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, the rationale for using pathogen reduction, 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, 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 aplasia is that in regular graft versus host disease,
if you will forward regular post bone marrow transplant,
the bone marrow is that of the recipient.
I'm sorry, the head of the donor.
So the donors bone marrow is basically replaced that of
basically replaced 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 host after a bone marrow transplant. The rash begins on the trunk and spreads to the extremities, 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,
even if the recipient is immunocompetent.

And you have an immuno competent donor from a blood transfusion.

What happens is let’s say the donor is homozygous? For HLA two or HLA B 44,

the recipient does not see the donor cells as being foreign because the recipient has a two and in this case be 44.

Whereas the donor cells are immuno competent,

it does see the host as being foreign.

and it reacts against the host giving the graft versus host disease as opposed to like a rejection of a heart or a kidney would be host versus graft.
So it’s either can occur. Also an immunocompromised host due to congenital or acquired. Aziz, or, or medications,

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

There was a fair amount of graft versus host disease.

TAA 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 perivascular infiltrates.

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 lossed, 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. 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 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,
00:08:55.490 --> 00:08:57.674 'cause people were donating for family
00:08:57.674 --> 00:08:59.845 members in the hope of preventing
00:08:59.845 --> 00:09:02.127 them from getting HIV at the time
00:09:02.127 --> 00:09:04.776 from unknown members of the blood supply.
00:09:04.780 --> 00:09:06.630 And that lets other problems
00:09:06.630 --> 00:09:09.060 as well because of the KGB HD.
00:09:09.060 --> 00:09:10.484 If it wasn’t irradiated,
00:09:10.484 --> 00:09:13.350 and if the blood component is HLA match,
00:09:13.350 --> 00:09:15.849 that should be also treated as well.
00:09:15.850 --> 00:09:17.986 Look, our reduction is not protective.
00:09:17.990 --> 00:09:19.254 You’re not removing enough.
00:09:19.254 --> 00:09:22.022 White cells are still four to five logs
00:09:22.022 --> 00:09:23.642 left after Leukoreduction standard
00:09:23.642 --> 00:09:25.490 blood washing doesn’t remove it.
00:09:25.490 --> 00:09:28.031 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 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,
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. 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
00:11:09.676 --> 00:11:10.600 Hodgkin's lymphoma?

00:11:10.600 --> 00:11:12.705 Patients need to have irradiated blood products with for life not even after they’ve been cured.

00:11:12.705 --> 00:11:15.280 But for life, lors, auto transplants, not irradiating the transplant.

00:11:15.280 --> 00:11:17.240 Of course, just any red cells that they get outside of the transplant.

00:11:17.240 --> 00:11:19.730 If it’s Rachel Emacs single donor platelets, or from relatives.

00:11:19.730 --> 00:11:21.390 not irradiating the transplant.

00:11:21.390 --> 00:11:22.220 Of course, just any red cells that they get outside of the transplant.

00:11:22.220 --> 00:11:24.404 If it’s Rachel Emacs single donor platelets, or from relatives.

00:11:24.404 --> 00:11:26.790 get outside of the transplant.

00:11:26.790 --> 00:11:30.950 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.
Getting Cam path anti CD.

NOTE Confidence: 0.847607553005219

antithymocyte globulin granulocytes?

NOTE Confidence: 0.847607553005219

If those products are used to treat

NOTE Confidence: 0.847607553005219

illnesses they should get irradiated blood

NOTE Confidence: 0.847607553005219

products not necessarily for aplastic anemia.

NOTE Confidence: 0.847607553005219

MD S Hodgkin’s lymphoma.

NOTE Confidence: 0.847607553005219

I’m sorry,

NOTE Confidence: 0.847607553005219

non Hodgkin’s lymphoma and non

NOTE Confidence: 0.847607553005219

Hodgkin’s leukemia is solid organs.

