1
00:00:04,460 --> 00:00:07,170
Hello and welcome
to Mayo Clinic Talks,

2
00:00:07,170 --> 00:00:09,030
The Opioid Edition.

3
00:00:09,030 --> 00:00:11,370
I'm Tracy McCray and
is was the second of

4
00:00:11,370 --> 00:00:14,145
two bonus episodes on
the opioid crisis.

5
00:00:14,145 --> 00:00:15,750
This podcast is brought to

6
00:00:15,750 --> 00:00:17,520
you by the opioid
conference,

7
00:00:17,520 --> 00:00:19,050
held each year as part of

8
00:00:19,050 --> 00:00:21,675
Mayo Clinic’s continuing
medical education.

9
00:00:21,675 --> 00:00:23,010
For more information on

10
00:00:23,010 --> 00:00:24,840
all opioid episodes

11
00:00:24,840 --> 00:00:28,395
available for credit, visit

12
00:00:28,395 --> 00:00:30,840
ce.mayo.edu/opioidpc.

13

00:00:30,840 --> 00:00:32,730
Today we are
showcasing Dr. Molly

14
00:00:32,730 --> 00:00:34,710
Feely, a consultant in
the division of

15
00:00:34,710 --> 00:00:36,150
General Internal Medicine

16
00:00:36,150 --> 00:00:37,815
at Mayo Clinic, Rochester.

17
00:00:37,815 --> 00:00:39,930
She will be sharing
best practices for

18
00:00:39,930 --> 00:00:42,684
management of opioid
side effects.

19
00:00:42,684 --> 00:00:44,810
I'm going to spend
a little time talking

20
00:00:44,810 --> 00:00:47,090
about opioid side effects.

21
00:00:47,090 --> 00:00:48,200
And I have no financial

22
00:00:48,200 --> 00:00:49,610
relationships with anybody.

23
00:00:49,610 --> 00:00:51,845
I am going to talk
about a number of

24
00:00:51,845 --> 00:00:53,929
off-label uses
of medications

25
00:00:53,929 --> 00:00:55,790
and I'll talk about
that as I go along.

26
00:00:55,790 --> 00:00:57,920
There's a lot
of side effects

27
00:00:57,920 --> 00:01:00,500
related to opioid
pain medications.

28
00:01:00,500 --> 00:01:02,870
And pointing out
the fact that

29
00:01:02,870 --> 00:01:03,890
we're really only
going to talk

30
00:01:03,890 --> 00:01:05,345
about four of them today.

31
00:01:05,345 --> 00:01:07,400
And what we're going
to try to talk about;

32
00:01:07,400 --> 00:01:09,470
our objectives
are recognizing

33
00:01:09,470 --> 00:01:11,510
which opiate side
effects are typically

34
00:01:11,510 --> 00:01:14,480
transient and which
are more pervasive.

35
00:01:14,480 --> 00:01:16,700
To talk about
management options for

36
00:01:16,700 --> 00:01:19,385
each opioid side
effect discussed

37
00:01:19,385 --> 00:01:21,830
and distinguish
when to rotate to

38
00:01:21,830 --> 00:01:23,540
a different opioid
versus when

39
00:01:23,540 --> 00:01:25,595
to just treat
through the symptom.

40
00:01:25,595 --> 00:01:27,290
And the way we're
gonna do this is we're

41
00:01:27,290 --> 00:01:29,495
going to have a case

42
00:01:29,495 --> 00:01:30,560
and then we're going to

43
00:01:30,560 --> 00:01:31,790
talk about the principles

44
00:01:31,790 --> 00:01:34,370
related to that
opioid side-effect,

45
00:01:34,370 --> 00:01:36,050
talk about some
tips and manage

46
00:01:36,050 --> 00:01:37,850
mean that opioid
side effect,

47
00:01:37,850 --> 00:01:40,265

and then we'll have
some take-home points

48
00:01:40,265 --> 00:01:41,510
and we'll do that for each

49
00:01:41,510 --> 00:01:42,950
side effect we talk about.

50
00:01:42,950 --> 00:01:45,125
We're talking about
constipation first,

51
00:01:45,125 --> 00:01:47,390
and this is an actual
patient I took care of.

52
00:01:47,390 --> 00:01:49,550
It's probably been
about two years now,

53
00:01:49,550 --> 00:01:51,710
but she was 37-years-old.

54
00:01:51,710 --> 00:01:53,750
She had widely metastatic

55
00:01:53,750 --> 00:01:56,465
breast cancer to the bones

56
00:01:56,465 --> 00:01:58,850
and she when she
presented to my office,

57
00:01:58,850 --> 00:02:01,565
she had had no bowel
movement in the last 8

58
00:02:01,565 --> 00:02:04,955
days and she was miserable.

59
00:02:04,955 --> 00:02:06,560

She was so miserable

60
00:02:06,560 --> 00:02:08,060
that she actually
quit taking

61
00:02:08,060 --> 00:02:10,385
all of her opioid
pain medications

62
00:02:10,385 --> 00:02:13,160
a couple days prior to
coming to my office,

63
00:02:13,160 --> 00:02:14,675
and that's significant.

64
00:02:14,675 --> 00:02:17,975
She took off her 75
microgram fentanyl patch

65
00:02:17,975 --> 00:02:19,220
and she stopped all of

66
00:02:19,220 --> 00:02:21,065
her oral hydromorphone.

67
00:02:21,065 --> 00:02:23,480
She did have a bowel
regimen at home.

68
00:02:23,480 --> 00:02:25,070
She had docusate, a

69
00:02:25,070 --> 00:02:27,845
100-milligrams, as-
needed twice a day.

70
00:02:27,845 --> 00:02:29,810
She had milk of magnesia 30cc’s

71
00:02:29,810 --> 00:02:32,825

three times
a day, as needed

72
00:02:32,825 --> 00:02:35,300
and Miralax 17 grams

73
00:02:35,300 --> 00:02:37,805
in water, daily as needed.

74
00:02:37,805 --> 00:02:39,695
So my question is,

75
00:02:39,695 --> 00:02:42,290
in addition to a
successful enema

76
00:02:42,290 --> 00:02:43,670
in the office,

77
00:02:43,670 --> 00:02:45,260
which of the
following would be

78
00:02:45,260 --> 00:02:46,835
the next best step

79
00:02:46,835 --> 00:02:48,695
in managing her
constipation?

80
00:02:48,695 --> 00:02:53,600
Adding sorbitol 30cc's
BO PO BID PRN,

81
00:02:53,600 --> 00:02:56,150
adding a scheduled
fiber supplement,

82
00:02:56,150 --> 00:02:58,535
adding a scheduled
stimulant laxative,

83

00:02:58,535 --> 00:03:00,215
or adding
methylnaltrexone?

84
00:03:00,215 --> 00:03:02,270
I agree with
stimulant laxative.

85
00:03:02,270 --> 00:03:04,250
We'll talk in a
minute about why I

86
00:03:04,250 --> 00:03:05,600
think that's

87
00:03:05,600 --> 00:03:07,985
a better answer than
methylnaltrexone.

88
00:03:07,985 --> 00:03:11,195
So managing opioid-
induced constipation,

89
00:03:11,195 --> 00:03:12,800
Opioid-induced constipation

90
00:03:12,800 --> 00:03:14,345
is almost universal,

91
00:03:14,345 --> 00:03:15,950
with scheduled opioids,

92
00:03:15,950 --> 00:03:18,020
almost everybody gets it.

93
00:03:18,020 --> 00:03:20,705
So you really do need
to anticipate it

94
00:03:20,705 --> 00:03:23,000
and tolerance does not

95

00:03:23,000 --> 00:03:25,610
develop to opioid-
induced constipation.

96
00:03:25,610 --> 00:03:27,065
You go up on the dose,

97
00:03:27,065 --> 00:03:28,190
the constipation gets

98
00:03:28,190 --> 00:03:29,570
worse, it doesn't
get better,

99
00:03:29,570 --> 00:03:31,040
the body doesn't
get used to it,

100
00:03:31,040 --> 00:03:33,320
the bowel does not get
used to it over time.

