.

47
00:01:59,766 --> 00:02:01,233
AND HIS BACHELOR
OF SCIENCE DEGREE

48
00:02:01,233 --> 00:02:03,500
FROM THE UNIVERSITY OF FLORIDA
IN PHYSICS AND ASTRONOMY.

49
00:02:03,500 --> 00:02:07,433
YOU KNOW, ANOTHER, YOU KNOW,
SEMI-WELL-KNOWN PLACE.

50
00:02:07,433 --> 00:02:09,766
HE COULDN'T GET INTO MICHIGAN.

51
00:02:09,766 --> 00:02:11,200
[laughter]

52
00:02:11,200 --> 00:02:12,966
BUT I--ALL--
ALL KIDDING ASIDE.

53
00:02:12,966 --> 00:02:16,233
JOSH IS ONE OF OUR MOST

DISTINGUISHED RESEARCHERS.

54
00:02:16,233 --> 00:02:20,466
HE RECENTLY COMPLETED
HIS NASA POSTDOCTORAL PROGRAM

55
00:02:20,466 --> 00:02:22,100
HERE AT AMES.

56
00:02:22,100 --> 00:02:25,533
BUT ON APRIL OF THIS YEAR,
AND I AM REALLY PROUD OF JOSH

57
00:02:25,533 --> 00:02:27,233
AND I THINK THAT
THE WHOLE CENTER SHOULD BE,

58
00:02:27,233 --> 00:02:28,866
HE WAS HONORED
AT THE WHITE HOUSE--

59
00:02:28,866 --> 00:02:30,933
SOME OF YOU MIGHT HAVE
HEARD OF THAT--

60
00:02:30,933 --> 00:02:33,133
BY PRESIDENT OBAMA--SOME OF YOU
MIGHT HAVE HEARD OF HIM--

61
00:02:33,133 --> 00:02:35,166
AND HE WAS NAMED ONE--

62
00:02:35,166 --> 00:02:38,266
HE WAS ONE OF THE FIVE
NASA RESEARCHERS

63
00:02:38,266 --> 00:02:40,500
THAT WAS A RECIPIENT
OF THE 2012

64
00:02:40,500 --> 00:02:43,100
PRESIDENTIAL EARLY CAREER AWARD
FOR SCIENTISTS AND ENGINEERS.

65
00:02:43,100 --> 00:02:45,600
SO JOSH IS GONNA TALK TODAY

66
00:02:45,600 --> 00:02:48,966
ABOUT "TO THE BONE: SPACEFLIGHT
AND THE SKELETAL SYSTEM."

67
00:02:48,966 --> 00:02:51,566
I ALSO NOTE, YOU KNOW--

68
00:02:51,566 --> 00:02:54,833
YOU KNOW, SINCE I WORE
KIND OF AN INTERESTING OUTFIT,

69
00:02:54,833 --> 00:02:56,566
THAT JOSH HAS TODAY, TOO,

70
00:02:56,566 --> 00:02:57,933
'CAUSE YOU USUALLY
DON'T SEE HIM IN A SUIT.

71
00:02:57,933 --> 00:03:01,266
SO PLEASE JOIN ME IN WELCOMING
DR. JOSH ALWOOD.

72
00:03:01,266 --> 00:03:04,366
[applause]

73
00:03:04,366 --> 00:03:08,166
- THANK YOU, PETE.

74
00:03:08,166 --> 00:03:10,300
WELL, THANK YOU
FOR THE INTRODUCTION, PETE.

75
00:03:10,300 --> 00:03:13,133
AND THANK YOU FOR INVITING ME
TO PARTICIPATE

76
00:03:13,133 --> 00:03:15,500
IN THIS COLLOQUIUM SERIES
THIS SUMMER.

77
00:03:15,500 --> 00:03:17,900
AND AS YOU CAN TELL
BY THE PROPS ON THE STAGE

78
00:03:17,900 --> 00:03:20,400
AND THE MUSIC,
THE--THE PERSIAN RUG,

79
00:03:20,400 --> 00:03:22,400
WE'RE GONNA HAVE
A LITTLE BIT OF FUN TODAY.

80
00:03:22,400 --> 00:03:24,466
AND I WAS CHALLENGED
TO WEAR A COSTUME,

81
00:03:24,466 --> 00:03:26,466
AND I DIDN'T--I WOULDN'T HAVE
COUNTED THIS AS A COSTUME,

82
00:03:26,466 --> 00:03:30,433
BUT I GUARANTEE ONE COSTUME
DURING THE PRESENTATION TODAY.

83
00:03:30,433 --> 00:03:33,066
SO KEEP YOUR EYES OPEN.

84
00:03:33,066 --> 00:03:35,933
SO, AS PETE SAID, I'M
A NEWLY HIRED SCIENTIST HERE

85

00:03:35,933 --> 00:03:38,266
AT NASA AMES IN SPACE BIOLOGY.

86
00:03:38,266 --> 00:03:40,533
IN TODAY'S TALK,
I'D LIKE TO BROADLY COVER

87
00:03:40,533 --> 00:03:44,033
THE BODY OF KNOWLEDGE
IN SKELETAL BIOLOGY

88
00:03:44,033 --> 00:03:46,500
AND BIOMECHANICS
DURING SPACEFLIGHT.

89
00:03:46,500 --> 00:03:49,400
AND I AM TO CONVEY THE RISKS
OF BONE LOSS

90
00:03:49,400 --> 00:03:50,966
DURING THE SPACE MISSIONS

91
00:03:50,966 --> 00:03:53,133
AND THAT RESEARCH--
FUNDAMENTAL RESEARCH

92
00:03:53,133 --> 00:03:55,800
IN THIS AREA IS AN IMPORTANT
COMPONENT OF ANY SPACE PROGRAM

93
00:03:55,800 --> 00:03:57,366
FOR TWO REASONS--

94
00:03:57,366 --> 00:04:01,066
THE FIRST BEING TO UNCOVER
BASIC BIOLOGICAL MECHANISMS

95
00:04:01,066 --> 00:04:03,633
THAT IMPROVE OUR UNDERSTANDING
OF THESE CONDITIONS,

96
00:04:03,633 --> 00:04:07,200
AS WELL AS TO TEST
PROTECTIVE TREATMENTS,

97
00:04:07,200 --> 00:04:10,133
REFERRED TO IN THE TALK
AS COUNTERMEASURES,

98
00:04:10,133 --> 00:04:12,433
THAT ENABLE HUMAN EXPLORATION
OF SPACE.

99
00:04:12,433 --> 00:04:14,200
AND THIS IS A PROCESS

100
00:04:14,200 --> 00:04:16,200
OF TRANSLATING BASIC
SCIENCE RESULTS

101
00:04:16,200 --> 00:04:18,900
INTO--INTO PRACTICE
AND INTO SOLUTIONS.

102
00:04:18,900 --> 00:04:22,600
AND THIS IS NICELY ENCAPSULATED
BY THE AMES LOGO, ACTUALLY--

103
00:04:22,600 --> 00:04:25,366
DISCOVERY LEADING TO INNOVATIONS
LEADING TO SOLUTIONS.

104
00:04:25,366 --> 00:04:27,866
AND YOU CAN SEE
THE LITTLE CELL--

105
00:04:27,866 --> 00:04:30,300
THE FLUORESCENT GREEN HERE
ARE CELLS,

106
00:04:30,300 --> 00:04:33,800
AND SO THAT REALLY ILLUSTRATES
THE PROCESS WE'LL BE TAKING

107
00:04:33,800 --> 00:04:35,766
WITH THIS TRANSLATIONAL
PIPELINE.

108
00:04:35,766 --> 00:04:37,133
AND WHEN I WAS
AT THE WHITE HOUSE,

109
00:04:37,133 --> 00:04:39,733
PRESIDENT OBAMA ACTUALLY
IS VERY IN TUNE

110
00:04:39,733 --> 00:04:41,500
WITH TRANSLATIONAL RESEARCH.

111
00:04:41,500 --> 00:04:44,066
HE ACTUALLY EMPHASIZED
THAT IT'S REALLY IMPORTANT

112
00:04:44,066 --> 00:04:46,066
FOR BASIC SCIENTISTS
TO TRANSLATE THEIR WORK

113
00:04:46,066 --> 00:04:49,100
TO HELP HUMAN PROBLEMS.

114
00:04:49,100 --> 00:04:52,600
SO IF I HAD TO SUMMARIZE
MY TALK IN ONE SLIDE,

115
00:04:52,600 --> 00:04:54,466
SPACEFLIGHT IS BAD FOR THE BONE

116
00:04:54,466 --> 00:04:56,400
THOROGOOD ALMOST GOT IT RIGHT.

117
00:04:56,400 --> 00:05:00,966
AND SO SPACEFLIGHT IS--PRESENTS
UNIQUE BIOLOGICAL CHALLENGES

118
00:05:00,966 --> 00:05:04,600
TO THE SURVIVAL AND EQUILIBRIUM
OF LIVING SYSTEMS.

119
00:05:04,600 --> 00:05:07,566
AND TWO NOTABLE ASPECTS
OF THE ENVIRONMENT

120
00:05:07,566 --> 00:05:10,266
ARE WEIGHTLESSNESS ASSOCIATED
WITH MICROGRAVITY

121
00:05:10,266 --> 00:05:12,800
AS WELL AS IONIZING RADIATION
EXPOSURE

122
00:05:12,800 --> 00:05:15,966
FROM SOLAR PARTICLE EVENTS,
WHICH ARE MAINLY PROTONS

123
00:05:15,966 --> 00:05:19,766
AND GALACTIC COSMIC RAYS,
WHICH ARE VERY HIGH ENERGY

124
00:05:19,766 --> 00:05:22,800
AND VERY HARD TO SHIELD
AND CAN--

125
00:05:22,800 --> 00:05:26,300
AND DO GREAT DAMAGE
IN BIOLOGICAL ORGANISMS.

126
00:05:26,300 --> 00:05:29,566
IT'S WIDELY KNOWN
THAT WEIGHTLESSNESS

127
00:05:29,566 --> 00:05:31,333
INDUCES BONE LOSS,

128
00:05:31,333 --> 00:05:34,300
BUT LESS WELL-KNOWN ARE
THE EFFECTS OF SPACE RADIATION.

129
00:05:34,300 --> 00:05:36,166
AND THIS WILL BECOME
VERY IMPORTANT

130
00:05:36,166 --> 00:05:38,266
ONCE WE VENTURE OUTSIDE
OF THE EARTH'S MAGNETIC FIELDS,

131
00:05:38,266 --> 00:05:39,666
WHICH ARE CURRENTLY
PROTECTING US

132
00:05:39,666 --> 00:05:42,400
FROM SOME OF THESE
HIGH-ENERGY COSMIC RAYS.

133
00:05:42,400 --> 00:05:45,200
AND SO THIS KIND OF ILLUSTRATES
THAT TRANSLATIONAL PIPELINE.

134
00:05:45,200 --> 00:05:47,433
WHY DO WE STUDY BONE LOSS?

135
00:05:47,433 --> 00:05:50,366
WELL, THERE'S THE BASIC
HYPOTHESIS-DRIVEN SCIENCE

136
00:05:50,366 --> 00:05:53,800
AND DISCOVERY OF NEW KNOWLEDGE

137
00:05:53,800 --> 00:05:56,866

BUT ALSO TRYING TO ENABLE
LONGER DURATION MISSIONS

138
00:05:56,866 --> 00:05:59,200
THAT ARE FARTHER AWAY
FROM OUR HOME HERE ON EARTH.

139
00:05:59,200 --> 00:06:02,566
AT THE SAME TIME, WE ALSO WANT
TO HELP PEOPLE ON EARTH

140
00:06:02,566 --> 00:06:05,900
IN TERMS OF UNDERSTANDING
OSTEOPOROSIS BETTER,

141
00:06:05,900 --> 00:06:08,633
UNDERSTANDING WHAT IS--

142
00:06:08,633 --> 00:06:10,700
WHAT ARE THE MECHANISMS
OF AGING,

143
00:06:10,700 --> 00:06:14,166
WHAT ARE THE NEGATIVE EFFECTS OF
BED REST, SEDENTARY LIFESTYLES,

144
00:06:14,166 --> 00:06:17,033
RADIATION ON--
FROM OCCUPATIONAL EXPOSURE

145
00:06:17,033 --> 00:06:19,800
AND RADIO THERAPY,
AND THINKING BIG,

146
00:06:19,800 --> 00:06:23,033
OPENING UP NEW POSSIBILITIES
FOR HUMANITY'S ROLE IN SPACE.

147
00:06:23,033 --> 00:06:25,233
BEFORE I DELVE INTO SCIENCE,

148
00:06:25,233 --> 00:06:27,766
I'D LIKE TO SHARE WHERE
MY INTEREST ORIGINATED FROM

149
00:06:27,766 --> 00:06:30,000
AND THE PATH I TOOK
TO BECOME A SCIENTIST.

150
00:06:30,000 --> 00:06:32,233
AND AS YOU HEARD
IN THE INTRODUCTION,

151
00:06:32,233 --> 00:06:34,166
MY BACKGROUND IS
SOMEWHAT STAGGERED.

152
00:06:34,166 --> 00:06:36,866
BUT LOOKING BACK,
I WAS PURSUING AN INTEREST

153
00:06:36,866 --> 00:06:41,066
THAT RESIDED IN THE NEXUS OF
THREE SEEMINGLY SEPARATE AREAS,

154
00:06:41,066 --> 00:06:43,433
AND I'VE KIND OF GENERALIZED
THESE ELEMENTS

155
00:06:43,433 --> 00:06:46,033
AS FORCE, LIFE, AND SPACE.

156
00:06:46,033 --> 00:06:49,533
AND SO I THINK IT STARTED WITH
SCIENTIFIC CURIOSITY,

157
00:06:49,533 --> 00:06:52,233
ASKING QUESTIONS,
SEEKING UNDERSTANDING,

158
00:06:52,233 --> 00:06:54,533
AND THEN WITH--
WITH MY RESEARCH,

159
00:06:54,533 --> 00:06:56,533
LEARNING HOW TO FORM
A HYPOTHESIS

160
00:06:56,533 --> 00:06:59,233
AND--AND ANSWER
THAT HYPOTHESIS.