NOTE Confidence: 0.847607553005219

Unless they’re being treated

NOTE Confidence: 0.847607553005219

with one of these purine analogs

NOTE Confidence: 0.847607553005219

or other types of therapies,

NOTE Confidence: 0.847607553005219

so aplastic anemia getting ATG

NOTE Confidence: 0.847607553005219

therapy would be a candidate.

NOTE Confidence: 0.847607553005219

AA would.

NOTE Confidence: 0.847607553005219

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 places 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.
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 of 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.

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 cross
links 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.

Does the same thing as radiation would. In fact it doesn’t,

There are some non envelope virus.

is that it 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
have time to talk about riboflavin, which is also a photosensitizing agent intercalates into nucleic acids as well, and UV B light is used rather than UV A and that promotes oxygen radicals. UVC is another technology that's used in Europe. There is no photoactive photosensitizing agent. The UVC itself acts to induce peering, permitting dimers, and that was discussed by Jake Owen Delaney, transfusion recently. This is a manuscript that we wrote for 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 .

32
00:18:04.524 --> 00:18:07.609 micrograms per kilo you wind up
NOTE Confidence: 0.82047164440155
00:18:07.609 --> 00:18:10.034 with 1100 picograms and after
NOTE Confidence: 0.82047164440155
00:18:10.034 --> 00:18:13.728 about 6 hours or so it’s down to
NOTE Confidence: 0.82047164440155
00:18:13.728 --> 00:18:16.742 about 100 to 200 picograms per milliliter
NOTE Confidence: 0.82047164440155
00:18:16.742 --> 00:18:19.794 so it gets quite gets reduced to
NOTE Confidence: 0.82047164440155
00:18:19.794 --> 00:18:22.888 quite rapidly and studies on HPLC
NOTE Confidence: 0.82047164440155
00:18:22.888 --> 00:18:25.448 show as far as toxicology.
NOTE Confidence: 0.82047164440155
00:18:25.450 --> 00:18:27.850 This is before you V A.
NOTE Confidence: 0.82047164440155
00:18:27.850 --> 00:18:29.590 This is the HPLC.
NOTE Confidence: 0.82047164440155
00:18:29.590 --> 00:18:30.460 You see,
NOTE Confidence: 0.82047164440155
00:18:30.460 --> 00:18:32.165 after you via the photo
NOTE Confidence: 0.82047164440155
00:18:32.165 --> 00:18:33.870 products have formed over here.
NOTE Confidence: 0.82047164440155
00:18:33.870 --> 00:18:35.700 This is a standard and these
NOTE Confidence: 0.82047164440155
00:18:35.700 --> 00:18:38.147 sort of products are removed by a
NOTE Confidence: 0.82047164440155
00:18:38.147 --> 00:18:40.077 filtration technique that is used
NOTE Confidence: 0.82047164440155
00:18:40.077 --> 00:18:42.191 called compound or compound and sort
Device which is really call us.

Tyramine that absorbs the photo products.

So the amount of of the S 59 that’s goes into a recipient is minimal.

It’s in the the picogram quantities the same thing with plasma.

Here’s plasma after you VA with multiple photo products and hear the

photo products are pretty much gone after.

Compound resource if device absorption.

We’ve been using this product the platelet

one at Yale since 2017 we started.

We were among the first and we’ve been

the leaders nationally for this product.

This is the average.
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 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,

we went to all the C-Suite folks in the Department.

