Transfusion medicine, reduce morbidity, improve efficiency and really in some respects understand how we can always do better. And it's been a phenomenal service to our patients and to the mission of the Cancer Center and an Ed today is going to talk about GV HD and blood pathogens and the work he's done. So add, thank you. Thank you very much Charlie. It’s a pleasure to be here and we can get this. Working right, I’ll have to screen share, right?
Yes. Sure there it is.

OK, that looks like it's it works.

Work yes, OK, well thank you very much.

I'm going to talk today on prevention of transfusion, associated GVHD, and the role of a bladder radiation and pathogen reduction.

If I can get the slides to move, there you go for conflict of interest I do.

I am running three clinical trials on platelets and two on red cells for the serious Corporation.

but I get no personal honor area. All the money goes to the University and support my salary for that effort,
not for me.

Personally, so I’m going to review the pathophysiology of transfusion, associated GVHD review, addressed the types of pathogen reduction, provide data on the toxicology study, talk a little bit about the clinical studies, and then compare the pathogen reduction versus gamma radiation for preventing PA GVHD so.

Yale New Haven’s got about 1600 beds.

We have one transfuse, about 11,000 people a year. We transfuse about 54,000 products a year,
broken down, as you see, below red cells, platelets, plasma, where first transfusion associated GVHD, therefore, is potential with many of these transfusions. And unfortunately, we don’t see it for a variety of reasons. We will talk about TH GV HD occurs less than one per million transfusions. It’s pretty rare. Clinical signs began about 8 to 10 days after transfusion, with somewhere between 3 and 30 days. Usually is a rash associated with fever enterocolitis,
watery diarrhea, and elevated LFTS. A key sign is pancytopenia with a higher risk being in men. The reason for the aplasia is that in regular versus host disease, if you will forward regular post bone marrow transplant, the bone marrow is that of the recipient and the donors T cells therefore do not attack it because it’s the donors own cells in transfusion associated GVHD,
the host, or the recipients of bone marrow is there so that the donor cells attack the bone marrow as well as the liver and the skin. So that the a pleasure is due to GVHD involving the bone marrow of the recipient, and it is almost always fatal, and that’s why it’s that kind of fatality is not seen with affecting the bone marrow and graph versus the bone marrow and graph after a bone marrow transplant. The rash begins on the trunk and spreads to the extremities, and diagnosis with usually a biopsy and death,
00:03:40.470 --> 00:03:43.406 occurs one to three weeks after the symptoms.
NOTE Confidence: 0.894347965717316

00:03:43.410 --> 00:03:46.350 The mechanism is that transfused lymphocytes.
NOTE Confidence: 0.894347965717316

00:03:46.350 --> 00:03:48.590 From an immuno competent donor,
NOTE Confidence: 0.894347965717316

00:03:48.590 --> 00:03:51.158 recognized the host HLA is being
NOTE Confidence: 0.894347965717316

00:03:51.158 --> 00:03:53.401 foreign and former response and
NOTE Confidence: 0.894347965717316

00:03:53.401 --> 00:03:55.696 then the host counterattacks with
NOTE Confidence: 0.894347965717316

00:03:55.696 --> 00:03:57.073 its own lymphocytes.
NOTE Confidence: 0.894347965717316

00:03:57.080 --> 00:04:00.209 However, in cases of TAA GV HD,
NOTE Confidence: 0.816627144813538

00:04:00.210 --> 00:04:02.440 there is no counter attack.
NOTE Confidence: 0.816627144813538

00:04:02.440 --> 00:04:05.608 If you will and you just get in
NOTE Confidence: 0.816627144813538

00:04:05.608 --> 00:04:07.810 continued growth and engraftment.
NOTE Confidence: 0.816627144813538

00:04:07.810 --> 00:04:11.365 If you will, of the donor T cells which
NOTE Confidence: 0.816627144813538

00:04:11.365 --> 00:04:14.507 caused the graft versus host problems,
NOTE Confidence: 0.816627144813538

00:04:14.510 --> 00:04:16.270 the lack of neutralization.
NOTE Confidence: 0.816627144813538

00:04:16.270 --> 00:04:19.335 And what does this do to? Well,
NOTE Confidence: 0.816627144813538

00:04:19.335 --> 00:04:22.310 it’s do when the recipient several times,
NOTE Confidence: 0.816627144813538
00:04:22.310 --> 00:04:25.550 even if the recipient is immunocompetence.

NOTE Confidence: 0.816627144813538
00:04:25.550 --> 00:04:27.494 And you have an immuno competent

NOTE Confidence: 0.816627144813538
00:04:27.494 --> 00:04:29.620 donor from a blood transfusion.

NOTE Confidence: 0.816627144813538
00:04:29.620 --> 00:04:31.950 What happens is let’s say

NOTE Confidence: 0.816627144813538
00:04:31.950 --> 00:04:33.814 the donor is homozygous?

NOTE Confidence: 0.816627144813538
00:04:33.820 --> 00:04:36.725 For HLA two or HLA B 44,

NOTE Confidence: 0.816627144813538
00:04:36.730 --> 00:04:40.322 the recipient does not see the donor cells

NOTE Confidence: 0.816627144813538
00:04:40.322 --> 00:04:43.111 as being foreign because the recipient

NOTE Confidence: 0.816627144813538
00:04:43.111 --> 00:04:46.869 has a two and in this case be 44.

NOTE Confidence: 0.816627144813538
00:04:46.870 --> 00:04:49.950 Whereas the donor cells are immuno competent,

NOTE Confidence: 0.816627144813538
00:04:49.950 --> 00:04:53.046 it does see the host as being foreign

NOTE Confidence: 0.816627144813538
00:04:53.046 --> 00:04:56.550 and it reacts against the host giving

NOTE Confidence: 0.816627144813538
00:04:56.550 --> 00:05:00.052 the graft versus host disease as opposed

NOTE Confidence: 0.816627144813538
00:05:00.052 --> 00:05:03.590 to like a rejection of a heart or a

NOTE Confidence: 0.816627144813538
00:05:03.590 --> 00:05:06.230 kidney would be host versus graft.

NOTE Confidence: 0.816627144813538
So it’s either can occur.

Also an immunocompromised hosts due to congenital or acquired.

Aziz, or, or medications,

can do this, as we’ll see in in.

In a short while.

So the whole concept here is that the host is incapable of eliminating the immunocompetent T cells.

And they in graft.

And they attacked the bone marrow and that causes the ATA associated graft versus host.

So the requirements are to need to have a difference in donor recipient.

HLA immuno competent competent donor
cells need to be transfused and the host must be incapable of rejecting the immuno competent cells due to either disease or medication or congenital disease risk factors.

The degree of recipient, cellular immunodeficiency plays a role.

The number of viable T cells in the transfused product.

The minimum number is not known. It is known some products like granulocytes are associated with GV HD more than other products.

Also, the genetic diversity of the
population is important.

There was a fair amount of graft versus host disease.

T AA GVHD in Japan and they thought was that it was more of a closed population because of the fact that it was an isolated island and therefore the genetic diversity was not as great as would be in.

In a larger population.

Also fresher cellular blood products like red cells stored list in a couple of weeks have a higher risk of GV HD.

Also, for reasons that I’m not familiar with, I’m not sure if they’re known.
the differential diagnosis.

Once you start seeing things are ash you wonder about drug reaction or viral illness.

So skin biopsy is done when it’s done. It shows superficial

Here’s Grade 123 and then four in the lower right.

You see bullae formation, and you can see bullae formation starting here with these white circles.

And then you loss of reedy ridges, which are these intrusions into the dermis.