161
00:06:59,233 --> 00:07:00,833
I GREW UP IN FLORIDA

162
00:07:00,833 --> 00:07:03,933
AND WAS REALLY ABLE TO SEE
FIRSTHAND

163
00:07:03,933 --> 00:07:05,633
THE SPACE SHUTTLE LAUNCHES.

164
00:07:05,633 --> 00:07:08,200
AND SO THIS IS A PICTURE
I TOOK IN HIGH SCHOOL,

165
00:07:08,200 --> 00:07:11,166
AND THIS REALLY CAPTIVATED
MY IMAGINATION

166
00:07:11,166 --> 00:07:13,866
AND PROPELLED ME
INTO STUDYING PHYSICS

167
00:07:13,866 --> 00:07:17,366
AND, LATER,
STRUCTURAL ENGINEERING.

168
00:07:17,366 --> 00:07:20,166

AND SO IF ANY OF YOU
RECOGNIZE

169
00:07:20,166 --> 00:07:21,433
THE LAST FORMULA THERE,

170
00:07:21,433 --> 00:07:23,166
YOU CAN GO AHEAD
AND HEAD TO THE RECEPTION,

171
00:07:23,166 --> 00:07:25,466
'CAUSE YOU'LL--YOU UNDERSTAND
THE TALK ALREADY.

172
00:07:25,466 --> 00:07:28,500
AND SO I THINK I WAS--

173
00:07:28,500 --> 00:07:32,266
FROM MY CHILDHOOD, WHEN I WAS
ABOUT MAYBE HALF THE SIZE

174
00:07:32,266 --> 00:07:34,266
THAT I CURRENTLY AM,

175
00:07:34,266 --> 00:07:37,500
I WAS FASCINATED WITH BONE
AS A LIVING STRUCTURE--

176
00:07:37,500 --> 00:07:40,600
AND I'LL KIND OF EXPLAIN
WHAT A LIVING STRUCTURE IS

177
00:07:40,600 --> 00:07:43,833
IN A COUPLE SLIDES--

178
00:07:43,833 --> 00:07:48,033
BUT I REALLY IMMERSED
INTO SKELETAL BIOLOGY RESEARCH

179

00:07:48,033 --> 00:07:51,233
AND--AND SO THE THING
THAT TIES THIS ALL TOGETHER

180
00:07:51,233 --> 00:07:55,000
IS THE EFFECTS OF SPACEFLIGHT
ON THE HUMAN BODY

181
00:07:55,000 --> 00:07:57,700
AND ON THE SKELETON.

182
00:07:59,233 --> 00:08:01,633
I'VE ALSO--I ALSO
SOON IMMERSED IN--

183
00:08:01,633 --> 00:08:03,300
FOLLOWING HIGH SCHOOL,

184
00:08:03,300 --> 00:08:05,133
IMMERSED IN SCIENTIFIC RESEARCH.

185
00:08:05,133 --> 00:08:08,433
AND WAS A PARTICIPANT
IN A NUMBER OF PROGRAMS,

186
00:08:08,433 --> 00:08:10,000
EDUCATIONAL PROGRAMS.

187
00:08:10,000 --> 00:08:12,333
AND I WANT TO EMPHASIZE
TO THE STUDENTS IN THE AUDIENCE,

188
00:08:12,333 --> 00:08:14,633
YOU ALREADY KNOW THIS,
BUT GET INVOLVED,

189
00:08:14,633 --> 00:08:18,100
BROADEN YOUR INTERESTS,
AND--AND REALLY DEVELOP

190
00:08:18,100 --> 00:08:20,400
YOUR--YOUR EXPERTISE
AND INTERESTS.

191
00:08:20,400 --> 00:08:23,533
AND THOSE ON THE WEB,
HERE ARE SOME PROGRAMS

192
00:08:23,533 --> 00:08:26,233
THAT NASA PROVIDES.

193
00:08:26,233 --> 00:08:28,366
SO MOVING NOW TO THE SCIENCE.

194
00:08:28,366 --> 00:08:30,200
I'LL START AT
THE STRUCTURAL LEVEL.

195
00:08:30,200 --> 00:08:34,500
SO THINKING ABOUT BONES
AS LIVING STRUCTURES,

196
00:08:34,500 --> 00:08:36,533
AND SO WHAT I HAVE HERE

197
00:08:36,533 --> 00:08:39,033
IS A RAT SKELETON
AND A HUMAN SKELETON,

198
00:08:39,033 --> 00:08:41,700
JUST TO COMPARE AND CONTRAST
THE DIFFERENT

199
00:08:41,700 --> 00:08:44,466
MORPHOLOGIES AND SIZES

200
00:08:44,466 --> 00:08:47,233
AND THAT RESEARCH WITH
SOME OF THESE MODEL ORGANISMS

201
00:08:47,233 --> 00:08:49,000
CAN COMPLEMENT OUR KNOWLEDGE

202
00:08:49,000 --> 00:08:51,633
OF BONE LOSS IN ASTRONAUTS.

203
00:08:51,633 --> 00:08:53,333
AND THEN
I'LL PROGRESSIVELY GO

204
00:08:53,333 --> 00:08:55,100
TO SMALLER AND SMALLER
LINK SCALES

205
00:08:55,100 --> 00:08:57,033
SO THEN WORKING
AT THE CELLULAR LEVEL

206
00:08:57,033 --> 00:09:00,533
AS WELL AS
THE MOLECULAR LEVEL.

207
00:09:00,533 --> 00:09:03,233
SO IN ADDITION
TO SKELETAL EFFECTS,

208
00:09:03,233 --> 00:09:07,600
GENERALLY SPACEFLIGHT IS
BAD FOR THE ENTIRE BODY.

209
00:09:07,600 --> 00:09:11,800
AMONG A NUMBER OF RESPONSES
IN THE BODY,

210
00:09:11,800 --> 00:09:14,266
THERE'S FLUID REDISTRIBUTION
TO THE TORSO,

211

00:09:14,266 --> 00:09:17,166
THERE ARE VISUAL CHANGES,
AMONG OTHERS.

212
00:09:17,166 --> 00:09:19,533
AND WE--YOU KNOW,
THIS UNDERSCORES

213
00:09:19,533 --> 00:09:21,166
THAT WE'VE EVOLVED AT 1G.

214
00:09:21,166 --> 00:09:22,966
IT'S BEEN CONSTANT.

215
00:09:22,966 --> 00:09:25,200
AND WE INTIMATELY DEPEND
ON GRAVITY

216
00:09:25,200 --> 00:09:27,200
FOR--FOR SKELETAL HOMEOSTASIS

217
00:09:27,200 --> 00:09:29,566
AND HOMEOSTASIS
IN THE BODY.

218
00:09:29,566 --> 00:09:31,566
IT'S AN INTERESTING FACT

219
00:09:31,566 --> 00:09:33,333
THAT BREAKING DOWN THE BONE
MAY INCREASE--

220
00:09:33,333 --> 00:09:36,266
LEAD TO INCREASED RISK
OF KIDNEY STONES

221
00:09:36,266 --> 00:09:39,766
AS THE CALCIUM IS EXCRETED
IN THE URINE.

222
00:09:39,766 --> 00:09:42,700
AND THIS--THIS HAS BECOME
A PROBLEM

223
00:09:42,700 --> 00:09:45,233
IN THE PLUMBING ON ISS.

224
00:09:45,233 --> 00:09:48,800
SO THIS IS--YOU KNOW,
SPACEFLIGHT IS BAD

225
00:09:48,800 --> 00:09:50,966
AND THE LOSS OF SKELETAL MINERAL
IS BAD

226
00:09:50,966 --> 00:09:52,733
FOR THE ISS HARDWARE AS WELL.

227
00:09:52,733 --> 00:09:55,300
THIS IS A URINE PROCESSING
ASSEMBLY

228
00:09:55,300 --> 00:09:57,366
THAT RECYCLES URINE
INTO DRINKING WATER.

229
00:09:57,366 --> 00:10:01,200
AND--AND THIS
WAS ACTUALLY CLOGGED

230
00:10:01,200 --> 00:10:04,066
BY ELEVATED CALCIUM
CONCENTRATIONS,

231
00:10:04,066 --> 00:10:07,800
IN PART DUE TO THE HEIGHTENED
BONE LOSS IN ASTRONAUTS.

232
00:10:09,533 --> 00:10:14,166

GETTING BACK TO THE SKELETON
AS A LIVING STRUCTURE.

233
00:10:14,166 --> 00:10:15,666
THIS IS--THIS IS ONE REASON

234
00:10:15,666 --> 00:10:19,400
WHY BONE
REALLY FASCINATES ME.

235
00:10:19,400 --> 00:10:21,500
WHAT DOES
A LIVING STRUCTURE MEAN?

236
00:10:21,500 --> 00:10:25,233
WELL, CONTRAST BONE
TO A BRIDGE

237
00:10:25,233 --> 00:10:27,300
MADE OF CONCRETE AND STEEL.

238
00:10:27,300 --> 00:10:30,966
THEY BOTH CARRY
THE EFFECTIVE LOAD, AND--

239
00:10:30,966 --> 00:10:33,166
HOWEVER, THE SKELETON
ACTIVELY SENSES

240
00:10:33,166 --> 00:10:36,033
AND ADAPTS TO THE DEMANDS
OF ITS MECHANICAL ENVIRONMENT--

241
00:10:36,033 --> 00:10:38,833
LIKE MUSCULAR FORCES,
GROUND REACTION FORCES--

242
00:10:38,833 --> 00:10:42,266
BY DISTRIBUTING MINERAL--
MINERALIZED TISSUE

243
00:10:42,266 --> 00:10:45,733
WHERE IT'S MOST NEEDED
AND REMOVING IT WHERE IT'S NOT.

244
00:10:45,733 --> 00:10:47,533
AND SO OVER--THIS IS--

245
00:10:47,533 --> 00:10:50,000
THIS LINE OF THINKING EXTENDS
BACK OVER 100 YEARS

246
00:10:50,000 --> 00:10:53,200
WITH AN ORTHOPEDIST
NAMED JULIUS WOLFF

247
00:10:53,200 --> 00:10:54,566
WHERE HE PROPOSED THESE IDEAS

248
00:10:54,566 --> 00:10:57,366
AFTER OBSERVING THE ORGANIZATION
OF THE FEMORAL HEAD.

249
00:10:57,366 --> 00:10:59,500
AND SO THAT'S SHOWN
IN CROSS SECTION HERE.

250
00:10:59,500 --> 00:11:02,066
SO THIS IS THE HIP JOINT

251
00:11:02,066 --> 00:11:04,266
KIND OF IN--
THIS IS THE PROXIMAL--

252
00:11:04,266 --> 00:11:06,966
PROXIMAL FEMUR
IN A LONGITUDINAL CROSS SECTION.

253
00:11:06,966 --> 00:11:09,466

NOW, WHAT YOU SEE
WHEN YOU CRACK OPEN A FEMUR

254
00:11:09,466 --> 00:11:12,000
IS YOU SEE KIND OF THIS HOLLOW
TUBULAR STRUCTURE

255
00:11:12,000 --> 00:11:13,666
IN THE MIDSHAFT,

256
00:11:13,666 --> 00:11:16,266
WHICH IS THE REALLY, REALLY
DENSE CORTICAL BONE.

257
00:11:16,266 --> 00:11:18,633
AS YOU GET UP TO THE JOINT,
THE HIP JOINT,

258
00:11:18,633 --> 00:11:22,233
YOU SEE THIS VERY--
HIGHLY STRIATED

259
00:11:22,233 --> 00:11:25,700
AND HIGHLY POROUS CANCELLOUS
OR TRABECULAR BONE.

260
00:11:25,700 --> 00:11:27,566
AND WHAT WOLFF RECOGNIZED

261
00:11:27,566 --> 00:11:30,600
IS THAT LIKE A CANTILEVERED BEAM
AND BENDING,

262
00:11:30,600 --> 00:11:33,766
THE FEMUR HAS COMPRESSIVE
STRUTS.

263
00:11:33,766 --> 00:11:35,300
IT HAS TENSILE STRUTS,

264
00:11:35,300 --> 00:11:37,266
AND THAT THESE
ARE UNIQUE LOAD PATHS

265
00:11:37,266 --> 00:11:39,400
THAT TRANSFER FORCE
INTO THE CORTICAL BONE.

266
00:11:41,300 --> 00:11:45,133
IT'S IMPORTANT TO NOTE
THAT LOCATIONS OF FRACTURE

267
00:11:45,133 --> 00:11:47,100
IN OSTEOPOROTIC PATIENTS,

268
00:11:47,100 --> 00:11:49,433
AS WELL AS POTENTIALLY
IN ASTRONAUTS,

269
00:11:49,433 --> 00:11:52,700
OCCURS IN THESE HIGHLY POROUS
CANCELLOUS REGIONS.

270
00:11:52,700 --> 00:11:55,033
SO IF YOU DISTURB
THE--THE TISSUE THERE,

271
00:11:55,033 --> 00:11:57,933
IT'S VERY FRAGILE TISSUE

272
00:11:57,933 --> 00:12:00,666
AND THAT CAN LEAD
TO A HEIGHTENED PROPENSITY

273
00:12:00,666 --> 00:12:04,100
FOR FRACTURE.

274
00:12:04,100 --> 00:12:05,966
ZOOMING IN NOW

TO THE CELLULAR LEVEL,

275
00:12:05,966 --> 00:12:08,966
THERE ARE THREE CELL TYPES
THAT I'LL TALK ABOUT TODAY.

276
00:12:08,966 --> 00:12:12,333
THE FIRST IS THE OSTEOBLAST

277
00:12:12,333 --> 00:12:13,966
THESE ARE BONE-FORMING CELLS

278
00:12:13,966 --> 00:12:16,166
THAT RESIDE AT THE SURFACE
OF THE BONE.

