

0:00:00 -> 0:00:02.34 Support for Yale Cancer Answers
0:00:02.34 -> 0:00:04.212 comes from AstraZeneca,
0:00:04.22 -> 0:00:06.036 proud partner in personalized
0:00:06.036 -> 0:00:07.398 medicine developing tailored
0:00:07.398 -> 0:00:09.33 treatments for cancer patients.
0:00:09.33 -> 0:00:13.71 Learn more at [AstraZeneca-usa.com](https://www.astrazeneca-usa.com).
0:00:13.71 -> 0:00:15.142 Welcome to Yale Cancer
0:00:15.142 -> 0:00:16.574 Answers with your host
0:00:16.58 -> 0:00:18.38 Doctor Anees Chagpar.
0:00:18.38 -> 0:00:19.888 Yale Cancer Answers features
0:00:19.888 -> 0:00:21.773 the latest information on cancer
0:00:21.773 -> 0:00:23.703 care by welcoming oncologists and
0:00:23.703 -> 0:00:25.935 specialists who are on the forefront
0:00:25.993 -> 0:00:27.709 of the battle to fight cancer.
0:00:27.71 -> 0:00:29.744 This week is a conversation about
0:00:29.744 -> 0:00:32.289 the role of obesity and insulin in
0:00:32.289 -> 0:00:34.164 cancer with doctor Rachel Perry.
0:00:34.17 -> 0:00:36.138 Doctor Perry is an assistant professor
0:00:36.138 -> 0:00:38.12 in Medicine and Endocrinology
0:00:38.12 -> 0:00:39.8 and cellular and Molecular Physiology
0:00:39.8 -> 0:00:42.07 at the Yale School of Medicine,
0:00:42.07 -> 0:00:44.998 where doctor Chagpar is a
0:00:44.998 -> 0:00:46.95 professor of surgical oncology.
0:00:46.95 -> 0:00:47.32 Rachel,
0:00:47.32 -> 0:00:49.366 maybe we can start by talking
0:00:49.366 -> 0:00:51.37 a little bit about obesity.
0:00:55.05 -> 0:00:57.06 They talk about it
0:00:57.06 -> 0:00:59.09 being like the other pandemic.
0:00:59.09 -> 0:01:00.562 It's really something that's
0:01:00.562 -> 0:01:02.402 prevalent across the world,
0:01:02.41 -> 0:01:04.718 is that right?

0:01:04.72 -> 0:01:05.995 Yes, that is absolutely true.
0:01:05.995 -> 0:01:09.666 So at this point we're coming up on close
0:01:09.666 -> 0:01:12.764 to 50% of Americans who are obese and
0:01:12.764 -> 0:01:15.04 large numbers really worldwide as well.
0:01:15.04 -> 0:01:17.623 And with that obesity is a problem
0:01:17.623 -> 0:01:20.598 in and of itself, it increases
0:01:20.598 -> 0:01:22.578 the risk of cardiovascular disease,
0:01:22.58 -> 0:01:24.168 stroke and cancer which we will discuss
0:01:24.168 -> 0:01:25.756 today and other conditions,
0:01:25.76 -> 0:01:28.406 but it also brings with it an
0:01:28.406 -> 0:01:30.92 increased risk of type 2 diabetes
0:01:36.4 -> 0:01:38.548 which can be caused by obesity and
0:01:38.548 -> 0:01:40.698 is expected to effect 100% of
0:01:40.698 -> 0:01:42.488 Americans, or would affect 100%
0:01:42.49 -> 0:01:44.28 of Americans if current trends
0:01:44.28 -> 0:01:46.07 continue by the year 2050.
0:01:46.07 -> 0:01:48.58 That really is mazing.
0:01:48.58 -> 0:01:51.076 So that tells us we need to do
0:01:51.076 -> 0:01:52.869 something to intervene here.
0:01:52.87 -> 0:01:54.43 Two statistics that
0:01:54.43 -> 0:01:56.876 you put out in a single sentence
0:01:56.876 -> 0:01:59.318 that just completely blew me away.
0:01:59.32 -> 0:02:02.392 The first is that almost half of all
0:02:02.392 -> 0:02:05.045 Americans are obese and all of us are
0:02:05.045 -> 0:02:07.94 going to end up with Type 2 diabetes
0:02:07.94 -> 0:02:09.592 in 30 short years,
0:02:09.592 -> 0:02:11.24 that's incredible.
0:02:11.24 -> 0:02:13.718 I just have to correct myself.
0:02:13.72 -> 0:02:15.79 Overweight or obese, almost 50%.
0:02:15.79 -> 0:02:19.086 I was gonna ask about that.
0:02:19.09 -> 0:02:22.394 So what really is the definition of obesity?

0:02:22.4 -> 0:02:25.165 I mean are we talking about
0:02:25.165 -> 0:02:28.128 that last five or 10
0:02:28.128 -> 0:02:30.654 pounds that everyone has to lose?
0:02:30.66 -> 0:02:32.946 Or are we talking about people
0:02:32.946 -> 0:02:34.991 who are seriously several pounds
0:02:34.991 -> 0:02:37.256 or several 100 pounds overweight?
0:02:37.26 -> 0:02:40.165 Somewhere in between the two.
0:02:40.17 -> 0:02:41.562 Technically, obesity is defined
0:02:41.562 -> 0:02:43.9 as a body mass index over 30,
0:02:43.9 -> 0:02:45.51 and that really corresponds to
0:02:45.51 -> 0:02:47.63 being about 30 to 50 pounds,
0:02:47.63 -> 0:02:49.32 closer to 50 pounds over
0:02:49.32 -> 0:02:50.672 our ideal body weight,
0:02:50.68 -> 0:02:52.708 and so we're not talking about,
0:02:52.71 -> 0:02:54.606 you know the last five or
0:02:54.606 -> 0:02:56.44 10 pounds from high school.
0:02:56.44 -> 0:02:59.144 That may put us into the overweight category,
0:02:59.15 -> 0:03:02.264 but we don't need to be hundreds of pounds
0:03:02.264 -> 0:03:04.579 overweight to be in that obese category.
0:03:04.58 -> 0:03:06.326 That can really increase our risk
0:03:06.326 -> 0:03:08.649 of a number of health conditions,
0:03:08.65 -> 0:03:11.594 and so one of those conditions is cancer.
0:03:11.6 -> 0:03:14.849 Can you give us a metric?
0:03:14.85 -> 0:03:16.655 How much does obesity really
0:03:16.655 -> 0:03:19.184 increase your risk? I know a
0:03:19.184 -> 0:03:21.35 lot of people worry about cancer,
0:03:21.35 -> 0:03:23.155 I mean certainly they worry
0:03:23.155 -> 0:03:24.96 about diabetes and heart disease,
0:03:24.96 -> 0:03:27.624 all of those are some of the
0:03:27.624 -> 0:03:30.368 key killers of Americans these days.
0:03:30.37 -> 0:03:32.175 But how much does obesity

