

TRANSCRIPT - SURGEON GENERAL'S (KOOB) AD HOC COMMITTEE ON

"NON-DENTAL HEALTH EFFECTS OF FLUORIDE," APRIL 18 - 19, 1983

TRANSCRIPT OF PROCEEDINGS

NATIONAL INSTITUTES OF HEALTH

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Pages 282 - 476

MEETING OF
THE FLUORIDE PANEL

ORIGINAL

DAY II

Date: April 19, 1983

Location: Bethesda, Maryland

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EPA file (list of panel)

Surgeon General's AD HOC Committee on the "NON-Dental Effects of Fluoride," April 18-19, 1983

A G E N D A

FLUORIDE PANEL MEETING

THE CLINICAL CENTER, ROOM 2C116
NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND

MONDAY, APRIL 18

9:00 A.M.	Introductions:	Jay R. Shapiro, M.D. Acting Director, Clinical Center, NIH
	Summary of the Issues:	Robert Mecklenburg, D.D.S., M.P.H. Chief Dental Officer, USPHS
	Safe Drinking Water Act:	Joseph A. Cotruvo, Ph.D. Director, Criteria and Standards Division, Office of Drinking Water US Environmental Protection Agency
	Epidemiology of Fluoride in Drinking Water:	A. Richey Sharrett, M.D., Dr.P.H. Epidemiology Branch, National Heart, Lung, and Blood Institute, NIH
	Fluoride Metabolism, an Overview:	Frank A. Smith, M.D. Associate Professor of Toxicology University of Rochester Medical Center Rochester, New York
	Tissue Effects of Fluoride Intake:	Vincent Vigorita, M.D. Department of Pathology The Hospital for Special Surgery New York, New York
	Clinical Studies:	Michael Kleerekoper, M.D. Bone and Mineral Division Henry Ford Hospital Detroit, Michigan; Jay R. Shapiro, M.D.

DISCUSSION

TUESDAY, APRIL 19

9:00 A.M.	Animal Studies:	James L. Shupe, D.V.M. Professor of Pathology and Toxicology College of Agriculture Utah State University Logan, Utah
	Summary of Economic Issues:	Joseph A. Cotruvo, Ph.D.

DISCUSSION

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APRIL 18-19, 1983
THE CLINICAL CENTER, ROOM 2C116
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* * * AGENDA * * *

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9629 * * * FLUORIDE TOXICOLOGY ASSESSMENT * * *

9630 - - -

9631

9632 DR. SHAPIRO: For the moment, I would like
9633 to keep the discussion off the issue of the dental
9634 problem for the moment and then come back to it.

9635 Would someone like to suggest a definition
9636 of an adverse effect in terms of non-dental toxicity,
9637 either known or unknown?

9638 Certainly, an adverse effect is
9639 osteosclerosis. Is there a lesser stage based on your
9640 information that you would like to--

9641 DR. MARX: I don't think we agreed that
9642 osteosclerosis presents an adverse health effect.

9643 DR. SHAPIRO: Okay. Well, let's discuss it.
9644 If we agree that crippling fluorosis is an adverse
9645 health effect. How would you deal with this question
9646 of the lag period that was raised or do you think
9647 that the evidence to date suggests that the lag--

9648 DR. WALLACH: That comes under the next
9649 one, "Potential Adverse."

9650 DR. SHAPIRO: All right. So, crippling
9651 fluorosis we consider an adverse effect. Does anyone
9652 disagree with that? Are there any others?

9653 DR. WALLACH: What about the things Michael

9654 brings up, the fibrocystic or arthralgic?

9655 DR. KLEEREKOPER: That is really part of
9656 crippling fluorosis, I think, isn't it?

9657 DR. SHAPIRO: We don't know. That might be
9658 a potential adverse effect.

9659 DR. MARX: Oh, it is an adverse effect.

9660 DR. SHAPIRO: Okay.

9661 DR. KLEEREKOPER: I can't accept that as
9662 readily as a known adverse effect. I mean, if you are
9663 going to put down an adverse effect in terms of
9664 fluoride toxicity, if you want to take this to the
9665 letter of the law, an adverse effect of fluoride
9666 toxicity is death.

9667 DR. MARX: That is an adverse effect.

9668 DR. KLEEREKOPER: Death is;
9669 gastrointestinal hemorrhage is; gastrointestinal
9670 irritation-- if the question is "are there any
9671 adverse effects from fluoride? Is there any fluoride
9672 toxicity?" The answer is absolutely yes, all the way
9673 to death. That has been well-established by Dr.
9674 Smith's presentation yesterday.

9675 DR. SPENCER: I would like to say that I
9676 disagree. I would say that osteosclerosis is an
9677 adverse effect because we don't know what the later
9678 effect will be.

9679 DR. KLEEREKOPER: That is potential.

9680 DR. SPENCER: Potential effects, yes.

9681 DR. KLEEREKOPER: But recognized adverse
9682 effects of fluoride is clearly death,
9683 gastrointestinal hemorrhage, gastrointestinal
9684 irritation, arthralgias and crippling fluorosis. They
9685 are clearly recognized adverse effects.

9686 DR. SHAPIRO: Does anybody disagree with
9687 those adverse effects?

9688 DR. VIGORITA: Yes. The arthralgias, in our
9689 experience, have been transient and many things
9690 pursuant to medical therapy are transient and not
9691 considered adverse effect.

9692 So, I would consider an adverse health
9693 effect something that triggers an allergic response
9694 that leads--

9695 DR. MARX: But somebody that has arthralgia
9696 is compromised by it. He is not in good health if he
9697 is having arthralgia.

9698 DR. KLEEREKOPER: Not only that, but, if
9699 someone is getting arthralgias from fluoride in the
9700 drinking water, how do you stop it? So, I can't
9701 accept that.

9702 DR. SPENCER: I believe that we ought to
9703 differentiate these adverse effects from therapeutic

9704 doses and from amounts in—

9705 DR. KLEEREKOPER: That wasn't the question.
9706 The question is "Are there adverse effects from
9707 fluoride administration?" The answer is yes. At least,
9708 I think there are and maybe others.

9709 DR. WALLACH: Jay, why don't you redefine
9710 what we are talking about. We are talking about
9711 fluoridation, fluoride content of the drinking water
9712 or are we talking about fluoride administration in
9713 general?

9714 DR. SHAPIRO: I think we have to be talking
9715 about fluoride in drinking water. I don't think we
9716 have to be concerned with the pharmacological effects
9717 of fluoride right now.

9718 DR. WALLACH: Well, then I think we
9719 probably ought to throw out the GI effects.

9720 DR. SHAPIRO: Well, you can throw them out.
9721 Some of them, I think you may not have all the
9722 information you need. If you go up to eight parts per
9723 million, some people drinking that will have GI
9724 irritation.

9725 DR. KLEEREKOPER: Can we ask Joe what he is
9726 asking here in this paper? This is your baby. What
9727 did you want to know about any adverse effects in
9728 health? Are you really only interested in drinking

9729 water or are you interested in fluoride?