279
00:12:16,166 --> 00:12:19,500
OCCASIONALLY, SOME OF
THESE OSTEOBLAST CELLS

280
00:12:19,500 --> 00:12:21,866
BECOME TRAPPED
IN THEIR OWN MATRIX

281
00:12:21,866 --> 00:12:23,533
IN MINERALIZED TISSUE

282
00:12:23,533 --> 00:12:26,900
AND BECOME EMBEDDED
INTO CAVE-LIKE LACUNAE,

283
00:12:26,900 --> 00:12:29,666
AND THESE ARE DEEMED OSTEOCYTES.

284
00:12:32,100 --> 00:12:35,766
THERE'S A THIRD TYPE OF CELL
CALLED OSTEOCLASTS,

285
00:12:35,766 --> 00:12:38,933

AND THESE ARE GIANT
MULTINUCLEATED CELLS

286
00:12:38,933 --> 00:12:40,300
THAT ATTACH TO THE BONE

287
00:12:40,300 --> 00:12:43,300
AND DISSOLVE AWAY
THIS MATRIX AND MINERAL.

288
00:12:43,300 --> 00:12:46,066
AND COORDINATED--COORDINATED
ACTIVITY OF THESE CELLS

289
00:12:46,066 --> 00:12:50,033
IS CALLED BONE REMODELING
AND ALLOW SHAPING OF THE BONE,

290
00:12:50,033 --> 00:12:52,533
AND IT'S A REMARKABLY DYNAMIC
PROCESS.

291
00:12:52,533 --> 00:12:55,666
FOR EXAMPLE, THE SKELETON
COMPLETELY REMODELS ITSELF

292
00:12:55,666 --> 00:12:57,733
ABOUT ONCE EVERY DECADE.

293
00:12:57,733 --> 00:13:01,366
LOOKING AT THE ULTRASTRUCTURE
OF THE OSTEOCYTE,

294
00:13:01,366 --> 00:13:03,066
WHICH IS
IN THE LOWER RIGHT HERE,

295
00:13:03,066 --> 00:13:05,533
WHAT YOU CAN SEE IS
A WATERMELON-SHAPED CELL BODY

296
00:13:05,533 --> 00:13:08,800
AND PROCESSES
THAT EXTEND OUT

297
00:13:08,800 --> 00:13:10,733
INTO THE MINERALIZED TISSUE.

298
00:13:10,733 --> 00:13:14,266
SO THESE CELLS FORM NETWORKS
WITH OTHER OSTEOCYTES,

299
00:13:14,266 --> 00:13:18,133
AND THESE CELLS ARE THOUGHT TO
SENSE THE MECHANICAL ENVIRONMENT

300
00:13:18,133 --> 00:13:21,233
IN TERMS OF MECHANICAL STRAIN,

301
00:13:21,233 --> 00:13:23,633
FLUID SHEAR STRESS,
ACCELERATION.

302
00:13:23,633 --> 00:13:27,066
AND THESE CELLS ARE THOUGHT
TO DIRECT BONE REMODELING.

303
00:13:28,933 --> 00:13:31,066
SO WE HAVE
A SPECIAL PERFORMANCE NOW.

304
00:13:31,066 --> 00:13:34,700
BIOLOGY'S AN INHERENTLY
COLLABORATIVE FIELD.

305
00:13:34,700 --> 00:13:38,000
AND SO TO ILLUSTRATE THIS
PROCESS OF BONE REMODELING,

306

00:13:38,000 --> 00:13:42,033
WE HAVE AN ACTOR WHO'S--
ANN-SOFIE--

307
00:13:42,033 --> 00:13:43,933
WHO'S AN ASTRONAUT.

308
00:13:43,933 --> 00:13:48,600
AND WE'RE GONNA DEMONSTRATE
THE PROCESS OF BONE REMODELING.

309
00:13:48,600 --> 00:13:52,100
SO PLEASE WELCOME THE BONE
AND SIGNALING LAB ACTING TROUPE.

310
00:13:52,100 --> 00:13:54,833
[cheers and applause]

311
00:13:57,900 --> 00:14:01,933
SO FIRST, WE'LL COVER
BONE RESORPTION.

312
00:14:01,933 --> 00:14:05,466
SO OSTEOCYTES, WHICH--
[Pac-Man music]

313
00:14:05,466 --> 00:14:08,400
AH, WE HAVE A--WE HAVE A SIGNAL
BEING SENT.

314
00:14:08,400 --> 00:14:10,966
[laughs]
SO OSTEOCYTES,

315
00:14:10,966 --> 00:14:12,800
WHICH ARE THE CELLS THAT RESIDE
WITHIN THE BONE,

316
00:14:12,800 --> 00:14:15,333
THEY SEND A MOLECULAR SIGNAL

TO THE MARROW

317
00:14:15,333 --> 00:14:17,300
AND TO OSTEOCLAST PRECURSORS.

318
00:14:17,300 --> 00:14:19,433
THESE CELLS THEN HOME
TO THE BONE SURFACE,

319
00:14:19,433 --> 00:14:22,533
ATTACH, AND DEPOSIT ACID

320
00:14:22,533 --> 00:14:24,700
AND ACTIVELY DEGRADE AWAY
THE MATRIX

321
00:14:24,700 --> 00:14:26,233
AND THE MINERALIZED TISSUE.

322
00:14:26,233 --> 00:14:28,666
BY THAT MECHANISM,

323
00:14:28,666 --> 00:14:31,333
WE GET CHANGES
IN STRUCTURAL VOLUME.

324
00:14:31,333 --> 00:14:34,233
NEXT, THE OTHER COMPONENT
OF BONE REMODELING

325
00:14:34,233 --> 00:14:36,366
IS BONE FORMATION.

326
00:14:36,366 --> 00:14:38,600
SO AGAIN, WE HAVE
A UNIQUE MOLECULAR SIGNAL

327
00:14:38,600 --> 00:14:41,566
SENT TO

THE OSTEOBLAST PROGENITOR,

328
00:14:41,566 --> 00:14:43,533
WHICH THEN COMES TO
THE BONES SURFACE

329
00:14:43,533 --> 00:14:45,866
AND CREATES NEW MATRIX
AND NEW MINERAL.

330
00:14:45,866 --> 00:14:48,000
AND BY THAT--BY THIS PROCESS,
THE COORDINATED ACT--

331
00:14:48,000 --> 00:14:51,666
ACTIVITY OF THESE CELLS,
WE HAVE FRESH NEW BONE

332
00:14:51,666 --> 00:14:53,400
AND SKELETAL HOMEOSTASIS.

333
00:14:53,400 --> 00:14:55,966
AND IN ASTRONAUTS, WE SEE
THAT THESE PROCESSES GO AWRY.

334
00:14:55,966 --> 00:14:58,300
SO WITH THAT, PLEASE--

335
00:14:58,300 --> 00:15:00,433
PLEASE THANK ANN-SOFIE
AS THE ASTRONAUT.

336
00:15:00,433 --> 00:15:01,833
[applause]

337
00:15:01,833 --> 00:15:04,233
MOHIT, BETSABEL, AND REBECCA.

338
00:15:08,533 --> 00:15:10,700

[chuckles]

339
00:15:10,700 --> 00:15:13,066
I DEFINITELY OWE YOU ALL
SOME BEERS AFTER THIS.

340
00:15:13,066 --> 00:15:15,066
[laughs]

341
00:15:18,900 --> 00:15:22,033
SO BUILDING ON THIS IDEA
OF BONE IS A LIVING STRUCTURE

342
00:15:22,033 --> 00:15:23,766
AND THE PROCESS
OF BONE REMODELING,

343
00:15:23,766 --> 00:15:26,033
IT'S NOT TOO FAR A LEAP
TO STATE

344
00:15:26,033 --> 00:15:27,600
THAT BONE REMODELING
IS A FUNCTION

345
00:15:27,600 --> 00:15:29,566
OF THE MECHANICAL
LOADING ENVIRONMENT.

346
00:15:29,566 --> 00:15:32,800
AND SO IN MORE SPECIFICITY

347
00:15:32,800 --> 00:15:34,866
THE MECHANICAL STRAIN
EXPERIENCED

348
00:15:34,866 --> 00:15:37,266
BY THE DEFORMATION OF THE BONE,

349

00:15:37,266 --> 00:15:40,100
FLUID SHEAR STRESS AS IT PASSES
OVER THE SURFACE OF THE BONE,

350
00:15:40,100 --> 00:15:43,266
HYDROSTATIC PRESSURE,
AND ALSO GRAVITY

351
00:15:43,266 --> 00:15:46,233
IN TERMS OF
GRAVITATIONAL ACCELERATION.

352
00:15:46,233 --> 00:15:48,066
THESE ELEVATIONS
IN MECHANICAL LOADING,

353
00:15:48,066 --> 00:15:51,200
WHEN THEY'RE ELEVATED,
CAUSE, FOR EXAMPLE,

354
00:15:51,200 --> 00:15:54,366
DURING EXERCISE,
CAUSE CHANGES IN BONE VOLUME.

355
00:15:54,366 --> 00:15:56,800
AND THIS IS THE DOMAIN
OF THE OSTEOBLASTS.

356
00:15:56,800 --> 00:15:59,466
IN THE--
IN THE OPPOSITE DIRECTION,

357
00:15:59,466 --> 00:16:03,433
IN MICROGRAVITY,
WEIGHTLESSNESS, AND BED REST,

358
00:16:03,433 --> 00:16:07,600
THIS IS IN THE DOMAIN
OF THE OSTEOCLAST CELLS,

359

00:16:07,600 --> 00:16:11,866
AND SO WE SEE NEGATIVE CHANGES
IN BONE VOLUME.

360
00:16:11,866 --> 00:16:13,800
TO ILLUSTRATE THESE IDEAS
IN MORE DEPTH,

361
00:16:13,800 --> 00:16:17,133
WE'LL LOOK AT THE RIGHT AND LEFT
ARM OF A TENNIS PLAYER

362
00:16:17,133 --> 00:16:19,866
AS A MODEL OF ELEVATED
MECHANICAL LOADING.

363
00:16:19,866 --> 00:16:22,366
SO LOOKING AT THIS X-RAY,

364
00:16:22,366 --> 00:16:24,500
WHAT WE SEE IS THAT
ELITE TENNIS PLAYERS

365
00:16:24,500 --> 00:16:26,433
WHO HAVE PLAYED
THEIR WHOLE LIFE

366
00:16:26,433 --> 00:16:28,666
WITH HITTING--HITTING
THE TENNIS BALL WITH ONE HAND,

367
00:16:28,666 --> 00:16:32,166
THEY HAVE--THEY SHOW, YOU KNOW,
IMMEDIATE DIFFERENCES

368
00:16:32,166 --> 00:16:36,300
IN THE MINERAL DENSITY
AND ALSO THE GEOMETRY

369
00:16:36,300 --> 00:16:38,033

OF--OF THEIR ARMS.

370
00:16:38,033 --> 00:16:42,500
AND SO THAT MANIFESTS
IN BONE MINERAL CONTENT

371
00:16:42,500 --> 00:16:44,800
AS WELL AS DIAMETER

372
00:16:44,800 --> 00:16:46,366
AND THICKNESS OF THE BONE.

373
00:16:46,366 --> 00:16:50,366
AND UNDOUBTEDLY THESE GEOMETRIC
AND MATERIAL CHANGES

374
00:16:50,366 --> 00:16:53,600
CAN IMPROVE STRENGTH AS WELL.

375
00:16:53,600 --> 00:16:56,666
IN CONTRAST, ASTRONAUTS
EXPERIENCE WEIGHTLESSNESS

376
00:16:56,666 --> 00:16:58,366
DURING MICROGRAVITY.

377
00:16:58,366 --> 00:17:01,733
THIS DOESN'T MEAN INACTIVITY
JUST DIFFERENT LOADING PROFILE

378
00:17:01,733 --> 00:17:03,266
THAN WHAT'S EXPERIENCED
ON EARTH.

379
00:17:03,266 --> 00:17:05,533
AND SO WHAT THIS HISTOGRAM SHOWS

380
00:17:05,533 --> 00:17:08,366
IS THE NUMBER

OF LOADING OCCURRENCES

381
00:17:08,366 --> 00:17:12,866
VERSUS THE--EACH PEAK FORCE
OF EACH OCCURRENCE.

382
00:17:12,866 --> 00:17:16,166
AND SO IN BLACK,
YOU SEE NORMAL ACTIVITY

383
00:17:16,166 --> 00:17:19,233
LIKE WALKING AND RUNNING

384
00:17:19,233 --> 00:17:20,966
ON 1G HERE ON EARTH.

385
00:17:20,966 --> 00:17:24,666
AND IN GRAY, YOU SEE
THE INTERNATIONAL SPACE STATION.

386
00:17:24,666 --> 00:17:28,566
SO RUNNING ON THE COLD,
BARE TREADMILL, FOR EXAMPLE,

387
00:17:28,566 --> 00:17:31,700
THAT GETS A PEAK FORCE
OF ABOUT 1.4

388
00:17:31,700 --> 00:17:34,366
ON ISS,
1.4 TIMES BODY WEIGHT.

389
00:17:34,366 --> 00:17:37,100
WHEREAS ON EARTH,
IT'S ABOUT 2.5.

390
00:17:37,100 --> 00:17:40,566
AND SO THIS IS--SUNI WILLIAMS,
WHEN SHE RAN THE BOSTON MARATHON

391
00:17:40,566 --> 00:17:42,666
IN SPACE,
SHE--SHE SAID

392
00:17:42,666 --> 00:17:46,300
THAT SHE WAS GETTING ABOUT
75 TO 85% OF HER BODY WEIGHT

393
00:17:46,300 --> 00:17:48,700
LOADING ON THE--
ON THE TREADMILL.