0:03:32.175 -> 0:03:33.258 really impact cancer?
0:03:33.26 -> 0:03:35.773 And does it affect all kinds of
0:03:35.773 -> 0:03:37.948 cancer or just a select few?
0:03:37.95 -> 0:03:39.039 Well, those are
0:03:39.04 -> 0:03:41.044 both great questions and in the
0:03:41.044 -> 0:03:43.04 answer to the first question,
0:03:43.04 -> 0:03:45.476 how much does obesity affect cancer risk,
0:03:45.48 -> 0:03:47.7 it's difficult to answer because it
0:03:47.7 -> 0:03:49.912 really depends on the tumor type
0:03:49.912 -> 0:03:52.222 and so I'm going to answer your
0:03:52.222 -> 0:03:54.6 second question first and that is
0:03:56.976 -> 0:03:59.451 at this point there are 13 tumor types
0:03:59.451 -> 0:04:02.335 that the Centers for Disease Control have
0:04:02.335 -> 0:04:04.616 associated with obesity and that means,
0:04:04.62 -> 0:04:06.738 with obesity increasing the risk and
0:04:06.738 -> 0:04:09.215 causing a worse prognosis of those tumor
0:04:09.215 -> 0:04:11.225 types and those include breast cancer,
0:04:11.23 -> 0:04:12.274 ovarian, uterine, renal,
0:04:12.274 -> 0:04:13.408 pancreatic, thyroid, colorectal,
0:04:13.408 -> 0:04:15.598 as well as several others.
0:04:15.6 -> 0:04:18.113 And but there are few tumor types
0:04:18.113 -> 0:04:20.41 where there's no risk of obesity,
0:04:20.41 -> 0:04:23.105 and we really don't understand what causes
0:04:23.105 -> 0:04:25.958 some tumor types to be worse with obesity,
0:04:25.96 -> 0:04:28.179 and other tumor types not to be
0:04:28.179 -> 0:04:30.508 worse within the tumor types that
0:04:30.508 -> 0:04:32.244 are associated with obesity,
0:04:32.25 -> 0:04:34.882 there are some where obesity brings with it
0:04:34.882 -> 0:04:37.429 a relatively lower risk in breast cancer.
0:04:37.43 -> 0:04:39.65 I believe the increase is about
0:04:39.65 -> 0:04:42.2 20 to 30% of an increased risk

0:04:42.2 -> 0:04:44 with obesity, still very significant
0:04:44 -> 0:04:45.609 but smaller than others.
0:04:45.61 -> 0:04:47.102 Whereas with pancreatic cancer,
0:04:47.102 -> 0:04:50.329 risk is a couple fold, ovarian cancer as well,
0:04:50.33 -> 0:04:52.864 a couple fold greater risk with obesity.
0:04:52.87 -> 0:04:54.69 So as I said
0:04:54.69 -> 0:04:57.224 it really depends on the tumor type.
0:04:57.23 -> 0:04:59.701 But because these 13 cancer types that
0:04:59.701 -> 0:05:01.927 are associated with obesity are among
0:05:01.927 -> 0:05:04.489 the most prevalent cancer types out there,
0:05:04.49 -> 0:05:06.3 it really translates to a
0:05:06.3 -> 0:05:07.386 significant excess risk.
0:05:07.39 -> 0:05:08.842 From an epidemiological standpoint
0:05:08.842 -> 0:05:09.568 that comes
0:05:09.57 -> 0:05:10.659 with obesity.
0:05:10.659 -> 0:05:13.562 And we really don't know why.
0:05:13.562 -> 0:05:16.578 Even 20 to 30% increased risk of breast
0:05:16.578 -> 0:05:18.93 cancer seems pretty significant to me.
0:05:18.93 -> 0:05:21.716 But why is that 20 to 30%
0:05:21.72 -> 0:05:23.715 but in ovarian cancer we're
0:05:23.715 -> 0:05:25.71 talking about more like 200%?
0:05:25.71 -> 0:05:28.91 Do we know why that is?
0:05:28.91 -> 0:05:31.458 Why it is that obesity effects more
0:05:31.458 -> 0:05:34.49 cancers in some situations than in others?
0:05:34.49 -> 0:05:35.687 We really don't,
0:05:35.687 -> 0:05:38.48 and that is a tremendous open question
0:05:38.48 -> 0:05:40.88 that we need to figure out.
0:05:40.88 -> 0:05:43.19 Because if we could figure out
0:05:43.19 -> 0:05:44.73 why obesity worsens certain
0:05:44.8 -> 0:05:46.86 cancer risks worse than others,
0:05:46.86 -> 0:05:49.604 then perhaps we would have a better handle

0:05:49.604 -> 0:05:52.46 on why obesity increases cancer risk
0:05:52.46 -> 0:05:54.791 at all, and that would be the
0:05:54.791 -> 0:05:56.984 target that would be where we
0:05:56.984 -> 0:05:58.844 can intervene in this process.
0:05:58.85 -> 0:06:02.4 A lot of labs, mine included as well as
0:06:02.4 -> 0:06:04.38 many others are working on this
0:06:04.38 -> 0:06:07.02 question to try to uncover number one,
0:06:07.02 -> 0:06:09.216 why are certain tumor types affected
0:06:09.216 -> 0:06:11.279 and not others and #2 why are
0:06:11.28 -> 0:06:13.596 certain tumor types affected worse than
0:06:13.596 -> 0:06:15.512 others because there's really going
0:06:15.512 -> 0:06:17.668 to be a major epidemiological role for
0:06:17.67 -> 0:06:19.09 uncovering that information.
0:06:20.51 -> 0:06:23.598 Do we know what exactly or how exactly
0:06:23.598 -> 0:06:25.817 obesity increases your risk of cancer?
0:06:28.64 -> 0:06:30.761 We're still working on that and there
0:06:30.761 -> 0:06:33.32 have been a number of potential mediators
0:06:33.32 -> 0:06:35.696 that people have thrown out there.
0:06:35.7 -> 0:06:37.776 One that my lab studies is
0:06:37.776 -> 0:06:39.59 insulin and related to that,
0:06:39.59 -> 0:06:41.35 insulin-like growth factor one.
0:06:41.35 -> 0:06:43.185 The concentrations of these molecules
0:06:43.185 -> 0:06:45.695 increase with obesity and we and others
0:06:45.695 -> 0:06:47.837 have shown that in vitro those molecules
0:06:47.837 -> 0:06:49.82 can increase tumor cell division.
0:06:49.82 -> 0:06:52.644 We can talk a little bit later about
0:06:52.644 -> 0:06:55.119 the mechanism by which that may occur,
0:06:55.12 -> 0:06:56.071 if you'd like.
0:06:56.071 -> 0:06:58.779 But there have been a number of other
0:06:58.779 -> 0:07:01.677 factors that people have proposed as well,
0:07:01.68 -> 0:07:02.805 including inflammatory cytokines.