9730 DR. COTRUVO: Fluoride per se and then you
9731 back down--

9732 DR. KLEEREKOPER: To the levels. So, I
9733 think the things we have mentioned are adverse
9734 effects on health. We can take them out afterwards in
9735 drinking water.

9736 DR. WALLACH: At all doses and all manners
9737 of administration. Is that what you are after?

9738 DR. COTRUVO: Yes.

9739 DR. WALLACH: Okay.

9740 DR. KLEEREKOPER: Then osteosclerosis
9741 should stay.

9742 DR. SHAPIRO: I think we are divided on
9743 that.

9744 DR. KELLER: Unless the adverse effects
9745 from fluoride and then we can talk about for each one
9746 what we know about levels.

9747 DR. KLEEREKOPER: Would you read those
9748 again?

9749 DR. SHAPIRO: Death, crippling fluorosis,
9750 GI irritation, arthralgias.

9751 DR. KLEEREKOPER: GI bleeding.

9752 DR. SHAPIRO: I have GI irritation and
9753 bleeding. We are not talking about the cardiac

9754 effects. Those are potential. Osteosclerosis, is
9755 there a feeling that this represents a potential
9756 rather than a real adverse effect?

9757 DR. WALLACH: It is more potential than
9758 real.

9759 DR. KLEEREKOPER: I don't know whether
9760 there is a component of the crippling fluorosis that
9761 is related to osteosclerosis.

9762 DR. WALLACH: If you don't know, that makes
9763 it potential.

9764 DR. SHAPIRO: That is the point. You don't
9765 really know what is happening. I think it is
9766 reasonable to leave it as a potential adverse effect.

9767 DR. MARX: I would take a position that,
9768 just as dental fluorosis is a manifestation of
9769 moderately low levels of fluoride excess,
9770 osteosclerosis is the next stage and crippling
9771 fluorosis is a much more severe stage.

9772 I haven't seen any evidence in the two
9773 studies that were cited to suggest that, if you take
9774 a large population, a small fraction of them in Texas
9775 will have osteosclerosis, but those people are not
9776 health compromised.

9777 DR. KLEEREKOPER: That is in the States,
9778 but in India osteosclerosis may be one of the

9779 components.

9780 DR. MARX: It is a component of crippling
9781 fluorosis.

9782 DR. KLEEREKOPER: Is osteomalacia a side
9783 effect of fluoride toxicity? Can you induce
9784 osteomalacia with fluoride? The answer to that
9785 question is also yes, I think.

9786 DR. SHAPIRO: I think you would have to
9787 define "adverse" in the broadest sense of the word.

9788 DR. WALLACH: I would say osteodoses; I
9789 wouldn't say osteomalacia.

9790 DR. KLEEREKOPER: True clinical
9791 osteomalacia can be induced by fluoride in the right
9792 circumstances, as a direct side effect of fluoride.

9793 DR. VIGORITA: That data has not been
9794 presented in the last two days. That has not been
9795 presented.

9796 DR. KLEEREKOPER: Lancet, 1981. I have the
9797 paper in my bag, if you want to see it. We didn't
9798 mention it. Do you want the paper?

9799 DR. VIGORITA: Yes, I am curious.

9800 DR. KLEEREKOPER: It is right down at the
9801 bottom of my dirty underwear and all.

9802 MR. SMALL: No, don't open the bag.

9803 (Laughter)

9804 DR. KLEEREKOPER: You really want that
9805 paper.

9806 DR. SHAPIRO: I think, from a clinical
9807 standpoint, it is hard to say some grade of osteoid
9808 malacia or osteosclerosis is anything other than a
9809 potentially adverse effect, potential when impacted
9810 by other factors.

9811 DR. MARX: I don't think it is a
9812 potentially adverse effect. A potentially adverse
9813 effect is something that is adverse that might occur.
9814 Osteosclerosis is an effect that we don't think is
9815 adverse.

9816 DR. SHAPIRO: Are you sure that in children
9817 it is not adverse? Does it limit the rate of skeletal
9818 growth if it occurred in a child?

9819 DR. MARX: Osteosclerosis I don't think is
9820 adverse. Compromise of skeletal growth, if it occurs,
9821 is adverse. I don't think osteosclerosis is adverse.

9822 DR. SHAPIRO: But we don't know--

9823 DR. MARX: If you want to say that delayed
9824 skeletal maturity is a potential adverse effect--it
9825 is undesirable and we don't know if it occurs.

9826 DR. MARCUS: What Jay is trying to get you
9827 to address is whether you know in your heart that the
9828 lesion of osteosclerosis does not, in itself, cause

9829 the delay in skeletal maturation, not that skeletal
9830 maturation is--

9831 DR. MARX: For my part, I don't think that
9832 osteosclerosis, per se, is bad.

9833 DR. SHAPIRO: Look at it from this
9834 standpoint. If it doesn't naturally happen and you
9835 are inducing it by permitting this contaminant in
9836 water, does that--

9837 DR. MARX: But you could say the same thing
9838 for dental mottling. It doesn't normally happen. Mild
9839 changes in the dental composition don't imply that
9840 the skeleton is compromised. I would say the same for
9841 osteosclerosis.

9842 DR. ROWE: If those same changes were
9843 occurring in your daughter, you wouldn't be upset
9844 about it?

9845 DR. MARX: No.

9846 DR. SPENCER: If you were taking an x-ray
9847 of someone who lives in an area--

9848 DR. MARX: Let's also say that these
9849 sclerotic effects have been observed at age 50 and
9850 beyond. In these communities where there is life-long
9851 exposure, nobody decided to change.

9852 DR. ROWE: If it were my daughter, I would
9853 be concerned. We can say all of those things, but

9854 when you see a change occurring in the bones that we
9855 don't know what its implications are, but it is
9856 clearly recognized as two standard deviations from
9857 the norm--

9858 DR. KLEEREKOPER: Let's get away for a
9859 minute from the drinking water. Can you induce
9860 osteosclerosis in humans with fluoride? And the
9861 answer to that is yes.

9862 Can osteosclerosis, either on its own or
9863 induced by fluoride, cause adverse effects on health
9864 and the answer to that, in my opinion, Steve, is yes.
9865 I think it does cause certainly marble bone disease
9866 which is a form of osteosclerosis. Now, that may not
9867 be the same disease that you can induce with
9868 fluoride. I am not sure of that. That is clearly
9869 causing adverse effects.

9870 DR. VIGORITA: Marble bone disease refers
9871 to osteopetrosis. It is a completely different
9872 entity. If you are going to use the terms on record,
9873 you have to use them correctly.

9874 DR. KLEEREKOPER: Let me put it this way.
9875 There are osteosclerotic diseases that do have
9876 adverse effects. Whether it is the same disease that
9877 is induced by fluoride or not, I really don't know.

9878 DR. SHAPIRO: Let's just say, because we

9879 really don't have the information to come off of
9880 this, that osteosclerosis occurs and we really don't
9881 know whether it is potentially adverse or not. We
9882 don't have the data.