101
00:03:33,320 --> 00:03:34,580
And for patients who are

102
00:03:34,580 --> 00:03:36,454
on scheduled opioids,

103
00:03:36,454 --> 00:03:37,760
they really ought to be on

104
00:03:37,760 --> 00:03:39,770
a scheduled
stimulant laxative.

105
00:03:39,770 --> 00:03:42,380
This is a
suggested regiment

106
00:03:42,380 --> 00:03:44,510
that is not the only
regiment out there,

107
00:03:44,510 --> 00:03:46,640
but this is
typically what I do.

108
00:03:46,640 --> 00:03:48,875
And I'll point out
a couple of things

109
00:03:48,875 --> 00:03:51,800
about managing opioid-
induced constipation.

110
00:03:51,800 --> 00:03:53,360
First of all, I
would actually

111
00:03:53,360 --> 00:03:55,145
cross out docusate,

112
00:03:55,145 --> 00:03:57,680
there's actually
several very

113
00:03:57,680 --> 00:04:00,590
good placebo-controlled
double-blind studies

114
00:04:00,590 --> 00:04:01,730
that really showed

115
00:04:01,730 --> 00:04:03,020
docusate is
no better than

116
00:04:03,020 --> 00:04:05,900
placebo in any
patient population,

117
00:04:05,900 --> 00:04:07,400
whether they have
serious illness

118

00:04:07,400 --> 00:04:08,735
or whether they
are healthy,

119
00:04:08,735 --> 00:04:10,865
this drug does not
work very well.

120
00:04:10,865 --> 00:04:13,160
And then I'll point
out that you max

121
00:04:13,160 --> 00:04:15,860
out one drug before
you add another drug.

122
00:04:15,860 --> 00:04:17,060
If you'd go back to what

123
00:04:17,060 --> 00:04:18,230
my patient was taking,

124
00:04:18,230 --> 00:04:20,840
she was taking PRN

125
00:04:20,840 --> 00:04:23,300
docusate, PRN
milk of magnesia,

126
00:04:23,300 --> 00:04:25,580
PRN Miralax and
what that amounts

127
00:04:25,580 --> 00:04:28,160
to in a day is
she takes the

128
00:04:28,160 --> 00:04:29,300
docusate, it doesn't work,

129
00:04:29,300 --> 00:04:30,740
so four hours
later she takes

130
00:04:30,740 --> 00:04:32,660
a dose of milk of mag,
that doesn't work,

131
00:04:32,660 --> 00:04:34,910
so four hours after that
she takes Miralax.

132
00:04:34,910 --> 00:04:37,205
And she's essentially
taken one dose,

133
00:04:37,205 --> 00:04:39,875
three drugs a day,

134
00:04:39,875 --> 00:04:41,690
which is very low dose.

135
00:04:41,690 --> 00:04:43,280
So max out one drug

136
00:04:43,280 --> 00:04:45,874
first and then
you start adding

137
00:04:45,874 --> 00:04:48,260
and you get to
methylnaltrexone because

138
00:04:48,260 --> 00:04:49,280
methylnaltrexone

139
00:04:49,280 --> 00:04:50,540
is something
that's indicated

140
00:04:50,540 --> 00:04:51,950
if you've maxed out

141
00:04:51,950 --> 00:04:53,495
a good bowel regimen.

142
00:04:53,495 --> 00:04:55,310
Schedule your laxatives,

143
00:04:55,310 --> 00:04:56,810
and then adjust accordingly.

144
00:04:56,810 --> 00:04:58,160
If their stools
are too loose,

145
00:04:58,160 --> 00:05:00,215
back off but schedule them,

146
00:05:00,215 --> 00:05:01,400
don't give them PRN.

147
00:05:01,400 --> 00:05:02,570
How do they
know whether

148
00:05:02,570 --> 00:05:03,680
they should take
the milk of

149
00:05:03,680 --> 00:05:06,650
mag or the Miralax
or the docusate?

150
00:05:06,650 --> 00:05:08,420
So fiber isn't really

151
00:05:08,420 --> 00:05:10,760
helpful in opioid-
induced constipation.

152
00:05:10,760 --> 00:05:14,270
In the words of one of my
esteemed colleagues,

153
00:05:14,270 --> 00:05:17,750
opioids turn your

stool to concrete,

154
00:05:17,750 --> 00:05:20,675
adding fiber just gives
you fibrous concrete.

155
00:05:20,675 --> 00:05:22,040
Not that I'm anti-fiber.

156
00:05:22,040 --> 00:05:23,420
Fiber is lovely, it just

157
00:05:23,420 --> 00:05:24,980
does not work for this.

158
00:05:24,980 --> 00:05:26,255
And consider

159
00:05:26,255 --> 00:05:27,920
a peripherally-acting Mu

160
00:05:27,920 --> 00:05:29,810
opioid receptor antagonist

161
00:05:29,810 --> 00:05:30,950
if you've maxed
out a bowel

162
00:05:30,950 --> 00:05:32,300
regimen and you
aren't getting

163
00:05:32,300 --> 00:05:33,710
very far and you've

164
00:05:33,710 --> 00:05:35,315
ruled out a bowel
obstruction.

165
00:05:35,315 --> 00:05:37,399
So what are these
peripherally-

166
00:05:37,399 --> 00:05:40,190
acting Mu opioid
receptor antagonists?

167
00:05:40,190 --> 00:05:40,820
Well, we're going to talk

168
00:05:40,820 --> 00:05:42,410
about methylnaltrexone first.

169
00:05:42,410 --> 00:05:44,360
It is the first
one that came out.

170
00:05:44,360 --> 00:05:46,760
It first came out
in a sub-q form.

171
00:05:46,760 --> 00:05:47,900
and what it is, is it's

172
00:05:47,900 --> 00:05:50,480
a mu opioid
receptor antagonist

173
00:05:50,480 --> 00:05:52,910
that does not cross the
blood-brain barrier.

174
00:05:52,910 --> 00:05:55,910
So it reverses the
effect of opioids on

175
00:05:55,910 --> 00:05:56,990
the mu receptor in

176
00:05:56,990 --> 00:05:58,850
the periphery but not

177
00:05:58,850 --> 00:06:00,305
in the central

nervous system.

178
00:06:00,305 --> 00:06:03,320
So it blocks the opioid
effect on the gut,

179
00:06:03,320 --> 00:06:06,890
inducing laxation
without reversing

180
00:06:06,890 --> 00:06:08,300
the pain control within

181
00:06:08,300 --> 00:06:09,860
the central nervous system,

182
00:06:09,860 --> 00:06:14,000
and it is highly
effective. If you have

183
00:06:14,000 --> 00:06:15,200
the right diagnosis and

184
00:06:15,200 --> 00:06:16,565
the patient has
opioid-induced

185
00:06:16,565 --> 00:06:18,710
constipation and you give

186
00:06:18,710 --> 00:06:19,760
this and it doesn't work,

187
00:06:19,760 --> 00:06:20,810
and you give a second dose

188
00:06:20,810 --> 00:06:22,340
the next day and
it doesn't work,

189
00:06:22,340 --> 00:06:23,915
question your diagnosis.

190
00:06:23,915 --> 00:06:25,160
It is that effective

191
00:06:25,160 --> 00:06:27,245
for opioid-induced
constipation.

192
00:06:27,245 --> 00:06:28,790
But it ain't cheap -

193
00:06:28,790 --> 00:06:30,530
it's about a $100 a dose

194
00:06:30,530 --> 00:06:32,420
and it's dosed
based on weight.

195
00:06:32,420 --> 00:06:34,280
They do have an oral
methylnaltrexone

196
00:06:34,280 --> 00:06:36,620
now. The FDA
indication for

197
00:06:36,620 --> 00:06:38,570
the oral methylnaltrexone
pill is

198
00:06:38,570 --> 00:06:41,300
only for non-cancer
related pain.

199
00:06:41,300 --> 00:06:42,950
Bowel obstruction is still

200
00:06:42,950 --> 00:06:44,840
an absolute
contraindication and it

201
00:06:44,840 --> 00:06:46,340

is also highly effective

202
00:06:46,340 --> 00:06:48,500
for opioid-induced
constipation.