Chairs have 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.
NOTE Confidence: 0.837122082710266
00:21:57.066 --> 00:21:58.686 of platelets in the pH drops,
NOTE Confidence: 0.837122082710266
00:21:58.690 --> 00:22:00.713 the acid causes the platelets to clump
NOTE Confidence: 0.837122082710266
00:22:00.713 --> 00:22:02.812 and you get this, which is obvious.
NOTE Confidence: 0.837122082710266
00:22:02.812 --> 00:22:03.988 What we’re worried about,
NOTE Confidence: 0.837122082710266
00:22:03.990 --> 00:22:05.445 or those that are contaminated
NOTE Confidence: 0.837122082710266
00:22:05.445 --> 00:22:06.318 and look normal.
NOTE Confidence: 0.837122082710266
00:22:06.320 --> 00:22:07.112 That’s the problem,
NOTE Confidence: 0.837122082710266
00:22:07.112 --> 00:22:08.696 and that’s why we’ve had six
NOTE Confidence: 0.837122082710266
00:22:08.696 --> 00:22:09.810 near misses recently,
NOTE Confidence: 0.837122082710266
00:22:09.810 --> 00:22:12.008 and we’ve had two deaths at this
NOTE Confidence: 0.837122082710266
00:22:12.008 --> 00:22:12.950 institution from contaminated
NOTE Confidence: 0.837122082710266
00:22:13.008 --> 00:22:14.622 platelets or what actually one plate
NOTE Confidence: 0.837122082710266
00:22:14.622 --> 00:22:16.508 and one red cell over the years,
NOTE Confidence: 0.837122082710266
00:22:16.510 --> 00:22:18.838 and we’ve had a lot of near misses.
NOTE Confidence: 0.837122082710266
00:22:18.840 --> 00:22:19.130 Fortunately,
our blood bank staff could pick up something if it looks strange. If there’s a lack of platelets world, 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.

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
00:24:53.120 --> 00:24:55.418 actually up to 96 hours later,

00:24:55.420 --> 00:24:56.728 subsequent red cell transfusions.

00:24:56.728 --> 00:24:58.036 The platelets didn’t work.

00:24:58.040 --> 00:24:59.945 They would probably transfuse more

00:24:59.945 --> 00:25:02.232 red cells that the patient would

00:25:02.232 --> 00:25:04.458 still be bleeding and there was a

00:25:04.458 --> 00:25:06.235 little more less again point units

00:25:06.235 --> 00:25:10.580 .2 more of a unit in the conventional

00:25:10.638 --> 00:25:12.513 wasn’t the pathogen reduction group

00:25:12.513 --> 00:25:14.388 showing that the platelets worked.

00:25:14.390 --> 00:25:16.847 There may have been a little more

00:25:16.847 --> 00:25:18.970 platelets used port part of a unit,

00:25:18.970 --> 00:25:20.635 but nothing substantial and was

00:25:20.635 --> 00:25:21.634 in my approach.

NOTE Confidence: 0.861809194087982
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
beneficial that it prevents
the loss of removes 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,

uh 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. 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, 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.
00:28:46.498 --> 00:28:48.128 consent obviously went through the
NOTE Confidence: 0.852834582328796
00:28:48.128 --> 00:28:50.172 IRB to whether they get pathogen
NOTE Confidence: 0.852834582328796
00:28:50.172 --> 00:28:51.842 reduced or conventional red cells,
NOTE Confidence: 0.852834582328796
00:28:51.850 --> 00:28:53.788 and they’re not transfused for this
NOTE Confidence: 0.852834582328796
00:28:53.788 --> 00:28:56.164 study if their doctor says they need
NOTE Confidence: 0.852834582328796
00:28:56.164 --> 00:28:57.864 a transfusion and they’ve agreed.
NOTE Confidence: 0.852834582328796
00:28:57.870 --> 00:29:00.470 We will give them one or the other,
NOTE Confidence: 0.830222129821777
00:29:00.470 --> 00:29:02.934 but we’re not going to radiate the
NOTE Confidence: 0.830222129821777
00:29:02.934 --> 00:29:04.722 pathogen reduced product because that
NOTE Confidence: 0.830222129821777
00:29:04.722 --> 00:29:07.060 would cause a double damage to the
NOTE Confidence: 0.830222129821777
00:29:07.060 --> 00:29:09.250 platelet or the OR the red cell rather.
NOTE Confidence: 0.830222129821777
00:29:09.250 --> 00:29:11.091 So the purpose of this talk was
NOTE Confidence: 0.830222129821777
00:29:11.091 --> 00:29:13.060 also to reassure everyone that the
NOTE Confidence: 0.830222129821777
00:29:13.060 --> 00:29:14.925 data show clearly that pathogen
NOTE Confidence: 0.830222129821777
00:29:14.925 --> 00:29:16.718 reduction prevents graft versus host.
NOTE Confidence: 0.830222129821777
00:29:16.720 --> 00:29:18.995 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, 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. Let me fix this. Sorry about that, OK. Let me fix this. Sorry about that, OK.