9883 DR. MARX: But we can still vote on it.
9884 That is what we are here for.

9885 DR. SHAPIRO: All right. Let's have a vote.
9886 How many feel that osteosclerosis should be included
9887 as an adverse effect?

9888 DR. MARCUS: As a potential--

9889 DR. SHAPIRO: No. I said adverse effect.
9890 Who believes that osteosclerosis is a known adverse
9891 effect, that there is something wrong with having it?

9892 DR. SHUPE: May I ask a question. I will go
9893 back to the work of Lente and some of them where he
9894 broke down osteofluorosis into the chemical, the
9895 sclerotic, pleurotic, the malacic and he based it
9896 into degrees. The problem I am having is to define
9897 what you mean by osteosclerosis.

9898 DR. MARX: What we are talking about is is
9899 it a healthy animal or an unhealthy animal. We are
9900 not talking about the histology and we are not
9901 talking about the chemistry, but whether the animal
9902 is in bad health.

9903 DR. VIGORITA: I would like to make a

9904 comment because I see what Dr. Shupe is saying. If
9905 the osteosclerosis in fluoride refers to the changes
9906 that Dr. Shupe showed and Riggs has referred to as
9907 calcified ligaments, I think that is an adverse
9908 effect on health.

9909 We have not observed that in our experience
9910 and we haven't discussed it in this group from
9911 others' experience. So, I wouldn't consider that
9912 without the calcified tendons an adverse effect on
9913 health.

9914 So, perhaps the blanket statement is
9915 unfair. Maybe we want to modify it.

9916 DR. MARCUS: My interpretation of the
9917 discussion is osteofluorosis is a histologic change
9918 which is an increase in trabecular width and some of
9919 the things you showed yesterday. That is what I think
9920 we are talking about. We are not talking about any
9921 disease which is radiologically apparent. We are
9922 already recognizing that. That is osteofluorosis. Is
9923 that what you called it?

9924 DR. SPENCER: Talk about radiologically
9925 again.

9926 DR. MARCUS: We have already talked about
9927 that as an adverse thing. That is agreed on. We have
9928 moved that aside.

bone fractures

9929 DR. SHAPIRO: No, no. We have not agreed
9930 that early radiologic change is an adverse effect
9931 because in everything we read nobody says it is an
9932 adverse effect.

9933 DR. MARCUS: How far do you want to take
9934 this definition of what we are voting on.

9935 DR. KLEEREKOPER: To me, adverse effects of
9936 skeletal disease are either pain and invisible
9937 fracture. I don't know of any other clinical
9938 manifestation of skeletal disease.

9939 DR. MARCUS: Growth abnormalities.

9940 DR. SHAPIRO: That can happen to.

9941 DR. KLEEREKOPER: What do we know about
9942 fractures in bones treated with fluoride? What do we
9943 know about the strength?

9944 DR. SHAPIRO: These articles all say that
9945 there is nothing to say that it occurs. It has not
9946 been cited.

9947 DR. KLEEREKOPER: What do we know about
9948 pain as a symptom in these patients who get even
9949 severe radiographic changes?

9950 DR. SHAPIRO: It can occur after very, very
9951 prolonged levels of fluoride. But at ambient levels
9952 it occurs in a very, very small level.

9953 DR. KLEEREKOPER: But it is not something

9954 that occurs.

9955 DR. SHAPIRO: And it may not be related to
9956 fluoride.

9957 DR. KLEEREKOPER: So you have no fractures,
9958 no pain, no tenderness.

9959 DR. SHAPIRO: That is right.

9960 DR. KLEEREKOPER: I think from that point
9961 of view, it is not an adverse effect on health. If
9962 you wanted to include the exosdoses as part of the
9963 osteosclerosis symptom, then you have a different
9964 ballgame. I am not sure I can, but just taking
9965 osteosclerosis, leaving the joint component out,
9966 osteosclerosis doesn't have pain, tenderness or
9967 fracture.

9968 DR. VIGORITA: I think I have a way out of
9969 this. If we said something to the effect of a
9970 radio-dense skeleton--that is implying an x-ray
9971 change--a radio-dense skelton, as seen in association
9972 with the fluoride, without soft tissue changes, does
9973 not appear to have an adverse effect on health and
9974 that gets us away from the calcified ligaments, from
9975 potential soft tissue changes and confines it to a
9976 Roentgenographic radio-dense skeleton because I can
9977 certainly accept that.

9978 DR. SHAPIRO: Okay, but again you are

radiographic change
no pain, no fracture,
no tenderness
... not a health effect

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9979 talking about something that has not generally been
9980 observed.

9981 DR. VIGORITA: Well, osteosclerosis, I
9982 believe, we are referring to Roentgenographic
9983 radio-density.

9984 DR. KELLER: I think there is evidence. It
9985 is controversial and it has not even been repeated
9986 that often. But there is evidence to the contrary,
9987 that radio-dense skeletons are protected against
9988 fractures, at least. Now, I don't know about pain.

9989 The North Dakota study certainly indicated
9990 less compression fractions in women, I think it was,
9991 accompanied with radio-dense skeletons in very high
9992 fluoride areas.

9993 DR. MARX: But, again, we are not trying to
9994 address protective levels.

9995 DR. KELLER: I understand, but we are
9996 asking the question does radio-dense skeleton, which
9997 is a clinical indication of osteosclerosis, imply
9998 adverse effects which have been defined as pain,
9999 tenderness or fracture and I am saying one of those
10000 three not only doesn't imply an increase in fracture,
10001 it implies the reverse, a decrease in fracture.

10002 DR. MARX: How about something in the line
10003 of osteosclerosis, as has been observed in water

→ 8 ppm no further
↳ send

10004 levels up to eight parts per million, is not
10005 associated with adverse health effects. That leaves
10006 open the fact that osteosclerosis is a part of
10007 crippling fluorosis. But the degrees that have been
10008 seen, which are relatively mild, have not been
10009 associated with that.

10010 DR. SHAPIRO: So, what you are saying is
10011 you don't think it should be listed as a potential
10012 adverse effect?

10013 DR. MARX: Getting back into the definition
10014 of what is a potential adverse effect, fraction^{we} is a
10015 potential effect; pain is a potential adverse effect;
10016 I don't think that a radiographic change is an
10017 adverse health effect.

10018 DR. SHAPIRO: All right. Are there
10019 other--the value of the potential, by the way, I
10020 think is highlighting some possible changes and
10021 perhaps later on leading to some recommendations
10022 about information that we would have to get, for
10023 example, in terms of cardiotoxic, in terms of
10024 impairment of skeletal growth in children who have
10025 early changes.

10026 DR. WALLACH: I would also include the
10027 possibility of reduced turn-over of the young
10028 skeleton and the retention in the skeleon of other

(adverse water well)

10029 adverse effects.

10030 DR. SHAPIRO: Going along with Joe's
10031 suggestion, what is the highest no observed adverse
10032 effect exposure level? Now, remember, the water group
10033 when they discussed this they sort of split. Half of
10034 them--

10035 DR. MARX: Before we address any of that,
10036 we have got to decide whether we consider dental to
10037 be an adverse health effect because that is the
10038 threshold effect for a lot of things.