203
00:06:48,500 --> 00:06:51,500
It is 400, the dose
is 450 milligrams

204
00:06:51,500 --> 00:06:54,230
a day and it comes as
a 150 milligram pill.

205
00:06:54,230 --> 00:06:56,720
So that's three
tablets once a day.

206
00:06:56,720 --> 00:06:58,730
And it's about $1500 a

207
00:06:58,730 --> 00:07:00,710
month for a one-
month supply.

208
00:07:00,710 --> 00:07:02,360
So it is very expensive.

209
00:07:02,360 --> 00:07:05,720
Naloxegol also is an oral

210
00:07:05,720 --> 00:07:07,100
peripheral-acting Mu

211
00:07:07,100 --> 00:07:08,720
opioid receptor
antagonist.

212
00:07:08,720 --> 00:07:10,325
This is a
PEGylated derivative

213

00:07:10,325 --> 00:07:11,630
of naloxone,

214
00:07:11,630 --> 00:07:13,339
so that it acts
peripherally

215
00:07:13,339 --> 00:07:15,170
without crossing the
blood-brain barrier.

216
00:07:15,170 --> 00:07:16,970
It is also highly
effective for

217
00:07:16,970 --> 00:07:19,130
opioid-induced
constipation if

218
00:07:19,130 --> 00:07:20,945
you have the
right diagnosis.

219
00:07:20,945 --> 00:07:23,550
Very rare episodes of
opiate withdrawal occur,

220
00:07:23,550 --> 00:07:25,760
predominantly with
methadone patients.

221
00:07:25,760 --> 00:07:27,560
Some GI side effects

222
00:07:27,560 --> 00:07:29,540
early on within the
first few days,

223
00:07:29,540 --> 00:07:32,090
again, primarily in
patients on methadone.

224
00:07:32,090 --> 00:07:33,620

The downside of
the naloxegol

225
00:07:33,620 --> 00:07:35,630
is that it has

226
00:07:35,630 --> 00:07:37,535
multiple drug interactions

227
00:07:37,535 --> 00:07:38,810
that you really have to

228
00:07:38,810 --> 00:07:39,860
make sure that you're

229
00:07:39,860 --> 00:07:42,290
not interacting
with other drugs.

230
00:07:42,290 --> 00:07:44,585
It comes as a low
dose and a high dose

231
00:07:44,585 --> 00:07:48,110
and it's only about
$330 a month.

232
00:07:48,110 --> 00:07:50,330
Just a chart
comparing them

233
00:07:50,330 --> 00:07:51,770
and I would just
point out that for

234
00:07:51,770 --> 00:07:53,540
advanced illness
or cancer pain,

235
00:07:53,540 --> 00:07:55,460
the subcutaneous
methylnaltrexone

236
00:07:55,460 --> 00:07:56,270
is the only one that's

237
00:07:56,270 --> 00:07:57,830
FDA indicated for

238
00:07:57,830 --> 00:07:59,915
opioid-induced
constipation.

239
00:07:59,915 --> 00:08:01,760
I would keep your
eyes and ears

240
00:08:01,760 --> 00:08:03,800
open because I suspect in

241
00:08:03,800 --> 00:08:05,180
the coming months and years

242
00:08:05,180 --> 00:08:06,530
we're going to
hear more and more

243
00:08:06,530 --> 00:08:09,290
about the oral products
and their safety in

244
00:08:09,290 --> 00:08:10,520
use in patients with

245
00:08:10,520 --> 00:08:12,950
cancer or serious illness.

246
00:08:12,950 --> 00:08:14,885
So keep your eyes peeled.

247
00:08:14,885 --> 00:08:16,880
Bowel obstruction is
a contraindication

248

00:08:16,880 --> 00:08:18,185
for all of them.

249
00:08:18,185 --> 00:08:20,060
All of them have only have

250
00:08:20,060 --> 00:08:22,685
safety profiles going
out about a year.

251
00:08:22,685 --> 00:08:24,965
Certainly that data
will trick in...

252
00:08:24,965 --> 00:08:27,620
trickle in over time of
safety beyond a year,

253
00:08:27,620 --> 00:08:29,345
but that's something
to consider,

254
00:08:29,345 --> 00:08:32,600
and then the cost as
noted. And all of them,

255
00:08:32,600 --> 00:08:34,250
if you have a bowel
wall that has

256
00:08:34,250 --> 00:08:36,725
integrity issues such as

257
00:08:36,725 --> 00:08:38,210
a cancer growing
through it,

258
00:08:38,210 --> 00:08:39,590
you can run the risk

259
00:08:39,590 --> 00:08:42,380
of perforation in
those bowels

260
00:08:42,380 --> 00:08:43,430
so that's
something to think

261
00:08:43,430 --> 00:08:44,540
about as well; that is

262
00:08:44,540 --> 00:08:47,840
a very rare but
catastrophic complication.

263
00:08:47,840 --> 00:08:49,040
And this is kind of how I

264
00:08:49,040 --> 00:08:50,825
think about using it

265
00:08:50,825 --> 00:08:53,270
in an algorithm where

266
00:08:53,270 --> 00:08:55,100
if they have advanced
illness or cancer,

267
00:08:55,100 --> 00:08:57,080
I'm going straight
to the subcu[taneous].

268
00:08:57,080 --> 00:08:58,880
If they have
non-cancer pain,

269
00:08:58,880 --> 00:09:00,140
my question is, do we have

270
00:09:00,140 --> 00:09:02,180
hepatic failure or
drug interactions?

271
00:09:02,180 --> 00:09:03,875
If we do, I'm going

272
00:09:03,875 --> 00:09:05,630
to oral methylnaltrexone.

273
00:09:05,630 --> 00:09:06,740
If we don't have that,

274
00:09:06,740 --> 00:09:08,105
you can use either one.

275
00:09:08,105 --> 00:09:09,410
So my take-home points

276
00:09:09,410 --> 00:09:11,585
for opioid-induced
constipation, is that

277
00:09:11,585 --> 00:09:13,940
it is virtually
universal in patients

278
00:09:13,940 --> 00:09:15,680
on scheduled opioids,

279
00:09:15,680 --> 00:09:18,395
no tolerance
develops over time,

280
00:09:18,395 --> 00:09:18,980
if you're going to

281
00:09:18,980 --> 00:09:20,720
have someone on
scheduled opioids,

282
00:09:20,720 --> 00:09:21,770
you should really have them

283
00:09:21,770 --> 00:09:22,970
on a scheduled stimulant

284

00:09:22,970 --> 00:09:27,065
laxative, fiber is a no-no
for these patients,

285
00:09:27,065 --> 00:09:29,270
and consider a
peripherally-acting

286
00:09:29,270 --> 00:09:31,160
mu opioid receptor
antagonist

287
00:09:31,160 --> 00:09:32,345
if you've maxed out

288
00:09:32,345 --> 00:09:34,400
a bowel regimen and
you've ruled out

289
00:09:34,400 --> 00:09:36,440
bowel obstruction.
And the role of

290
00:09:36,440 --> 00:09:37,835
the oral opioid

291
00:09:37,835 --> 00:09:39,590
antagonist in
advanced illnesses

292
00:09:39,590 --> 00:09:40,700
and cancer is probably

293
00:09:40,700 --> 00:09:41,930
evolving and we're probably

294
00:09:41,930 --> 00:09:44,345
going to see more and
more about that. Nausea.

295
00:09:44,345 --> 00:09:46,160
This is a young 18-year-old

296
00:09:46,160 --> 00:09:47,480
woman who really has

297
00:09:47,480 --> 00:09:50,750
horrific systemic
lupus erythematosus

298
00:09:50,750 --> 00:09:53,495
and she has a severe
destructive arthritis

299
00:09:53,495 --> 00:09:56,390
related to her Lupus,
and that severe

300
00:09:56,390 --> 00:09:57,740
joint pain really limits

301
00:09:57,740 --> 00:10:00,500
her mobility and
her functionality.