394
00:17:48,700 --> 00:17:51,066
APPARENTLY IT WASN'T DESIGNED
TO DO MARATHONS IN SPACE,

395
00:17:51,066 --> 00:17:55,100
AND SO IT WAS VERY UNCOMFORTABLE
TO RUN 26.2 MILES.

396
00:17:55,100 --> 00:17:58,933
INTERESTING NOTE, WHEN SHE
RETURNED THE YEAR AFTER

397
00:17:58,933 --> 00:18:00,466
AND SHE RAN
THE BOSTON MARATHON,

398
00:18:00,466 --> 00:18:03,966
SHE SHAVED ABOUT HALF AN HOUR
OFF OF HER TIME.

399
00:18:03,966 --> 00:18:07,200
SO, YOU KNOW,
YOU CAN IMMEDIATELY SEE

400
00:18:07,200 --> 00:18:11,133
THAT THE HIGH FORCE EXERCISE
STIMULATION IS MISSING

401
00:18:11,133 --> 00:18:12,900
ON ISS.

402
00:18:12,900 --> 00:18:16,266
AND THIS WAS A GAP IN THE--IN
THE CADRE OF EXERCISE EQUIPMENT

403
00:18:16,266 --> 00:18:17,966
FOR SOME TIME.

404
00:18:17,966 --> 00:18:19,966
AND THOUGH THIS HAS SINCE
BEEN RECTIFIED,

405
00:18:19,966 --> 00:18:22,833
AND I'LL SHARE THOSE RESULTS
WITH YOU IN A MOMENT.

406
00:18:22,833 --> 00:18:26,166
SO WHAT HAVE WE LEARNED FROM
THE--FROM THE PAST DECADES

407
00:18:26,166 --> 00:18:27,900
OF RESEARCH INTO THIS AREA?

408
00:18:27,900 --> 00:18:29,800
SO THIS IS REALLY THE KEY DATA
FROM ASTRONAUTS

409
00:18:29,800 --> 00:18:31,433
THAT CHARACTERIZE THE PROBLEM,

410
00:18:31,433 --> 00:18:33,300
AND THIS IS GENERATED THROUGH
DEXA SCANS

411
00:18:33,300 --> 00:18:35,700
AND MORE RECENTLY
THROUGH CT SCANS.

412
00:18:35,700 --> 00:18:38,566
SO--SO RIGHT HERE,
IT'S SHOWN--

413
00:18:38,566 --> 00:18:40,366
THIS IS DATA FROM MIR,

414
00:18:40,366 --> 00:18:44,200
AND SO WHAT YOU SEE IS THAT
IN LONG-DURATION MISSIONS

415
00:18:44,200 --> 00:18:47,066
BONE LOSS MANIFESTS,
AND IT APPEARS AT A RATE

416
00:18:47,066 --> 00:18:50,433
OF ABOUT 1% LOSS OF BONE
MINERAL DENSITY PER MONTH.

417
00:18:50,433 --> 00:18:52,866
THIS OCCURS
IN THE WEIGHT-BEARING BONES,

418
00:18:52,866 --> 00:18:55,566
LIKE THE SPINE,

419
00:18:55,566 --> 00:18:58,833
THE FEMORAL NECK,
THE TIBIA.

420
00:18:58,833 --> 00:19:01,533
BUT IT DOESN'T MANIFEST
IN THE UPPER EXTREMITIES,

421
00:19:01,533 --> 00:19:04,233
LIKE THE HUMERUS.

422
00:19:04,233 --> 00:19:06,900

SO THESE WEIGHT-BEARING BONES
ARE REALLY--

423
00:19:06,900 --> 00:19:09,433
THEY NEED THIS
MECHANICAL FORCE TO SURVIVE

424
00:19:09,433 --> 00:19:12,533
AND TO MAINTAIN HOMEOSTASIS.

425
00:19:12,533 --> 00:19:15,700
IN MORE DEPTH,
THE SKELETAL TURNOVER

426
00:19:15,700 --> 00:19:18,000
IS MORE PRONOUNCED
IN THE CANCELLOUS TISSUE.

427
00:19:18,000 --> 00:19:20,600
AND ONCE THE ASTRONAUTS
RETURN TO EARTH,

428
00:19:20,600 --> 00:19:23,266
IT TAKES A LONG TIME
TO RECOVER.

429
00:19:23,266 --> 00:19:25,766
AND IN FACT,
IT MAY NOT EVER RECOVER

430
00:19:25,766 --> 00:19:29,466
AFTER--AFTER ONE YEAR
EARTHBOUND.

431
00:19:31,366 --> 00:19:35,666
AND AS A RESULT
OF CANCELLOUS DEFICITS,

432
00:19:35,666 --> 00:19:37,566
THERE'S AN EXPANSION

OF THE CORTICAL BONE

433
00:19:37,566 --> 00:19:39,433
THAT--THAT TAKES PLACE
IN ASTRONAUTS

434
00:19:39,433 --> 00:19:41,566
AFTER THEY'VE RETURNED
TO NORMAL LOADING.

435
00:19:43,166 --> 00:19:45,466
SO, YOU KNOW,
TAKEN TOGETHER,

436
00:19:45,466 --> 00:19:47,766
I THINK THIS REALLY IS
A CONCERN

437
00:19:47,766 --> 00:19:50,066
IN TERMS OF
ASTRONAUT FRACTURE RISK.

438
00:19:52,233 --> 00:19:54,466
IN FACT, WE CAN QUANTIFY
THIS RISK IN MORE DETAIL

439
00:19:54,466 --> 00:19:56,533
WITH COMPUTER MODELING.

440
00:19:56,533 --> 00:19:59,466
SO FROM THE IN VIVO CT SCANS

441
00:19:59,466 --> 00:20:01,166
FROM THE ASTRONAUT BONES,

442
00:20:01,166 --> 00:20:02,900
ONE CAN GENERATE
STRUCTURAL ANALYSES--

443

00:20:02,900 --> 00:20:04,900
IN THIS CASE,
FINITE ELEMENTS--

444
00:20:04,900 --> 00:20:07,400
AND INVESTIGATE
THE DISTRIBUTION OF STRESS

445
00:20:07,400 --> 00:20:09,033
WITHIN BONES.

446
00:20:09,033 --> 00:20:11,800
AND SO THIS IS THE CONCENTRATION
OF FORCE WITHIN AN AREA.

447
00:20:11,800 --> 00:20:14,833
THIS EXEMPLARY FIGURE
SHOWS HIGH STRESS

448
00:20:14,833 --> 00:20:17,733
IN THE FEMORAL HEAD,

449
00:20:17,733 --> 00:20:19,600
WITH RED BEING
HIGH SHEAR STRESS

450
00:20:19,600 --> 00:20:21,666
AND BLUE BEING LOW.

451
00:20:23,333 --> 00:20:26,000
AND SO THIS TYPE OF ANALYSIS

452
00:20:26,000 --> 00:20:28,266
WAS PERFORMED BEFORE
AND AFTER FLIGHT

453
00:20:28,266 --> 00:20:29,833
ON ASTRONAUTS.

454

00:20:29,833 --> 00:20:31,900
AND SO THE DATA
IS HERE ON THE LEFT

455
00:20:31,900 --> 00:20:35,400
WITH A STANCE LOADING
CONFIGURATION

456
00:20:35,400 --> 00:20:37,500
AND A FALL LOADING
CONFIGURATION.

457
00:20:37,500 --> 00:20:39,500
AND SO EACH LINE HERE
IS AN INDEPENDENT ASTRONAUT

458
00:20:39,500 --> 00:20:41,633
BEFORE AND AFTER FLIGHT.

459
00:20:41,633 --> 00:20:45,000
AND SO ACROSS THE BOARD, YOU CAN
SEE THERE'S A LARGE MAJORITY

460
00:20:45,000 --> 00:20:46,933
OF NEGATIVE SLOPES

461
00:20:46,933 --> 00:20:50,000
IN EACH LOADING CONFIGURATION.

462
00:20:50,000 --> 00:20:51,633
AND WITH THE STANCE
CONFIGURATION,

463
00:20:51,633 --> 00:20:54,700
THERE'S ABOUT A 2.5%
DECREMENT PER MONTH

464
00:20:54,700 --> 00:20:58,133
IN--IN THE BONE STRENGTH

465
00:20:58,133 --> 00:21:00,433
NORMALIZED PER BODY WEIGHT.

466
00:21:00,433 --> 00:21:02,866
AND THESE DATA SUGGEST THAT
THE FORCES ARE CONCENTRATING

467
00:21:02,866 --> 00:21:05,300
WITHIN THE ASTRONAUT BONES

468
00:21:05,300 --> 00:21:08,400
AND SUGGEST ASTRONAUT BONES
HAVE REDUCED STRENGTH.

469
00:21:10,433 --> 00:21:13,900
AND NOW, TRANSITIONING TO
MODEL ORGANISMS

470
00:21:13,900 --> 00:21:15,200
THAT HAVE BEEN FLOWN INTO SPACE

471
00:21:15,200 --> 00:21:17,400
AS WELL AS GROUND-BASED MODELS

472
00:21:17,400 --> 00:21:19,333
THAT INCORPORATE MODEL ORGANISMS

473
00:21:19,333 --> 00:21:22,666
AND--AND HUMAN MODELS
OF WEIGHTLESSNESS.

474
00:21:22,666 --> 00:21:25,933
IT'S--THESE TYPES OF ANALYSES

475
00:21:25,933 --> 00:21:27,933
COMPLEMENT THOSE
PRIMARY DATA SETS

476

00:21:27,933 --> 00:21:30,766
THAT WE JUST WENT OVER
FROM THE ASTRONAUTS.

477
00:21:32,133 --> 00:21:35,133
AND SO WE CAN COMPARE THE DATA
THAT WE JUST REVIEWED

478
00:21:35,133 --> 00:21:36,900
AND ALSO EXTEND
OUR UNDERSTANDING

479
00:21:36,900 --> 00:21:40,033
AND LOOK AT MORE
FUNDAMENTAL BIOLOGY MECHANISMS,

480
00:21:40,033 --> 00:21:42,633
LOOK AT THE CELLULAR
AND MOLECULAR CHANGES

481
00:21:42,633 --> 00:21:45,233
THAT THE ANIMALS OR THE HUMANS
ARE EXPERIENCING.

482
00:21:45,233 --> 00:21:47,700
AND SO IN 1978,

483
00:21:47,700 --> 00:21:49,900
IT WAS OBSERVED WITH ANIMALS
FLOWN IN SPACE

484
00:21:49,900 --> 00:21:51,533
THAT THERE WAS DECREASED
MINERALIZATION

485
00:21:51,533 --> 00:21:53,733
BY OSTEOBLAST CELLS.

486
00:21:53,733 --> 00:21:58,633
MORE RECENTLY, THERE'S--IN

A SIMULATION OF WEIGHTLESSNESS,

487
00:21:58,633 --> 00:22:00,333
SHOWN HERE--

488
00:22:00,333 --> 00:22:02,133
THIS IS CALLED
THE HINDLIMB UNLOADING MODEL

489
00:22:02,133 --> 00:22:04,133
OF--USED FOR RODENTS
TO SIMULATE WEIGHTLESSNESS

490
00:22:04,133 --> 00:22:07,000
ON THE TIBIA AND FEMUR.

491
00:22:07,000 --> 00:22:09,766
THEY--THESE RESEARCHERS
IDENTIFIED

492
00:22:09,766 --> 00:22:11,800
ELEVATED OSTEOCLAST ACTIVITY,

493
00:22:11,800 --> 00:22:14,000
AND THIS IS MOST LIKELY
RESPONSIBLE

494
00:22:14,000 --> 00:22:17,566
FOR BONE LOSS OBSERVED
IN SIMULATED WEIGHTLESSNESS.

495
00:22:17,566 --> 00:22:20,433
AND THERE'S--THIS DATA
WAS ALSO CONFIRMED IN HUMANS

496
00:22:20,433 --> 00:22:22,233
WHO WERE UNDERGOING BED REST.

497
00:22:22,233 --> 00:22:24,300

SO 12 WEEKS OF BED REST

498
00:22:24,300 --> 00:22:26,766
LISTED ELEVATIONS
IN OSTEOCLAST ACTIVITY

499
00:22:26,766 --> 00:22:29,666
AND DECREASES
IN OSTEOBLAST ACTIVITY.

500
00:22:29,666 --> 00:22:31,933
SO THESE--THINKING BACK
TO THE BONE REMODELING,

501
00:22:31,933 --> 00:22:35,733
THESE ARE ALL REALLY NEGATIVE
FOR--

502
00:22:35,733 --> 00:22:38,700
FOR SKELETAL STRUCTURE AND--

503
00:22:38,700 --> 00:22:41,366
AND THIS PROVIDES
CELLULAR MECHANISMS

504
00:22:41,366 --> 00:22:43,700
THAT UNDERLIE
THOSE VOLUMETRIC CHANGES.

505
00:22:45,733 --> 00:22:47,433
WITH ANIMALS FLOWN IN SPACE,

506
00:22:47,433 --> 00:22:50,533
WE CAN OBSERVE THE SKELETON
WITH GREATER RESOLUTION.

507
00:22:50,533 --> 00:22:53,500
AND SO WHAT'S SHOWN HERE
ARE THE PELVIC ISCHIA

508
00:22:53,500 --> 00:22:55,966
OF GROUND CONTROL ON THE LEFT

509
00:22:55,966 --> 00:22:58,666
AND 15 DAYS OF SPACEFLIGHT
ON THE RIGHT.

510
00:22:58,666 --> 00:23:00,966
THESE WERE IMAGED
WITH MICRO-CT BY COLLEAGUES

511
00:23:00,966 --> 00:23:03,333
IN THE BONE AND SIGNALING LAB
HERE AT AMES.

512
00:23:03,333 --> 00:23:05,566
AND WHAT THESE SHOW

513
00:23:05,566 --> 00:23:08,000
IS THAT BONE LOSS OCCURRED
IN THE PELVIC AREA

514
00:23:08,000 --> 00:23:10,300
THROUGH THINNING
OF THE CORTICAL BONE.