10039 DR. SHAPIRO: We don't know what bone looks
10040 like, unless Jim tells us the answer, we really don't
10041 know what bone looks like when you have a level of
10042 dental change which is acceptable at the two part per
10043 million level? Is that right? Over two parts per
10044 million in the drinking water, you are going to get
10045 more than grade two mottling in a small percent.

10046 DR. COTRUVO: In a small percentage.

10047 DR. SHAPIRO: We already know what that
10048 level is. That level that would be acceptable is,
10049 say, two parts per million or 2.4 part per million.
10050 What is the level?

10051 DR. COTRUVO: Well, 2.4 is the highest.

10052 DR. SHAPIRO: So, 2.4. Okay.

10053 DR. MARX: So you want to qualify. We are

10054 talking about the highest level for non-dental.

10055 DR. SHAPIRO: At the moment, yes. We know
10056 what happens at eight. Is eight an acceptable primary
10057 level? Is the risk so small that one can generalize
10058 to the--

10059 DR. WALLACH: You are talking about known
10060 risk or potential risk?

10061 DR. SHAPIRO: I am talking about known
10062 risk.

10063 DR. WALLACH: I will agree with eight for
10064 known risk.

10065 DR. SHAPIRO: You would agree with eight?

10066 DR. WALLACH: For known risk.

10067 DR. SHAPIRO: Right.

10068 MR. SMALL: I am concerned with something
10069 here that we keep going by and I would like to pin
10070 down. Joe shares this, I am sure, in the regulatory
10071 write-up the regulation refers to twice the optimal
10072 for an area which may vary. Eight PPM versus, for
10073 instance, being selected for research done in an area
10074 in Texas where the optimum was a particular level
10075 might not be equally all right some place else where
10076 the optimal is different. The multiples of optimal
10077 would be based on not only--

10078 DR. SHAPIRO: Do you feel any concern about

10079 this?

10080 DR. COTRUVO: No, because our feeling, in
10081 fact, for the future, is to move away from that, to
10082 try to set a standard based on specific numeric
10083 values.

10084 DR. MARX: I think right now what we are
10085 trying to do is establish the toxicology. We are not
10086 concerned with what is therapeutic. We just want to
10087 find out--

10088 MR. SMALL: No, it is just the terminology
10089 to be applied later in other areas where the optimal
10090 is different.

10091 DR. COTRUVO: Just dosages.

10092 DR. SHAPIRO: There is nothing that we have
10093 examined that says we should go above eight. Clearly,
10094 at eight, a small percentage of the population will
10095 at least have recognizable osteosclerosis. Some of
10096 them may have even more severe disease than that.
10097 There may be a smaller percentage who are clinically
10098 more effected, have an adverse effect.

10099 Now, is there any reason to move lower than
10100 that? Is there a reason to say or is there a reason
10101 to segregate out a certain population in which you
10102 say that is fine, but we will tell you right now, for
10103 this population, our best information is that we have

10104 to set that level here.

10105 DR. WALLACH: Jay, I personally feel that
10106 there is every reason in the world to go lower than
10107 that for the potential risks. Again, as a practical
10108 matter, I would set four for adults over the age of
10109 50 and, frankly, I would stick with the two for
10110 children and young adults. That is my personal
10111 feeling, not based on known effects, but based on the
10112 potential adverse effects.

10113 DR. KLEEREKOPER: Jay, this is something I
10114 should know, but I really can't remember off the top
10115 of my head. What is the level of fluoride in the
10116 drinking water in those communities that get
10117 clinically significant endemic fluorosis?

10118 DR. SHAPIRO: It depends.

10119 DR. KLEEREKOPER: The stuff Jeremy writes
10120 about for example.

10121 DR. KELLER: Bone fluorosis or dental
10122 fluorosis?

10123 DR. KLEEREKOPER: Bone fluorosis, crippling
10124 endemic bone fluorosis that Thiosus(?) has published
10125 widely on and many other people have.

10126 DR. SHAPIRO: You are talking about very
10127 high intakes for very long periods of time.

10128 DR. KLEEREKOPER: I understand, but what is

10129 the level of fluoride in the drinking water?

10130 DR. SMITH: Nine to ten and up.

10131 DR. SHAPIRO: You don't know what the level
10132 is, but certainly you are talking eight to ten and
10133 above.

WRONG

10134 DR. KLEEREKOPER: Or are we talking about
10135 four and above?

10136 MR. SMALL: No and you are talking about a
10137 tropical climate largely too.

10138 DR. KLEEREKOPER: I understand that. The
10139 question that we are asking is what is the lowest
10140 level of fluoride in drinking water that has not been
10141 reported to be adverse effect. If you want to define
10142 that in the United States—

10143 DR. VIGORITA: My records show that, at ten
10144 parts per million, if you drink ten liters like that
10145 Indian community did, you may develop crippling
10146 fluorosis. So, the lowest figure that I have access
10147 to from my material is ten, if you drink a lot of
10148 water.

WRONG

10149 DR. CHANIAN: I have here a 1963 by Singe
10150 that says 1.2 to 16.2 milligrams per liter showed
10151 morphological changes.

10152 DR. MARX: Why don't you say for the group
10153 what you just mentioned about those levels from the

1 Donald & Jones
1-7 & 2-6 pm

10154 Indian studies.

10155 DR. SMITH: I was just remarking that the
10156 problem with that literature is that they tell you
10157 that the population lives in an area of the Punjab
10158 where waters contain 1.6 to 15 or 18 or 23 PPM and
10159 you never know what well the guy is using that shows
10160 this.

}
→
wrong

10161 Let me quote you a paper. You were speaking
10162 of '63, was it? This is a paper of '65 by Sabrun(?)
10163 et al. There is only one subject, of course, but he
10164 states that he appears to have been drinking for 43
10165 years water of the concentrations of fluoride from
10166 2.4 to 3.5 PPM. Now, he had polydipsia of unknown
10167 origin, but he did have fluorotic radical myelopathy.

10168 DR. SHAPIRO: I think a possible answer is
10169 we know from the Hodge study, the one I quoted
10170 earlier, that there was no effect at three parts per
10171 million. You know on the other hand that you do get
10172 an effect between four and eight. I think there is
10173 some literature that suggests that.

10174 Around four seems to be the level at which
10175 you don't see anything, based on the available data.

10176 DR. KLEEREKOPER: So, to answer the
10177 question what is the lowest observed effect level,
10178 the answer, of course, is four.

lower than level of 4

10179 DR. SHAPIRO: It could be an adverse effect
10180 in an individual depending on other factors such as
10181 the amount that they are taking in every day, but I
10182 am talking about the development of radiologic
10183 change. That would occur in very small numbers.

10184 DR. KLEEREKOPER: In endemic areas, it
10185 occurs at the level of four.

10186 DR. SHAPIRO: Right.

10187 DR. MARX: For osteosclerosis.

10188 DR. KLEEREKOPER: Endemic fluorosis has
10189 been reported from communities, not in the United
10190 States, but it has been reported in communities
10191 drinking levels as low as four. No one is saying it
10192 is for 43 years with long term studies. That is what
10193 we are talking about and we are talking about people
10194 taking fluoride in drinking water from age zero to
10195 age 103. The reports outside of the United States,
10196 taking everything into consideration, do get
10197 clinically observable adverse effects certainly at
10198 four or above. There are plenty of papers.