302
00:10:00,500 --> 00:10:02,360
In addition to
that, she has

303
00:10:02,360 --> 00:10:03,950
multi-organ
dysfunction due to

304
00:10:03,950 --> 00:10:05,240
her lupus and she

305
00:10:05,240 --> 00:10:06,320
does have a limited life

306
00:10:06,320 --> 00:10:07,580
expectancy because of

307
00:10:07,580 --> 00:10:09,995
the severe progressive
disease that she has.

308
00:10:09,995 --> 00:10:12,200
So you elect to start
her on hydromorphone,

309
00:10:12,200 --> 00:10:13,700
two milligrams, PO q

310
00:10:13,700 --> 00:10:17,000
four hours PRN
for her pain,

311
00:10:17,000 --> 00:10:19,580
hoping to improve her
function as she has

312
00:10:19,580 --> 00:10:22,565
failed all other
adjuvant therapies.

313
00:10:22,565 --> 00:10:24,110
And 24 hours later

314
00:10:24,110 --> 00:10:25,640
she tells you
she's miserable

315
00:10:25,640 --> 00:10:27,140
with nausea and
vomiting and

316
00:10:27,140 --> 00:10:28,895
cannot take this
medication.

317
00:10:28,895 --> 00:10:31,220
Alternative
etiologies of nausea

318
00:10:31,220 --> 00:10:32,570
have been ruled out.

319

00:10:32,570 --> 00:10:34,880
What is the next best step

320
00:10:34,880 --> 00:10:37,190
to manage her nausea?
Opiate rotate

321
00:10:37,190 --> 00:10:38,765
her to fentanyl,
switch her to

322
00:10:38,765 --> 00:10:40,970
IV hydromorphone,
add scheduled

323
00:10:40,970 --> 00:10:42,440
prochlorperazine (which is

324
00:10:42,440 --> 00:10:44,840
Compazine), add PRN
ondansetron

325
00:10:44,840 --> 00:10:46,610
(which is Zofran)? Alright.

326
00:10:46,610 --> 00:10:47,690
Well I'm going to try and

327
00:10:47,690 --> 00:10:49,340
convince you that
adding scheduled

328
00:10:49,340 --> 00:10:50,540
prochlorperazine is

329
00:10:50,540 --> 00:10:52,235
actually the right
answer here.

330
00:10:52,235 --> 00:10:55,145
So opioid-induced
nausea is not rare.

331
00:10:55,145 --> 00:10:58,100
It's not as common
as we worry about,

332
00:10:58,100 --> 00:10:59,315
but it's not rare.

333
00:10:59,315 --> 00:11:01,070
Depending on what
study you look at it

334
00:11:01,070 --> 00:11:04,520
somewhere between
15% and 40% of patients.

335
00:11:04,520 --> 00:11:06,440
There are multiple
mechanisms by

336
00:11:06,440 --> 00:11:09,080
which opioids cause nausea.

337
00:11:09,080 --> 00:11:10,370
Obviously gut inertia and

338
00:11:10,370 --> 00:11:12,590
constipation is one
of the big ones.

339
00:11:12,590 --> 00:11:15,799
It can affect the
vestibular function

340
00:11:15,799 --> 00:11:17,270
and give nausea that way.

341
00:11:17,270 --> 00:11:18,440
But by far the most

342
00:11:18,440 --> 00:11:20,000
common way that
opioids induce

343
00:11:20,000 --> 00:11:21,470
nausea is through

344
00:11:21,470 --> 00:11:23,570
the chemo receptor
trigger zone.

345
00:11:23,570 --> 00:11:24,995
Here's the kicker though.

346
00:11:24,995 --> 00:11:27,470
Nausea from
opioids, patients

347
00:11:27,470 --> 00:11:29,810
develop tolerance to
it and it goes away

348
00:11:29,810 --> 00:11:31,280
in about 90% of

349
00:11:31,280 --> 00:11:33,410
patients in three
to seven days,

350
00:11:33,410 --> 00:11:35,330
if you just wait
long enough.

351
00:11:35,330 --> 00:11:38,330
In almost everybody,
the nausea goes away.

352
00:11:38,330 --> 00:11:40,100
Anti-dopaminergic
agents are

353
00:11:40,100 --> 00:11:41,360
first-line for opioid-

354
00:11:41,360 --> 00:11:42,770

induced nausea
and vomiting

355
00:11:42,770 --> 00:11:45,440
and the reason for
that is for nausea

356
00:11:45,440 --> 00:11:46,700
that is relayed through

357
00:11:46,700 --> 00:11:48,290
the chemo receptor
triggers zone,

358
00:11:48,290 --> 00:11:49,790
that's either
a dopaminergic

359
00:11:49,790 --> 00:11:51,635
or a serotonergic
phenomenon

360
00:11:51,635 --> 00:11:53,240
and you simply, simply need

361
00:11:53,240 --> 00:11:54,920
to know the piece of trivia

362
00:11:54,920 --> 00:11:57,230
that opioids that
go through there as

363
00:11:57,230 --> 00:11:59,510
a dopaminergic
phenomenon more

364
00:11:59,510 --> 00:12:01,370
than a serotonergic
phenomenon.

365
00:12:01,370 --> 00:12:02,780
And there's little
evidence to

366
00:12:02,780 --> 00:12:05,390
support the use of one
opioid over another,

367
00:12:05,390 --> 00:12:07,430
meaning that all
of the opioids

368
00:12:07,430 --> 00:12:09,725
induce nausea
at equal rates.

369
00:12:09,725 --> 00:12:13,520
Therefore, if you switch
opioids on day one,

370
00:12:13,520 --> 00:12:15,710
all you've done is
reset the clock at

371
00:12:15,710 --> 00:12:17,570
0 and they're likely to get

372
00:12:17,570 --> 00:12:19,910
nausea from that
opioid as well.

373
00:12:19,910 --> 00:12:22,130
So the key here
is try not to

374
00:12:22,130 --> 00:12:25,640
switch the opioids until
three to seven days

375
00:12:25,640 --> 00:12:27,230
and this is where I
try to treat through

376
00:12:27,230 --> 00:12:29,375
the nausea for three
to seven days.

377
00:12:29,375 --> 00:12:30,800
If we're seven
days out and we're

378
00:12:30,800 --> 00:12:32,510
still struggling
with nausea,

379
00:12:32,510 --> 00:12:33,980
then I switch to
a different drug.

380
00:12:33,980 --> 00:12:35,150
There was a study that came

381
00:12:35,150 --> 00:12:36,920
out about a year ago

382
00:12:36,920 --> 00:12:39,140
that showed that
tapentadol had

383
00:12:39,140 --> 00:12:40,580
significantly less GI

384
00:12:40,580 --> 00:12:42,365
side effects
than oxycodone.

385
00:12:42,365 --> 00:12:44,360
And that's a first study
that's really showed

386
00:12:44,360 --> 00:12:46,370
one opioid to be better

387
00:12:46,370 --> 00:12:47,960
than another and it had

388
00:12:47,960 --> 00:12:49,340
less constipation and

389
00:12:49,340 --> 00:12:51,170
less nausea related to it.

390
00:12:51,170 --> 00:12:52,970
So I have to put a
little asterisk there.

391
00:12:52,970 --> 00:12:53,990
It's a single study.

392
00:12:53,990 --> 00:12:56,105
It's only compared
it to oxycodone,

393
00:12:56,105 --> 00:12:59,060
but it is something to
think about and watch

394
00:12:59,060 --> 00:13:00,530
for if you have
someone who has a

395
00:13:00,530 --> 00:13:02,195
really, really touchy gut.