Can you see the screen? Can you see the screen? Can you see the screen?

OK yes, OK great wonderful again. OK yes, OK great wonderful again. OK yes, OK great wonderful again.

Thank you for inviting me to speak to this group today, speak to this group today, speak to this group today.

so I’m going to give you a tell so I’m going to give you a tell so I’m going to give you a tell.

you about something which is you about something which is 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 this debate or about these products

00:33:15.864 --> 00:33:18.268 and what the concern is relating to these.

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 and presentation 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. 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
00:34:57.296 --> 00:34:59.617
products amongst youth.

So there's an increased risk of exposure to nicotine, nicotine addiction, future disease risks, and even amongst adults who switched to using this product, there is a great deal of concern of dual use behavior. What adults are doing is not necessarily switching completely to use of these products, but are choosing to use both cigarettes and E-cigarettes depending on convenience and where they can use these.
products and that is not good either. And of course, then there’s a secondhand aerosol exposure issue, which again we know very little about, so these products are Sony on the market. So just to take a step back, as I said, this is the top public health concern which is cigarette smoking or tobacco smoking a cigar. Use all these combustible products that create havoc on multiple organ systems and also have contribute to cancer risks. So over the years in the US we’ve done
As many of you know, and most recently the one that has. I’ve been quite influential. 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 get this role. 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
is a very simple, really simple.
I should say I don’t know if you
even college and equipment or a device.
There is a. There’s a power component
here which charges the E cigarettes.
Not all of them look like this.
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
here 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 into the market 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

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,

devices or drug devices,

so they also ruled that 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. The FDA is actually coming up with a whole new way that these products can be regulated 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 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 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. 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 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
differs in terms of whether
it is a closed system in the sense
that the nicotine is contained in
it and you 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
filled and you just slide them in.

Now this is also left you a huge black market, so even with the pod devices now you can buy unfilled parts that you can then fill with whatever you want, and this has led to a huge increase in rates of marijuana use and use a variety of other products because people are filling pods with all kinds of different things and making them so. This is basically just to give you an idea of what exists, and this shows you the sales that has in Nielsen tracked retail channels by Brandon. You can see the amount of sales.
00:41:58.187 --> 00:42:00.170 that go towards E cigarettes.
00:42:00.170 --> 00:42:01.298 And obviously a very
00:42:01.298 --> 00:42:02.144 very profitable market,
00:42:02.150 --> 00:42:04.376 which is why a lot of people
00:42:04.376 --> 00:42:06.460 are investing in these products.
00:42:06.460 --> 00:42:08.483 So I bring you back now to
00:42:08.483 --> 00:42:10.409 what I started the talk with,
00:42:10.410 --> 00:42:12.168 which is let’s not talk about
00:42:12.168 --> 00:42:13.760 the benefits of the harms.
00:42:13.760 --> 00:42:15.275 So let’s proceed to talking
00:42:15.275 --> 00:42:16.487 about times or toxicity.
00:42:16.490 --> 00:42:16.794 First,
00:42:16.794 --> 00:42:19.530 I’m just going to show you snippets of data.
00:42:19.530 --> 00:42:21.360 There’s a huge literature out there,
00:42:21.360 --> 00:42:23.178 but in the interest of time,
let’s ask the first question.

When you look at E cigarettes, 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 like NNN.

And in case and some of these compounds, tobacco specific nitrosamine’s that have been shown to be toxic.

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. Anna 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, 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 not generally recognized as safe for inhalational use.

but they are not generally recognized as safe for edible use.

not for any Hill inhalation.