0:07:02.805 -> 0:07:04.68 Obesity is a pro inflammatory
0:07:04.68 -> 0:07:06.531 state and so inflammatory cytokines
0:07:06.531 -> 0:07:08.266 are up in obese individuals.
0:07:08.27 -> 0:07:11.006 There's leptin, a protein that is
0:07:11.006 -> 0:07:14.019 secreted by the fat and has been shown in
0:07:14.019 -> 0:07:16.699 certain models to accelerate tumor growth.
0:07:16.7 -> 0:07:19.29 There are other hormones that
0:07:19.29 -> 0:07:20.844 may be involved, we
0:07:20.85 -> 0:07:21.89 mentioned insulin,
0:07:21.89 -> 0:07:23.97 but also potentially Glucagon,
0:07:23.97 -> 0:07:24.752 Adiponectin.
0:07:24.752 -> 0:07:27.88 And any and all of these have
0:07:27.956 -> 0:07:29.38 been shown in vitro,
0:07:29.38 -> 0:07:30.985 so in cell culture studies,
0:07:30.985 -> 0:07:32.269 to accelerate tumor growth,
0:07:32.27 -> 0:07:33.554 and there's been increasing
0:07:33.554 -> 0:07:35.159 work in mice in humans,
0:07:35.16 -> 0:07:37.026 it's a little bit more difficult
0:07:37.026 -> 0:07:39.307 to tell the answer because you know
0:07:39.307 -> 0:07:41.257 a patient comes in with cancer.
0:07:41.26 -> 0:07:43.675 you can't do all these types of
0:07:43.675 -> 0:07:45.264 interventions that we're able to
0:07:45.264 -> 0:07:47.674 do in the lab to really be able to
0:07:47.674 -> 0:07:49.609 pick out certain positive factors,
0:07:49.61 -> 0:07:51.591 but all of these hormones and cytokines
0:07:51.591 -> 0:07:53.839 that I just listed correlate with
0:07:53.839 -> 0:07:55.619 tumor appearance and progression.
0:07:57.77 -> 0:07:58.45 And a point
0:07:58.45 -> 0:08:00.83 I wanted to make related to the
0:08:00.83 -> 0:08:02.08 role of obesity,
0:08:02.08 -> 0:08:04.425 we talked about how obesity may increase

0:08:04.425 -> 0:08:07.11 the risk of certain types of cancers,
0:08:07.11 -> 0:08:09.258 but it also worsens the progression
0:08:09.26 -> 0:08:11.408 and increases the rate of recurrence
0:08:11.408 -> 0:08:12.482 of the cancer.
0:08:12.49 -> 0:08:15.338 So when we say that obesity may increase
0:08:15.338 -> 0:08:17.877 the risk of breast cancer by 20%,
0:08:17.88 -> 0:08:20.238 it also worsens the prognosis of
0:08:20.238 -> 0:08:22.197 someone who's already diagnosed with
0:08:22.197 -> 0:08:24.111 breast cancer as well as increasing
0:08:24.111 -> 0:08:26.489 her risk of recurrence, so that 20%
0:08:26.49 -> 0:08:29.01 increased risk is really not just 20%.
0:08:29.01 -> 0:08:31.11 Because the increased risk continues
0:08:31.11 -> 0:08:34.029 down the line and we really need
0:08:34.029 -> 0:08:36.612 to figure out what the reason for
0:08:36.612 -> 0:08:39.268 that is so that we can intervene in
0:08:39.27 -> 0:08:40.79 a mechanistically driven manner.
0:08:40.79 -> 0:08:43.796 And I think that the
0:08:43.796 -> 0:08:45.764 other problem now that you mention
0:08:45.764 -> 0:08:48.173 it, is the fact that obesity really
0:08:48.173 -> 0:08:50.283 increases the risk of recurrence,
0:08:50.29 -> 0:08:52.185 particularly in breast cancer and
0:08:52.185 -> 0:08:54.47 maybe in other cancers as well.
0:08:54.47 -> 0:08:57.011 Some of the therapies that we use
0:08:57.011 -> 0:08:59.493 actually make you gain weight, so
0:08:59.493 -> 0:09:01.808 many breast cancer survivors actually
0:09:01.808 -> 0:09:04.61 gain weight during therapy and then on
0:09:04.61 -> 0:09:07.196 top of that that weight gain or that
0:09:07.196 -> 0:09:09.998 obesity increases their risk of recurrence.
0:09:10 -> 0:09:13.888 So have people looked at that?
0:09:13.89 -> 0:09:16.49 I mean, is the weight that you gain
0:09:16.49 -> 0:09:18.426 during therapy versus simply just

0:09:18.426 -> 0:09:20.456 being overweight to begin with?
0:09:20.46 -> 0:09:22.285 Does that make a difference
0:09:22.285 -> 0:09:23.38 to your recurrence?
0:09:23.38 -> 0:09:25.21 If you were normal weight,
0:09:25.21 -> 0:09:27.576 for example, when you were diagnosed and
0:09:27.576 -> 0:09:30.318 then you gained weight with your treatment,
0:09:30.32 -> 0:09:32.882 does that increase your risk of
0:09:32.882 -> 0:09:35.024 recurrence because that weight gain
0:09:35.024 -> 0:09:37.214 was related to your treatment versus
0:09:37.214 -> 0:09:40.098 if you were overweight to begin with?
0:09:40.42 -> 0:09:41.5 In fact it does.
0:09:41.5 -> 0:09:43.95 So people have looked at this specifically,
0:09:43.95 -> 0:09:45.798 the change of weight during
0:09:45.798 -> 0:09:47.749 the course of treatment and those
0:09:47.749 -> 0:09:49.409 who gain weight during treatment.
0:09:49.41 -> 0:09:50.373 Actually specifically for
0:09:50.373 -> 0:09:51.978 breast cancer as you mentioned,
0:09:51.98 -> 0:09:54.031 are in fact at a higher risk
0:09:54.031 -> 0:09:55.83 of recurrence of their cancer,
0:09:55.83 -> 0:09:57.714 and so that's something that absolutely
0:09:57.714 -> 0:10:00.317 needs to be kept in mind during therapy.
0:10:00.32 -> 0:10:01.211 Now that said,
0:10:01.211 -> 0:10:03.85 it's not as simple as it may appear,
0:10:03.85 -> 0:10:05.435 because those who lose weight
0:10:05.435 -> 0:10:06.703 during treatment
0:10:06.703 -> 0:10:08.347 also have a poorer prognosis.
0:10:08.35 -> 0:10:11.006 This gets into the issue of cancer cachexia.
0:10:11.01 -> 0:10:12.25 So when patients are
0:10:12.25 -> 0:10:13.49 being treated for cancer,
0:10:13.49 -> 0:10:15.35 have cancer and they lose a
0:10:15.35 -> 0:10:16.59 significant amount of weight,

0:10:16.59 -> 0:10:18.865 a very large amount of weight so
0:10:18.865 -> 0:10:21.299 that they lose a lot of fat and
0:10:21.299 -> 0:10:23.1 start to lose muscle as well,
0:10:23.1 -> 0:10:24.65 those patients are also at
0:10:24.65 -> 0:10:26.2 higher risk for poorer outcomes,
0:10:26.2 -> 0:10:28.37 and so we can't simply tell people,
0:10:28.37 -> 0:10:29.92 just go and lose weight,
0:10:29.92 -> 0:10:32.167 and that's really why we need to
0:10:32.167 -> 0:10:33.468 understand mechanistically what this
0:10:33.468 -> 0:10:35.184 link is between obesity and cancer,
0:10:35.19 -> 0:10:37.05 so that instead of telling people,
0:10:37.05 -> 0:10:38.91 oh, just go and lose weight,
0:10:38.91 -> 0:10:40.806 we can give them a mechanistically
0:10:40.806 -> 0:10:41.438 driven intervention
0:10:41.44 -> 0:10:44.176 that may help mitigate that risk of obesity,
0:10:44.18 -> 0:10:45.544 while not predisposing them
0:10:45.544 -> 0:10:46.567 to cancer cachexia.
0:10:47.33 -> 0:10:50.466 So let's unpack that a little bit more.
0:10:50.47 -> 0:10:53.221 What do you mean by a mechanistically
0:10:53.221 -> 0:10:55.578 driven intervention?
0:10:55.58 -> 0:10:57.758 We want to understand what the molecule is or
0:10:57.758 -> 0:11:00.123 molecules are that are responsible for
0:11:00.123 -> 0:11:02.655 this link between obesity and cancer.
0:11:02.66 -> 0:11:04.82 For instance, if the link is
0:11:04.82 -> 0:11:06.98 at least in part insulin,
0:11:06.98 -> 0:11:08.95 one of my favorite hypothesis,
0:11:08.95 -> 0:11:11.934 there are ways that we can lower insulin
0:11:11.934 -> 0:11:15.229 while not forcing a patient to lose weight.
0:11:15.23 -> 0:11:17.618 There are different drugs that work
0:11:17.62 -> 0:11:20.574 in different ways that would all lower
0:11:20.574 -> 0:11:22.52 circulating insulin and that would