10199 I mean, you may say you don't like that
10200 one, but there are other papers that show you do get
10201 that at four.

10202 DR. SPENCER: I don't believe that we can
10203 compare a report in Indian which is a tropical

10204 country where you don't know how much water you take
10205 in, where the nutritional status is very poor, where
10206 they don't have any milk and little meat; therefore,
10207 no calcium, no phosphorus and magnesium and one
10208 cannot compare this to the high fluoride areas in
10209 this country.

10210 DR. SMITH: I think you are going to find
10211 some populations of that sort in this country too.

10212 DR. SPENCER: Then we should see more
10213 pathologic indication of myelopathy and fluorosis in
10214 this country. Why don't we see it in the areas of
10215 four PPM?

10216 DR. SHAPIRO: I think that you have to
10217 conclude that we haven't looked for it and we really
10218 don't know. What we are being driven by in this
10219 argument is that slide of fluoride content in water
10220 because we know that you are dealing with a relative
10221 small number of people. That is a major part of this
10222 and also inadequate data in terms of this.

10223 DR. MARCUS: I think we are going to be
10224 drive by the list of potential effects even further
10225 than we are by the list of well-defined effects. So,
10226 perhaps we should move on with that.

10227 DR. SHAPIRO: Let me restate what Stanley
10228 said though. What Stanley said was he suggested that

10229 we set a level of four parts per million for an adult
10230 population. You want to say over 50 and that might be
10231 kind of hard to work, but at least for an adult
10232 population.

10233 Two parts per million for children and
10234 young adults, as levels at which one would think that
10235 you are approaching a mean level of safety. You still
10236 don't know what is happening at that point, but you
10237 are approaching a mean level of safety.

10238 DR. KLEEREKOPER: That is a totally
10239 impractical suggestion.

10240 DR. SHAPIRO: Why?

10241 DR. KLEEREKOPER: Any family with kids,
10242 which is every community clearly, has to have a two
10243 level.

10244 DR. WALLACH: Then so be it.

10245 DR. SHAPIRO: Is that impractical? In other
10246 words, can you say that, if you have children in your
10247 house up to a certain age, as a primary regulation
10248 the water coming through your facet should not
10249 contain more than two parts per million of fluoride?

10250 DR. COTRUVO: That can be done. The
10251 question of how this is all done is a matter of the
10252 law.

10253 DR. SHAPIRO: We are just looking at the

10254 data and I don't think we have to worry about how
10255 that would be implemented, if one seriously believes
10256 going above that and allowing children to take in
10257 four parts per million would be compromising their
10258 health. Unfortunately, we don't have the answer one
10259 way or the other.

10260 DR. WALLACH: I hate to put this on a
10261 personal level, but how many people here, if they had
10262 a child born today or tomorrow, would want their
10263 child to drink four parts per million for most of
10264 their lives?

10265 DR. KLEEREKOPER: And why would they not
10266 want them to drink four parts per million?

10267 DR. WALLACH: Because of the potential
10268 adverse effects?

10269 DR. KLEEREKOPER: No. Because of
10270 unequivocal expected dental fluorosis, unacceptable.
10271 If you ask me why I don't want my daughter to have
10272 four parts per million, I don't want her to have
10273 Stage III or IV dental fluorosis.

10274 DR. SHAPIRO: What I am talking about is,
10275 if I know I enter toxicity for 15 percent or whatever
10276 it is between four and eight, then I don't know how
10277 you can go above that level because you get into a
10278 range that is potentially toxic for some people,

10279 depending on variables that you can't control.

10280 DR. WALLACH: You would have to have rocks
10281 in your head, in my opinion, to allow your child much
10282 more than two parts per million.

10283 DR. ROWE: I think we all agree on that.

10284 DR. SHAPIRO: How many disagree with
10285 setting a primary standard of four parts for adults
10286 and no more than two parts for children.

10287 DR. MARX: One at a time.

10288 DR. CARLOS: Can we define "adult", the age
10289 of adult?

10290 DR. SHAPIRO: Post-puberty.

10291 DR. MARX: I think Michael and I, at least,
10292 see the age cut-off as a dental issue. There is some
10293 disagreement about that.

10294 DR. MECKLENBURG: In dental areas, the data
10295 is quite variable in this too. More recent studies
10296 now in Texas with 3.8, 3.9, they are showing no
10297 severe fluorosis at all. But there are other places
10298 that were. Only in some studies. Some don't report
10299 any of the higher level, where you know it has to be
10300 or it seems like it has to be, but, if you look
10301 across the range of studies, the confidence interval
10302 in the studies, it appears that you are running on
10303 the range of moderate to severe fluorosis, maybe

10304 showing up a little bit, one percent, two percent.

10305 Optimum, twice optimum, three times optimum. You are
10306 getting up maybe to three or four percent risk.

10307 DR. MARX: Up until what age?

10308 DR. MECKLENBURG: Around six or seven. To
10309 be safe, the Surgeon General said less than age nine,
10310 to have a safety margin.

10311 DR. MARCUS: Even for third molars which
10312 don't come out until--

10313 DR. MARX: That is not cosmetic though.

10314 DR. MECKLENBURG: You see some evidence
10315 back there, but it is not significant in any respect.

10316 DR. KLEEREKOPER: And you don't smile with
10317 your back teeth.

10318 DR. MECKLENBURG: No, you don't smile back
10319 there. This isn't significant.

10320 DR. WALLACH: Shall we say age 14?

10321 DR. MARCUS: Age nine.

10322 DR. REDDI: I think the question that Dr.
10323 Wallach brought up in terms of turn-over, if we are
10324 interested more about the norm, I would say the age
10325 of the closure of the epiphysis which might be more
10326 meaningful and more physiological.

10327 DR. KLEEREKOPER: We have no idea what
10328 happens when you go through the accelerated growth

10329 spurt. We have no idea, if you are talking about
10330 potential toxicity, we have no idea whether it is 18
10331 or puberty. We have no idea.

10332 DR. WALLACH: But the point is being made
10333 that we ought to at least pick a point at which
10334 skeletal turnover begins to slow down.

10335 DR. REDDI: Turnover of the major growth
10336 spurt, at least for clinical parameters, I would say
10337 is the closure of the epiphysis.

10338 DR. WALLACH: Well, while they are not all
10339 closed at 18, most of your epiphyses are closed at
10340 18.

10341 DR. KLEEREKOPER: As long as you are not
10342 hypothyroid.

10343 DR. REDDI: Even in legal matters, I would
10344 say that closure of epiphysis or voting age where the
10345 person decides for himself what is good for him, even
10346 on a legal parameter because now we can decide for
10347 our children. At the age of 18, he will decide how
10348 much fluoride he wants to have.