Using isn’t very important distinction

and what we’re finding through a lot of
the cellular toxicity work going on is that many of these flavor molecules are have. Are toxic to cells, some of them also have been known to have diseased risks. An example of this is diacetyl, which is a chemical which is included to produce butter flavor and it has been known to be associated popcorn lung disease which is actually found in people who are working in popcorn factories, so this chemical is still used in many of these eliquids as a flavoring chemical, so there are concerns about toxicity of these flavors.
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. Be 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 se. We really started becoming very concerned about this in the US and we're really concerned about it. We really started becoming very concerned about it.
00:48:09.710 --> 00:48:11.550 concerned about it because of
NOTE Confidence: 0.818998157978058
00:48:11.617 --> 00:48:13.427 the extensive use among youth.
NOTE Confidence: 0.818998157978058
00:48:13.430 --> 00:48:14.188 This show.
NOTE Confidence: 0.818998157978058
00:48:14.188 --> 00:48:16.462 This shows you the current tobacco
NOTE Confidence: 0.818998157978058
00:48:16.462 --> 00:48:18.785 product use amongst high school students
NOTE Confidence: 0.818998157978058
00:48:18.785 --> 00:48:21.430 in the US from the National Youth
NOTE Confidence: 0.818998157978058
00:48:21.430 --> 00:48:23.817 Tobacco data and you see here this,
NOTE Confidence: 0.818998157978058
00:48:23.820 --> 00:48:26.788 this red line is indicative of E cigarettes.
NOTE Confidence: 0.818998157978058
00:48:26.790 --> 00:48:29.238 Now their their rates were significantly
NOTE Confidence: 0.818998157978058
00:48:29.238 --> 00:48:31.299 increasing through 2019 and in 20.
NOTE Confidence: 0.818998157978058
00:48:31.300 --> 00:48:33.916 18 and 2019 we discovered a lot of
NOTE Confidence: 0.818998157978058
00:48:33.916 --> 00:48:35.893 these increasing rates was because of
NOTE Confidence: 0.818998157978058
00:48:35.893 --> 00:48:38.205 the presence of jewel in the market
NOTE Confidence: 0.818998157978058
00:48:38.205 --> 00:48:40.000 and they were certain regulations
NOTE Confidence: 0.818998157978058
00:48:40.000 --> 00:48:41.777 put on jewel in 2019.
NOTE Confidence: 0.818998157978058
00:48:41.777 --> 00:48:44.136 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 in. Amongst you have gone down because
of lack of access and lack of
the same kind of cues that they
experience in schools from seeing
their peers use and so
whether it’s regulatory or related to kovid,
but the rates have gone down at least in
the early 2020 to what it was in 2018.
That’s still not low,
but it’s still, you know,
did head in the right direction.
Youth are using multiple kinds of devices,
so this is the other concern BC youth using
every device that’s available on the market.
There is a lot of concern about nicotine
00:49:50.642 --> 00:49:53.407 use in these devices because devices like
00:49:53.407 --> 00:49:56.359 the jewel contain very high levels of
00:49:56.359 --> 00:49:59.208 nicotine and the adolescent brain is more
00:49:59.208 --> 00:50:01.918 sensitive to nicotine than the adult Bremen.
00:50:01.920 --> 00:50:02.684 Israeli tobacco,
00:50:02.684 --> 00:50:03.830 nicotine exposure, primes,
00:50:03.830 --> 00:50:06.128 the adolescent brain for nicotine addiction,
00:50:06.130 --> 00:50:08.040 addiction to other substances that
00:50:08.040 --> 00:50:09.543 alters developmental maturing, and.
00:50:09.543 --> 00:50:12.367 It can also have effects on multiple organs.
00:50:12.370 --> 00:50:14.354 I’m sure you are all well aware of
00:50:14.354 --> 00:50:16.680 the of the acetyl choline or the
00:50:16.680 --> 00:50:18.440 cholinergic system and know that
00:50:18.501 --> 00:50:20.591 nicotine binds to cholinergic receptors
00:50:20.591 --> 00:50:23.191 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
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
else in the product, and most likely that it’s probably a cannabis related product. And as I said the there is multiple papers on this, but this is one of our papers which shows that E cigarette use, amongst Euclides to cigarette use. So let’s now move on to talking about smoking cessation. So we’ve talked about all the bad things. Now let’s see. Well, is it actually doing what it was? What it set out to do? Which is help smokers quit smoking. 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, few.
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 of E cigarettes do have some, albeit 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, 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 a product that is really having an impact on youth. There is limited evidence that the product may help. Um people stop smoking cigarettes completely. 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, in illiquid. 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
00:55:10.292 --> 00:55:11.918 regulating nicotine levels,
00:55:11.920 --> 00:55:13.284 we could regulate flavors.
00:55:14.650 --> 00:55:16.690 They removed all flavors in Eliquids,
00:55:16.690 --> 00:55:19.741 but then there is a concern that smokers may
00:55:19.741 --> 00:55:22.259 actually need the flavors to quit smoking.
00:55:22.260 --> 00:55:24.264 We know this is something that
00:55:24.264 --> 00:55:25.958 will definitely be beneficial for
00:55:25.958 --> 00:55:27.458 youth because Uther really drawn
00:55:27.458 --> 00:55:29.390 to the flavors in the product.
00:55:29.390 --> 00:55:31.005 We could regulate the kind
00:55:31.980 --> 00:55:33.768 You know, I talked about these
00:55:33.768 --> 00:55:35.540 open and close system products,
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