Here’s the epidermis on top, and then here’s the dermis,
the Rady Ridges,
where the blood vessels go are losted,
and the dermis of the epidermis separate.
Here you can see this set of little circles.
They have a whole.
This whole line shows the separation
of the Germans to the epidermis of
complete sloughing of that issue,
and that of course leads to infection
and causes problems as well.
So that is what?
The TA GV HD looks like on skin biopsy.
This is a bone marrow showing
a hypoplastic marrow.
As you can see,
this is patients back showing the rash.
Here the rash on the extremities and this other one in the lower right before he seemed so the treatment there really is no treatment. It’s a uniformly fatal condition, pretty much because of the marrow aplasia and in Allo transplants. You know when you give someone a unit of blood does this. a unit of blood does this. This can cause problems because again the transplanted bone marrow is that of the marrow donor or not. If necessary, the transfusion donor. Which is usually not the same.
Immuno suppression is rarely helpful. The radiation or whatever you’re using to look to eliminate the T cells in this in the donor products does not apply to FFP cryoprecipitate derivatives and also frozen red cells. Interestingly, because they’re washed multiple times, but it’s not been reported with non cellular products or with frozen cells as far as I know it’s frozen. You would need to irradiate the. Or in our case passage and reduce the product if it comes from a blood relative. If it’s a directed donation which was more common in the age era than it is now,
'cause people were donating for family members in the hope of preventing them from getting HIV at the time from unknown members of the blood supply. And that lets other problems as well because of the KGB HD. If it wasn’t irradiated, If the blood component is HLA match, that should be also treated as well. Look, our reduction is not protective. You’re not removing enough. White cells are still four to five logs left after Leukoreduction standard blood washing doesn’t remove it. You either need to gamma irradiate it.
The federal government wants to get rid of gamma radiation because of the potential to form dirty bombs. And we’ll talk about that in a couple seconds and then pathogen reduction as you will see, is also protective. And what if you give a pathogen reduced product? We do not irradiate the product at all, so this is what a bloody radiator looks like. The blood red cells and or platelets, whatever is put into this canister. The canister is here where the rent is is rotating in a circle and then
that whole thing rotates around to
where the source of the cesium sources here.
There are two pencils.
As I said this, the great material is led.
The person is standing over here watching the red cells
swivel around like a lazy suzan. It’s exposed for 456 minutes depending
on the strength of the radiation source that last years and years and years,
and then when the time is up, it automatically comes back to
the opening and then it’s removed. So that’s what the gamma cell is.
The concern is that terrorists will break in and rip open several tons of lead and take out the pencil source can be done, but the government would like to get rid of this and move to X Ray devices. And if with gamma rate with pathogen reduction you won’t need any kind of device at all actually. All the indications for radiated components, who are those that are immunosuppressed. Intrauterine transfusions, low birth weight. Exchange transfusions in newborns and you should’ve radiate the red cells for that. Patients with DiGeorge syndrome, where does he sell immunodeficiency
Hodgkin’s lymphoma?

Patients need to have irradiated blood products with for life not even after they’ve been cured. But for life, lors, auto transplants, not irradiating the transplant. Of course, just any red cells that they get outside of the transplant. If it’s Rachel Emacs single donor platelets, or from relatives. Or someone’s got various illnesses and are getting a purine analogue like fludarabine, cladribine, bendamustine, and other drugs as they come along patients.
00:11:41.510 --> 00:11:43.800 Getting Cam path anti CD.
NOTE Confidence: 0.847607553005219
00:11:43.800 --> 00:11:45.572 52 antithymocyte globulin granulocytes?
NOTE Confidence: 0.847607553005219
00:11:45.572 --> 00:11:48.768 If those products are used to treat
NOTE Confidence: 0.847607553005219
00:11:48.768 --> 00:11:51.582 illnesses they should get irradiated blood
NOTE Confidence: 0.847607553005219
00:11:51.582 --> 00:11:54.339 products not necessarily for aplastic anemia.
NOTE Confidence: 0.847607553005219
00:11:54.340 --> 00:11:56.172 MD S Hodgkin’s lymphoma.
NOTE Confidence: 0.847607553005219
00:11:56.172 --> 00:11:57.088 I’m sorry,
NOTE Confidence: 0.847607553005219
00:11:57.090 --> 00:11:59.380 non Hodgkin’s lymphoma and non
NOTE Confidence: 0.847607553005219
00:11:59.380 --> 00:12:01.670 Hodgkin’s leukemia is solid organs.
NOTE Confidence: 0.847607553005219
00:12:01.670 --> 00:12:02.906 Unless they’re being treated
NOTE Confidence: 0.847607553005219
00:12:02.906 --> 00:12:04.760 with one of these purine analogs
NOTE Confidence: 0.847607553005219
00:12:04.811 --> 00:12:06.226 or other types of therapies,
NOTE Confidence: 0.847607553005219
00:12:06.230 --> 00:12:07.750 so aplastic anemia getting ATG
NOTE Confidence: 0.847607553005219
00:12:07.750 --> 00:12:09.270 therapy would be a candidate.
NOTE Confidence: 0.847607553005219
00:12:09.270 --> 00:12:09.878 AA would.
NOTE Confidence: 0.847607553005219
00:12:09.878 --> 00:12:12.006 If you don’t know what it is,
I’m not going to give you a laundry list called The Blood Bank and ask the Blood Bank what their policy is right now. What happens if someone requests it? We’ve provided irradiated blood and then we review the indication and see if it needs to continue or not. So please call the Blood Bank for specific information on your patient.

Interesting, Lee, when they reviewed the use of these products. They found that not all institutions follow the same criteria. Here are three institutions from Canada and one from Boston,
and as you can see, not everybody irradiates for the same thing term.

Infants MGH does not place in Canada. Don’t do it for acute leukemias or chronic leukemias or stem cell donors during the harvest.

Children with solid tumors, it varies, and it’s an amazing amount of variability.

Again, give us a call and we’ll be happy to talk about your patient if there’s a new patient. And you have questions.
So now that we know about TTA GVHD, what is the pathogen reduction?
Well, that is a technology that attempts to eliminate pathogens contained in units of blood. The only thing in it what it does, it does it by binding DNA or RNA, single or double stranded, whether it’s viral or bacterial, and it prevents it from replicating. There’s nothing in blood that should have DNA except a pathogen. Well, it shouldn’t be in there,
but there’s nothing in blood that has DNA or RNA except a pathogen there is. I know there’s mitochondrial DNA, but that’s not what we’re discussing in platelets here, and there’s a little RNA left in red cells from the ridiculous site, but we’re not discussing that. We’re talking about pathogens, and that’s where the material is attacked. Emerging pathogens just showed you as a concern. If COVID-19 was Bloodborne and was transmissible by blood, things would be even worse.
If you can imagine that they are now and maybe covid 29 if it comes along. Hopefully not. Maybe Bloodborne, and we need to have pathogen reduction technology in place to mitigate that. So the therapies are two one for platelets and plasma and one for red cells with the service technology. The active agent is called S 59. Is is a sorrel in call dammit oslin is added to the playlist at the time is collection by the Blood Center and the mcauslan goes through the cell membrane and binds to the DNA.
or RNA double or single stranded and then it’s exposed to UV. A light in an illuminator. And it crosslinks preventing replication. That’s how it inactivates pathogens S 303. It has to be used for red cells, because hemoglobin A will absorb the UV A and it will not provide an appropriate and effective. Mitigation technology so this material, which is an alkylating agent, goes into the blood into the red cells and intercalates quickly and crosslinks without any illumination at all, and then it degrades very rapidly into a non reactive material is 300.
so and this has been approved by the FDA since 2014 the platelets or plasma and the red cell one is in phase three clinical trials. Which is what we’re doing here at Yale, and I’ll talk about that.

So what types of pathogens is it and activate both the red cell and the platelet forms those two agents? 59 and S 303 and activate the envelope viruses that we do. Blood tests for lots of other envelope viruses. Chikungunya dengue, influenza A gram. All the gram negatives.
Most of the gram.

Almost all the grammar negatives

and positives, spirochetes, protozoa, and leukocytes.

And this is where pathogen reduction eliminates the need for gamma radiation.