10349 DR. SHAPIRO: I think there is no data on
10350 that point. I think, if you are talking about a
10351 regulation that has some impact, I think you have to
10352 be very conservative in that.

10353 DR. WALLACH: I know I mentioned every age

10354 under the sun. I guess I will settle with a
10355 recommendation for 18.

10356 DR. SHAPIRO: How many feel it should be
10357 18?

10358 DR. VIGORITA: I would like to make one
10359 comment. I think I would go along with Dr. Reddi. I
10360 mentioned just briefly in the discussion the
10361 skeletally mature individual. If we are concerned
10362 about teeth and bones are really teeth, I think that
10363 is a safe way of going, skeletally mature individual
10364 and that leaves it subject to the pediatrician of
10365 knowing when they are skeletally mature.

10366 MR. SMALL: But it is not the pediatrician;
10367 it is the water department and the medical society
10368 that is going to have to make that decision.

10369 DR. WALLACH: And this may have to be
10370 defended in court.

10371 DR. KLEEREKOPER: This is an aside and it
10372 may be the wrong question to ask. Joe, if we set an
10373 upper limit and you have a fluoridation program--of
10374 course, there are many places having fluoride
10375 added--would you then add fluoride to a level of two
10376 or what factors would you use to determine the level
10377 of fluoride you would add?

10378 DR. COTRUVO: First of all, fluoridation is

10379 voluntary. So, the community decides whether they are
10380 going to fluoridate or not. The amount they add
10381 usually is up to about one milligram per liter
10382 because that is what is listed as the optimal and
10383 that is also economic. When you add two, it costs
10384 twice as much money. So, they generally add up to
10385 one.

10386 So, a number of two and above--well, number
10387 one and above really wouldn't affect that at all.

10388 DR. WALLACH: Two would not conflict with
10389 that?

10390 DR. KLEEREKOPER: So, you do not regulate
10391 what they put in?

10392 DR. COTRUVO: No, as long as they don't put
10393 in more.

10394 DR. SHAPIRO: There were one or two people
10395 interested in 18. How many people are interested in
10396 nine which is the point at which teeth become--

10397 (There was a show of hands.)

10398 DR. SHAPIRO: And how many have any other
10399 recommendations?

10400 DR. MARCUS: I have a recommendation, but I
10401 am very worried about breaking in the ages.

10402 DR. KLEEREKOPER: So am I. I would like to
10403 make a recommendation that, from all the available

10404 data, we can't state that there is no apparent
10405 adverse health effects on a water fluoride level of
10406 two parts per million or below. There may be higher
10407 levels that you can go without adverse effects on
10408 health. That high level may change as a function of
10409 age, but we don't have enough data to recommend at
10410 this stage that a higher level of two parts per
10411 million is safe for all age groups.

10412 DR. SHAPIRO: I think you are being unduly
10413 cautious. I think there is data that allows you to
10414 make--

10415 DR. KLEEREKOPER: At all age groups?

10416 DR. SHAPIRO: Yes, that is my impression.

10417 DR. KLEEREKOPER: Maybe I am unduly
10418 cautious, but--

10419 DR. MARX: Any recommendation we make is
10420 for the time-being. If new data comes up tomorrow,
10421 then the recommendation can be changed.

10422 DR. SHAPIRO: Let me just expand on that.
10423 Is it possible for us to come up with a
10424 recommendation that requests specific studies? Is it
10425 possible to request reevaluation. The law requires it
10426 how frequently?

10427 DR. COTRUVO: Every three years.

10428 DR. SHAPIRO: Every three years. Michael,

10429 the law requires this to go on every three years.

10430 DR. COTRUVO: Not necessarily like this,
10431 but a review every three years.

10432 DR. SHAPIRO: So, is it farfetched for us
10433 to recommend to the EPA that certain studies be
10434 carried out with regard to children?]

10435 DR. COTRUVO: No, that is fine, in addition
10436 to your other recommendations.

10437 DR. SHAPIRO: In addition to our other
10438 recommendations.

10439 DR. KLEEREKOPER: Let me ask again a
10440 practical question. In practical terms, what is
10441 harder for the ODW to look at? A global
10442 recommendation of two or a recommendation of two up to
10443 age nine and four beyond that? Which is a more
10444 difficult situation for you to live with in a
10445 practical sense?

10446 DR. COTRUVO: They are both really okay
10447 and, in fact, the latter is good. It is perfectly
10448 fine to put qualifiers on. It is perfectly fine to
10449 say this is the outside limit that we are talking
10450 about that would protect the whole population;
10451 however, in addition to that, there are certain
10452 individuals who are at less risk or at more risk or
10453 there are certain times in their lives where they

10454 will be at risk. It is perfectly fine to do that.

10455 Now, ultimately, we have to pick a number,
10456 but all of that additional information helps in the
10457 application of that number.

10458 DR. KLEEREKOPER: Let's just say that there
10459 are two options that I can personally live, two
10460 across the board or two up to age nine and four
10461 beyond that.

10462 DR. COTRUVO: Either one of those are okay.

10463 DR. KLEEREKOPER: And easily workable?

10464 DR. COTRUVO: Because, let's suppose, the
10465 two across the board is obvious, but the second
10466 recommendation, two for a certain age group and four
10467 and above for another age group, really says the
10468 standard is really two because there is a large
10469 number of people who are at that age group; however,
10470 if you run into situations where you have segments of
10471 people that don't include the high risk group, you
10472 may be able to deal with that a little differently.
10473 You can be more liberal in the way you apply the
10474 thing. That kind of device is helpful.

10475 DR. MARX: In looking at the system, they
10476 have to go with the two.

10477 DR. MARCUS: In looking at this graph that
10478 was shown on the water content, out of the 5000

10479 communities that were out of compliance, 68 percent
10480 of those, if we set a new level now at two, will be
10481 in compliance. I am not sure that two or three are
10482 substantially different. My own view, I would find
10483 three acceptable. That would take care of another
10484 1000 or 940.

10485 If we say a level of three, it would save
10486 so much money in terms of what would be necessary to
10487 put them into compliance that you could actually get
10488 involved in trying to separate age groups or do
10489 on-site, point of use. You could be dealing with
10490 point of use. You would be dealing with a very small
10491 number of communities in terms of cost efficacy which
10492 I understand we are not necessarily considering here,
10493 but I think a level of three would have a substantial
10494 impact.

10495 Extending that to four wouldn't have much
10496 more impact. So, it would seem to me that we have
10497 already agreed that four is probably not--

10498 DR. COTRUVO: But that is a cost benefit
10499 judgment and a risk-benefit judgment. What we would
10500 ask you to say is what are the consequences of two,
10501 three, four, five.

10502 DR. MARCUS: Four, we all agreed that we
10503 are concerned about. The cost benefit issue wouldn't

10504 be substantial anyway. So, I see no pressure to even
10505 consider four further. I can see some pressures maybe
10506 to consider three.

10507 DR. WALLACH: Three wouldn't protect the
10508 individual with renal insufficiency; it would protect
10509 the polydipsic individual.]