0:11:22.52 -> 0:11:24.968 not require the patient to go on a
0:11:25.04 -> 0:11:27.15 restrictive diet or put themselves
0:11:27.15 -> 0:11:29.647 at risk for cancer cachexia syndrome.
0:11:29.647 -> 0:11:31.582 Similarly, if the link were
0:11:31.582 -> 0:11:32.743 certain inflammatory cytokine,
0:11:32.75 -> 0:11:34.43 there are various antibodies that
0:11:34.43 -> 0:11:36.673 are being developed to block certain
0:11:36.673 -> 0:11:38.179 inflammatory cytokine action,
0:11:38.18 -> 0:11:40.256 and so we could potentially give
0:11:40.256 -> 0:11:42.572 folks an antibody to that particular
0:11:42.572 -> 0:11:45.164 cytokine that might lower their risk,
0:11:45.17 -> 0:11:45.944 while again,
0:11:45.944 -> 0:11:48.266 not requiring them to lose weight.
0:11:48.27 -> 0:11:51.825 So it would just allow us to more safely
0:11:51.83 -> 0:11:53.705 intervene in this link between
0:11:53.705 -> 0:11:54.83 obesity and cancer
0:11:54.83 -> 0:11:56.33 if we could understand
0:11:56.33 -> 0:11:57.83 exactly what mediates it.
0:11:57.83 -> 0:12:00.038 Except that they'd still be at
0:12:00.038 -> 0:12:01.955 increased risk of heart disease
0:12:01.955 -> 0:12:03.83 and diabetes if they were
0:12:03.83 -> 0:12:04.958 overweight, right?
0:12:04.958 -> 0:12:06.462 Yes, certainly weight loss
0:12:06.462 -> 0:12:07.96 within a healthy range,
0:12:07.96 -> 0:12:10.21 so not becoming underweight but
0:12:10.21 -> 0:12:12.18 weight loss within a healthy
0:12:12.18 -> 0:12:14.913 range is probably going to be the
0:12:14.913 -> 0:12:16.959 best way to mitigate this risk.
0:12:16.96 -> 0:12:19.21 Overall though it may be very
0:12:19.21 -> 0:12:20.71 difficult during cancer treatment,
0:12:20.71 -> 0:12:21.73 as you mentioned.

0:12:21.73 -> 0:12:23.09 Cancer treatment tends to
0:12:23.09 -> 0:12:24.86 cause people to gain weight,
0:12:24.86 -> 0:12:27.17 and so during that short period of
0:12:27.17 -> 0:12:29.819 time it may be better to focus on
0:12:29.82 -> 0:12:32.137 what we can do from
0:12:32.137 -> 0:12:33.13 a cancer standpoint,
0:12:33.13 -> 0:12:34.785 to mechanistically intervene in this
0:12:34.785 -> 0:12:36.44 link between obesity and cancer,
0:12:36.44 -> 0:12:38.426 rather than focusing on weight loss.
0:12:38.43 -> 0:12:40.747 But long term from a population standpoint,
0:12:40.75 -> 0:12:42.688 absolutely we should all be encouraging
0:12:42.688 -> 0:12:44.719 our patients and ourselves to
0:12:44.72 -> 0:12:46.706 maintain a healthy weight.
0:12:46.71 -> 0:12:49.662 Rachel, I want to dig a little bit deeper into
0:12:49.662 -> 0:12:52.364 what your lab is doing in terms of
0:12:52.37 -> 0:12:54.638 insulin and its link to obesity.
0:12:54.64 -> 0:12:56.944 One of the statistics that you
0:12:56.944 -> 0:12:59.929 gave us at the top of the show,
0:12:59.93 -> 0:13:01.815 which was the link between
0:13:01.815 -> 0:13:02.946 obesity and diabetes,
0:13:02.95 -> 0:13:05.218 was just mind blowing to me.
0:13:05.22 -> 0:13:07.747 So talk a little bit about that
0:13:07.747 -> 0:13:10.14 and how insulin plays into that,
0:13:10.14 -> 0:13:12.025 as well as into this
0:13:12.025 -> 0:13:13.533 whole concept of obesity.
0:13:14.19 -> 0:13:16.075 Yeah, so my training was
0:13:16.075 -> 0:13:17.583 in straight metabolism.
0:13:17.59 -> 0:13:19.665 I studied diabetes and substrate
0:13:19.665 -> 0:13:21.74 metabolism during my graduate work
0:13:21.804 -> 0:13:23.75 and my post doc and we developed
0:13:23.75 -> 0:13:25.935 methods to be able to assess

0:13:25.935 -> 0:13:28.07 metabolism in different tissues and
0:13:28.07 -> 0:13:30.246 different settings and so one of
0:13:30.246 -> 0:13:32.746 the hormones that we focus on in
0:13:32.746 -> 0:13:34.976 the metabolism world is insulin.
0:13:34.98 -> 0:13:37.368 Insulin is secreted by the endocrine
0:13:37.368 -> 0:13:39.519 pancreas when we eat a meal.
0:13:39.52 -> 0:13:41.776 When blood sugar levels go up,
0:13:41.78 -> 0:13:42.914 insulin is secreted.
0:13:42.914 -> 0:13:45.182 Insulin helps ourselves to take up
0:13:45.19 -> 0:13:47.71 glucose or sugar so that the sugar
0:13:47.71 -> 0:13:50.157 is taken out of the bloodstream
0:13:50.157 -> 0:13:51.865 and into the tissues.
0:13:51.87 -> 0:13:53.84 And when we do that,
0:13:53.84 -> 0:13:55.778 the tissues or even tumors in
0:13:55.778 -> 0:13:58.319 certain cases can use that sugar as
0:13:58.319 -> 0:14:00.284 fuel for themselves while lowering
0:14:00.284 -> 0:14:02.09 blood glucose concentrations.
0:14:02.09 -> 0:14:03.266 So in diabetes,
0:14:03.266 -> 0:14:05.226 that process doesn't happen efficiently.
0:14:05.23 -> 0:14:07.588 People tend to become insulin resistant,
0:14:07.59 -> 0:14:10.418 so their bodies don't respond as well
0:14:10.418 -> 0:14:13.712 as they need to insulin and so it
0:14:13.712 -> 0:14:16.66 either needs to be given by injection,
0:14:16.66 -> 0:14:18.375 or certain interventions need to
0:14:18.375 -> 0:14:20.781 take place to allow the body to
0:14:20.781 -> 0:14:22.341 respond better to insulin and
0:14:22.341 -> 0:14:24.388 the work that we've been doing
0:14:24.39 -> 0:14:26.598 in my lab in the last
0:14:26.598 -> 0:14:28.401 several years has been specifically
0:14:28.401 -> 0:14:30.765 looking at this link between insulin,
0:14:30.77 -> 0:14:31.778 obesity and cancer.