about what you can do as clinicians.

People working in this area,

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
not over using E cigarettes and getting in more nicotine than what they normally will do. They also need to have a plan for quitting cigarettes completely. No dual use behaviors, you know they shouldn’t just use the product whenever convenient and they should have a plan to quit E cigarettes as well. We don’t want to have a generation just dependent on nicotine either because we don’t know what the long term consequences of this are. You can also educate your parents and help educate communities and
00:57:02.441 --> 00:57:04.457 local schools to really advise them

00:57:04.457 --> 00:57:06.669 of what these products could do.

00:57:06.670 --> 00:57:09.526 And finally I would say really help us

00:57:09.526 --> 00:57:11.868 collect scientific evidence on E cigarettes.

00:57:11.870 --> 00:57:14.806 I know that E cigarettes was on the

00:57:14.806 --> 00:57:17.022 grand challenge during the retreat and

00:57:17.022 --> 00:57:19.595 I hope that this push will continue

00:57:19.595 --> 00:57:22.262 and that you all will be involved

00:57:22.262 --> 00:57:24.626 in helping us collect more toxicity,

00:57:24.626 --> 00:57:26.621 safety and efficacy data on

00:57:26.621 --> 00:57:28.308 these product so we can.

00:57:28.310 --> 00:57:29.345 Regulate them appropriately.

00:57:29.345 --> 00:57:32.490 The point is they are out in the market.

00:57:32.490 --> 00:57:34.940 Everybody is using them and we are

00:57:34.940 --> 00:57:37.008 trying to develop all the signs.

00:57:37.008 --> 00:57:39.008 And finally I would say really help us

00:57:39.008 --> 00:57:41.214 collect scientific evidence on E cigarettes.

00:57:41.214 --> 00:57:43.704 I know that E cigarettes was on the

00:57:43.704 --> 00:57:45.951 grand challenge during the retreat and

00:57:45.951 --> 00:57:48.485 I hope that this push will continue

00:57:48.485 --> 00:57:51.785 and that you all will be involved

00:57:51.785 --> 00:57:54.173 in helping us collect more toxicity,

00:57:54.173 --> 00:57:56.168 safety and efficacy data on

00:57:56.168 --> 00:57:58.178 these product so we can.

00:57:58.178 --> 00:57:59.208 Regulate them appropriately.

00:57:59.208 --> 00:58:01.890 The point is they are out in the market.