515
00:23:10,300 --> 00:23:12,100
AND IN OTHER--IN THE FEMUR,

516
00:23:12,100 --> 00:23:15,400
IT ACTUALLY SHOWED THINNING
OF BOTH THE CORTEX

517
00:23:15,400 --> 00:23:17,533
AS WELL AS
THE TRABECULAR STRUTS.

518
00:23:19,266 --> 00:23:21,033
AND WHAT--

519
00:23:21,033 --> 00:23:23,133
SO THIS IS A TRABECULAR STRUT
ON THE RIGHT.

520
00:23:23,133 --> 00:23:25,933
AND SO BASICALLY
JUST A RADIAL DECREASE

521
00:23:25,933 --> 00:23:28,266
IN--IN THAT STRUCTURE.

522
00:23:28,266 --> 00:23:31,633
AND THEN IN COMPLEMENTARY
GROUND-BASED MODELS

523
00:23:31,633 --> 00:23:33,833
THIS SHOWS PROGRESSIVE THINNING

524
00:23:33,833 --> 00:23:36,766
AND EVENTUALLY REMOVAL
OF THESE TRABECULAE

525
00:23:36,766 --> 00:23:39,633
WITH--WITH LONGER DURATION
SPACEFLIGHT.

526
00:23:39,633 --> 00:23:42,933
SO IT'S THE PROGRESSION OVER
THE COURSE OF A COUPLE MONTHS,

527
00:23:42,933 --> 00:23:44,433
OR WEEKS TO MONTHS,

528
00:23:44,433 --> 00:23:47,400
THAT THE SURFACE MEDIATED
RESORPTION

529
00:23:47,400 --> 00:23:51,366

STARTS TO REMOVE AWAY
THESE TRABECULAR STRUTS.

530
00:23:51,366 --> 00:23:53,333
AND ONCE THEY'RE REMOVED,

531
00:23:53,333 --> 00:23:55,866
THEY CANNOT BE CREATED DE NOVO.

532
00:23:55,866 --> 00:23:58,200
SO THAT'S--THIS UNDERSCORES

533
00:23:58,200 --> 00:24:00,266
KIND OF A STRUCTURAL MECHANISM

534
00:24:00,266 --> 00:24:02,900
UNDERLYING THESE REALLY
PERSISTENT DEFICITS

535
00:24:02,900 --> 00:24:04,766
IN THE ASTRONAUT
CANCELLOUS TISSUE

536
00:24:04,766 --> 00:24:06,966
AND WHY THE CORTICAL BONE

537
00:24:06,966 --> 00:24:09,400
SEEMS TO COMPENSATE
WITH AN EXPANSION.

538
00:24:11,466 --> 00:24:15,233
ADDITIONALLY, BONES
FROM SPACEFLIGHT ANIMALS

539
00:24:15,233 --> 00:24:17,233
AND GROUND-BASED MODELS
HAVE CONFIRMED

540
00:24:17,233 --> 00:24:20,500

THAT MECHANICAL PROPERTIES
AND BONE STRENGTH ARE REDUCED

541
00:24:20,500 --> 00:24:24,100
FOLLOWING WEIGHTLESSNESS.

542
00:24:24,100 --> 00:24:25,866
WITHIN THESE SAME MICE
WE ASKED,

543
00:24:25,866 --> 00:24:28,166
HOW ARE THE OSTEOCYTES
RESPONDING?

544
00:24:28,166 --> 00:24:30,100
WE ANALYZED
THE SPACE-FLOWN BONES

545
00:24:30,100 --> 00:24:32,000
AT SLAC NATIONAL LAB

546
00:24:32,000 --> 00:24:35,833
WITH A 30 NANOMETER X-RAY
TRANSITION MICROSCOPE--

547
00:24:35,833 --> 00:24:37,500
TRANSMISSION MICROSCOPE.

548
00:24:37,500 --> 00:24:39,033
AND SO THESE IMAGES
ARE PICTURED HERE.

549
00:24:39,033 --> 00:24:40,966
THE GROUND CONTROL
ON THE LEFT

550
00:24:40,966 --> 00:24:43,266
AND THE SPACE-FLOWN ANIMALS
ON THE RIGHT.

551
00:24:43,266 --> 00:24:45,600
AND WE ASKED WHETHER
THE LOCAL TISSUE DENSITY

552
00:24:45,600 --> 00:24:47,466
WAS ALTERED DURING SPACEFLIGHT,

553
00:24:47,466 --> 00:24:49,266
AND WHETHER
THE OSTEOCYTES SHOWED

554
00:24:49,266 --> 00:24:51,300
ANY MORPHOLOGICAL CHANGES,

555
00:24:51,300 --> 00:24:53,500
AND THE RESULTS WERE SURPRISING.

556
00:24:53,500 --> 00:24:56,133
WE DID NOT SEE ANY
TISSUE LEVEL DENSITY CHANGES,

557
00:24:56,133 --> 00:24:58,333
BUT WE DID SEE THE LACUNAE--

558
00:24:58,333 --> 00:25:01,133
THESE ARE THE APARTMENTS
OF THE OSTEOCYTES--

559
00:25:01,133 --> 00:25:04,066
THESE WERE BECOMING LARGER

560
00:25:04,066 --> 00:25:06,700
IN TERMS OF THEIR AREA
AND PERIMETER.

561
00:25:06,700 --> 00:25:10,033
AND THESE DATA SUGGEST
AN ADDITIONAL METHOD

562
00:25:10,033 --> 00:25:12,033
OF BONE REMODELING

563
00:25:12,033 --> 00:25:14,933
IN ADDITION TO THE SURFACE
MEDIATED OSTEOCLAST RESORPTION.

564
00:25:14,933 --> 00:25:18,200
NAMELY, THESE BONES ARE
REMODELING FROM THE INSIDE OUT.

565
00:25:18,200 --> 00:25:21,100
AND COLLEAGUES IN THE BONE
AND SIGNALING LAB CONFIRMED

566
00:25:21,100 --> 00:25:24,366
THIS REMODELING PHENOTYPE

567
00:25:24,366 --> 00:25:26,966
WITH PROTEIN MARKERS OF MATRIX

568
00:25:26,966 --> 00:25:30,100
AND MINERAL REMODELING
WITHIN THE OSTEOCYTE LACUNAE.

569
00:25:32,833 --> 00:25:34,733
SO STEPPING BACK TO ASTRONAUTS

570
00:25:34,733 --> 00:25:38,100
AND INTRODUCING THE IDEA OF
EXERCISE AS A COUNTERMEASURE,

571
00:25:38,100 --> 00:25:41,233
RECALL THAT THE LACK
OF HIGH-FORCE EXERCISES

572
00:25:41,233 --> 00:25:43,900
COULD BE A CRITICAL WEAKNESS

573
00:25:43,900 --> 00:25:48,066
OF UNDERLYING THE BONE LOSS
THAT WE TALKED ABOUT EARLIER.

574
00:25:48,066 --> 00:25:50,433
AND THIS RELATIVELY NEW DEVICE,

575
00:25:50,433 --> 00:25:53,300
THE ADVANCED RESISTIVE
EXERCISE DEVICE

576
00:25:53,300 --> 00:25:55,166
PICTURED HERE,

577
00:25:55,166 --> 00:25:57,066
HAS BECOME THE FIRST EFFECTIVE
COUNTERMEASURE

578
00:25:57,066 --> 00:25:59,900
AT PREVENTING BONE LOSS
EXPERIENCED BY ASTRONAUTS.

579
00:25:59,900 --> 00:26:03,166
SO WITH THIS DEVICE, THEY CAN
GET ABOUT 500 POUNDS OF FORCE

580
00:26:03,166 --> 00:26:04,966
IN A SQUAT EXERCISE.

581
00:26:04,966 --> 00:26:07,233
THEY CAN DO HEEL RAISES

582
00:26:07,233 --> 00:26:09,966
AND REALLY REINTRODUCE

583
00:26:09,966 --> 00:26:12,766
THIS--THIS HIGH-FORCE EXERCISE
ONTO THE WEIGHT-BEARING BONES.

584
00:26:12,766 --> 00:26:15,133
AND WHAT THE DATA SUGGESTS

585
00:26:15,133 --> 00:26:17,433
ARE IN THE SPINE AND THE FEMUR

586
00:26:17,433 --> 00:26:19,700
AND THE PELVIS,
THAT THIS IS PREVENTING

587
00:26:19,700 --> 00:26:22,700
THAT--THE BONE LOSS
THAT WE TALKED ABOUT EARLIER.

588
00:26:22,700 --> 00:26:25,133
HOWEVER, WE'RE NOT
OUT OF THE WOODS YET.

589
00:26:25,133 --> 00:26:27,700
WHEN YOU LOOK AT THE BLOOD
AND THE URINE,

590
00:26:27,700 --> 00:26:29,600
THE SKELETON IS IN
A HIGH-TURNOVER STATE.

591
00:26:29,600 --> 00:26:32,066
SO WHAT THAT MEANS
IS FORMATION IS HIGH,

592
00:26:32,066 --> 00:26:34,366
WHICH IS A GOOD THING,
BUT RESORPTION IS STILL HIGH.

593
00:26:34,366 --> 00:26:37,633
SO THE OSTEOCLASTS ARE STILL
IN AN ACTIVE STATE.

594
00:26:37,633 --> 00:26:40,166

SO I DON'T THINK WE'VE
FULLY SOLVED THE PROBLEM,

595
00:26:40,166 --> 00:26:42,900
AND WE DON'T KNOW
AT WHAT QUALITY THE BONE IS

596
00:26:42,900 --> 00:26:45,766
THAT FORMS UNDER
THIS HIGH-TURNOVER STATE.

597
00:26:45,766 --> 00:26:49,500
NONETHELESS, THIS IS THE FIRST
EFFECTIVE COUNTERMEASURE

598
00:26:49,500 --> 00:26:52,266
THAT--THAT--TO PREVENT
BONE LOSS IN SPACE.

599
00:26:54,466 --> 00:26:57,233
LESS WELL-KNOWN ARE THE EFFECTS
OF SPACE RADIATION

600
00:26:57,233 --> 00:26:58,966
ON THE BODY
AND ON THE SKELETON,

601
00:26:58,966 --> 00:27:02,666
AND AS THE EARTH MAGNETIC FIELD
IS CURRENTLY SHIELDING

602
00:27:02,666 --> 00:27:04,933
MOST OF
THE CHARGED PARTICLE FLUX.

603
00:27:04,933 --> 00:27:07,600
THE RAD DOSIMETER,
WHICH SHOWED--

604
00:27:07,600 --> 00:27:09,700

WHICH TOOK DATA
ON THE CRUISE PHASE TO MARS

605
00:27:09,700 --> 00:27:12,300
WITH THE "CURIOSITY" ROVER

606
00:27:12,300 --> 00:27:16,300
HAS MEASURED THE DOSE RATES OF
THE GALACTIC COSMIC RADIATION,

607
00:27:16,300 --> 00:27:20,200
WHICH IS THIS
LOW CHRONIC EXPOSURE

608
00:27:20,200 --> 00:27:21,933
THAT ASTRONAUTS
WOULD BE EXPERIENCING,

609
00:27:21,933 --> 00:27:24,033
AS WELL AS
SOLAR PARTICLE EVENTS--

610
00:27:24,033 --> 00:27:27,000
THESE LITTLE SPIKES
IN THE DOSE RATE

611
00:27:27,000 --> 00:27:29,200
VERSUS TIME CHART HERE.

612
00:27:29,200 --> 00:27:32,600
AND THE GCR PARTICLES
ARE REALLY THE ONES OF CONCERN.

613
00:27:32,600 --> 00:27:35,033
THE--THEY'RE REALLY HARD
TO SHIELD,

614
00:27:35,033 --> 00:27:37,866
AND THEY CAN DO
REALLY INTENSE DAMAGE.

615
00:27:37,866 --> 00:27:42,833
AND THAT'S SHOWN HERE
IN A PROTEIN--IN GREEN HERE,

616
00:27:42,833 --> 00:27:46,500
THAT LABELS ACTIVE DNA DAMAGE
REPAIR OCCURRING.

617
00:27:46,500 --> 00:27:49,200
AND SO AT DOSES HERE
THAT ARE ACHIEVABLE

618
00:27:49,200 --> 00:27:51,400
DURING A MARS--
A ROUND-TRIP MARS MISSION,

619
00:27:51,400 --> 00:27:54,900
YOU CAN SEE THAT THESE TYPES
OF EXPOSURES

620
00:27:54,900 --> 00:27:57,433
ARE ELICITING DNA DAMAGE

621
00:27:57,433 --> 00:27:58,900
AND IN ADDITION,

622
00:27:58,900 --> 00:28:02,466
THEY CAN ELICIT FREE RADICAL
STRESS TO ORGANISMS.

623
00:28:04,033 --> 00:28:06,733
AND SO DURING
MY POSTDOCTORAL FELLOWSHIP,

624
00:28:06,733 --> 00:28:08,833
WE AIMED TO BETTER QUANTIFY
THE EFFECTS

625

00:28:08,833 --> 00:28:11,566
OF SPACE RADIATION
ON THE SKELETAL TISSUE.

626
00:28:14,600 --> 00:28:18,300
AND SO TO SIMULATE SPACE
RADIATION, IONS AND ENERGIES,

627
00:28:18,300 --> 00:28:20,766
WE WENT TO
THE NASA SPACE RADIATION LAB

628
00:28:20,766 --> 00:28:23,700
AT BROOKHAVEN NATIONAL LAB
IN LONG ISLAND

629
00:28:23,700 --> 00:28:26,500
WERE WE USED
A GAMMA RADIATION SOURCE.

630
00:28:26,500 --> 00:28:28,533
AND WE FOUND THAT
RADIATION EXPOSURE

631
00:28:28,533 --> 00:28:31,266
CAUSES RAPID
AND IRREVERSIBLE BONE LOSS.