Cousin and activates leukocytes by binding to the DNA of the T cells and therefore. Does the same thing as radiation would. In fact it doesn’t, as you’ll see much more efficiently. There are some non envelope virus that also has affected as it doesn’t affect parvovirus very well. Does it affect spores,
hepatitis A or hepatitis E which
are not lipid envelope but
don’t cause a chronic problems
generally in patients.
So it is quite robust and all the
other technologies to remove bacteria
don’t have any effect on removing.
Viruses, which is why I felt that
pathogen reduction was the way to go,
rather than using other bacterial
technologies to prevent bacterial
contamination that did nothing for
viruses and certainly didn’t do
anything for leukocytes either.
There other technologies we don’t
00:16:59.985 --> 00:17:02.290 have time to talk about riboflavin,
NOTE Confidence: 0.82047164440155
00:17:02.290 --> 00:17:04.558 which is also a photosensitizing agent
NOTE Confidence: 0.82047164440155
00:17:04.558 --> 00:17:06.560 intercalates into nucleic acids as well,
NOTE Confidence: 0.82047164440155
00:17:06.560 --> 00:17:09.089 and UV B light is used rather than UV
NOTE Confidence: 0.82047164440155
00:17:09.089 --> 00:17:11.896 A and that promotes oxygen radicals.
NOTE Confidence: 0.82047164440155
00:17:11.900 --> 00:17:13.324 UVC is another technology
NOTE Confidence: 0.82047164440155
00:17:13.324 --> 00:17:14.748 that’s used in Europe.
NOTE Confidence: 0.82047164440155
00:17:14.750 --> 00:17:16.022 Make a pharma.
NOTE Confidence: 0.82047164440155
00:17:16.022 --> 00:17:17.718 There is no photoactive
NOTE Confidence: 0.82047164440155
00:17:17.718 --> 00:17:18.566 photosensitizing agent.
NOTE Confidence: 0.82047164440155
00:17:18.570 --> 00:17:21.699 The UVC itself acts to induce peering,
NOTE Confidence: 0.82047164440155
00:17:21.700 --> 00:17:22.594 permitting dimers,
NOTE Confidence: 0.82047164440155
00:17:22.594 --> 00:17:26.170 and that was discussed by Jake Owen Delaney,
NOTE Confidence: 0.82047164440155
00:17:26.170 --> 00:17:27.064 transfusion recently.
NOTE Confidence: 0.82047164440155
00:17:27.064 --> 00:17:30.640 This is a manuscript that we wrote for
NOTE Confidence: 0.82047164440155
00:17:30.715 --> 00:17:33.767 New England Journal of several years ago,
but still accurate.

I hope the sorlin works by forming DNA and RNA, adults, and cross linking the riboflavin.

I mentioned cause direct DNA and RNA damage, guanine modification.

And the UV C causes finding dimer formation.

That’s for the platelets.

Similarly, and there are other types of pathogen reducing agents.

We don’t have time to discuss, but it’s in this manuscript.

If you give us Orland people, this was studied by serious .
micrograms per kg you wind up with 1100 picograms and after about 6 hours or so it’s down to about 100 to 200 picograms per ml so it gets quite gets reduced to quite rapidly and studies on HPLC show as far as toxicology. This is before you VA. This is the HPLC. You see, after you via the photo products have formed over here. This is a standard and these sort of products are removed by a filtration technique that is used called compound or compound and sort
00:18:42.191 --> 00:18:44.441 of device which is really call us
NOTE Confidence: 0.82047164440155
00:18:44.441 --> 00:18:46.487 tyramine that absorbs the photo products.
NOTE Confidence: 0.82047164440155
00:18:46.490 --> 00:18:49.154 So the amount of of the S 59 that’s
NOTE Confidence: 0.82047164440155
00:18:49.154 --> 00:18:51.596 goes into a recipient is minimal.
NOTE Confidence: 0.82047164440155
00:18:51.600 --> 00:18:53.574 It’s in the in the picogram
NOTE Confidence: 0.82047164440155
00:18:53.574 --> 00:18:55.699 quantities the same thing with plasma.
NOTE Confidence: 0.82047164440155
00:18:55.700 --> 00:18:57.788 Here’s plasma after you VA with
NOTE Confidence: 0.82047164440155
00:18:57.788 --> 00:18:59.909 multiple photo products and hear the
NOTE Confidence: 0.82047164440155
00:18:59.909 --> 00:19:02.247 photo products are pretty much gone after.
NOTE Confidence: 0.82047164440155
00:19:02.250 --> 00:19:05.590 Compound resource if device absorption.
NOTE Confidence: 0.82047164440155
00:19:05.590 --> 00:19:08.033 We’ve been using this product the platelet
NOTE Confidence: 0.82047164440155
00:19:08.033 --> 00:19:10.567 one at Yale since 2017 we started.
NOTE Confidence: 0.82047164440155
00:19:10.570 --> 00:19:13.090 We were among the first and we’ve been
NOTE Confidence: 0.82047164440155
00:19:13.090 --> 00:19:15.559 the leaders nationally for this product.
NOTE Confidence: 0.82047164440155
00:19:15.560 --> 00:19:16.820 This is the average.
NOTE Confidence: 0.82047164440155
These are in the units of platelets. This is per year the average per year. Green is all the platelets. Red is pathogen reduced and blue is the play list that are not pathogen reduced. And as you can see there’s been a steady decline. This is average for fiscal year 1718 and 19. Reminders going up and it has now them. Starting here, it’s monthly, so this goes all the way out to fiscal year 2020. Now we’re in fiscal year 2021. We are probably going to have about 100 non pathogen reduced a month and about 8 to 900 pathogen
00:19:53.437 --> 00:19:55.178 reduced non pathogen reduced about
00:19:55.178 --> 00:19:58.251 100 to 150 or so 900 or so pathogen
00:19:58.251 --> 00:20:00.820 reduced and that’s the kind of the
00:20:00.897 --> 00:20:03.513 way it’s been for a long long time.
00:20:03.520 --> 00:20:05.697 So we have a lot of data
00:20:05.697 --> 00:20:07.830 and a lot of patience.
00:20:07.830 --> 00:20:09.720 This is what the am Apostle.
00:20:09.720 --> 00:20:12.240 It looks like this is the regular shorland.
00:20:12.240 --> 00:20:14.196 This is the eight mop that’s
00:20:14.196 --> 00:20:16.690 used for T cell lymphoma’s and.
00:20:16.690 --> 00:20:20.560 sort of content of food,
00:20:20.560 --> 00:20:22.710 not exactly the same sorlin,
00:20:22.710 --> 00:20:24.860 but in celery and celeriac
00:20:24.860 --> 00:20:26.580 which is celery root,
milligram quantities and we’re talking picogram so you have milligram and then you go to nanograms in micrograms that picogram. So it’s quite a low amount that’s infused as far as the toxicology is concerned on the FDA, therefore had no problem in allowing the psoralen treated platelets to be used for every patient. In the hospital, including neonates and preemies, including those receiving for the therapy which for reasons we don’t have time to discuss, pregnancy, nursing mothers.
It’s been used in jail since 2017.

We have a 3 1/2 year experience.

We’ve transfused 10s of thousands

of hundreds of thousands of

patients of of units and we haven’t

had knock on pressboard,

but any problems it’s used for everyone.

Jehovah’s Witnesses,

obviously because of their religious beliefs,

it’s not acceptable to them generally.

Before we brought it in,

got their approval.

Also the business office,
’cause it is more expensive.

We went all the clinical group Center, and.

Train them on the new product ’cause the bags look different.

The plasma will look different color.

We got all the service lines involved so it was a very large effort which we described in a manuscript that we wrote. This is what we’re trying to prevent. This is what we call classical.

EDS stands for egg drop soup if you will because that’s what it looks like. It’s a bacteria growing in this case staff orias in a unit.
00:21:57.066 --> 00:21:58.686 of platelets in the pH drops,

00:21:58.690 --> 00:22:00.713 the acid causes the platelets to clump

00:22:00.713 --> 00:22:02.812 and you get this, which is obvious.

00:22:02.812 --> 00:22:03.988 What we’re worried about,

00:22:03.990 --> 00:22:05.445 or those that are contaminated

00:22:05.445 --> 00:22:06.318 and look normal.

00:22:06.320 --> 00:22:07.112 That’s the problem,

00:22:07.112 --> 00:22:08.696 and that’s why we’ve had six

00:22:08.696 --> 00:22:09.810 near misses recently,

00:22:09.810 --> 00:22:12.008 and we’ve had two deaths at this

00:22:12.008 --> 00:22:12.950 institution from contaminated

00:22:14.622 platelets or what actually one plate

00:22:16.508 and one red cell over the years,

00:22:18.838 and we’ve had a lot of near misses.