00:58:01.890 --> 00:58:03.970 Everybody is using them and we are

00:58:03.970 --> 00:58:06.000 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. I know we’re a little late, I just actually Melinda Irwin sent more comment than a question, but I think it’s it’s important she writes important talk an area focus. 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 3 cigarettes,
NOTE Confidence: 0.822980761528015
00:58:15.850 --> 00:58:18.544 do you perceive that that actually
NOTE Confidence: 0.822980761528015
00:58:18.544 --> 00:58:21.690 could reverse the trend, as it were?
NOTE Confidence: 0.822980761528015
00:58:22.730 --> 00:58:26.706 I'm hoping not. No, but we do.
NOTE Confidence: 0.889474877289363
00:58:26.710 --> 00:58:28.060 I think the question is
NOTE Confidence: 0.889474877289363
00:58:28.060 --> 00:58:29.850 can we get all these youth?
NOTE Confidence: 0.889474877289363
00:58:29.850 --> 00:58:31.275 Who are the new entrants
NOTE Confidence: 0.889474877289363
00:58:31.275 --> 00:58:32.700 into this area to stop?
NOTE Confidence: 0.889474877289363
00:58:32.700 --> 00:58:34.980 And that’s what a lot of prevention work.
NOTE Confidence: 0.889474877289363
00:58:34.980 --> 00:58:36.690 And also our work at Yale.
NOTE Confidence: 0.889474877289363
00:58:36.690 --> 00:58:38.115 We’re doing a lot of
NOTE Confidence: 0.889474877289363
00:58:38.115 --> 00:58:39.730 cessation related program,
NOTE Confidence: 0.889474877289363
00:58:39.730 --> 00:58:40.958 so we’re doing a lot of education,
NOTE Confidence: 0.889474877289363
00:58:40.960 --> 00:58:42.670 prevention and cessation and high schools.
NOTE Confidence: 0.889474877289363
00:58:42.670 --> 00:58:45.340 So if you or any of you are aware of
NOTE Confidence: 0.889474877289363
00:58:45.421 --> 00:58:47.698 the need, please send me a note and
NOTE Confidence: 0.889474877289363
00:58:47.698 --> 00:58:49.861 we can certainly go out and talk to
NOTE Confidence: 0.889474877289363
00:58:49.861 --> 00:58:52.360 the group if we can prevent these entrance,
NOTE Confidence: 0.889474877289363
00:58:52.360 --> 00:58:53.790 I think we would be.
NOTE Confidence: 0.889474877289363
00:58:53.790 --> 00:58:55.235 We would really serve public
NOTE Confidence: 0.889474877289363
00:58:55.235 --> 00:58:56.680 health very well because we.
NOTE Confidence: 0.889474877289363
00:58:56.680 --> 00:58:59.304 One thing we don’t want them to do,
NOTE Confidence: 0.889474877289363
00:59:01.098 --> 00:59:02.930 we don’t want them to then
NOTE Confidence: 0.889474877289363
00:59:02.930 --> 00:59:04.855 convert to using the products.
NOTE Confidence: 0.889474877289363
00:59:04.855 --> 00:59:06.879 These are all all these kids are
NOTE Confidence: 0.889474877289363
00:59:06.880 --> 00:59:09.176 If E cigarettes don’t serve them well,
NOTE Confidence: 0.889474877289363
00:59:09.154 --> 00:59:11.154 they’re going to want to move
NOTE Confidence: 0.889474877289363
00:59:11.154 --> 00:59:12.470 on to product switch.
NOTE Confidence: 0.889474877289363
00:59:12.470 --> 00:59:13.460 Serve them better.
NOTE Confidence: 0.889474877289363
00:59:13.460 --> 00:59:14.450 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.
00:59:43.030 --> 00:59:44.960 Thank you all for attending

NOTE Confidence: 0.821239793300628

00:59:44.960 --> 00:59:47.679 and enjoy the rest of your day.

NOTE Confidence: 0.821239793300628

00:59:47.680 --> 00:59:51.572 Thank you bye bye.