0:14:32.35 -> 0:14:34.338 I think there's a lot more
0:14:34.338 -> 0:14:36.689 we need to learn about obesity,
0:14:36.69 -> 0:14:37.692 insulin, and cancer,
0:14:37.692 -> 0:14:40.03 and how all of that plays together.
0:14:40.03 -> 0:14:42.165 But first we need to take a
0:14:42.165 -> 0:14:44.369 short break for a medical minute.
0:14:44.37 -> 0:14:46.045 Please stay tuned to learn
0:14:46.045 -> 0:14:47.383 more about obesity, insulin,
0:14:47.383 -> 0:14:50.047 and cancer with my guest doctor Rachel Perry.
0:14:50.68 -> 0:14:53.05 Support for Yale Cancer Answers
0:14:53.05 -> 0:14:54.946 comes from AstraZeneca,
0:14:54.95 -> 0:14:57.245 a bio pharmaceutical business that
0:14:57.245 -> 0:15:00.1 is pushing the boundaries of science
0:15:00.1 -> 0:15:02.525 to deliver new cancer medicines.
0:15:02.53 -> 0:15:05.73 More information at astrazeneca-us.com.
0:15:05.73 -> 0:15:08.677 This is a medical minute about genetic
0:15:08.677 -> 0:15:11.239 testing which can be useful for
0:15:11.239 -> 0:15:13.675 people with certain types of cancer
0:15:13.675 -> 0:15:16.418 that seem to run in their families.
0:15:16.42 -> 0:15:18.94 Patients that are considered at risk
0:15:18.94 -> 0:15:21.431 receive genetic counseling and testing so
0:15:21.431 -> 0:15:23.651 informed medical decisions can be based
0:15:23.651 -> 0:15:26.279 on their own personal risk assessment.
0:15:26.28 -> 0:15:28.1 Resources for genetic counseling and
0:15:28.1 -> 0:15:29.92 testing are available at federally
0:15:29.976 -> 0:15:32.028 designated comprehensive cancer centers.
0:15:32.03 -> 0:15:33.674 Interdisciplinary teams include geneticists,
0:15:33.674 -> 0:15:34.96 genetic counselors, physicians,
0:15:34.96 -> 0:15:35.88 and nurses who
0:15:35.88 -> 0:15:38.18 work together to provide
0:15:38.18 -> 0:15:40.36 risk assessment and steps to

0:15:40.36 -> 0:15:42.345 prevent the development of cancer.
0:15:42.35 -> 0:15:44.11 More information is available
0:15:44.11 -> 0:15:44.99 at yalecancercenter.org.
0:15:44.99 -> 0:15:47.63 You're listening to Connecticut public radio.
0:15:48.84 -> 0:15:50.742 This is doctor Anees Chagpar
0:15:50.742 -> 0:15:52.831 and I'm joined tonight by
0:15:52.831 -> 0:15:54.716 my guest doctor Rachel Perry.
0:15:54.72 -> 0:15:56.796 We're talking about the role of
0:15:56.796 -> 0:15:58.986 obesity and insulin in cancer and
0:15:58.986 -> 0:16:01.212 right before the break Rachel, you
0:16:01.212 -> 0:16:03.559 were starting to tell us a little
0:16:03.559 -> 0:16:05.742 bit about how insulin really works in
0:16:05.742 -> 0:16:07.989 terms of causing obesity and how that
0:16:07.989 -> 0:16:10.29 plays into the development of cancer.
0:16:10.29 -> 0:16:12.972 Can you take us back a couple of
0:16:12.972 -> 0:16:15.83 steps and talk about insulin and obesity?
0:16:15.83 -> 0:16:17.738 I know insulin is a hormone
0:16:17.738 -> 0:16:20.029 it's made by the pancreas,
0:16:20.03 -> 0:16:23.648 but how does that cause us to be obese?
0:16:23.65 -> 0:16:26.457 And if all of us make insulin,
0:16:26.46 -> 0:16:27.669 how come not
0:16:27.67 -> 0:16:29.68 all of us are obese?
0:16:29.68 -> 0:16:32.086 Those are both important questions,
0:16:32.09 -> 0:16:34.834 and honestly, we're still not certain the
0:16:34.834 -> 0:16:37.213 metabolic community is still not certain
0:16:37.213 -> 0:16:39.493 to what extent insulin causes obesity
0:16:39.493 -> 0:16:42.139 versus obesity causing high insulin levels.
0:16:42.14 -> 0:16:44.42 We know that obesity causes high
0:16:44.42 -> 0:16:46.437 insulin levels because as individuals
0:16:46.437 -> 0:16:48.567 become more and more obese,
0:16:48.57 -> 0:16:50.65 they become more and more

0:16:50.65 -> 0:16:53.45 insulin resistant and that's due to increased
0:16:53.45 -> 0:16:56.427 levels of lipid or fat in various tissues.
0:16:56.43 -> 0:16:58.35 When we become insulin resistant,
0:16:58.35 -> 0:17:00.28 that means we don't respond,
0:17:00.28 -> 0:17:02.814 our bodies don't respond very well to
0:17:02.814 -> 0:17:05.887 insulin and so our body has to secrete
0:17:05.887 -> 0:17:08.36 more insulin to counteract that effect.
0:17:08.36 -> 0:17:10.436 Now the question of whether insulin
0:17:10.436 -> 0:17:12.6 causes obesity is very interesting
0:17:12.6 -> 0:17:14.91 in sort of a chicken and
0:17:14.91 -> 0:17:16.45 egg type of question,
0:17:16.45 -> 0:17:18.718 and there are a number of
0:17:18.718 -> 0:17:20.7 studies that do suggest that
0:17:20.7 -> 0:17:23.479 insulin may itself independently cause
0:17:23.479 -> 0:17:26.684 obesity and that's at least in large part
0:17:26.684 -> 0:17:28.634 because insulin causes fat deposition.
0:17:28.64 -> 0:17:30.645 It causes those small molecules
0:17:30.645 -> 0:17:33.116 of carbohydrate and fat that are
0:17:33.116 -> 0:17:35.48 floating by in our bloodstream to
0:17:35.48 -> 0:17:37.879 actually be deposited in tissues in
0:17:37.879 -> 0:17:40.165 subcutaneous fat depots and form larger
0:17:40.165 -> 0:17:42.926 and larger pieces of fat, and so
0:17:42.93 -> 0:17:44.121 in that regard,
0:17:44.121 -> 0:17:46.9 it is likely that insulin causes obesity,
0:17:46.9 -> 0:17:48.89 at least to some extent.
0:17:48.89 -> 0:17:51.69 But as I said, it's more certain
0:17:51.69 -> 0:17:53.074 that obesity causes hyperinsulinemia
0:17:53.074 -> 0:17:55.15 or high insulin levels because of
0:17:55.207 -> 0:17:56.939 that insulin resistance phenomenon.
0:17:56.94 -> 0:17:58.065 As you said,
0:17:58.065 -> 0:18:00.315 we all need to have insulin.