632
00:28:31,266 --> 00:28:33,866
AND THINKING OF
THE CANCELLOUS TISSUE,

633
00:28:33,866 --> 00:28:38,200
THIS WAS AFFECTED BY REMOVAL
OF THE CANCELLOUS STRUTS.

634
00:28:38,200 --> 00:28:40,666
SO THIS IS A SIMILAR
PROGRESSIVE BONE LOSS

635

00:28:40,666 --> 00:28:43,266
BUT IT--AS SIMULATED
WEIGHTLESSNESS

636
00:28:43,266 --> 00:28:45,466
OR SPACEFLIGHT,

637
00:28:45,466 --> 00:28:49,233
BUT IT JUST HAPPENS
MUCH, MUCH MORE RAPIDLY.

638
00:28:49,233 --> 00:28:52,166
AND SO THIS IS ATTRIBUTED TO
THE OSTEOCLAST CELLS.

639
00:28:52,166 --> 00:28:55,766
THEY'RE MORE IN NUMBER.
THEY'RE GREATER IN SIZE.

640
00:28:55,766 --> 00:28:58,600
AND THIS PERSISTED

641
00:28:58,600 --> 00:29:01,900
UNTIL--UNTIL
AGE-RELATED BONE LOSS

642
00:29:01,900 --> 00:29:04,666
OVERTOOK THAT
STRUCTURAL DECREMENT.

643
00:29:04,666 --> 00:29:07,033
SO WHAT'S SHOWN HERE
IN BLACK IS--

644
00:29:07,033 --> 00:29:09,333
CHARACTERIZES AGE-RELATED
BONE LOSS OVER--

645
00:29:09,333 --> 00:29:12,333
IN A MOUSE OVER A PERIOD

OF ABOUT FOUR MONTHS.

646
00:29:12,333 --> 00:29:15,700
AND YOU CAN SEE THE REMOVAL
OF TRABECULAR STRUTS

647
00:29:15,700 --> 00:29:18,466
REDUCING THIS PARAMETER
CALLED TRABECULAR NUMBER,

648
00:29:18,466 --> 00:29:20,633
AND THEN THAT--THIS TISSUE
NEVER RECOVERS.

649
00:29:20,633 --> 00:29:23,100
IT JUST GETS OVERTAKEN
BY AGE-RELATED BONE LOSS.

650
00:29:25,633 --> 00:29:28,500
FURTHER, WE--

651
00:29:28,500 --> 00:29:30,333
WE PERFORMED FINE ELEMENT
MODELING

652
00:29:30,333 --> 00:29:32,000
ON THE VERTEBRA

653
00:29:32,000 --> 00:29:34,166
FROM SPECIMENS THAT HAD BEEN
IRRADIATED

654
00:29:34,166 --> 00:29:37,366
AND EXPERIENCED THIS TYPE
OF REMOVAL OF TRABECULAR STRUTS.

655
00:29:37,366 --> 00:29:40,400
AND WHAT WE SAW WAS THAT
THE STRESS IN THESE BONES

656
00:29:40,400 --> 00:29:42,433
CONCENTRATES WITHIN
THE REMAINING TISSUE

657
00:29:42,433 --> 00:29:44,233
ON THE CANCELLOUS BONE.

658
00:29:44,233 --> 00:29:46,900
ALSO, BECAUSE OF THE REMOVAL
OF THESE LOAD PATHS,

659
00:29:46,900 --> 00:29:49,566
THERE'S MORE STRESS ON
THE SURROUNDING CORTICAL SHELL.

660
00:29:49,566 --> 00:29:51,566
SO THIS IS--THIS IS--

661
00:29:51,566 --> 00:29:54,500
THIS IS A REAL RISK
FOR ASTRONAUT BONE STRENGTH

662
00:29:54,500 --> 00:29:57,466
ONCE THEY REACH
THIS RADIATION DOSE.

663
00:29:59,666 --> 00:30:02,600
I'D LIKE TO KIND OF
TAPER DOWN THE TALK

664
00:30:02,600 --> 00:30:04,100
AT THE MOLECULAR LEVEL

665
00:30:04,100 --> 00:30:06,766
AND THIS IS THE REALM
OF PROTEINS,

666
00:30:06,766 --> 00:30:08,800
RECEPTORS, AND LIGANDS.

667
00:30:08,800 --> 00:30:10,833
THESE ARE CELL MACHINERY

668
00:30:10,833 --> 00:30:13,000
THAT ENGAGE WITH CELLS--

669
00:30:13,000 --> 00:30:15,166
ALLOW THEM TO ENGAGE
WITH THE ENVIRONMENT

670
00:30:15,166 --> 00:30:16,733
IN TRANSDUCED
MECHANICAL SIGNALS

671
00:30:16,733 --> 00:30:19,600
AND ALSO TO COMMUNICATE
WITH NEIGHBORING CELLS.

672
00:30:19,600 --> 00:30:21,866
SO WE DEMONSTRATED EARLIER

673
00:30:21,866 --> 00:30:24,600
THAT OSTEOCYTES CONTROL
BONE REMODELING

674
00:30:24,600 --> 00:30:27,500
HOWEVER, THE SIGNALING MOLECULES

675
00:30:27,500 --> 00:30:29,400
THAT ELICIT THESE--
THIS CONTROL

676
00:30:29,400 --> 00:30:32,366
HAVE BEEN FAIRLY RECENTLY
DISCOVERED

677
00:30:32,366 --> 00:30:34,200
IN THE PAST 15 YEARS OR SO.

678
00:30:34,200 --> 00:30:36,200
AND SO WE ASKED--
WELL, THE FIELD ASKED,

679
00:30:36,200 --> 00:30:39,066
HOW DO THESE MOLECULES CHANGE
DURING SIMULATED SPACEFLIGHT?

680
00:30:39,066 --> 00:30:41,766
AND SO THERE ARE THREE KEY
SIGNALING MOLECULES

681
00:30:41,766 --> 00:30:43,000
THAT I'LL TALK ABOUT TODAY.

682
00:30:43,000 --> 00:30:45,233
THE FIRST IS SCLEROSTIN.

683
00:30:45,233 --> 00:30:48,266
THIS IS A UNIQUE PROTEIN
THAT OSTEOCYTES PRODUCE

684
00:30:48,266 --> 00:30:52,766
AND SECRETE INTO
THE EXTRA CELLULAR SPACE.

685
00:30:52,766 --> 00:30:56,933
AND THIS SCLEROSTIN
INHIBITS BONE FORMATION,

686
00:30:56,933 --> 00:30:58,900
AND SO THUS, IT ESTABLISHES
NEGATIVE FEEDBACK

687
00:30:58,900 --> 00:31:01,400
WITHIN THIS OSTEOBLAST LINEAGE,

688
00:31:01,400 --> 00:31:03,400

WHERE HIGHER SCLEROSTIN LEVELS

689
00:31:03,400 --> 00:31:05,600
CAUSE LESS BONE FORMATION.

690
00:31:07,233 --> 00:31:10,200
THE NEXT MOLECULAR SIGNAL
IS RANK LIGAND.

691
00:31:10,200 --> 00:31:14,533
AND THIS IS A LIGAND
NOT UNIQUE TO OSTEOCYTES,

692
00:31:14,533 --> 00:31:17,433
HOWEVER THIS IS
AN IMPORTANT FACTOR

693
00:31:17,433 --> 00:31:19,700
FOR DRIVING
OSTEOCLAST FORMATION

694
00:31:19,700 --> 00:31:22,966
AND INITIATING THE PROCESS
OF BONE RESORPTION.

695
00:31:22,966 --> 00:31:25,866
THERE'S A THIRD PLAYER

696
00:31:25,866 --> 00:31:27,966
NAMED OSTEOPROTEGERIN,

697
00:31:27,966 --> 00:31:30,900
WHICH IS OPG,
SECRETED BY OSTEOCYTES

698
00:31:30,900 --> 00:31:32,766
AND OTHER CELLS

699
00:31:32,766 --> 00:31:35,600

THAT INHIBITS
THIS RANK LIGAND MOLECULE.

700
00:31:35,600 --> 00:31:38,200
AND SO THIS STARTS TO--

701
00:31:38,200 --> 00:31:41,433
IF THESE ARE IMPLICATED IN
SPACEFLIGHT-INDUCED BONE LOSS,

702
00:31:41,433 --> 00:31:43,466
THEN THESE PROTEINS BECOME
TRANSLATIONAL TARGETS

703
00:31:43,466 --> 00:31:45,366
FOR OUR COUNTERMEASURE
DEVELOPMENT.

704
00:31:47,233 --> 00:31:50,166
NOW, RECALL THAT BONE FORMATION
IS LOW IN SPACEFLIGHT.

705
00:31:50,166 --> 00:31:54,433
AND SIMULATIONS OF MICROGRAVITY

706
00:31:54,433 --> 00:31:57,733
HAVE SHOWN THAT
SCLEROSTIN LEVELS ARE HIGH

707
00:31:57,733 --> 00:32:00,766
IN BED REST AND IN
HINDLIMB UNLOADING MODELS.

708
00:32:00,766 --> 00:32:03,666
OPPOSITELY,
PHYSIOLOGIC LOADING,

709
00:32:03,666 --> 00:32:07,233
LIKE EXERCISE
OR PRESCRIBED MECHANICAL FORCE,

710
00:32:07,233 --> 00:32:09,466
DECREASE THESE SCLEROSTIN LEVELS

711
00:32:09,466 --> 00:32:13,433
AND NEGATIVELY REGULATE
BONE FORMATION.

712
00:32:13,433 --> 00:32:15,966
SO TAKEN TOGETHER,
INHIBITING SCLEROSTIN

713
00:32:15,966 --> 00:32:19,166
SHOULD RESTORE BONE FORMATION
IN ASTRONAUTS.

714
00:32:19,166 --> 00:32:22,266
AND THIS IDEA WAS SHOWN
TO BE CORRECT

715
00:32:22,266 --> 00:32:24,166
IN A SIMULATION
OF WEIGHTLESSNESS.

716
00:32:24,166 --> 00:32:27,733
AND SO WHAT THEY DID WAS
HINDLIMB UNLOAD ANIMALS

717
00:32:27,733 --> 00:32:30,333
AND TREAT THEM
WITH AN ANTIBODY

718
00:32:30,333 --> 00:32:32,833
FOR THIS SCLEROSTIN MOLECULE,

719
00:32:32,833 --> 00:32:35,866
NEUTRALIZING THE ACTIVITY
OF THAT MOLECULE.

720

00:32:35,866 --> 00:32:39,400
AND THIS WAS SHOWN TO
STIMULATE BONE FORMATION

721
00:32:39,400 --> 00:32:41,400
IN THE CANCELLOUS TISSUE
AND THE CORTICAL TISSUE

722
00:32:41,400 --> 00:32:44,366
AND PREVENT THE NEGATIVE
CONSEQUENCES

723
00:32:44,366 --> 00:32:48,100
OF CONCENTRATING STRESS,
SHOWN HERE IN RED,

724
00:32:48,100 --> 00:32:51,766
THAT WEIGHTLESSNESS AFFECTS.

725
00:32:51,766 --> 00:32:55,266
FURTHER, THIS ANTIBODY WAS
TESTED ON STS-135,

726
00:32:55,266 --> 00:32:58,033
AND RESULTS ARE STILL
FORTHCOMING.

727
00:32:58,033 --> 00:33:00,966
THIS MOLECULE--
THIS ANTIBODY TREATMENT

728
00:33:00,966 --> 00:33:03,533
IS CURRENTLY UNDERGOING
CLINICAL TRIALS

729
00:33:03,533 --> 00:33:07,000
FOR OSTEOPOROSIS TREATMENT.

730
00:33:07,000 --> 00:33:09,700
SO THIS IS ONE LEVER OF

MOLECULAR CONTROL

731
00:33:09,700 --> 00:33:11,966
OF BONE FORMATION
THAT COULD HELP ASTRONAUTS

732
00:33:11,966 --> 00:33:14,033
PROTECT THEIR
SKELETAL STRUCTURE.

733
00:33:15,800 --> 00:33:17,900
MOVING TO BONE RESORPTION,

734
00:33:17,900 --> 00:33:19,666
RECALL THAT IT'S HIGH
IN SPACEFLIGHT.

735
00:33:19,666 --> 00:33:22,200
AND IN SIMULATIONS
OF WEIGHTLESSNESS,

736
00:33:22,200 --> 00:33:25,433
IT'S BEEN SHOWN THAT RANK LIGAND
EXPRESSION IS ELEVATED.

737
00:33:25,433 --> 00:33:29,100
ADDITIONALLY, AFTER HIGH DOSES
OF RADIATION,

738
00:33:29,100 --> 00:33:31,966
RANK LIGAND IS ALSO ELEVATED,

739
00:33:31,966 --> 00:33:34,400
AS IS BONE RESORPTION.

740
00:33:34,400 --> 00:33:36,666
AND WE'RE ACTIVELY INVESTIGATING
WHETHER RANK LIGAND

741

00:33:36,666 --> 00:33:39,566
PLAYS A ROLE IN THE RESPONSE
TO SPACE RADIATION EXPOSURE.

742
00:33:41,333 --> 00:33:43,000
SO THIS INFORMATION SUGGESTS
RANK LIGAND

743
00:33:43,000 --> 00:33:45,500
IS DRIVING OSTEOCLAST FORMATION

744
00:33:45,500 --> 00:33:47,800
AND BONE FORMATION
IN ASTRONAUTS,

745
00:33:47,800 --> 00:33:50,900
AND RESEARCHERS HAVE ASKED,

746
00:33:50,900 --> 00:33:52,900
WHAT ROLE DO OSTEOCYTES PLAY

747
00:33:52,900 --> 00:33:56,200
IN CREATING RANK LIGAND?