00:22:19.130 Fortunately,
our blood bank staff could pick something up if it looks strange. If there’s a lack of platelets worldwide, which is something we could talk about it another time. Probably never will talk about it, but I just say that, but this is what we’re trying to prevent data from Europe because you say, well, three years of data. They’ve used a total of 3.3 million trailer units of platelets.
Transfused in these three countries between 2006 and 2017. There was 76 contaminated products in 12 deaths. There were 700 and 5000 intercept platelets transfused during that time. Admittedly, it’s a fourth of it, but there were no deaths and no infections at all. And now that we have more data that Europe doesn’t give the data out as as frequently as we would like to see it, but there’s been no reports that I know of any problems with the exception of one or two cases of Acinetobacter,
which is a separate issue

which we don’t have time to talk about.

Today we published our results in the

British Journal of Hematology are Yale

results with the weight Schultz and and.

And these were we had five

There were septic reactions with

conventional products about 9000 and

they were about 12,000 pathogen.

Reduced products had none.

This was statistically significant.

There were no other differences in

any of the other types of reactions,

basically.
Then we did data who did studies which we don’t have much time to talk about. Looking at the the number of subsequent platelet transfusions of platelets were damaged by the material and didn’t work. Did they need to give another play live very quickly and with PR there was a slight amount of damage. We will list it 1/2 of 1/4 of a unit. More was needed. Cafe unit here. 24 hours later maybe .6 of unit here was 1.2 of a unit versus 1 blue is the conventional non pathogen reduced? This is the pathogen reduced,
and none of these were irradiated, obviously. Well, obvious to me anyway, and as you got out 96 hours there was, you know, a little more so the PR does a little damage, but the tradeoff is you’ve got a product that is not pathogen potentially pathogen contaminated. And this was the time between the next platelet transfusion. Again, if it didn’t work, they would give play that sooner and there was no significant difference between the two. And as far as rental utilization
actually 2448 up to 96 hours later, subsequent red cell transfusions. The platelets didn’t work. They would probably transfuse more red cells that the patient would still be bleeding and there was a little more less again point units .2 more of a unit in the conventional group than all the way out that it wasn’t the pathogen reduction group showing that the platelets worked. There may have been a little more platelets used port part of a unit, but nothing substantial and was in my approach.
Expression of that of most, the reviewer says that it was worth the tradeoff.

We also looked at our data for Pediatric patients as well, 'cause it’s very little and we showed almost exactly the same results as far as the efficacy and the utilization. And there was really no difference between the conventional for neonates, infants, or pediatric up to 18 years for both conventional versus pathogen reduced in pediatric groups as well. So what we have is. A product that appears to be
It is beneficial that it prevents the loss of pathogens, but it also allows platelets to function properly and be even statically effective. We finished a phase four trial called Piper with 3000 patients, comparing patients getting conventional versus intercept treated in the mock group and we trance. We contributed about 50. About 530 patients of the 3000. They would let us do more because they didn’t want to overweight. This is being analyzed and will hopefully be in a New England Journal.
article near you at sometime in the future or another Journal, perhaps, but is the largest study looking at a group of patients getting conventional versus pathogen reduced platelets? The second part, just to close up, is with the red cell pathogens. Again, you want to have a pathogen material. Reduced by for red cells as well. This study is in phase three clinical trials, which we’re doing now at Yale. We have two groups of patients were studying again, the benefit if you don’t have a red cell product that you’re not going to be able
to get rid of the gamma irradiators, but you need to provide the radiation. Also eliminate not only the viruses and bacteria, but also beesia and also will eliminate the need to irradiate the white cells for the same reason. This technology the S 303 intercalates into the DNA. Or RNA the cross links by chemical reaction. It doesn’t require light incurs faster than the linker degrades, allowing a blockage of replication so it does inactivate the pathogens. And then at the grades to Anon.
A non toxic product it is

A quitter in which is, those of you know there are some concerns but it inactivates quite rapidly and is washed and it’s essentially removed and the data which I don’t have time to share unfortunately shows that there is not a risk of toxicology associated with this and this is not used routinely in Europe. And is now being in phase three clinical trials here at Yale. It’s again for up to 42 days of storage. We were studying two groups of patients, the which I’ll talk about in a second of the log reduction.
Dissimilar to what the psoralen is.

5 log reductions, and 99.9 is 3 log reduction, so these are 56 logs with various viruses and bacteria.
The studies were doing the acute study in the cardiac surgery and we’re doing one in chronically anemic patients getting simple transfusions called Redis, which is what we’re going to be doing on the 7th floor and in the outpatient clinics where patients who need a blood transfusion will get randomized after they signed written informed consent.
consent obviously went through the IRB to whether they get pathogen reduced or conventional red cells, and they’re not transfused for this study if their doctor says they need a transfusion and they’ve agreed. We will give them one or the other, but we’re not going to radiate the pathogen reduced product because that would cause a double damage to the platelet or the red cell rather. So the purpose of this talk was also to reassure everyone that the data show clearly that pathogen reduction prevents graft versus host. So for those of your chemotherapy patients,
that may need it. Pathogen reduction would be acceptable.

And here's the major data showing the number of adduct formation with gamma radiation, one in every 37 thousand base pairs forms an adult which is enough to block references host 'cause that's the standard with S 59 plus UV A it's one in every 80 three base pairs shown in this cartoon. The data is in blood 1998 and for S 303 the data is have been published yet, but you get an even more robust and up formation with whole blood. Or with red cells,
it’s an average of water every 38 to one in every 53 orders of magnitude more than the adult formation with gamma radiation. So there’s no reason to believe that using pathogen reduced product in lieu of gamma radiated product will be as safe or not showing. It’s obviously better, but as safe and then other studies coming out of Europe showed no reported

PA GVHD with irradiated products. Conventional amat asselyn 186 thousand. Again, no reported cases. Again, orders of magnitude less, but in that Switzerland similarly
no reports with the. With the. With the use of the Sourland TAA GV HD in summary is rare, but fatal treatment is unsuccessful. Prevention is best in attention. The only approach death due to marrow, a pleasure, gamma radiation or pathogen reduction are both acceptable to the FDA to the IRB. In Europe, the data are there PR playlist, usamma, TASSELL and UV. A red cells use a muscle in nucleic acid. After formation is more robust and there’s no need to do both and this.
will produce unwanted cellular damage.

And there are a couple of references here.

An I will end there and thank you for your attention.

Go ahead, thank you.

It's a terrific work and really in advance and transfusion medicine that obviously addresses multiple complications just because we're running a little late I think will probably not will, will ask people to send you questions directly and turn to our next speaker so our next lecture is Doctor Suchitra Krishnan Sarin and Suchitra is, you know, is a professor of
psychiatry and the chair of the Human Investigations Committee. Yeah, and her work over the years has really been. As a leader in understanding tobacco treatment control and the interventions and risk factors associated with it, her work was instrumental in the Surgeon General’s report of preventing tobacco use among young people. She served on the FDA’s tobacco product Scientific Advisory Committee and currently serves on the CDC’s Interagency Commission on Smoking and Health and her work on E...
cigarettes really has been critical, particularly as these. Have become far more trendy, sadly, particularly among young people, so Skeeter thank you for sharing your work with us.

You run, I think your video and sound and audio is off.

Let me fix this. Sorry about that, OK.

Can you see the screen?

OK yes, OK great wonderful again.