396
00:13:02,195 --> 00:13:03,620
So my take-home points

397
00:13:03,620 --> 00:13:05,870
for nausea and vomiting,

398
00:13:05,870 --> 00:13:09,095
are address alternative
sources of nausea,

399
00:13:09,095 --> 00:13:11,060
try to avoid
opioid rotation

400
00:13:11,060 --> 00:13:12,440
in the first five

to seven days -

401
00:13:12,440 --> 00:13:14,960
try to treat through
for five to seven days,

402
00:13:14,960 --> 00:13:16,730
anti-dopaminergic
agents are

403
00:13:16,730 --> 00:13:19,355
first line and I
schedule them -

404
00:13:19,355 --> 00:13:20,630
if through that first

405
00:13:20,630 --> 00:13:22,160
five to seven
days and then I

406
00:13:22,160 --> 00:13:24,845
taper them off, and
consider tapentadol

407
00:13:24,845 --> 00:13:26,270
if you have someone
who has a really,

408
00:13:26,270 --> 00:13:27,290
really touchy gut that

409
00:13:27,290 --> 00:13:29,960
you'd need to use...
someone...use it for in

410
00:13:29,960 --> 00:13:32,239
the right
situation. Sedation

411
00:13:32,239 --> 00:13:33,545
related to opioids.

412
00:13:33,545 --> 00:13:34,925
If you are interested in

413
00:13:34,925 --> 00:13:36,395
learning more
about this topic,

414
00:13:36,395 --> 00:13:37,820
Dr. Molly Feely speaks at

415
00:13:37,820 --> 00:13:40,355
the annual Mayo Clinic
opioid conference.

416
00:13:40,355 --> 00:13:42,200
Mayo Clinic offers
hundreds of

417
00:13:42,200 --> 00:13:43,670
continuing
medical education

418
00:13:43,670 --> 00:13:45,305
conferences worldwide.

419
00:13:45,305 --> 00:13:48,560
Visit ce.mayo.edu and

420
00:13:48,560 --> 00:13:49,610
register today for

421
00:13:49,610 --> 00:13:52,010
the Mayo Clinic
opioid conference.

422
00:13:52,010 --> 00:13:54,290
So this is one of my
favorite patients

423
00:13:54,290 --> 00:13:56,570
that I've ever cared
for in my career.

424
00:13:56,570 --> 00:13:58,550
He's 50 years
old and he is in

425
00:13:58,550 --> 00:14:00,620
remission from non-
Hodgkin’s lymphoma.

426
00:14:00,620 --> 00:14:02,960
Unfortunately, he had
pretty bad chemotherapy-

427
00:14:02,960 --> 00:14:05,210
induce peripheral
neuropathy for which he

428
00:14:05,210 --> 00:14:07,550
has been on chronic
opioids because

429
00:14:07,550 --> 00:14:09,965
he has failed trials
of everything else.

430
00:14:09,965 --> 00:14:11,435
And when I mean failed

431
00:14:11,435 --> 00:14:13,460
he got horrible edema from

432
00:14:13,460 --> 00:14:15,530
gabapentin and so I

433
00:14:15,530 --> 00:14:17,195
switched him to pregabalin.

434
00:14:17,195 --> 00:14:20,540
You got horrible edema
from pregabalin that I

435
00:14:20,540 --> 00:14:22,340

tried to treat through
with Lasix and

436
00:14:22,340 --> 00:14:24,500
compression garments;
that did not work.

437
00:14:24,500 --> 00:14:26,585
So I put them on
carbamazepine.

438
00:14:26,585 --> 00:14:28,459
The carbamazepine,
I successfully

439
00:14:28,459 --> 00:14:29,810
drove his sodium down to

440
00:14:29,810 --> 00:14:33,050
a 108, personal record
for me at the time.

441
00:14:33,050 --> 00:14:35,060
So I put him
on topiramate.

442
00:14:35,060 --> 00:14:36,740
If anybody...if
you've ever seen

443
00:14:36,740 --> 00:14:37,760
the issues with

444
00:14:37,760 --> 00:14:39,110
concen...concentration

445
00:14:39,110 --> 00:14:40,595
and memory with topiramate?

446
00:14:40,595 --> 00:14:43,160
He got that. Couldn't
remember anything.

447
00:14:43,160 --> 00:14:45,080
So I put them
on lamotrigine.

448
00:14:45,080 --> 00:14:46,400
I don't know if any
of you have had

449
00:14:46,400 --> 00:14:47,480
the luxury of

450
00:14:47,480 --> 00:14:49,490
inducing the
lamotrigine rash in

451
00:14:49,490 --> 00:14:51,290
one of your patients;
I'm here to tell you it

452
00:14:51,290 --> 00:14:54,440
is horrible, horrible rash.

453
00:14:54,440 --> 00:14:56,120
And so in the end
I put them on

454
00:14:56,120 --> 00:14:58,100
tricyclics and
we literally had

455
00:14:58,100 --> 00:15:00,065
to shock him out of v tach

456
00:15:00,065 --> 00:15:01,835
from the tricyclics.

457
00:15:01,835 --> 00:15:04,070
So he was on
opiates and he had

458
00:15:04,070 --> 00:15:06,230
failed all of the opiates

459
00:15:06,230 --> 00:15:08,390
including methadone
until I had

460
00:15:08,390 --> 00:15:10,700
him on a fentanyl patch.

461
00:15:10,700 --> 00:15:12,380
It was a long-time
stable dose.

462
00:15:12,380 --> 00:15:14,105
He had no aberrant
behavior.

463
00:15:14,105 --> 00:15:16,250
The issue was that the same

464
00:15:16,250 --> 00:15:18,290
with a fentanyl patch
that he'd had with

465
00:15:18,290 --> 00:15:19,730
all of the other opioids is

466
00:15:19,730 --> 00:15:21,320
that they made
him really sleepy

467
00:15:21,320 --> 00:15:23,180
and it was interfering
with his ability

468
00:15:23,180 --> 00:15:25,190
to do his job at work.

469
00:15:25,190 --> 00:15:27,290
And the only medication
that he was on was

470
00:15:27,290 --> 00:15:29,000

a 25 microgram fentanyl

471
00:15:29,000 --> 00:15:30,350
patch every other day.

472
00:15:30,350 --> 00:15:33,140
So what's the next
best step to help with

473
00:15:33,140 --> 00:15:36,620
this guy's somnolence?
Add modafinil

474
00:15:36,620 --> 00:15:38,000
(which is Provigil), tell

475
00:15:38,000 --> 00:15:39,140
him he can't be on opioids

476
00:15:39,140 --> 00:15:40,505
anymore because
he doesn't have

477
00:15:40,505 --> 00:15:41,840
cancer-related pain,

478
00:15:41,840 --> 00:15:43,550
tell him he should
quit his job and go on

479
00:15:43,550 --> 00:15:45,995
disability, or start
him on an SSRI?

480
00:15:45,995 --> 00:15:48,185
I'd agree with
add modafinil.

481
00:15:48,185 --> 00:15:49,550
He actually had multiple

482
00:15:49,550 --> 00:15:50,750

people telling
him he should

483
00:15:50,750 --> 00:15:51,860
quit his job and go on

484
00:15:51,860 --> 00:15:53,900
disability because
of this issue,

485
00:15:53,900 --> 00:15:56,540
and I just think
that would be

486
00:15:56,540 --> 00:15:59,780
a disaster for this
50, 50-year-old guy.

487
00:15:59,780 --> 00:16:02,165
So sedation-related
to opioids,

488
00:16:02,165 --> 00:16:03,770
it's not uncommon, but it's

489
00:16:03,770 --> 00:16:05,060
almost always transient

490
00:16:05,060 --> 00:16:06,080
and it usually goes away

491
00:16:06,080 --> 00:16:07,445
in a couple of days.

492
00:16:07,445 --> 00:16:09,635
If it doesn't go away,

493
00:16:09,635 --> 00:16:11,345
what else is going on?

494
00:16:11,345 --> 00:16:13,355
What else are you missing?

495
00:16:13,355 --> 00:16:15,080
Is there sleep apnea?

496
00:16:15,080 --> 00:16:16,190
What other drug got

497
00:16:16,190 --> 00:16:17,960
added? Nine times
out of ten

498
00:16:17,960 --> 00:16:19,940
it's a benzodiazepine
or a muscle

499
00:16:19,940 --> 00:16:22,580
relaxer, but what else

500
00:16:22,580 --> 00:16:24,890
is going on that's
driving the sedation if

501
00:16:24,890 --> 00:16:27,470
it doesn't go away in
two to three days.