748
00:33:56,200 --> 00:33:59,200
AND ADDITIONALLY, BECAUSE
RANK LIGAND IS A KEY PLAYER,

749
00:33:59,200 --> 00:34:01,500
THAT INHIBITOR OF RANK LIGAND,

750
00:34:01,500 --> 00:34:05,333
OPG, COULD BE
A TRANSLATIONAL--

751
00:34:05,333 --> 00:34:07,333
A COUNTERMEASURE
FOR ASTRONAUTS.

752

00:34:08,966 --> 00:34:11,033
SO TO IDENTIFY
THE CELLULAR SOURCE

753
00:34:11,033 --> 00:34:12,733
OF THIS RANK LIGAND,

754
00:34:12,733 --> 00:34:14,933
A GROUP OUT OF LITTLE ROCK

755
00:34:14,933 --> 00:34:17,400
CREATED
A TRANSGENIC MOUSE MODEL

756
00:34:17,400 --> 00:34:19,700
THAT DELETED
THE RANK LIGAND GENE

757
00:34:19,700 --> 00:34:22,400
UNIQUELY IN OSTEOCYTE CELLS.

758
00:34:22,400 --> 00:34:26,000
AND THIS IS
THE DMP1-CRE PROMOTER

759
00:34:26,000 --> 00:34:27,633
HERE ON THE RIGHT.

760
00:34:27,633 --> 00:34:29,633
SO WHAT THEIR EXPERIMENT SHOWS

761
00:34:29,633 --> 00:34:32,000
IS THAT, AS EXPECTED,

762
00:34:32,000 --> 00:34:34,366
THE SIMULATED WEIGHTLESSNESS
CAUSES BONE LOSS,

763
00:34:34,366 --> 00:34:40,166

HOWEVER, IN THE DELETED--
THE OSTEOCYTE-SPECIFIC DELETION

764
00:34:40,166 --> 00:34:43,400
ANIMALS WERE NOT LOSING BONE.

765
00:34:43,400 --> 00:34:46,300
AND SO THIS IS SAYING THAT, ONE,

766
00:34:46,300 --> 00:34:48,566
THAT THE OSTEOCYTES ARE
PRODUCING THE RANK LIGAND,

767
00:34:48,566 --> 00:34:51,100
AND THAT THIS IS
THE RESPONSIBLE MECHANISM

768
00:34:51,100 --> 00:34:53,933
FOR WEIGHTLESSNESS-INDUCED
BONE LOSS.

769
00:34:57,633 --> 00:35:01,400
LOOKING NEXT AT OPG

770
00:35:01,400 --> 00:35:05,066
AND A FAMILY OF MOLECULES
CALLED ANTIRESORPTIVES,

771
00:35:05,066 --> 00:35:07,633
IT'S BEEN--LONG BEEN KNOWN

772
00:35:07,633 --> 00:35:09,833
THAT BISPHOSPHONATES
ARE AN FDA APPROVED DRUG

773
00:35:09,833 --> 00:35:11,466
FOR OSTEOPOROSIS,

774
00:35:11,466 --> 00:35:13,866

AND THEY PREVENT
OSTEOCLAST ATTACHMENT

775
00:35:13,866 --> 00:35:16,466
AND PREVENT
OSTEOCLAST SURVIVAL.

776
00:35:16,466 --> 00:35:19,166
AND THEY HAVE BEEN TESTED
IN ASTRONAUTS,

777
00:35:19,166 --> 00:35:22,766
AND THIS IS SHOWN TO PREVENT THE
SPACEFLIGHT-INDUCED BONE LOSS.

778
00:35:22,766 --> 00:35:24,600
SO THIS IS THE SECOND
COUNTERMEASURE

779
00:35:24,600 --> 00:35:26,500
THAT IS IN OUR TOOLBOX

780
00:35:26,500 --> 00:35:29,033
TO PREVENT THESE NEGATIVE
CHANGES IN THE SKELETON.

781
00:35:29,033 --> 00:35:33,200
IN MICE, THIS FAMILY OF DRUGS,
BISPHOSPHONATES,

782
00:35:33,200 --> 00:35:35,766
ALSO PREVENTED RADIATION-INDUCED
BONE LOSS.

783
00:35:37,666 --> 00:35:39,500
AND LOOKING AT OPG,

784
00:35:39,500 --> 00:35:41,500
BASICALLY INHIBITING
THAT RANK LIGAND MOLECULE,

785
00:35:41,500 --> 00:35:44,900
THIS--IN MICE,
THIS WAS SHOWN IN STS-108,

786
00:35:44,900 --> 00:35:48,633
THAT IT PREVENTED
SPACEFLIGHT-INDUCED BONE LOSS.

787
00:35:48,633 --> 00:35:52,066
SO THIS IS ALL FINE AND GOOD,

788
00:35:52,066 --> 00:35:53,933
BUT THERE'S STILL
A NEGATIVE SIDE EFFECT

789
00:35:53,933 --> 00:35:56,600
OF PROLONGED USE OF SOME OF
THESE ANTIRESORPTIVES.

790
00:35:56,600 --> 00:35:59,400
AND THIS HAS SHOWN UP
IN OSTEOPOROTIC PATIENTS.

791
00:35:59,400 --> 00:36:01,566
THERE'S UNCOUPLING
OF BONE REMODELING,

792
00:36:01,566 --> 00:36:03,333
WHICH YOU ALL UNDERSTAND NOW,

793
00:36:03,333 --> 00:36:05,966
BUT THERE'S ALSO
OSTEONECROSIS OF THE JAW

794
00:36:05,966 --> 00:36:07,833
AND FEMORAL FRACTURES
THAT ARE ATYPICAL

795

00:36:07,833 --> 00:36:09,466
EMERGED WITH PROLONGED USE.

796
00:36:09,466 --> 00:36:12,233
SO I THINK THESE ANTIRESORPTIVES
ARE GOOD FOR THE SHORT DURATION,

797
00:36:12,233 --> 00:36:14,266
BUT NOT--THEY'RE NOT
A PERMANENT SOLUTION.

798
00:36:16,300 --> 00:36:20,100
SO IN SUMMARY, WE'VE REALLY JUST
SCRATCHED THE SURFACE TODAY,

799
00:36:20,100 --> 00:36:22,033
BUT THESE ARE
BY NO MEANS

800
00:36:22,033 --> 00:36:24,100
THE ONLY SIGNALING MOLECULES
OF RELEVANCE.

801
00:36:24,100 --> 00:36:25,633
BUT I HOPE THAT I'VE SUCCEEDED
IN COMMUNICATING

802
00:36:25,633 --> 00:36:29,600
THE VALUE AND IMPORTANCE
OF SPACE BIOLOGY

803
00:36:29,600 --> 00:36:32,500
AND STUDYING BONE LOSS
IN ASTRONAUTS.

804
00:36:32,500 --> 00:36:35,600
I THINK WE'VE ILLUSTRATED
THIS PROCESS OF DISCOVERY

805
00:36:35,600 --> 00:36:39,133

AND BRINGING SOLUTIONS

806
00:36:39,133 --> 00:36:41,600
TO THE ASTRONAUT.

807
00:36:41,600 --> 00:36:44,900
SO I'D LIKE TO CLOSE WITH JUST
A SNAPSHOT OF WHERE WE'RE GOING.

808
00:36:44,900 --> 00:36:47,766
AND THIS IS A SLIDE
THAT JEFF SMITH PROVIDED ME.

809
00:36:47,766 --> 00:36:50,466
THIS IS A--IT'S A PLOT OF
DISTANCE THAT WE'VE TRAVELED

810
00:36:50,466 --> 00:36:53,366
FROM EARTH VERSUS
THE MISSION DURATION.

811
00:36:53,366 --> 00:36:55,333
AND WHAT YOU SEE IS--

812
00:36:55,333 --> 00:36:57,933
THIS L-SHAPE
IN THE LOWER LEFT,

813
00:36:57,933 --> 00:37:00,466
THIS IS WHERE WE'VE BEEN SO FAR,

814
00:37:00,466 --> 00:37:03,733
AND THIS BIG ELLIPSE
IS WHERE WE WANNA GO.

815
00:37:03,733 --> 00:37:05,666
AND I THINK--

816
00:37:05,666 --> 00:37:07,900

I THINK WE CAN USE
MODEL ORGANISMS

817
00:37:07,900 --> 00:37:10,000
AND A BASIC BIOLOGY APPROACH

818
00:37:10,000 --> 00:37:12,733
TO REALLY HELP ENABLE
REACHING OUT

819
00:37:12,733 --> 00:37:15,933
AND EXTENDING DURATION
AND EXTENDING DISTANCE

820
00:37:15,933 --> 00:37:18,233
FROM--FROM EARTH.

821
00:37:18,233 --> 00:37:20,933
SO WITH THAT, I THANK YOU
FOR YOUR ATTENTION

822
00:37:20,933 --> 00:37:23,333
AND YOUR ATTENDANCE TODAY

823
00:37:23,333 --> 00:37:26,000
AND OPEN IT UP FOR QUESTIONS.

824
00:37:26,000 --> 00:37:29,000
[applause]

825
00:37:40,566 --> 00:37:43,066
- HI. I HAVE A QUESTION
IN REGARDS

826
00:37:43,066 --> 00:37:46,000
TO THE AGE OF THE SUBJECTS
THAT YOU WERE LOOKING AT.

827
00:37:46,000 --> 00:37:48,133

ARE THESE ALL YOUNG MICE
OR OLDER MICE

828
00:37:48,133 --> 00:37:50,466
OR HAVE YOU STUDIED
DIFFERENT AGE GROUPS?

829
00:37:50,466 --> 00:37:52,033
- THERE HAVE BEEN--

830
00:37:52,033 --> 00:37:54,133
I THINK THE ORIGINAL STUDIES
WERE WITH GROWING RATS.

831
00:37:54,133 --> 00:37:56,766
BUT THESE--I THINK THOSE

832
00:37:56,766 --> 00:37:58,966
ARE VERY KEENLY TUNED

833
00:37:58,966 --> 00:38:02,033
TO THE MECHANICAL ENVIRONMENT

834
00:38:02,033 --> 00:38:04,833
AND THOSE--THOSE SHOWED
THE FIRST NEGATIVE CHANGES

835
00:38:04,833 --> 00:38:06,433
IN THE OSTEOBLAST.

836
00:38:06,433 --> 00:38:08,300
HOWEVER, WITH ADULT ANIMALS,

837
00:38:08,300 --> 00:38:10,766
I THINK YOU SEE SOMETHING
MAYBE NOT AS DRAMATIC

838
00:38:10,766 --> 00:38:12,966
BUT SOMETHING

IN THE SAME DIRECTION.

839
00:38:15,866 --> 00:38:18,166
OH, AND ALSO
THE HUMAN BONE BIOPSY

840
00:38:18,166 --> 00:38:21,000
ALSO ACTUALLY SHOWED--
THESE WERE ADULT HUMANS,

841
00:38:21,000 --> 00:38:23,666
AND THAT SHOWED NEGATIVE
OSTEOBLAST CHANGES AS WELL.

842
00:38:25,100 --> 00:38:27,033
- FIRST, THANKS FOR PUTTING
AN O'NEILL CYLINDER

843
00:38:27,033 --> 00:38:29,166
ON YOUR SLIDES.
THAT WAS NICE.

844
00:38:29,166 --> 00:38:31,466
I HAVE A QUESTION ABOUT
CALCULATING THE--

845
00:38:31,466 --> 00:38:34,400
THE BIOLOGICAL EFFECTIVENESS
FOR GCR.

846
00:38:34,400 --> 00:38:36,266
- MM-HMM.
- I THINK,

847
00:38:36,266 --> 00:38:38,266
ALTHOUGH I MIGHT BE WRONG,
THAT ALMOST ALL THE DATA

848
00:38:38,266 --> 00:38:41,900
IS FROM A FAIRLY SHORT DURATION

AND A LITTLE HIGHER DOSES

849
00:38:41,900 --> 00:38:45,066
BUT YOU NEED TO UNDERSTAND
WHAT LOW DOSES

850
00:38:45,066 --> 00:38:47,000
OVER LONG PERIODS OF TIME,
AND HOW--

851
00:38:47,000 --> 00:38:49,366
IS THAT CONVERSION MADE
IN SOME AD HOC WAY,

852
00:38:49,366 --> 00:38:51,733
OR IS THERE SOMETHING
REALLY SOLID THAT DOES IT?

853
00:38:51,733 --> 00:38:53,166
- THAT'S--THAT'S
A TOUGH QUESTION.

854
00:38:53,166 --> 00:38:55,633
I THINK--I THINK IT'S
ON A TISSUE BY TISSUE BASIS.

855
00:38:55,633 --> 00:38:58,700
AND SO--AND IT DEPENDS
ON WHAT YOU'RE MEASURING.

856
00:38:58,700 --> 00:39:00,800
ARE YOU GONNA MEASURE
CELL DEATH?

857
00:39:00,800 --> 00:39:02,833
ARE YOU GONNA MEASURE
FREE RADICAL GENERATION

858
00:39:02,833 --> 00:39:04,333
OR DNA DAMAGE?

859
00:39:04,333 --> 00:39:06,133
AND SO I THINK EACH OF THOSE--
WHATEVER YOU MEASURE

860
00:39:06,133 --> 00:39:07,600
IS GONNA HAVE A DIFFERENT

861
00:39:07,600 --> 00:39:09,200
RELATIVE BIOLOGICAL
EFFECTIVENESS.

862
00:39:09,200 --> 00:39:11,000
I THINK MOST OF THE NUMBERS
USED RIGHT NOW

863
00:39:11,000 --> 00:39:13,633
ARE FROM CELL DEATH
OR EFFECTIVE CELL KILLING.

864
00:39:13,633 --> 00:39:15,666
- IS THAT HOW IT'S DONE
FOR BONE?

865
00:39:15,666 --> 00:39:17,400
- MM-HMM.