Thank you for inviting me to speak to this group today, so I’m going to give you a tell you about something which is
00:33:00.155 --> 00:33:01.991 completely different than what
00:33:01.991 --> 00:33:04.249 you’ve heard about from Ed and.
00:33:04.250 --> 00:33:06.122 This relates to this public health
00:33:06.122 --> 00:33:07.749 problem of E cigarettes and I.
00:33:07.750 --> 00:33:09.990 I’m going to kind of give you an
00:33:09.990 --> 00:33:11.665 overview because I figured that many
00:33:11.665 --> 00:33:13.944 of you may not have really heard about
00:33:13.944 --> 00:33:15.864 of you may not have really heard about
00:33:15.864 --> 00:33:18.268 this debate or about these products
00:33:18.270 --> 00:33:21.204 So I’m just going to give you a little
00:33:21.204 --> 00:33:23.706 basic overview and give you an update
00:33:23.706 --> 00:33:26.959 of where we are as a field in this area.
00:33:26.960 --> 00:33:33.626 Oh OK, there we go.
00:33:33.626 --> 00:33:36.231 So I have no conflicts of disclosures
00:33:36.231 --> 00:33:38.816 to report as was mentioned,
I have served as a member of FDA’s tobacco products Scientific Advisory Committee, which is a committee which reviews tobacco products and approves them for marketing in the US market. And I’m also a current member of CDC’s Icy SH and I also called the Tobacco Center of Regulatory Science at Yale. So just a brief presentation of what the problem is. So this is something I’m going to be coming back to later in my talk to. With E cigarettes there are two parts to the public health problem in question that is being debated a lot today one
00:34:21.225 --> 00:34:23.350 is potentially they pose benefits.

00:34:23.350 --> 00:34:25.642 They could help reduce disease risk

00:34:25.642 --> 00:34:28.070 for current smokers if they switched

00:34:28.070 --> 00:34:30.560 to using these products they could

00:34:30.560 --> 00:34:32.428 reduce disease morbidity for smokers

00:34:32.428 --> 00:34:35.450 and I'm sure this is a huge concern for

00:34:35.450 --> 00:34:37.730 this community because of the known

00:34:37.730 --> 00:34:39.219 relationship between tobacco use,

00:34:39.220 --> 00:34:40.860 smoking and cancer risks.

00:34:40.860 --> 00:34:43.830 So this is very very beneficial if it.

00:34:43.830 --> 00:34:45.846 If it works out that way,

00:34:45.850 --> 00:34:48.546 on the other hand, you have the harms,

00:34:48.550 --> 00:34:51.574 which is in the right hand side panel an.

00:34:51.580 --> 00:34:54.276 Unfortunately, as we have seen in the US,

00:34:54.280 --> 00:34:56.296 increased rates of use of these
00:34:56.296 --> 00:34:57.304 products amongst youth.
NOTE Confidence: 0.897755324840546
00:34:57.310 --> 00:34:58.990 So there's an increased risk
NOTE Confidence: 0.897755324840546
00:34:58.990 --> 00:35:00.334 of exposure to nicotine,
NOTE Confidence: 0.897755324840546
00:35:00.340 --> 00:35:02.030 nicotine addiction, future disease risks,
NOTE Confidence: 0.897755324840546
00:35:02.030 --> 00:35:03.710 Anna hold real knee renormalization
NOTE Confidence: 0.897755324840546
00:35:03.710 --> 00:35:05.054 of tobacco use behaviors,
NOTE Confidence: 0.897755324840546
00:35:05.060 --> 00:35:06.745 and even amongst adults who
NOTE Confidence: 0.897755324840546
00:35:06.745 --> 00:35:10.242 there is a great deal of
NOTE Confidence: 0.897755324840546
00:35:08.430 --> 00:35:10.242 concern of dual use behavior.
NOTE Confidence: 0.897755324840546
00:35:12.140 --> 00:35:15.220 So what a lot of adults are doing.
NOTE Confidence: 0.897755324840546
00:35:15.220 --> 00:35:16.564 Is not necessarily switching
NOTE Confidence: 0.897755324840546
00:35:16.564 --> 00:35:18.580 completely to use of these products,
NOTE Confidence: 0.897755324840546
00:35:18.580 --> 00:35:20.890 but are choosing to use both cigarettes
NOTE Confidence: 0.897755324840546
00:35:20.890 --> 00:35:22.678 and E cigarettes depending on
NOTE Confidence: 0.897755324840546
00:35:22.678 --> 00:35:25.240 convenience and where they can use these
00:35:25.240 --> 00:35:27.316 products and that is not good either.

00:35:27.320 --> 00:35:28.328 And of course,

00:35:28.328 --> 00:35:29.672 then there’s a secondhand

00:35:29.672 --> 00:35:30.680 aerosol exposure issue,

00:35:30.680 --> 00:35:33.025 which again we know very little about,

00:35:33.030 --> 00:35:36.654 so these products are Sony on the market.

00:35:36.660 --> 00:35:39.236 So just to take a step back,

00:35:39.240 --> 00:35:40.218 as I said,

00:35:40.218 --> 00:35:42.174 this is the top public health

00:35:42.174 --> 00:35:44.207 concern which is cigarette smoking

00:35:44.207 --> 00:35:46.247 or tobacco smoking a cigar.

00:35:46.250 --> 00:35:48.494 Use all these combustible products that

00:35:48.494 --> 00:35:50.767 create havoc on multiple organ systems

00:35:50.767 --> 00:35:53.266 and also have contribute to cancer risks.

00:35:53.270 --> 00:35:56.033 So over the years in the US we’ve done

NOTE Confidence: 0.897755324840546
We put into place multiple public health policies to try and address cigarette use behaviors. As many of you know, and most recently the one that has been quite influential. Is this FDA allowing the FDA to regulate these tobacco products? If for those who know this area, you know the FDA had been trying for a long time to get this role. For a long time to have the ability to regulate these products and that only went into place when this family smoking prevention and Tobacco Control Act was signed in 2009 by President Obama.
So since then, the FDA has been trying to put into place Regulations on the manufacture, distribution, and marketing of these products to protect public health. And that's where the cigarettes kind of come into the picture they were actually invented by a Chinese pharmacist who wanted to develop a cleaner form of nicotine to help smokers quit smoking. It was created in 2003, started appearing in the US in about 2009, and today. There are over 400 E.
Cigarette brands are basically cigarette

I should say I don’t know if you

There is a. There’s a power component

Obviously. I’ll show you some pictures.

There is a control element where

the user can push a button to

activate it and heat the juice,

which is located in this compartment

and at the other end there

is a there is a mouthpiece

that the user can then use to.

Get taken the papers that are created.
Um be started.
Address entering the US market in about 2009 and when they first entered the FDA, really tried to prevent them from entering the market by directing the Bottom Border Protection agencies to reject the entry of these products because they were unapproved drug delivery devices. They wanted to classify them as a drug delivery device, but there was a lawsuit that was brought against the FDA by a cigarette company at that time and they said that the FDA had
no authority over E cigarettes
because they were a tobacco product.
And that they were not a drug delivery
device or a drug device combination
because they were not being sold for
any therapeutic purpose in the US.
One would think that that would
have been turned down,
but they actually were successful
in the US District Court and US
District Court basically prohibited
the FDA from seizing the services,
the FDA could only regulate these signatures
of tobacco product.
Unless therapeutic claims are made, any product you see on the market can only be regulated as tobacco products. They’re not regulated yet, but they can only be regulated, and they cannot make any therapeutic claims. So the FDA is actually coming up with the whole series of a whole another way that these products can be regulated and they give them marketing claims and they can make certain claims about what the product can be used for. But it cannot be a direct therapeutic claim because they are not.
None of these companies are actually proceeding along the therapeutic side of FDA to get them approved as a cessation device. They're just getting them regulated or approved as a tobacco product. So essentially what I said here is that you know they can only be regulated as a tobacco product. The FSB TC, it did not cover them till almost 2016 because the original law that President Obama signed did not cover E cigarettes, so they actually incorporated it into the law only in 2016.
So therefore from 2010 to 2016 these products have been unregulated and they will probably remain unregulated through 2022 because as I said, the FDA has a different way of regulating them in.

All these companies are now submitting their safety data to the FDA through this premarket tobacco product application, which were all due September 9th, 2020. So the FDA is just reviewing products from thousands and thousands of companies or products.
To really see if they should be allowed to have any marketing claims. In the meantime, there has just been an evolution of or an explosion I should say in the market in terms of the products available, you get product switch look like cigarettes on the left hand side, going all the way to these pens, which you can replace eliquids in. You have these box mods which look nothing like a cigarette, but which allow you to change, you know, produce huge vapor clouds and all these other kinds of behaviors. And then you have the most recent
entrance which is the jewel which is that little black device you see.