0:18:00.32 -> 0:18:02.57 The body knows if it doesn't
0:18:02.57 -> 0:18:04.07 have enough functioning insulin,
0:18:04.07 -> 0:18:06.688 because when we don't have enough insulin,
0:18:06.69 -> 0:18:08.94 our blood glucose levels get high
0:18:08.94 -> 0:18:10.858 without insulin action on various
0:18:10.858 -> 0:18:13.308 tissues, we're not able to take up
0:18:13.308 -> 0:18:15.628 enough glucose or sugar from our
0:18:15.628 -> 0:18:17.184 bloodstream into those tissues,
0:18:17.19 -> 0:18:18.654 and when that happens,
0:18:18.654 -> 0:18:21.749 the body senses the high blood sugar level
0:18:21.75 -> 0:18:24.144 and secretes more insulin to try to
0:18:24.144 -> 0:18:26.56 counteract the effects of insulin resistance.
0:18:27.32 -> 0:18:30.312 So let me get this straight, obesity
0:18:30.312 -> 0:18:32.98 causes you to be insulin resistant,
0:18:32.98 -> 0:18:36.204 so your body needs to make more insulin.
0:18:36.21 -> 0:18:39.325 But that insulin takes sugar from your
0:18:39.325 -> 0:18:41.458 bloodstream and deposits it as fat,
0:18:41.46 -> 0:18:44.684 which then causes you to be more obese.
0:18:44.69 -> 0:18:47.12 So isn't this a vicious cycle?
0:18:47.76 -> 0:18:50.343 It absolutely is a vicious cycle and
0:18:50.343 -> 0:18:53.255 we and others have shown that if you
0:18:53.255 -> 0:18:55.88 intervene in any step of this cycle,
0:18:55.88 -> 0:18:58.769 so if you intervene in the step of eating
0:18:58.769 -> 0:19:01.259 too many calories, if you intervene
0:19:01.259 -> 0:19:03.747 in secreting too much insulin,
0:19:03.747 -> 0:19:06.201 if you intervene in depositing that
0:19:06.201 -> 0:19:08.514 sugar in tissues as fat if you
0:19:08.514 -> 0:19:10.639 intervene in any of these steps,
0:19:10.64 -> 0:19:12.716 you can intervene in the cycle
0:19:12.716 -> 0:19:14.7 of the development of obesity.
0:19:14.7 -> 0:19:15.819 But yes, absolutely,

0:19:15.819 -> 0:19:18.057 it's a vicious cycle and this
0:19:18.057 -> 0:19:19.575 absolutely contributes to this
0:19:19.575 -> 0:19:21.735 pandemic of obesity that we have
0:19:21.74 -> 0:19:23.95 in our country and worldwide.
0:19:23.95 -> 0:19:24.7 We're
0:19:24.7 -> 0:19:27.318 going to get back to exactly how
0:19:27.318 -> 0:19:29.936 we can intervene, but let's talk a
0:19:29.936 -> 0:19:32.18 little bit about the cancer part.
0:19:32.18 -> 0:19:34.844 So we talked a little bit at the
0:19:34.844 -> 0:19:37.622 beginning of the show about the fact
0:19:37.622 -> 0:19:39.657 that obesity really does drive,
0:19:39.66 -> 0:19:42.278 I think it was what 13 different
0:19:42.278 -> 0:19:43.4 types of cancer,
0:19:43.4 -> 0:19:46.384 but not all cancers are affected by obesity,
0:19:46.39 -> 0:19:49.374 but certainly a large number of cancers are.
0:19:49.38 -> 0:19:51.25 So how does that happen?
0:19:51.25 -> 0:19:53.12 And what does insulin have
0:19:53.12 -> 0:19:54.99 to do with it anyways?
0:19:55.04 -> 0:19:57.476 Right, so as we were discussing earlier,
0:19:57.48 -> 0:19:59.727 I think in reality there are a
0:19:59.727 -> 0:20:01.41 number of different factors that
0:20:01.41 -> 0:20:03.699 may mediate at least part of this
0:20:03.699 -> 0:20:05.828 link between obesity and cancer.
0:20:05.83 -> 0:20:08.542 But as you said, we focus on specifically
0:20:08.542 -> 0:20:10.698 how insulin may fuel tumor growth.
0:20:10.7 -> 0:20:12.04 So, as I mentioned,
0:20:12.04 -> 0:20:13.715 individuals with obesity frequently have
0:20:13.715 -> 0:20:15.523 high circulating insulin levels because
0:20:15.523 -> 0:20:17.653 they tend to be insulin resistant.
0:20:17.66 -> 0:20:20.38 And this is indeed a vicious cycle. We
0:20:20.38 -> 0:20:23.218 found in a few studies, both in vitro

0:20:23.218 -> 0:20:26.45 so in a dish and in vivo, in mice,
0:20:26.45 -> 0:20:28.385 that insulin can drive tumor
0:20:28.385 -> 0:20:30.32 glucose uptake and metabolism, that
0:20:30.381 -> 0:20:33.021 actually was a little bit surprising
0:20:33.021 -> 0:20:34.781 initially because conventional wisdom
0:20:34.848 -> 0:20:37.473 has said that tumor glucose or sugar
0:20:37.473 -> 0:20:39.302 metabolism is constitutively high,
0:20:39.302 -> 0:20:41.759 so it would always be high and
0:20:41.759 -> 0:20:44.27 not regulated by any hormones,
0:20:44.27 -> 0:20:47.294 but the surprising finding that we
0:20:47.294 -> 0:20:50.749 and that others have also shown is that in fact,
0:20:50.75 -> 0:20:52.37 tumor glucose or sugar
0:20:52.37 -> 0:20:53.99 metabolism is insulin dependent,
0:20:53.99 -> 0:20:56.846 and so in mice that are obese
0:20:56.85 -> 0:20:57.921 and insulin resistant,
0:20:57.921 -> 0:20:59.706 they have high circulating insulin
0:20:59.706 -> 0:21:01.458 levels and this causes glucose
0:21:01.458 -> 0:21:03.098 uptake into their tumor cells.
0:21:03.1 -> 0:21:05.529 After the tumor cells take up glucose,
0:21:05.53 -> 0:21:08.298 it can be used in two different ways.
0:21:08.3 -> 0:21:10.376 It can be used for metabolism,
0:21:10.38 -> 0:21:12.816 so simply to provide the fuel that
0:21:12.816 -> 0:21:14.89 allows the cells to keep going,
0:21:14.89 -> 0:21:17.586 and it can also be used to make
0:21:17.586 -> 0:21:19.059 building blocks for cells.
0:21:19.06 -> 0:21:21.587 So a unique feature about tumor cells
0:21:21.587 -> 0:21:24.258 is that in order to be a tumor,
0:21:24.26 -> 0:21:26.348 these cells need to be growing
0:21:26.348 -> 0:21:28.16 and dividing all the time.
0:21:28.16 -> 0:21:31.112 They grow and divide very rapidly and they
0:21:31.112 -> 0:21:33.836 need building blocks to be able to do that,