502
00:16:27,470 --> 00:16:29,780
And really, step three

503
00:16:29,780 --> 00:16:31,580
is really what
else is going on?

504
00:16:31,580 --> 00:16:34,385
Is this person hypogonadal
from the opioids?

505
00:16:34,385 --> 00:16:35,780
Are there alternative drugs

506
00:16:35,780 --> 00:16:37,130
other than the opioids?

507
00:16:37,130 --> 00:16:38,180
Can you switch them to

508
00:16:38,180 --> 00:16:40,130
a non-opioid medication?

509
00:16:40,130 --> 00:16:42,500
I think we
definitively gave

510
00:16:42,500 --> 00:16:44,990
that our very best shot
with this patient.

511
00:16:44,990 --> 00:16:48,485
Opioid...Is opioid
rotation an option?

512
00:16:48,485 --> 00:16:50,210
What else can we do?

513
00:16:50,210 --> 00:16:52,040
Because the last thing is

514
00:16:52,040 --> 00:16:53,930
to add a stimulant
medication.

515
00:16:53,930 --> 00:16:56,615
And as both a family doc

516
00:16:56,615 --> 00:16:57,830
and a general internist,

517
00:16:57,830 --> 00:16:59,330
I hate treating
the side effect

518
00:16:59,330 --> 00:17:00,830
of one drug with
another drug,

519
00:17:00,830 --> 00:17:02,720
but this is a case in

520
00:17:02,720 --> 00:17:04,640
a rare situation
where I would

521
00:17:04,640 --> 00:17:05,780
consider doing it with

522
00:17:05,780 --> 00:17:07,010
a stimulant medication.

523
00:17:07,010 --> 00:17:08,480
The two stimulants
out there that

524
00:17:08,480 --> 00:17:09,890
we use are methylphenidate,

525
00:17:09,890 --> 00:17:12,530
(or Ritalin) or modafinil
(or Provigil).

526
00:17:12,530 --> 00:17:13,550
They really have very

527
00:17:13,550 --> 00:17:15,769
similar side
effect profiles

528
00:17:15,769 --> 00:17:18,245
with some anxiety,
some tremulousness,

529
00:17:18,245 --> 00:17:20,000
some cardiac
dysrhythmia that

530
00:17:20,000 --> 00:17:22,460
is usually atrial in

531
00:17:22,460 --> 00:17:27,230
nature, usually but not
always, insomnia and

532
00:17:27,230 --> 00:17:29,300
anorexia is listed
by side effect.

533
00:17:29,300 --> 00:17:30,530
I will tell you
I've never seen

534
00:17:30,530 --> 00:17:31,700
that in an adult yet.

535
00:17:31,700 --> 00:17:33,560
I've never seen an
adult who had had

536
00:17:33,560 --> 00:17:35,615
significant problems
with that yet.

537
00:17:35,615 --> 00:17:38,630
The tips that I would
say is don't give

538
00:17:38,630 --> 00:17:39,830
the second dose after

539
00:17:39,830 --> 00:17:41,570
2:00 PM or they're
not going to sleep.

540
00:17:41,570 --> 00:17:45,650
So I usually dose it at
eight and noon or eight and two,

541
00:17:45,650 --> 00:17:46,970
but I won't go...but I try

542

00:17:46,970 --> 00:17:48,965
not to give it
after two o'clock.

543
00:17:48,965 --> 00:17:50,600
Methylphenidate is twice a day,

544
00:17:50,600 --> 00:17:52,490
I usually use modafinil
once a day;

545
00:17:52,490 --> 00:17:54,275
it's a little bit
longer-acting.

546
00:17:54,275 --> 00:17:55,610
So my sedation take-home

547
00:17:55,610 --> 00:17:57,455
points are:
it’s usually transient,

548
00:17:57,455 --> 00:17:59,000
try to wait a couple days,

549
00:17:59,000 --> 00:18:00,920
it almost always gets
better and go away,

550
00:18:00,920 --> 00:18:02,090
if it doesn't
get better and

551
00:18:02,090 --> 00:18:03,380
go away, I really,

552
00:18:03,380 --> 00:18:04,970
really look hard to try and

553
00:18:04,970 --> 00:18:06,710
figure out what
else is going on.

554
00:18:06,710 --> 00:18:08,150
And I would use
stimulants as

555
00:18:08,150 --> 00:18:09,650
an...as a last resort

556
00:18:09,650 --> 00:18:12,665
and only in the
right patient. Pruritus.

557
00:18:12,665 --> 00:18:14,180
So this is a 24-year-old

558
00:18:14,180 --> 00:18:15,410
young man who
is admitted to

559
00:18:15,410 --> 00:18:16,640
the hospital with a tib/fib

560
00:18:16,640 --> 00:18:18,320
fracture one night,

561
00:18:18,320 --> 00:18:20,180
planning to go to the
operating room the next

562
00:18:20,180 --> 00:18:22,835
morning to have a rod
put in his leg.

563
00:18:22,835 --> 00:18:24,500
Upon admission
to the hospital,

564
00:18:24,500 --> 00:18:26,600
he had reported
allergies to morphine,

565
00:18:26,600 --> 00:18:28,925
codeine, oxycodone,

and hydrocodone.

566
00:18:28,925 --> 00:18:31,250
Now why 24-year-old has

567
00:18:31,250 --> 00:18:32,750
had exposure to morphine,

568
00:18:32,750 --> 00:18:34,610
codeine, oxycodone,

569
00:18:34,610 --> 00:18:36,320
hydrocodone would
probably have

570
00:18:36,320 --> 00:18:38,180
been a good thing
for me to ask.

571
00:18:38,180 --> 00:18:39,980
At the time, I didn't

572
00:18:39,980 --> 00:18:42,050
he complaints of
pain and his pain

573
00:18:42,050 --> 00:18:45,965
is uncontrolled by
non-opioid regiments.

574
00:18:45,965 --> 00:18:47,600
So I ordered PO

575
00:18:47,600 --> 00:18:50,360
hydromorphone for his
pain and he almost

576
00:18:50,360 --> 00:18:52,160
immediately
started itching, his

577
00:18:52,160 --> 00:18:53,675

exam showed no rash.

578
00:18:53,675 --> 00:18:55,535
So how would you
manage his itching?

579
00:18:55,535 --> 00:18:57,425
Switch him to IV
hydromorphone,

580
00:18:57,425 --> 00:19:00,020
add PRN
diphenhydramine, schedule

581
00:19:00,020 --> 00:19:02,120
at a dean, switch
him to nalbuphine.

582
00:19:02,120 --> 00:19:03,230
I'm going to try
and convince you

583
00:19:03,230 --> 00:19:04,580
that actually switching

584
00:19:04,580 --> 00:19:05,630
him to nalbuphine is

585
00:19:05,630 --> 00:19:07,235
probably the best
answer here.

586
00:19:07,235 --> 00:19:09,650
So opioid-induced pruritus.

587
00:19:09,650 --> 00:19:11,900
So first of all, pruritus,
is not an allergy.

588
00:19:11,900 --> 00:19:13,970
You can have an
allergy to opioids,

589
00:19:13,970 --> 00:19:16,550
but a true opioid allergy
usually presents as

590
00:19:16,550 --> 00:19:17,690
hives or anaphylaxis

591
00:19:17,690 --> 00:19:20,375
and it's very impressive,

592
00:19:20,375 --> 00:19:22,340
and not very subtle. The pruritus

593
00:19:22,340 --> 00:19:24,035
and the itching
that people get

594
00:19:24,035 --> 00:19:25,790
from opioids that is more

595
00:19:25,790 --> 00:19:28,145
common is actually
not an allergy.

596
00:19:28,145 --> 00:19:33,110
It is common and it is
far more common with

597
00:19:33,110 --> 00:19:35,510
intrathecal or
axial opioids than

598
00:19:35,510 --> 00:19:38,060
it is with
systemic opioids.

599
00:19:38,060 --> 00:19:41,300
And it is not a histamine-
related phenomenon.