10510 DR. MARX: We are going to have to talk
10511 about special cases.

10512 DR. MARCUS: Do you think two would?

10513 DR. WALLACH: I think two is more likely to
10514 protect--

10515 DR. MARCUS: But, even if we settled at
10516 two, we are still talking about 68 percent of the
10517 problem.

10518 DR. KLEEREKOPER: No, less than 68 percent
10519 of the problem. You have only those communities on
10520 there that are out of compliance.

10521 DR. MARCUS: That is correct. Sixty-eight
10522 percent of the compliance problem is taken care of by
10523 a level of two.

10524 DR. COTRUVO: Some of those are in
10525 compliance because the standard stretches over that
10526 range. Many of those 3000 are in compliance.

10527 DR. KLEEREKOPER: Still, the bigger picture
10528 of 60,000 communities. There are only 1800 of those

10529 60,000 that have a level currently greater than two
10530 parts per million.

10531 Do we really have to have that rider of two
10532 to four for other age groups to take in that 1800
10533 communities? That is really the question I am asking
10534 myself. That is why maybe I am being
10535 over-conservative, but, in the real world, that rider
10536 doesn't serve very much purpose. The people are
10537 unhappy at having a fluoride level with a primary
10538 regulation. They are going to be unhappy no matter
10539 what you say.

10540 DR. WALLACH: It seems to me that we have
10541 three alternatives, as a practical matter, to decide
10542 upon. One is a level of two globally, a level of two
10543 up to age nine, or a level up to age 18. Why don't we
10544 address these three issues and make a decision.

10545 DR. KLEEREKOPER: I would like to make a
10546 recommendation that it is two globally.

10547 DR. SHAPIRO: Okay. There is a
10548 recommendation of two globally. Who is in favor of
10549 that recommendation?

10550 DR. MARX: Can we have a little discussion?
10551 I think that is too restrictive. I think that what we
10552 are supposed to be doing is setting limits for toxic
10553 effects for the general population. Eight is a level

10554 at which the general population doesn't have
10555 problems. I think four gives a limit of safety. I
10556 don't see any reason to be more restrictive than
10557 four.

10558 DR. SHAPIRO: The comment has been made
10559 that we should really talk about adverse rather than
10560 adverse health effects because the health effects are
10561 really minimal. That is a good point.

10562 DR. ROWE: Do you feel that for children
10563 too?

10564 DR. MARX: Right now we are talking about
10565 the general population.

10566 DR. SHAPIRO: All right. Any other
10567 discussion about two global?

10568 (No response.)

10569 DR. SHAPIRO: All right.

10570 DR. KLEEREKOPER: That includes kids.

10571 DR. MARX: I have another objection to two
10572 global. I think, if one considers bringing the level
10573 down that low, I think one should not talk in terms
10574 of a global absolute number, but something more
10575 adjusted for climate where water intake varies as
10576 well.

10577 DR. WALLACH: I think that two across the
10578 board is very restrictive. It is not really

10579 necessary.

10580 DR. KLEEREKOPER: Excuse me, but what is
10581 the current level? When you say this two is
10582 restrictive, what is the current level?

10583 DR. COTRUVO: 1.4 to 2.4.

10584 DR. KLEEREKOPER: So how restrictive is
10585 two?

10586 DR. SHAPIRO: No, that is optimal without
10587 being any trace of dental fluorosis.

10588 DR. KLEEREKOPER: How is that far different
10589 from what you have now?

10590 DR. WALLACH: We are being asked to
10591 reconsider the issue.

10592 DR. MECKLENBURG: You really start seeing
10593 the dental fluorosis that you are concerned about in
10594 moderate to severe once you hit four times. Once you
10595 hit four times and up, then you have a very good
10596 chance of having it. I started to say earlier about
10597 asking the wrong question. It bounces around down in
10598 that list of one or two percent, three percent
10599 through most of these areas, optimum, two times
10600 optimum, three times optimum. When you get four times
10601 optimum, zoom! You know you are going--

10602 DR. WALLACH: So, that is between .7 and
10603 1.2 is optimal.

10604 DR. SHAPIRO: But we are talking about the
10605 limits, four times that of 2.8 and roughly--

10606 DR. KLEEREKOPER: So, I don't see how a
10607 value of two is overly conservative nor overly
10608 different from what is in there now.

10609 DR. WALLACH: Except that the older
10610 population isn't at risk for dental fluorosis.

10611 DR. MECKLENBURG: Once you are past age
10612 eight, you are not at risk for dental fluorosis.

10613 DR. KLEEREKOPER: If we allow a level of
10614 eight, for example, and I am living near an aluminum
10615 or a phosphate plant, now I can contaminate my water
10616 up to a level of eight and be in compliance with the
10617 ODW and not worry about any effects for the large
10618 population that is going to have this? That is what
10619 you are saying.

10620 DR. SHAPIRO: That is what he is telling us
10621 the states are doing. That is making any of this a
10622 secondary regulation because nobody is going to pay
10623 any attention to it.

10624 MR. SMALL: This is your drinking water not
10625 discharge water.

10626 DR. KLEEREKOPER: Nevertheless, levels go
10627 up in areas surrounding--

10628 DR. SHAPIRO: The experience seems to be in

10629 these communities that they ignore it. Is that fair?

10630 DR. COTRUVO: Oh, way up the line, they
10631 don't drink the water. In the lower ends, those that
10632 can easily get into compliance do; those that have to
10633 build something, don't.

10634 DR. SHAPIRO: We differ in this discussion
10635 from the option that voted on levels to protect
10636 against dental fluorosis as a secondary regulation.
10637 We really differ. We are talking about them as a
10638 primary regulation. That is a very different story.

10639 DR. WALLACH: You know, we have kicked this
10640 around a lot. I think we all know the issues involved
10641 and we are going to disagree with each other. I think
10642 we are just going to have to get a consensus.

10643 DR. SHAPIRO: Okay. Do you want to talk
10644 about two up to age 18? Is there any further
10645 discussion required on that?

10646 DR. MARX: What?

10647 DR. SHAPIRO: Two parts per million
10648 standard up to age 18.

10649 DR. MARX: I think what we have to discuss
10650 is some of the concepts though. I think the issue on
10651 this 18 is that some people think that the potential
10652 adverse effect of impaired skeletal maturation is
10653 something to be concerned about and that is why they

10654 are recommending age 18.

10655 I think the real issue is how many people
10656 think that the potential adverse effect on skeletal
10657 maturation should be a concern? If it is a concern,
10658 then one would have to go up to age 18. The question
10659 is how many people think it is a concern and how many
10660 don't?

10661 DR. WALLACH: I feel it is a concern for
10662 two reasons: One, the intrinsic benefits of having
10663 normal maturation in general; the second one has to
10664 do with the presence in the skeleton of the
10665 contaminants that reduce greater maturation, reduce
10666 turn-over in general, if they occur.

10667 It will lead to a greater exposure to
10668 skeleton of noxious elements. There is a whole
10669 radio-biologic effort in England at the present time
10670 to be very concerned with the presence of such things
10671 as plutonium and americium in the animal and human
10672 skeleton.