0:21:33.84 -> 0:21:35.872 and glucose is a key fuel to be
0:21:35.872 -> 0:21:37.725 able to provide those building
0:21:37.725 -> 0:21:39.845 blocks for these tumor cells,
0:21:39.85 -> 0:21:41.848 and so in that way glucose
0:21:41.85 -> 0:21:43.86 and insulin which drives glucose uptake,
0:21:43.86 -> 0:21:45.53 is a key pathogenic factor in tumors.
0:21:47.25 -> 0:21:49.398 So let me ask you this,
0:21:49.4 -> 0:21:52.172 we know a lot of diabetics who
0:21:52.172 -> 0:21:55.125 are type one diabetics who take insulin.
0:21:55.13 -> 0:21:57.906 Does that mean that the insulin can actually
0:21:57.906 -> 0:22:00.498 be driving tumor growth in these people?
0:22:00.5 -> 0:22:02.582 Putting them at increased risk since
0:22:02.582 -> 0:22:04.43 their injecting themselves with insulin?
0:22:05.41 -> 0:22:07.486 You know that's a key question.
0:22:07.49 -> 0:22:08.874 A very important question,
0:22:08.874 -> 0:22:10.95 and frankly a personally relevant question, as
0:22:10.95 -> 0:22:13.12 I am a person with type one
0:22:13.12 -> 0:22:15.258 diabetes and so this is something
0:22:15.258 -> 0:22:17.52 that I am very curious about.
0:22:17.52 -> 0:22:18.9 The epidemiological evidence doesn't
0:22:18.9 -> 0:22:21.334 seem to support a strong role for
0:22:21.334 -> 0:22:22.874 exogenous insulin, that is injected
0:22:22.874 -> 0:22:24.557 insulin, in type one diabetic
0:22:24.557 -> 0:22:26.517 individuals in driving tumor growth,
0:22:26.52 -> 0:22:28.596 and there could be a few
0:22:28.596 -> 0:22:29.98 different reasons for that.
0:22:29.98 -> 0:22:32.05 It is a little bit surprising,
0:22:32.05 -> 0:22:33.805 but what we currently believe
0:22:33.805 -> 0:22:36.269 is that you may need two hits.
0:22:36.27 -> 0:22:36.946 That is,
0:22:36.946 -> 0:22:38.974 high glucose and high insulin levels,

0:22:38.98 -> 0:22:40.72 so type one diabetic individuals
0:22:40.72 -> 0:22:43.19 who take as much insulin as they
0:22:43.19 -> 0:22:45.17 need tend not to have chronically
0:22:45.17 -> 0:22:47.12 high glucose levels all the time,
0:22:47.12 -> 0:22:49.472 and so it may be that keeping blood
0:22:49.472 -> 0:22:51.814 sugar normal is also very important in
0:22:51.814 -> 0:22:53.954 these individuals who need to inject
0:22:53.954 -> 0:22:56.27 insulin exogeneously to stay alive.
0:22:56.27 -> 0:22:58.28 But that's a question that really
0:22:58.28 -> 0:23:00.356 is an open question and one
0:23:00.356 -> 0:23:02.026 that were very curious about.
0:23:02.03 -> 0:23:03.446 It's also entirely possible,
0:23:03.446 -> 0:23:05.963 and I think this is likely that
0:23:05.963 -> 0:23:08.217 insulin may not be the only factor
0:23:08.22 -> 0:23:09.6 that mediates the effects
0:23:09.6 -> 0:23:11.325 of obesity on tumor growth,
0:23:11.33 -> 0:23:13.874 so it may be that you need high
0:23:13.874 -> 0:23:16.061 insulin levels to have an obesity
0:23:16.061 -> 0:23:17.906 affect to drive tumor growth,
0:23:17.91 -> 0:23:20.549 but that you also need other factors
0:23:20.549 -> 0:23:22.02 like inflammatory cytokines or
0:23:22.02 -> 0:23:23.682 leptin or other hormones.
0:23:25.87 -> 0:23:28.243 And in these lean type one diabetic
0:23:28.243 -> 0:23:30.017 individuals they may have high
0:23:30.017 -> 0:23:32.087 insulin levels but not these other
0:23:32.087 -> 0:23:33.856 factors that may be required
0:23:33.856 -> 0:23:35.204 to mediate the effects.
0:23:37.08 -> 0:23:39.072 You know, and that makes me
0:23:39.072 -> 0:23:40.4 think of something else.
0:23:40.4 -> 0:23:42.254 Some people have these benign tumors
0:23:42.254 -> 0:23:44.38 in their pancreas that secrete insulin,

0:23:44.38 -> 0:23:46.767 so it's kind of a little insulin
0:23:46.767 -> 0:23:48.699 factory that they've got going on.
0:23:48.7 -> 0:23:50.36 Are those people at increased
0:23:50.36 -> 0:23:51.688 risk of developing cancer,
0:23:51.69 -> 0:23:53.974 or is it still this,
0:23:53.974 -> 0:23:55.846 you need the interplay of a
0:23:55.846 -> 0:23:57.917 number of factors so they may
0:23:57.917 -> 0:23:59.987 not really be at increased risk.
0:23:59.99 -> 0:24:01.65 So I believe that these
0:24:01.65 -> 0:24:04.298 folks and I could be wrong on this,
0:24:04.3 -> 0:24:05.96 this isn't particularly my field,
0:24:05.96 -> 0:24:07.97 but I believe that those folks
0:24:07.97 -> 0:24:10.298 are at higher risk of pancreatic,
0:24:10.3 -> 0:24:13.009 at least benign tumors of other types,
0:24:13.01 -> 0:24:14.95 and maybe at higher risk
0:24:14.95 -> 0:24:16.114 of pancreatic cancer,
0:24:16.12 -> 0:24:18.358 so that would suggest that insulin
0:24:18.358 -> 0:24:20.719 may be acting within the pancreas
0:24:20.719 -> 0:24:22.704 as a tumor promoting factor,
0:24:22.71 -> 0:24:24.984 but I don't believe they're at
0:24:24.984 -> 0:24:27.369 substantially higher risk in other sites.
0:24:27.37 -> 0:24:29.614 Now this could be because it's
0:24:29.614 -> 0:24:31.593 my understanding that those folks
0:24:31.593 -> 0:24:33.653 aren't allowed to go continuously
0:24:33.653 -> 0:24:35.729 forever with high insulin levels
0:24:35.729 -> 0:24:38.228 secreted by a tumor from the pancreas.
0:24:38.23 -> 0:24:40.878 The tumor will be either removed, or
0:24:40.878 -> 0:24:41.514 treated,
0:24:41.514 -> 0:24:43.422 they may be treated with somatostatin
0:24:43.422 -> 0:24:45.885 or some other agent to prevent the
0:24:45.885 -> 0:24:47.9 high insulin secretion,

0:24:47.9 -> 0:24:50.063 but I would expect that if someone
0:24:50.063 -> 0:24:51.43 were chronically having high
0:24:51.43 -> 0:24:52.946 insulin levels from continuous
0:24:52.946 -> 0:24:54.462 excess secretion of insulin,
0:24:54.47 -> 0:24:57.521 that they would in fact be at risk and
0:24:57.521 -> 0:25:00.7 that is a study that we've done in mice.
0:25:00.7 -> 0:25:03.268 So if you take mice and put a
0:25:03.268 -> 0:25:04.714 subcutaneous insulin pellet into
0:25:04.714 -> 0:25:06.928 them so that they
0:25:06.93 -> 0:25:09.006 chronically have high insulin levels,
0:25:09.01 -> 0:25:11.116 they do develop tumors more quickly
0:25:11.12 -> 0:25:13.46 and do worse with the tumors
0:25:13.46 -> 0:25:15.02 than mice that
0:25:15.02 -> 0:25:16.97 don't have too much circulating
0:25:16.97 -> 0:25:18.53 insulin all the time.
0:25:19.26 -> 0:25:21.507 And when we talked about the fact
0:25:21.507 -> 0:25:24.139 that some of the cancers are increased
0:25:24.139 -> 0:25:26.527 with obesity and insulin is one
0:25:26.602 -> 0:25:28.975 factor that may be playing a role,
0:25:28.98 -> 0:25:30.935 sometimes people talk
0:25:30.935 -> 0:25:32.89 about this thing called insulin
0:25:32.952 -> 0:25:34.377 growth factor or my IGF,
0:25:34.38 -> 0:25:36.9 which can be found in some cancers.
0:25:36.9 -> 0:25:37.959 Are those related?
0:25:37.959 -> 0:25:40.43 So we find that insulin plays more
0:25:40.5 -> 0:25:43.02 of role in people who have tumors
0:25:43.02 -> 0:25:44.82 that have receptors, for example,
0:25:44.82 -> 0:25:46.98 that are more responsive to insulin,
0:25:46.98 -> 0:25:49.86 or is this something that is more ubiquitous?
0:25:49.86 -> 0:25:52.38 At least in these 13 tumor types,
0:25:52.38 -> 0:25:54.19 regardless of whether or not