600
00:19:41,300 --> 00:19:43,040
It is true that opioids

601
00:19:43,040 --> 00:19:44,840
cause mast cell release,

602
00:19:44,840 --> 00:19:47,960
but it is not mast cell
release or histamine-

603
00:19:47,960 --> 00:19:50,255
related that causes the itching

604
00:19:50,255 --> 00:19:51,875
that people get
with opioids.

605
00:19:51,875 --> 00:19:53,720
So please, quit snowing

606
00:19:53,720 --> 00:19:55,700
these people with
Benadryl.

607
00:19:55,700 --> 00:19:57,140
They do sleep and they quit

608
00:19:57,140 --> 00:19:59,360
complaining because
they're schnockered,

609
00:19:59,360 --> 00:20:01,100
but they wake up itching.

610
00:20:01,100 --> 00:20:03,440
Unfortunately, there
is very little data

611
00:20:03,440 --> 00:20:05,000
on how to manage

612
00:20:05,000 --> 00:20:07,235
the itching outside of

613
00:20:07,235 --> 00:20:09,485
the intrathecal
administration,

614
00:20:09,485 --> 00:20:10,940
which makes it challenging.

615
00:20:10,940 --> 00:20:12,560
And management is largely

616
00:20:12,560 --> 00:20:14,255
based on expert opinion.

617
00:20:14,255 --> 00:20:16,670
So these are my tips

618
00:20:16,670 --> 00:20:19,475
for opioid-
induced pruritus.

619
00:20:19,475 --> 00:20:20,870
So for reasons we don't

620
00:20:20,870 --> 00:20:23,720
understand, hydromorphone,
fentanyl, oxymorphone,

621
00:20:23,720 --> 00:20:25,940
and tramadol seem to

622
00:20:25,940 --> 00:20:28,160
have less itching
associated with them.

623
00:20:28,160 --> 00:20:29,900
So that is always
my first step.

624
00:20:29,900 --> 00:20:31,100
If they're on oxycodone

625

00:20:31,100 --> 00:20:33,080
or hydrocodone or morphine,

626
00:20:33,080 --> 00:20:35,779
and I have the opportunity

627
00:20:35,779 --> 00:20:37,055
to opiate rotate them,

628
00:20:37,055 --> 00:20:39,110
these drugs
might cause less

629
00:20:39,110 --> 00:20:40,730
itching and some patients

630
00:20:40,730 --> 00:20:42,410
will tolerate
them much better.

631
00:20:42,410 --> 00:20:43,715
Oral or IV makes

632
00:20:43,715 --> 00:20:45,740
no difference.
Naloxone

633
00:20:45,740 --> 00:20:47,330
is indeed really,

634
00:20:47,330 --> 00:20:49,010
really effective
for getting

635
00:20:49,010 --> 00:20:50,975
rid of the opioid-
induced etching.

636
00:20:50,975 --> 00:20:52,190
The problem is it

637
00:20:52,190 --> 00:20:54,440

also reverses their
pain control

638
00:20:54,440 --> 00:20:56,420
and so that doesn't
really help you much in

639
00:20:56,420 --> 00:20:59,675
the practical management
of these patients.

640
00:20:59,675 --> 00:21:02,000
Partial opioid
agonists such as

641
00:21:02,000 --> 00:21:04,580
nalbuphine or butorphanol,

642
00:21:04,580 --> 00:21:06,680
butorphanol is Stadol,
nalbuphine is Nubain,

643
00:21:06,680 --> 00:21:09,485
seem to really
reduce itching a lot.

644
00:21:09,485 --> 00:21:11,090
These studies have
mostly been done in

645
00:21:11,090 --> 00:21:13,265
patients on intrathecal
opioids,

646
00:21:13,265 --> 00:21:15,170
so their pain is
being managed by

647
00:21:15,170 --> 00:21:17,210
their intrathecal
pump and they're

648

00:21:17,210 --> 00:21:18,650
given small doses of

649
00:21:18,650 --> 00:21:21,335
these opioids solely
to manage the itching,

650
00:21:21,335 --> 00:21:22,970
not to manage the pain.

651
00:21:22,970 --> 00:21:25,220
How you manage this
in someone like

652
00:21:25,220 --> 00:21:27,380
my patient who was having

653
00:21:27,380 --> 00:21:30,110
it based on systemic,
and how you use

654
00:21:30,110 --> 00:21:31,250
these medicines to treat

655
00:21:31,250 --> 00:21:34,115
both pain and itching
is less clear.

656
00:21:34,115 --> 00:21:35,840
I will tell you
with my guy,

657
00:21:35,840 --> 00:21:37,880
I went with Nubain
because I was somewhat

658
00:21:37,880 --> 00:21:39,200
familiar with it and using

659
00:21:39,200 --> 00:21:40,310
it in pregnant women.

660

00:21:40,310 --> 00:21:41,540
It was a very interesting

661
00:21:41,540 --> 00:21:42,830
20-minute conversation

662
00:21:42,830 --> 00:21:44,390
with the nighttime
pharmacists,

663
00:21:44,390 --> 00:21:45,470
trying to convince him

664
00:21:45,470 --> 00:21:47,000
that my 24-year-old man,

665
00:21:47,000 --> 00:21:48,860
I was indeed ordering
Nubain for

666
00:21:48,860 --> 00:21:50,510
my 24-year-old man and

667
00:21:50,510 --> 00:21:52,010
no, he was
not pregnant.

668
00:21:52,010 --> 00:21:53,450
But I eventually got it up,

669
00:21:53,450 --> 00:21:55,310
we used it for his
pain and it worked

670
00:21:55,310 --> 00:21:56,390
beautifully for both his

671
00:21:56,390 --> 00:21:57,755
pain and his itching.

672
00:21:57,755 --> 00:22:01,429
If this is a mu

receptor phenomenon,

673
00:22:01,429 --> 00:22:03,065
if the itching is
actually caused

674
00:22:03,065 --> 00:22:05,270
by a mu receptor phenomenon.

675
00:22:05,270 --> 00:22:06,860
How about these
peripherally-

676
00:22:06,860 --> 00:22:09,560
acting Mu, opioid
receptor antagonists?

677
00:22:09,560 --> 00:22:10,310
While in fact there are

678
00:22:10,310 --> 00:22:11,360
a couple of
studies out there

679
00:22:11,360 --> 00:22:14,150
now looking at managing

680
00:22:14,150 --> 00:22:15,740
itching with
methylnaltrexone.

681
00:22:15,740 --> 00:22:17,015
And disappointingly,

682
00:22:17,015 --> 00:22:18,980
it hasn't worked
in any of them.

683
00:22:18,980 --> 00:22:20,450
There's a reasonably good

684
00:22:20,450 --> 00:22:22,370

double-blind
placebo-controlled trial

685
00:22:22,370 --> 00:22:24,200
of 72 patients that had no,

686
00:22:24,200 --> 00:22:25,805
no benefit over placebo.

687
00:22:25,805 --> 00:22:28,400
That probably suggests
that this is more

688
00:22:28,400 --> 00:22:29,720
a central phenomenon than

689
00:22:29,720 --> 00:22:31,250
a peripheral
phenomenon

690
00:22:31,250 --> 00:22:32,300
and that makes sense

691
00:22:32,300 --> 00:22:33,440
based on that we see the

692
00:22:33,440 --> 00:22:35,180
itching more
common in intra-

693
00:22:35,180 --> 00:22:37,115
thecal and axial opioids.

694
00:22:37,115 --> 00:22:38,660
And the other thing
is, there might be

695
00:22:38,660 --> 00:22:39,950
a serotonin component to

696
00:22:39,950 --> 00:22:42,470
this because the serotonin

697
00:22:42,470 --> 00:22:45,425
blockers seem to
help the itching.

698
00:22:45,425 --> 00:22:47,930
There's not good
data for this,

699
00:22:47,930 --> 00:22:50,510
but using ondansetron,

700
00:22:50,510 --> 00:22:52,730
which is a serotonergic
blocker or,

701
00:22:52,730 --> 00:22:54,080
mirtazapine,

702
00:22:54,080 --> 00:22:55,850
in some studies have shown

703
00:22:55,850 --> 00:22:58,340
some benefit in
managing itching.