I'm a third from the right hand side and some other devices which are called pod devices, which essentially the way all these differs in terms of whether it is a closed system in the sense that the nicotine is contained in it and you vape it. Whether you can fill in new illiquid's like the weapons allow you to do, or these pod devices which are completely closed systems that come with these parts that are pre
00:41:21.723 --> 00:41:23.679 filled and you just slide them in.
NOTE Confidence: 0.879437804222107
00:41:23.680 --> 00:41:25.829 Now this is also left you a
NOTE Confidence: 0.879437804222107
00:41:25.829 --> 00:41:26.750 huge black market,
NOTE Confidence: 0.879437804222107
00:41:26.750 --> 00:41:29.880 so even with the pod devices now you can buy.
NOTE Confidence: 0.879437804222107
00:41:29.880 --> 00:41:31.998 Unfilled parts that you can then
NOTE Confidence: 0.879437804222107
00:41:31.998 --> 00:41:33.800 fill with whatever you want,
NOTE Confidence: 0.879437804222107
00:41:33.800 --> 00:41:36.192 and this has led to a huge increase
NOTE Confidence: 0.879437804222107
00:41:36.192 --> 00:41:38.979 in rates of marijuana use and use a
NOTE Confidence: 0.879437804222107
00:41:38.979 --> 00:41:40.867 variety of other products because
NOTE Confidence: 0.879437804222107
00:41:40.867 --> 00:41:43.674 people are filling pods with all kinds
NOTE Confidence: 0.879437804222107
00:41:43.674 --> 00:41:46.260 of different things and making them so.
NOTE Confidence: 0.879437804222107
00:41:46.260 --> 00:41:48.246 This is basically just to give
NOTE Confidence: 0.879437804222107
00:41:48.246 --> 00:41:50.529 you an idea of what exists,
NOTE Confidence: 0.879437804222107
00:41:50.530 --> 00:41:53.275 and this shows you the sales that has in
NOTE Confidence: 0.879437804222107
00:41:53.275 --> 00:41:55.870 Nielsen tracked retail channels by Brandon.
NOTE Confidence: 0.879437804222107
00:41:55.870 --> 00:41:58.187 You can see the amount of sales
that go towards E cigarettes. And obviously a very, very profitable market,
which is why a lot of people are investing in these products.
So I bring you back now to what I started the talk with, which is let’s not talk about the benefits of the harms.
First, I’m just going to show you snippets of data. There’s a huge literature out there, but in the interest of time,
let’s ask the first question.

When you look at E cigarettes, when you compare them to E cigarettes or combustible products, do they actually have reduced form? So if you do an apples to apples comparison and you look at things like some of the nitrosamine’s the NNN. And in case and some of these compounds, tobacco specific nitrosamine’s that have been shown to be toxic. enough significant cancer risk. When you look at the current content of these nitrosamine’s in combustible products versus E cigarettes, you definitely see that E cigarette
exposure results in less exposure to tobacco specific nitrosamine's does not completely eliminate them, but there's definitely lexical less exposure. But our concerns about this or not, just the nitrosamine’s. There are a variety of other products that. Our existing E cigarettes, which by which combined with the way these products are being used, which is almost in many people almost constantly used throughout the day, raises a lot of concerns about what some of these contents could do. So an example of some of these are
probably in glycol and vegetable glycerin which are used included as solvents or constituents.

There are a lot of flavor chemicals which are all aldehydes, and I’ll talk about them in a second. There are sweeteners that are present in these products and other solvents including alcohol and of course nicotine. A variety of metals and metals actually come from the coil when the coil is heated, it releases metals and so this is all part of what the individual is going to be inhaling when they inhale this particular product and the figure shows you some of the other ultrafine particles,
and so on, which could be.
Reduced Um, so I'll just briefly touch on
Flavors because that is a huge.
Focus of our tobacco center.
Here at Yale, we're really interested in understanding the role of flavors and appeal,
addiction and toxicity of these products,
and I'm going to address toxicity here so the flavors as you know it are made up of flavor chemicals,
so they're not just benign.
You know flavor molecules.
Some of these chemicals are
identified and are listed out here.

You’ll see many of them are aldehydes and depending on the concentration, can have significant health effects.

Not help to fix, I’m sorry. Let me back up significant toxicity.

There was an argument made initially that these are flavor chemicals and they are gras or generally recognized as safe, but they are not generally recognized as safe for inhalational use.

They are grass for edible use, not for any Hill inhalation.

Using isn’t very important distinction and what we’re finding through a lot of
NOTE Confidence: 0.83473414182663
00:45:13.044 --> 00:45:15.123 the cellular toxicity work going on is
NOTE Confidence: 0.83473414182663
00:45:15.186 --> 00:45:18.026 that many of these flavor molecules are have.
NOTE Confidence: 0.83473414182663
00:45:18.030 --> 00:45:19.434 Are toxic to cells,
NOTE Confidence: 0.83473414182663
00:45:19.434 --> 00:45:21.540 some of them also have been
NOTE Confidence: 0.83473414182663
00:45:21.621 --> 00:45:23.786 known to have diseased risks.
NOTE Confidence: 0.83473414182663
00:45:23.790 --> 00:45:26.478 So an example of this is diacetyl,
NOTE Confidence: 0.83473414182663
00:45:26.480 --> 00:45:29.182 which is a chemical which is included
NOTE Confidence: 0.83473414182663
00:45:29.182 --> 00:45:31.902 to produce butter flavor and it has
NOTE Confidence: 0.83473414182663
00:45:31.902 --> 00:45:34.134 been known to be associated popcorn
NOTE Confidence: 0.83473414182663
00:45:34.207 --> 00:45:36.860 lung disease which is actually found in
NOTE Confidence: 0.83473414182663
00:45:36.860 --> 00:45:39.576 people who are working in popcorn factories,
NOTE Confidence: 0.83473414182663
00:45:39.576 --> 00:45:43.098 so this chemical is still used in many of
NOTE Confidence: 0.83473414182663
00:45:43.098 --> 00:45:45.282 these eliquids as a flavoring chemical,
NOTE Confidence: 0.83473414182663
00:45:45.290 --> 00:45:47.220 so there are concerns about
NOTE Confidence: 0.83473414182663
00:45:47.220 --> 00:45:48.764 toxicity of these flavors.
NOTE Confidence: 0.83473414182663

82
And our tobacco center is also shown that his flavor aldehydes actually form what are called acetal addicts with the propylene glycol and glycerine in this illiquid and that these acetal out addicts that are formed when the salute are there just formed. When the illiquid just sitting on the shelf and these addicts we’re showing are actually stronger airway irritants in the original aldehydes itself, so like vanillin. Adult will actually be is a stronger airway, urgent than vanillin itself, so this is an area which we need to need a lot more research on.
The similar kind of work on all the other products that I listed earlier from E cigarettes from many other people in the country. And there was a National Academy of Science report which came out in 2018 and the public health consequences of E cigarettes which basically I’m presenting you with an overview of findings, but you should feel free to check it out an.