866
00:39:20,300 --> 00:39:23,533
- HI, JOSH.
ON ONE OF YOUR SLIDES,

867
00:39:23,533 --> 00:39:26,900
YOU SHOWED THE SPACEFLIGHT DATA
FROM ASTRONAUTS,

868
00:39:26,900 --> 00:39:29,066
THAT THEY LOSE
ABOUT 1% PER MONTH

869

00:39:29,066 --> 00:39:31,100
FOR THEIR WEIGHT-BEARING BONES

870
00:39:31,100 --> 00:39:33,566
BUT NOT FOR THE BONES
OF THE UPPER EXTREMITIES.

871
00:39:33,566 --> 00:39:35,833
I'M CURIOUS WHAT YOU KNOW
ABOUT THE MECHANISMS

872
00:39:35,833 --> 00:39:37,733
BY WHICH, YOU KNOW,
YOUR ARM BONES

873
00:39:37,733 --> 00:39:41,133
ARE ABLE TO MAINTAIN
HOMEOSTASIS,

874
00:39:41,133 --> 00:39:43,833
YOU KNOW,
REGARDLESS OF GRAVITY LOAD,

875
00:39:43,833 --> 00:39:47,066
AND IF THAT CAN OFFER
ANY INSIGHTS

876
00:39:47,066 --> 00:39:49,633
TO, YOU KNOW, HOW YOU CAN MANAGE
BONE REMODELING

877
00:39:49,633 --> 00:39:51,433
IN MICROGRAVITY.

878
00:39:51,433 --> 00:39:52,766
I GUESS THE LAST PART IS,

879
00:39:52,766 --> 00:39:54,700
IS THAT PATTERN ALSO REFLECTED

880
00:39:54,700 --> 00:39:57,300
IN NORMAL OSTEOPOROTIC DISEASE
PROCESSES

881
00:39:57,300 --> 00:39:59,600
FOR PATIENTS ON EARTH?

882
00:39:59,600 --> 00:40:02,100
- SO THE FIRST PART
OF THE QUESTION,

883
00:40:02,100 --> 00:40:04,266
WE--I'VE NEVER LOOKED AT THAT,
SO THAT'S A GOOD QUESTION.

884
00:40:04,266 --> 00:40:07,400
I WOULD PREDICT THAT IT UTILIZES
SOME OF THE SAME MOLECULES

885
00:40:07,400 --> 00:40:10,266
TO REGULATE BONE TURNOVER,

886
00:40:10,266 --> 00:40:14,200
AND SO WE SAW WITH THIS USE
IN THE BED REST,

887
00:40:14,200 --> 00:40:16,366
THE SCLEROSTIN WAS UP.

888
00:40:16,366 --> 00:40:20,000
AND SO I THINK THERE ARE
A COUPLE INTERPRETATIONS.

889
00:40:20,000 --> 00:40:23,066
PERHAPS THE BONE IS AT A LOWER
RATE OF TURNOVER TO BEGIN WITH,

890
00:40:23,066 --> 00:40:25,933
AND SO ANY CHANGE

WOULD TAKE LONGER TO MANIFEST.

891
00:40:25,933 --> 00:40:28,766
OR THE SCLEROSTIN LEVEL VARIES
BY TISSUE.

892
00:40:28,766 --> 00:40:31,866
AND MAYBE THAT HELPS EXPLAIN WHY

893
00:40:31,866 --> 00:40:35,933
THERE'S NOT A PHENOTYPE
IN THE UPPER EXTREMITY.

894
00:40:35,933 --> 00:40:38,300
AND THE SECOND QUESTION,
CAN YOU REPEAT?

895
00:40:38,300 --> 00:40:41,000
- WELL, COULD THAT--

896
00:40:41,000 --> 00:40:44,266
IS THAT ALSO THE CASE
FOR OSTEOPOROSIS ON EARTH?

897
00:40:44,266 --> 00:40:46,633
IS THERE A PATTERN
BETWEEN LOAD-BEARING

898
00:40:46,633 --> 00:40:49,233
AND UNLOAD-BEARING BONES?

899
00:40:49,233 --> 00:40:51,666
- I THINK OSTEOPOROSIS ON EARTH,

900
00:40:51,666 --> 00:40:54,100
THERE'S A COUPLE DIFFERENT FORMS
OF THE DISEASE.

901
00:40:54,100 --> 00:40:56,700

AND HORMONES PLAY
AN IMPORTANT ROLE

902
00:40:56,700 --> 00:41:00,200
IN POSTMENOPAUSAL OSTEOPOROSIS.

903
00:41:00,200 --> 00:41:02,400
AND SO I THINK
THERE ARE OTHER PLAYERS,

904
00:41:02,400 --> 00:41:05,100
BUT I THINK RANK LIGAND,
SCLEROSTIN

905
00:41:05,100 --> 00:41:07,566
PROBABLY PLAY A ROLE.

906
00:41:10,600 --> 00:41:12,666
- HI. I WANT TO TOUCH
ON A COUPLE DEEPER TOPICS

907
00:41:12,666 --> 00:41:14,566
THAT WE MAY
HAVE TO HAVE BEERS ABOUT.

908
00:41:14,566 --> 00:41:17,100
BUT, UM...

909
00:41:17,100 --> 00:41:20,600
SO FIRST, COUNTER TO
A LOT OF INTUITION,

910
00:41:20,600 --> 00:41:22,266
EVERYTHING I UNDERSTAND
ABOUT BONE DEVELOPMENT

911
00:41:22,266 --> 00:41:24,300
IS THAT, FOR INSTANCE,
COMPRESSION--

912
00:41:24,300 --> 00:41:26,600
COMPRESSIVE PRESSURE ON A BONE

913
00:41:26,600 --> 00:41:29,600
CAUSES THAT BONE TO DEGRADE
AND DISAPPEAR,

914
00:41:29,600 --> 00:41:32,033
VERSUS TENSION ON A BONE

915
00:41:32,033 --> 00:41:34,766
WILL CAUSE IT TO GROW,
LIKE A BONE SPUR.

916
00:41:34,766 --> 00:41:38,166
SO THIS TIES IN
TO SORT OF A DEEPER STORY

917
00:41:38,166 --> 00:41:40,800
OF, FOR INSTANCE,

918
00:41:40,800 --> 00:41:42,900
WHEN WE THINK OF
"WEIGHT-BEARING" SKELETON,

919
00:41:42,900 --> 00:41:44,966
IT'S NOT ACTUALLY BECAUSE
THE SKELETON IS BEING COMPRESSED

920
00:41:44,966 --> 00:41:46,566
BY THE WEIGHT OF THE BODY,

921
00:41:46,566 --> 00:41:49,633
IT'S BECAUSE IT'S EXPERIENCING
GREATER TENSILE LOADS

922
00:41:49,633 --> 00:41:52,700
FROM THE MUSCLES
SURROUNDING THEM.

923
00:41:52,700 --> 00:41:55,033
AND, UM...

924
00:41:55,033 --> 00:41:57,100
PART OF A SORT OF
TENSION NETWORK APPROACH

925
00:41:57,100 --> 00:41:58,633
TO UNDERSTANDING THE BODY.

926
00:41:58,633 --> 00:42:00,633
IT'S A VERY DIFFERENT APPROACH
THAN SORT OF COMMON SENSE,

927
00:42:00,633 --> 00:42:02,500
BUT THERE'S A LOT OF EVIDENCE
BACKING IT.

928
00:42:02,500 --> 00:42:04,800
AND SO THAT WOULD FIT IN
TO THIS IDEA

929
00:42:04,800 --> 00:42:07,433
THAT WHILE--
WHEN IN SPACEFLIGHT

930
00:42:07,433 --> 00:42:09,300
YOU ARE USING YOUR ARMS A LOT.

931
00:42:09,300 --> 00:42:10,966
YOU STILL NEED TO USE
MUSCULAR ACTIVITY

932
00:42:10,966 --> 00:42:13,766
TO MOVE THE MASS AND INERTIA
OF OBJECTS AROUND,

933
00:42:13,766 --> 00:42:16,300

AND ASTRONAUTS PUSH THEMSELVES
AROUND A LOT WITH THEIR ARMS.

934
00:42:16,300 --> 00:42:18,333
SO THOSE MUSCLES ARE ACTIVE,
THEREFORE THOSE BONES

935
00:42:18,333 --> 00:42:20,933
ARE GETTING LOTS OF LOAD
AND SO THEY DON'T DEGRADE.

936
00:42:20,933 --> 00:42:23,766
WHEREAS THE LEGS
AND OTHER PARTS OF THE BODY

937
00:42:23,766 --> 00:42:25,633
WHICH ARE ACCUSTOMED TO DEALING
WITH GRAVITY AREN'T,

938
00:42:25,633 --> 00:42:27,933
THEREFORE THEY ARE NOT
EXPERIENCING THAT SAME LEVEL

939
00:42:27,933 --> 00:42:29,666
OF TENSION.

940
00:42:29,666 --> 00:42:32,100
SO IT'S REALLY THE TENSION
OF THE MUSCLES THAT'S THE ISSUE,

941
00:42:32,100 --> 00:42:34,466
NOT THE WEIGHT-BEARING, PER SE.

942
00:42:34,466 --> 00:42:36,500
- YEAH. I THINK--

943
00:42:36,500 --> 00:42:39,833
YOU KNOW, A STATIC COMPRESSION
CAN CERTAINLY BE DAMAGING

944
00:42:39,833 --> 00:42:41,466
INTO SKELETAL TISSUE,

945
00:42:41,466 --> 00:42:43,400
BUT YOU KNOW,
INTERMITTENT COMPRESSION

946
00:42:43,400 --> 00:42:45,700
IS REALLY POSITIVE
FOR SKELETAL GROWTH.

947
00:42:45,700 --> 00:42:47,900
SO I THINK--YOU KNOW, I THINK
THE SKELETON IS SENSITIVE

948
00:42:47,900 --> 00:42:49,700
TO DIFFERENT TYPES OF FORCE.

949
00:42:49,700 --> 00:42:53,533
IT'S SENSITIVE TO TENSION,
SHEAR, INTERMITTENT COMPRESSION.

950
00:42:53,533 --> 00:42:56,300
SO I THINK ALL THESE THINGS
WOULD FEED INTO

951
00:42:56,300 --> 00:42:58,266
A PRETTY UNIQUE MODEL.

952
00:42:58,266 --> 00:43:01,866
BUT CERTAINLY, YOU'RE REMOVING
THIS CONSTANT COMPRESSION

953
00:43:01,866 --> 00:43:04,266
OF WEIGHT-BEARING,

954
00:43:04,266 --> 00:43:06,300
SO I THINK THAT'S--
THAT'S A GOOD POINT.

955
00:43:06,300 --> 00:43:09,233
- AND HAVE PEOPLE LOOKED
AT THE IDEA

956
00:43:09,233 --> 00:43:12,366
OF CONTINUOUS
RESISTIVE DEVICES?

957
00:43:12,366 --> 00:43:14,266
FOR INSTANCE, I'VE BEEN TALKING
WITH SOME FOLKS ABOUT,

958
00:43:14,266 --> 00:43:16,133
FOR INSTANCE, MAKING
INFLATABLE EXOSKELETONS

959
00:43:16,133 --> 00:43:18,066
THAT ASTRONAUTS COULD WEAR
ON A DAILY BASIS

960
00:43:18,066 --> 00:43:20,233
THAT WOULD RESIST ALL ACTIVITY
AND ALL DIRECTIONS

961
00:43:20,233 --> 00:43:22,533
AND THEREFORE APPLY
CONTINUAL LOADING?

962
00:43:22,533 --> 00:43:24,366
- YEAH, I THINK
IT'S AN INTERESTING IDEA.

963
00:43:24,366 --> 00:43:26,900
THE KEY THING
FROM THE HISTOGRAM CHART

964
00:43:26,900 --> 00:43:28,900
IS THAT YOU'D REALLY NEED

965
00:43:28,900 --> 00:43:31,333
TO GET UP TO THAT
TWO AND THREE BODY WEIGHT

966
00:43:31,333 --> 00:43:32,800
HIGH-FORCE EXERCISE.

967
00:43:32,800 --> 00:43:34,866
AND SO IF YOU COULD HAVE
A DEVICE THAT'S ABLE TO GET

968
00:43:34,866 --> 00:43:38,033
THAT FORCE REGIMEN, THEN YOU'RE
GONNA BE SOME REALLY POTENT

969
00:43:38,033 --> 00:43:41,233
STIMULATION FOR BONE.
- OKAY.

970
00:43:53,366 --> 00:43:56,166
- QUITE A FEW
IMPLANT MANUFACTURERS

971
00:43:56,166 --> 00:43:59,200
ARE SUFFERING FROM
THE SAME KIND OF PROBLEMS

972
00:43:59,200 --> 00:44:02,300
AS THE--YOU DESCRIBE
THE BONE WE SAW.

973
00:44:02,300 --> 00:44:05,600
SO FOR EXAMPLE, IF WE INSTALL
A FULLY NEW HIP

974
00:44:05,600 --> 00:44:07,000
FOR A PATIENT,

975
00:44:07,000 --> 00:44:09,866

THE LOWER PARTS OF THE--

976
00:44:09,866 --> 00:44:13,800
OF THE FEMUR BONE
ARE GOING TO START DEGRADING.

977
00:44:13,800 --> 00:44:16,233
HAVE YOU HAD ANY COLLABORATION

978
00:44:16,233 --> 00:44:18,733
WITH IMPLANT MANUFACTURERS
OR HOSPITALS

979
00:44:18,733 --> 00:44:20,666
REGARDS OF THIS?

980
00:44:20,666 --> 00:44:22,300
- WE HAVE NOT.
WE HAVE NOT.

981
00:44:22,300 --> 00:44:24,533
I MEAN, IT'S AN ACTIVE AREA
OF RESEARCH IN THE FIELD,

982
00:44:24,533 --> 00:44:28,100
BUT WE'VE NOT DONE ANY
DIRECT RESEARCH.

983
00:44:31,933 --> 00:44:34,766
- SO IF YOU COULD PLEASE JOIN ME
IN THANKING JOSH ALWOOD.

984
00:44:34,766 --> 00:44:37,766
[applause]