704
00:22:58,340 --> 00:23:00,815
I had a cancer
patient on high doses

705
00:23:00,815 --> 00:23:04,295
of oxymorphone who
had terrible itching

706
00:23:04,295 --> 00:23:06,650
and we put him
on scheduled

707
00:23:06,650 --> 00:23:07,940
ondansetron four times a

708
00:23:07,940 --> 00:23:09,620

day and didn't
eliminate the itching,

709
00:23:09,620 --> 00:23:11,660
but it made it...
decreased it enough to

710
00:23:11,660 --> 00:23:13,820
make it tolerable
for him to continue

711
00:23:13,820 --> 00:23:15,290
therapy. So my take-home

712
00:23:15,290 --> 00:23:16,790
points - it's not histamine,

713
00:23:16,790 --> 00:23:18,260
please stop the Benadryl.

714
00:23:18,260 --> 00:23:20,585
Consider a
partial agonist drug,

715
00:23:20,585 --> 00:23:22,580
if that's an option,
and possibly

716
00:23:22,580 --> 00:23:24,410
consider ondansetron or

717
00:23:24,410 --> 00:23:27,185
mirtazapine if...if...as a,

718
00:23:27,185 --> 00:23:28,475
as a management tool.

719
00:23:28,475 --> 00:23:29,960
So Dr. Feely we have a few

720
00:23:29,960 --> 00:23:30,680

specific questions

721
00:23:30,680 --> 00:23:31,550
about side effects for you.

722
00:23:31,550 --> 00:23:33,380
So what do you think about

723
00:23:33,380 --> 00:23:34,880
the person who's
on scheduled

724
00:23:34,880 --> 00:23:36,080
chronic narcotics,

725
00:23:36,080 --> 00:23:38,405
who denies they ever
have any constipation?

726
00:23:38,405 --> 00:23:40,115
Are they full of it?
I had...

727
00:23:40,115 --> 00:23:41,510
I had one patient who had

728
00:23:41,510 --> 00:23:43,070
chronic diarrhea
who, getting

729
00:23:43,070 --> 00:23:44,660
on chronic opioids for her

730
00:23:44,660 --> 00:23:46,280
calciphylaxis, was
the best thing that

731
00:23:46,280 --> 00:23:48,080
ever happened to her. And I

732
00:23:48,080 --> 00:23:49,940
had her on nothing

for laxatives because

733
00:23:49,940 --> 00:23:52,235
the opioid solved her
chronic diarrhea.

734
00:23:52,235 --> 00:23:53,930
So it can happen,

735
00:23:53,930 --> 00:23:55,985
but it is few
and far between.

736
00:23:55,985 --> 00:23:56,780
And then how would you

737
00:23:56,780 --> 00:23:57,920
handle a patient
who develops

738
00:23:57,920 --> 00:24:00,200
extrapyramidal symptoms
on the prochlorperazine

739
00:24:00,200 --> 00:24:01,250
that you're using to

740
00:24:01,250 --> 00:24:02,840
treat their nausea?

741
00:24:02,840 --> 00:24:04,100
I would put them on something

742
00:24:04,100 --> 00:24:05,810
that's not a
dopaminergic blocker.

743
00:24:05,810 --> 00:24:06,710
You'd...you'd have to go

744
00:24:06,710 --> 00:24:07,670
to something else because

745
00:24:07,670 --> 00:24:10,100
that's a side effect
of all dopaminergic

746
00:24:10,100 --> 00:24:12,020
antagonist drugs.

747
00:24:12,020 --> 00:24:13,370
And so you're going
to have to go

748
00:24:13,370 --> 00:24:16,775
to ondansetron or
something else.

749
00:24:16,775 --> 00:24:18,050
We've had a
couple questions

750
00:24:18,050 --> 00:24:18,830
throughout the
morning about

751
00:24:18,830 --> 00:24:21,005
hypogonadism as
a side effect.

752
00:24:21,005 --> 00:24:23,210
And is that
resolved simply by

753
00:24:23,210 --> 00:24:24,430
removing the opioid or

754
00:24:24,430 --> 00:24:25,340
is there ever a role for,

755
00:24:25,340 --> 00:24:27,290
for example,
testosterone treatment?

756

00:24:27,290 --> 00:24:29,030
It is actually resolved

757
00:24:29,030 --> 00:24:30,710
with getting them
off the opioids.

758
00:24:30,710 --> 00:24:32,630
The hypogonadism goes away,

759
00:24:32,630 --> 00:24:34,850
all of the woman who got

760
00:24:34,850 --> 00:24:37,385
pregnant as her
dose came down.

761
00:24:37,385 --> 00:24:39,650
So the ideal
situation would be

762
00:24:39,650 --> 00:24:41,870
to get them off the
opioids if they,

763
00:24:41,870 --> 00:24:44,000
if their diseases
such that getting

764
00:24:44,000 --> 00:24:46,520
them off the opioids
is not an option,

765
00:24:46,520 --> 00:24:48,755
treating them with
testosterone is effective.

766
00:24:48,755 --> 00:24:50,330
What's the rationale
for changing

767
00:24:50,330 --> 00:24:52,280
q2 two days?

768
00:24:52,280 --> 00:24:54,050
And then it would

769
00:24:54,050 --> 00:24:56,465
ketamine be an
alternative to fentanyl,

770
00:24:56,465 --> 00:24:57,170
when you're thinking

771
00:24:57,170 --> 00:24:58,340
about peri-operative use?

772
00:24:58,340 --> 00:25:00,335
For perioperative pain control,

773
00:25:00,335 --> 00:25:03,710
fentanyl patches are
work every third day

774
00:25:03,710 --> 00:25:07,370
for about 98 to
99% of people.

775
00:25:07,370 --> 00:25:10,130
And then there are some
people who are simply

776
00:25:10,130 --> 00:25:12,890
faster metabolizers
and they

777
00:25:12,890 --> 00:25:14,630
will see the dose

778
00:25:14,630 --> 00:25:16,070
will wear off on
that third day.

779
00:25:16,070 --> 00:25:17,840
And they'll come in

and say, I'm great,

780
00:25:17,840 --> 00:25:20,150
except that third day
is horrible.

781
00:25:20,150 --> 00:25:21,980
And so in those patients

782
00:25:21,980 --> 00:25:23,390
going to an,
every other day,

783
00:25:23,390 --> 00:25:26,705
fentanyl at the same
dose is very effective.

784
00:25:26,705 --> 00:25:28,430
I've seen that
predominantly in

785
00:25:28,430 --> 00:25:30,230
people who are profoundly

786
00:25:30,230 --> 00:25:32,240
cachectic and my hospice

787
00:25:32,240 --> 00:25:34,144
patients at the
very end of life,

788
00:25:34,144 --> 00:25:35,660
but the other
place where I've seen

789
00:25:35,660 --> 00:25:37,250
it is in real young people.

790
00:25:37,250 --> 00:25:38,270
Do you think that there's

791
00:25:38,270 --> 00:25:39,170

an opioid that causes

792
00:25:39,170 --> 00:25:41,810
less delirium and our
elderly patients or

793
00:25:41,810 --> 00:25:44,585
one that you would
choose over another? No,

794
00:25:44,585 --> 00:25:46,190
and it's not tramadol.

795
00:25:46,190 --> 00:25:48,530
They all have equal,
equal delirium.

796
00:25:48,530 --> 00:25:50,375
We've been talking
about management of

797
00:25:50,375 --> 00:25:52,730
opioid side effects
with Dr. Molly Feely,

798
00:25:52,730 --> 00:25:54,020
consultant in
the division of

799
00:25:54,020 --> 00:25:55,460
General Internal Medicine

800
00:25:55,460 --> 00:25:57,035
at Mayo Clinic, Rochester.

801
00:25:57,035 --> 00:25:59,525
Remember, if you enjoyed
Mayo Clinic Talks,

802
00:25:59,525 --> 00:26:01,805
please subscribe and
share with a friend.

803
00:26:01,805 --> 00:26:03,740
Healthcare professionals
looking to claim

804
00:26:03,740 --> 00:26:05,780
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