They concluded that E cigarettes were not risk free, while the current evidence suggests that they are far less harmful than combustible tobacco cigarettes and a.
smoker is exposed to lower levels of toxic substances other than nicotine. There may be some short term resulting in reduced short-term adverse health outcomes that there was very little data to assess the impact on cancer and health, heart disease risk. And there’s a lot more evidence coming out on heart disease risk at this point, but. I also thought you would be interested in seeing the specific cancer related section that they had in this public in this report. Essentially, what this says is there is no available
evidence that E-cigarette users associated with intermediate cancer endpoints, but that there is substantial evidence that some chemicals present in E-cigarette aerosol like formaldehyde and actually not capable of causing DNA damage in mutagenesis. But this has not panned out into a clinical outcome per say and. You know there’s more to come and much more work that needs to be done on this issue. So let’s move on to vivia concerned about this in the US and we're really concerned about it. We really started becoming very
00:48:09.710 --> 00:48:11.550 concerned about it because of the extensive use among youth.
NOTE Confidence: 0.818998157978058
00:48:13.430 --> 00:48:16.462 This show.
NOTE Confidence: 0.818998157978058
00:48:16.462 --> 00:48:18.785 This shows you the current tobacco product use amongst high school students in the US from the National Youth Tobacco data and you see here this, the presence of jewel in the market and they were certain regulations put on jewel in 2019. You do see a decrease in 2020,
but I will tell you that we don’t really know if this decreases because of the regulations that were put into place or whether it was covid related from 2 perspectives. First, this envy TS data collection of this data, which goes on pretty much through six months of the year. Had to be stopped because of Corbin’s only, but they only got a partial sample. And Secondly, we are also seeing in Connecticut that rates have gone down because
00:49:12.630 --> 00:49:14.938 of lack of access and lack of
NOTE Confidence: 0.818998157978058
00:49:14.938 --> 00:49:16.933 the same kind of cues that they
NOTE Confidence: 0.818998157978058
00:49:17.008 --> 00:49:18.868 experience in schools from seeing
NOTE Confidence: 0.818998157978058
00:49:18.868 --> 00:49:20.728 their peers use and so
NOTE Confidence: 0.857419550418854
00:49:20.730 --> 00:49:22.998 on and so forth so we don’t
NOTE Confidence: 0.857419550418854
00:49:22.998 --> 00:49:25.140 know what this is related to,
NOTE Confidence: 0.857419550418854
00:49:25.140 --> 00:49:27.506 whether it’s regulatory or related to kovid,
NOTE Confidence: 0.857419550418854
00:49:27.510 --> 00:49:30.561 but the rates have gone down at least in
NOTE Confidence: 0.857419550418854
00:49:30.561 --> 00:49:33.609 the early 2020 to what it was in 2018.
NOTE Confidence: 0.857419550418854
00:49:33.610 --> 00:49:34.970 That’s still not low,
NOTE Confidence: 0.857419550418854
00:49:34.970 --> 00:49:36.822 but it’s still, you know,
NOTE Confidence: 0.857419550418854
00:49:36.822 --> 00:49:39.318 did head in the right direction.
NOTE Confidence: 0.857419550418854
00:49:39.320 --> 00:49:41.994 Youth are using multiple kinds of devices,
NOTE Confidence: 0.857419550418854
00:49:42.000 --> 00:49:45.069 so this is the other concern BC youth using
NOTE Confidence: 0.857419550418854
00:49:45.069 --> 00:49:48.129 every device that’s available on the market.
NOTE Confidence: 0.857419550418854
00:49:48.130 --> 00:49:50.642 There is a lot of concern about nicotine
use in these devices because devices like the jewel contain very high levels of nicotine and the adolescent brain is more sensitive to nicotine than the adult Bremen.

I'm sure you are all well aware of the of the acetyl choline or the cholinergic system and know that nicotine binds to cholinergic receptors and can therefore influence a variety...
00:50:23.191 --> 00:50:26.197 of other organ systems shown here.

NOTE Confidence: 0.857419550418854

00:50:26.200 --> 00:50:27.928 You thought so use multiple flavors

NOTE Confidence: 0.857419550418854

00:50:27.928 --> 00:50:30.111 and I’ve already talked to you a little

NOTE Confidence: 0.857419550418854

00:50:30.111 --> 00:50:31.575 bit about the toxicity of flavors.

NOTE Confidence: 0.857419550418854

00:50:31.580 --> 00:50:33.188 Flavors are what draw youth to

NOTE Confidence: 0.857419550418854

00:50:33.188 --> 00:50:33.992 user these products,

NOTE Confidence: 0.857419550418854

00:50:34.000 --> 00:50:35.992 so this is a great deal

NOTE Confidence: 0.857419550418854

00:50:35.992 --> 00:50:37.320 of concern about this.

NOTE Confidence: 0.857419550418854

00:50:37.320 --> 00:50:39.005 You choose the cigarettes for

NOTE Confidence: 0.857419550418854

00:50:39.005 --> 00:50:40.016 many alternative purposes.

NOTE Confidence: 0.857419550418854

00:50:40.020 --> 00:50:42.708 You know they use them for vape tricks,

NOTE Confidence: 0.857419550418854

00:50:42.710 --> 00:50:45.160 which is a huge cloud competitions and

NOTE Confidence: 0.857419550418854

00:50:45.160 --> 00:50:47.430 vape clouds that you may have seen.

NOTE Confidence: 0.857419550418854

00:50:47.430 --> 00:50:49.120 They participate in cloud competitions.

NOTE Confidence: 0.857419550418854

00:50:49.120 --> 00:50:51.269 These are some of the clouds that

NOTE Confidence: 0.857419550418854

00:50:51.269 --> 00:50:53.382 you shapes that you can create

91
using these products. They use it for something called dripping, which means opening up the device and putting the E liquid directly onto the open battery and inhaling it. They use it for vaping cannabis so this has in fact gone up. Significantly, as I said, a lot of these products can be manipulated. So Uther actually adding in other things into these devices. So if you see somebody vaping, there's no guarantee there, just vaping nicotine. They could be using something
00:51:19.890 --> 00:51:21.106 else in the product,
NOTE Confidence: 0.857419550418854
00:51:21.110 --> 00:51:23.402 and most likely that it’s probably
NOTE Confidence: 0.857419550418854
00:51:23.402 --> 00:51:24.930 a cannabis related product.
NOTE Confidence: 0.857419550418854
00:51:24.930 --> 00:51:26.932 And as I said the there is
NOTE Confidence: 0.857419550418854
00:51:26.932 --> 00:51:28.180 multiple papers on this,
NOTE Confidence: 0.857419550418854
00:51:28.180 --> 00:51:30.133 but this is one of our papers
NOTE Confidence: 0.857419550418854
00:51:30.133 --> 00:51:32.009 which shows that E cigarette use,
NOTE Confidence: 0.857419550418854
00:51:32.010 --> 00:51:34.060 amongst Euclides to cigarette use.
NOTE Confidence: 0.857419550418854
00:51:34.060 --> 00:51:36.398 So let’s now move on to talking
NOTE Confidence: 0.857419550418854
00:51:36.398 --> 00:51:37.400 about smoking cessation.
NOTE Confidence: 0.857419550418854
00:51:37.400 --> 00:51:40.064 So we’ve talked about all the bad things.
NOTE Confidence: 0.857419550418854
00:51:40.070 --> 00:51:41.069 Now let’s see.
NOTE Confidence: 0.857419550418854
00:51:41.069 --> 00:51:43.750 Well, is it actually doing what it was?
NOTE Confidence: 0.857419550418854
00:51:43.750 --> 00:51:45.748 What it set out to do?
NOTE Confidence: 0.857419550418854
00:51:45.750 --> 00:51:47.748 Which is help smokers quit smoking.
NOTE Confidence: 0.857419550418854
00:51:47.750 --> 00:51:50.088 The evidence on that is still emerging.
Unfortunately, we don’t have clear cut answers yet because doing an RCT on this issue in the US is very, very difficult because of the way the products are regulated. Once the FDA gets more information on the toxicity and safety of some of these products, they would be willing to allow an RCT to proceed more easily for cessation purposes, but at this point that is very hard to do. There have been a few few. Weldon are our CTS and but the overall idea is based off based on some Cochrane
reviews is there are small sample sizes.