0:25:54.19 -> 0:25:56.12 the tumor secretes insulin or
0:25:56.12 -> 0:25:57.664 insulin related growth factor,
0:25:57.67 -> 0:25:58.828 there does seem
0:25:58.83 -> 0:26:00.378 to be a relationship
0:26:00.378 -> 0:26:02.313 between my IGF and insulin,
0:26:02.32 -> 0:26:05.029 so that comes in several different ways,
0:26:05.03 -> 0:26:07.487 mostly that the IGF1 and insulin
0:26:07.487 -> 0:26:09.877 receptors are very similar and both
0:26:09.877 -> 0:26:11.987 molecules can activate the other.
0:26:11.99 -> 0:26:15.086 So insulin can activate the IG F1 receptor
0:26:15.09 -> 0:26:17.922 and IG F1 can activate the insulin receptor
0:26:17.922 -> 0:26:21.438 and so I would absolutely expect there to
0:26:21.438 -> 0:26:23.99 be interplay between insulin an IG F1,
0:26:23.99 -> 0:26:25.574 particularly in those
0:26:25.574 -> 0:26:27.158 IGF one expressing tumors.
0:26:27.16 -> 0:26:29.362 This also brings up a good
0:26:29.362 -> 0:26:31.999 point that I want to highlight,
0:26:32 -> 0:26:34.821 and that is that the insulin receptor
0:26:34.821 -> 0:26:37.238 is not ubiquitously found in tumors.
0:26:37.24 -> 0:26:39.376 The tumor types that are associated
0:26:39.376 -> 0:26:41.347 with obesity on average have
0:26:41.347 -> 0:26:43.279 higher insulin receptor expression,
0:26:43.28 -> 0:26:46.094 but that's not 100% across the board,
0:26:46.1 -> 0:26:49.727 but because of this cross talk between IGF,1
0:26:49.73 -> 0:26:52.874 and insulin that may explain some of
0:26:52.874 -> 0:26:55.202 the discrepancies there where a tumor
0:26:55.202 -> 0:26:58.23 may be at least weakly obesity associated.
0:26:58.23 -> 0:27:00.211 But may not have the insulin receptor
0:27:00.211 -> 0:27:02.65 and that may be because the IGF1
0:27:02.65 -> 0:27:04.18 receptor compensates for that.
0:27:04.18 -> 0:27:04.543 Unfortunately,

0:27:04.543 -> 0:27:07.084 tumors are evolved to survive very well,
0:27:07.09 -> 0:27:09.876 and so they've sort of developed mechanisms
0:27:09.876 -> 0:27:12.547 in their evolution to be able to survive,
0:27:12.55 -> 0:27:14.74 and one that I think
0:27:14.74 -> 0:27:16.56 is the redundancy of insulin,
0:27:16.56 -> 0:27:18.38 and IGF1 action.
0:27:19.24 -> 0:27:21.824 In our last few
0:27:21.824 -> 0:27:24.454 minutes I really want to get back
0:27:24.454 -> 0:27:26.844 to something you said earlier which
0:27:26.844 -> 0:27:29.31 was breaking the cycle of obesity.
0:27:29.31 -> 0:27:32.294 Can have an impact on reducing cancer risk.
0:27:32.3 -> 0:27:35.276 I wanna make sure I got that straight.
0:27:35.28 -> 0:27:37.392 So if you're overweight and you
0:27:37.392 -> 0:27:39.648 decide to lose weight by cutting
0:27:39.648 -> 0:27:41.988 calories or exercise,
0:27:41.99 -> 0:27:44.594 that actually can reduce your cancer risk.
0:27:44.6 -> 0:27:45.719 Is that right?
0:27:46.24 -> 0:27:47.026 Absolutely, epidemiologically,
0:27:47.026 -> 0:27:49.384 even losing weight within the last
0:27:49.384 -> 0:27:51.48 couple years reduces your cancer risk,
0:27:51.48 -> 0:27:53.718 and so it's best
0:27:53.72 -> 0:27:55.958 of course, if we're normal weight,
0:27:55.96 -> 0:27:57.83 healthy weight throughout our lives.
0:27:57.83 -> 0:27:59.954 But it absolutely can have a
0:27:59.954 -> 0:28:02.319 huge impact to lower cancer risk.
0:28:02.32 -> 0:28:04.19 Losing a little bit of
0:28:04.19 -> 0:28:06.06 weight at really anytime.
0:28:06.06 -> 0:28:09.116 And you know the other point I want
0:28:09.116 -> 0:28:11.822 to highlight is we don't have to be
0:28:11.822 -> 0:28:14.659 back to our high school body weight.
0:28:14.66 -> 0:28:16.56 This is a case where

0:28:16.56 -> 0:28:18.541 Losing 5 to 10% of body weight
0:28:18.541 -> 0:28:20.869 if you're an overweight or obese
0:28:20.869 -> 0:28:23.209 individual can actually almost fully
0:28:23.209 -> 0:28:25.539 normalize your insulin sensitivity,
0:28:25.54 -> 0:28:28.116 and so that can be
0:28:28.116 -> 0:28:30.188 predicted to almost fully normalize
0:28:30.188 -> 0:28:33.289 or reduce the excess risk of obesity,
0:28:33.29 -> 0:28:36.265 and so that is something where
0:28:36.265 -> 0:28:39.068 that loss of five to 10% is something
0:28:39.068 -> 0:28:41.732 that would be much more achievable
0:28:41.732 -> 0:28:43.49 then returning to a quote
0:28:43.49 -> 0:28:46.339 unquote healthy weight for a lot of
0:28:46.34 -> 0:28:47.884 individuals.
0:28:47.884 -> 0:28:49.814 Doctor Rachel Perry is an assistant professor in
0:28:49.814 -> 0:28:51.369 medicine and Endocrinology
0:28:51.37 -> 0:28:53.165 and cellular and Molecular Physiology
0:28:53.165 -> 0:28:55.58 at the Yale School of Medicine.
0:28:55.58 -> 0:28:57.116 If you have questions,
0:28:57.116 -> 0:28:58.652 the address is canceranswers@yale.edu
0:28:58.652 -> 0:29:00.775 and past editions of the program
0:29:00.775 -> 0:29:02.713 are available in audio and written
0:29:02.773 -> 0:29:04.39 form at Yalecancercenter.org.
0:29:04.39 -> 0:29:07.286 We hope you'll join us next week to
0:29:07.286 -> 0:29:10.102 learn more about the fight against
0:29:10.102 -> 0:29:13.12 cancer here on Connecticut public radio.