Um, and but they do seem to show some efficacy, but there are multiple observation ull studies. So if you go out and talk to smokers that are many smokers, who will tell you that these products have helped them reduce use of cigarettes? If not, completely quit, which of course then leads to the concern I had raised earlier about use of both products at the same time. This is a result of an RCT which came out in New England Journal of Medicine from the UK, which shows you that use of E...
cigarettes versus nicotine replacement.
The outcomes at the end of 52 weeks.
After the initial start of the trial,
the outcome is better for E cigarettes
than it is for nicotine replacement,
and also that those who use E cigarettes
seem to have some benefits in terms of
some of the respiratory outcomes that
are associated with cigarette use.
This is another trial that just
came out from New Zealand,
where they showed again that
use E cigarettes do have some,
allbeit very small benefit over and above.
Using patches alone in terms of produce,
having an efficacy or helping smokers quit smoking so the jury is still out on this issue. Also and as the National Academy of Sciences report basically said there, there where they are very concerned about the use of the pump. When you consider the public health consequences of E cigarettes we have this huge divide of of a product that is really having an impact on youth. There is limited evidence that people stop smoking cigarettes completely. Um there seems to be more evidence of dual use behaviors,
so we really need more work to help people convert to E cigarettes.
And they also said that if people are able to completely switch from cigarettes to E cigarettes, it will reduce exposure to numerous toxins that cops imagines.
Now one might ask, well, is there some way of regulating these products to prevent use? You choose, but suppose smoking cessation and this is a debate that the field has been having for a very long time, and I will basically tell you.
that we haven’t reached any big

conclusions at this point,

I’ve listed some ways we could go.

We could regulate the nicotine levels.

You for example only allows a nicotine

level up to 20 milligrams per mil,

To give you an example,

jewel contains up to 60 milligrams per mil.

The concern here is that smokers

may actually need higher levels of

nicotine to quit smoking and get

satisfaction from their product,

so this issue has really not been

resolved and there doesn’t seem to

be that much movement in terms of
NOTE Confidence: 0.831678867340088
00:55:10.292 --> 00:55:11.918 regulating nicotine levels,
NOTE Confidence: 0.831678867340088
00:55:11.920 --> 00:55:13.284 we could regulate flavors.
NOTE Confidence: 0.831678867340088
NOTE Confidence: 0.831678867340088
00:55:14.650 --> 00:55:16.690 They removed all flavors in Eliquids,
NOTE Confidence: 0.831678867340088
00:55:16.690 --> 00:55:19.741 but then there is a concern that smokers may
NOTE Confidence: 0.831678867340088
00:55:19.741 --> 00:55:22.259 actually need the flavors to quit smoking.
NOTE Confidence: 0.831678867340088
00:55:22.260 --> 00:55:24.264 We know this is something that
NOTE Confidence: 0.831678867340088
00:55:24.264 --> 00:55:25.958 will definitely be beneficial for
NOTE Confidence: 0.831678867340088
00:55:25.958 --> 00:55:27.458 youth because Uther really drawn
NOTE Confidence: 0.831678867340088
00:55:27.458 --> 00:55:29.390 to the flavors in the product.
NOTE Confidence: 0.831678867340088
00:55:29.390 --> 00:55:31.005 We could regulate the kind
NOTE Confidence: 0.831678867340088
NOTE Confidence: 0.831678867340088
00:55:31.980 --> 00:55:33.768 You know, I talked about these
NOTE Confidence: 0.831678867340088
00:55:33.768 --> 00:55:35.540 open and close system products,
NOTE Confidence: 0.831678867340088
00:55:35.540 --> 00:55:36.515 open system products.
You can add things in. It can sleep through a variety of other behaviors, but you know, there's a concern about that also. And you could just allow close system devices but close system devices were the ones which are very popular amongst youth, so we really not reached any Consensus about this issue. So I just wanted to end with this So I would say continue to encourage your patients to quit smoking.
I don’t think there is. I think a combustible cigarette use is about the worst behavior, especially from a cancer risk, so that does need to continue. Use treatments that have been shown to work and that are approved like the existing behavioral interventions and gum and Chantix. And these are proven interventions have been shown to work. If nothing else works on your patients, want to use his cigarettes, then I think you could support them, but you need to warn them about.
00:56:34.694 --> 00:56:36.497 not over using E cigarettes and
NOTE Confidence: 0.831678867340088
00:56:36.497 --> 00:56:38.092 getting in more nicotine than
NOTE Confidence: 0.831678867340088
00:56:38.092 --> 00:56:39.760 what they normally will do.
NOTE Confidence: 0.831678867340088
00:56:39.760 --> 00:56:41.912 They also need to have a plan for
NOTE Confidence: 0.831678867340088
00:56:41.912 --> 00:56:43.060 quitting cigarettes completely.
NOTE Confidence: 0.831678867340088
00:56:43.060 --> 00:56:44.240 No dual use behaviors,
NOTE Confidence: 0.831678867340088
00:56:44.240 --> 00:56:46.010 you know they shouldn’t just use
NOTE Confidence: 0.831678867340088
00:56:46.072 --> 00:56:47.342 the product whenever convenient
NOTE Confidence: 0.831678867340088
00:56:47.342 --> 00:56:49.240 and they should have a plan
NOTE Confidence: 0.831678867340088
00:56:49.300 --> 00:56:50.860 to quit E cigarettes as well.
NOTE Confidence: 0.831678867340088
00:56:50.860 --> 00:56:52.813 We don’t want to have a generation
NOTE Confidence: 0.831678867340088
00:56:52.813 --> 00:56:54.306 just dependent on nicotine either
NOTE Confidence: 0.831678867340088
00:56:54.306 --> 00:56:56.406 because we don’t know what the long
NOTE Confidence: 0.831678867340088
00:56:56.406 --> 00:56:58.107 term consequences of this are.
NOTE Confidence: 0.831678867340088
00:56:58.110 --> 00:57:00.468 You can also educate your parents
NOTE Confidence: 0.831678867340088
00:57:00.468 --> 00:57:02.441 and help educate communities and
local schools to really advise them of what these products could do.

And finally I would say really help us collect scientific evidence on E cigarettes. I know that E cigarettes was on the grand challenge during the retreat and I hope that this push will continue and that you all will be involved in helping us collect more toxicity, safety and efficacy data on these products so we can regulate them appropriately. The point is they are out in the market. Everybody is using them and we are trying to develop all the signs.
It’s almost like backtracking on the development of science and that is where many of these concerns have risen. So I will stop there. Considering the time and happy to answer any questions. Mr Teacher, thank you.

Given the 50% of reduction in cancer mortality from the peak. Do the tobacco control and obviously I guess, given your point, this sort of...
00:58:13.340 --> 00:58:15.850 resurgence of exposure to 3 cigarettes,

00:58:15.850 --> 00:58:18.544 do you perceive that that actually

00:58:18.544 --> 00:58:21.690 could reverse the trend, as it were?

00:58:22.730 --> 00:58:26.706 I’m hoping not. No, but we do.

00:58:26.710 --> 00:58:28.060 I think the question is

00:58:28.060 --> 00:58:29.850 can we get all these youth?

00:58:29.850 --> 00:58:31.275 Who are the new entrants

00:58:31.275 --> 00:58:32.700 into this area to stop?

00:58:32.700 --> 00:58:34.980 And that’s what a lot of prevention work.

00:58:34.980 --> 00:58:36.690 And also our work at Yale.

00:58:36.690 --> 00:58:38.115 We’re doing a lot of

00:58:38.115 --> 00:58:38.970 cessation related program,

00:58:38.970 --> 00:58:40.958 so we’re doing a lot of education,

00:58:40.960 --> 00:58:42.670 prevention and cessation and high schools.

00:58:42.670 --> 00:58:45.340 So if you or any of you are aware of

00:58:45.350 --> 00:58:47.174 the new entrants, please reach out to us.

00:58:47.174 --> 00:58:50.000 And I hope to see you all back here in two years.

00:58:50.000 --> 00:58:51.595 Thank you.
the need, please send me a note and we can certainly go out and talk to the group if we can prevent these entrance,

I think we would be. We would really serve public health very well because we.

One thing we don’t want them to do, we don’t want them to then convert to using the products. These are all these kids are going to be nicotine addicted. If E cigarettes don’t serve them well, they’re going to want to move on to product switch. Serve them better. Which are cigarettes.
Cigarette is one of the best nicotine delivery devices I have ever seen, so that’s the biggest concern which is will there be a re emergence of combustible tobacco and nicotine use and will that then lead to? The problems we’ve seen earlier, so I can’t answer that question. Melinda, it’s a very good one though. Well, thank you. Excellent talk, you know it. It’s 103 so I think will will break. But I wanted to say thank you teacher and Ed for two superb talks.
Thank you all for attending and enjoy the rest of your day.

Thank you bye bye.