10673 I asked one of the people in that group, a
10674 fellow named Priest. I said why are you worried about
10675 this? Are you really worried that, if somebody drops
10676 a bomb, there will be enough of us around?

10677 He said there is, in fact, present
10678 contamination of our environment with these elements.

10679 I said give me an example and he said smoke detectors
10680 and there are radio-biologically active contaminants
10681 in our environment that get into our skeletons. They
10682 are all long-lived and, if we don't turn-over our
10683 skeletons at a reasonable rate and get rid of these
10684 things in due course, we have undue and excessive
10685 radiation.

10686 DR. REDDI: Although the levels of fluoride
10687 which were used by Dr. Shupe in his studies are much
10688 higher than what we are discussing now, in his own
10689 studies we saw that there was a clear difference
10690 between when the fluoride was initiated in the young.
10691 They had large amounts.

10692 DR. VIGORITA: I would like to raise a
10693 question. I think we should deal in terms of
10694 physiology and not age limits per se because the
10695 concept I think Dr. Reddi referred to was that the
10696 epiphysis be closed and that the patient be
10697 skeletally mature. That isn't necessarily at age 18.

10698 So, to be physiologic, since we are a group
10699 of scientists, I think we should use those terms and
10700 not numbers. Now, Dr. Mecklenburg referred to nine as
10701 dental maturity in most people. I accept that because
10702 I don't know, but in a skeleton it varies.

10703 DR. SHAPIRO: Let me make another

10704 recommendation to you. That you pick a number that
10705 allows you to have some impact at this point on the
10706 population you think may be most at risk, although
10707 you don't know, and do that with the caveat that it
10708 be studied and that at the time of the next review
10709 this be one of the major considerations in looking at
10710 that number again, insofar as it applies to children.

10711 My own feeling would be that I would go to
10712 nine since the best information you have, at least as
10713 far as teeth are concerned, but I would make it very,
10714 very clear that we know nothing about this issue and
10715 maybe it should be 14, maybe it should be 18. Is
10716 there going to be any global impact of our postponing
10717 this issue for three years or so and the answer is
10718 that I don't think there is.

10719 So, rather than provoke something in an
10720 area that we really have no information on, I would
10721 be a little conservative there, try to protect the
10722 relatively young in terms of a time when I know bone
10723 turn-over is particularly high and I know it is going
10724 to affect the teeth at that point which may have
10725 something to do or may not with what is happening
10726 with bone. I don't know. I can't say because I don't
10727 have the information, but make it is very clear that
10728 that is something I have to look at again.

10729 DR. MARX: We know already that there are
10730 lots of communities in Texas and other parts of the
10731 United States where people have had relatively high
10732 fluoride consumptions throughout their bone growth
10733 and into maturity and the most that has been observed
10734 in those communities so far is a little bit of
10735 osteosclerosis.

10736 DR. SHAPIRO: But you really don't know
10737 that. Maybe they should all be five or six. Maybe
10738 they had Heberden's nodes when they are 40 years old.

10739 MR. HANSON: Maybe I can add something to
10740 that. In Texas, which took a stand on fluoride and
10741 said anything higher than five you had to do
10742 something else, you weren't allowed to drink that
10743 water, and really you aren't seeing any exposure
10744 above five milligrams per liter.

10745 DR. MARX: Not anymore, but at one time
10746 they did.

10747 MR. SMALL: And they did intense medical
10748 examinations.

10749 DR. HUGHES: I would agree with you, except
10750 that I would take the conservative and pick the age
10751 18 or 20, some number, when in most people the
10752 epiphysis is closed until that question can be
10753 answered.

10754 Is there a community in which that question
10755 can be looked at?

10756 DR. MARCUS: I think the Pima Indians are a
10757 good one because they are under constant scrutiny
10758 anyway and they live in a high fluoride area and they
10759 are known in the earlier part of the century to have
10760 a high prevalence of dental fluorosis. My
10761 recollection of the Pima data from Public Health
10762 Service is that, in fact, they are a relatively short
10763 statured group of people.

10764 DR. WALLACH: And they all get diabetes.

10765 DR. MARCUS: There are many confounding
10766 things.

10767 DR. SHAPIRO: Do they have a high incidence
10768 of dental fluorosis?

10769 DR. MECKLENBURG: I am not aware that they
10770 have a high incidence.

10771 DR. MARCUS: There is a book from the PHS
10772 that was published around ten years ago, a nice
10773 hard-bound book that I got when I was here at NIH. It
10774 was sort of a history of fluoridation.

10775 MR. SMALL: Frank McClure's.

10776 DR. MARCUS: That is right and he describes
10777 these country dentists that went around on bule-back
10778 looking in mouths. He said in that book that there

10779 was a high prevalence among the Pima.

10780 DR. KLEEREKOPER: Certainly, nobody would
10781 have any question globally about two. I don't think
10782 anybody would have any concern about two up to age
10783 nine, whether we are allowed to talk about dental
10784 fluorosis or otherwise. Is that reasonable?

10785 DR. MARX: I think we can have a range. I
10786 don't think we have to set an absolute limit because
10787 I think water intake varies, depending on climate.

10788 DR. SHAPIRO: Yes, it depends on other
10789 factors.

10790 DR. MARCUS: Well, we are going to have to
10791 learn to set that range. I am not sure what is the
10792 fudge factor.

10793 DR. KLEEREKOPER: I think everybody is in
10794 agreement including the dental aspects that, after
10795 age nine, four is without harm, both observed or even
10796 potential.

10797 DR. HUGHES: No, I am not in agreement with
10798 that. I am not sure that a ten year old is going to
10799 have no harm from four. I am not sure what it is
10800 going to do to their bone turn-over rate and to the
10801 concerns that have been expressed here.

10802 I think that that data can probably be
10803 gotten by looking at growth curves in children who

10804 were examined in Bartlett, Texas and in North Dakota.
10805 I think that this could be gotten by somebody with a
10806 lot of energy and a lot of time to get at this data.
10807 I am sure it is available in bits and pieces.

10808 DR. ROWE: At bone age of nine, you have
10809 about--I am trying to remember the table--about 60 to
10810 70 percent of your total bone growth. So, you still
10811 have a lot of bone growth left to go at bone age
10812 nine.

10813 DR. SHAPIRO: All right. How many people
10814 feel that 18, picking that one out of the air, is a
10815 more appropriate age at which to run the two parts
10816 per million up to than nine?

10817 (There was a show of hands.)

10818 DR. SHAPIRO: Four, okay.

10819 DR. KLEEREKOPER: I can certainly live with
10820 that.

10821 DR. SPENCER: I believe a study should be
10822 done as suggested and not with Indians, but in areas
10823 like in Texas and in North Dakota and to look at the
10824 growth curves. This is very important. This can be
10825 done and would not take such a long time.

10826 DR. SHAPIRO: How many feel that they would
10827 limit the two parts by primary regulation up to age
10828 nine?

10829 (There was a show of hands.)

10830 DR. WALLACH: I will vote for 18.

10831 DR. SHAPIRO: That made it five. How many
10832 for nine? Who isn't voting? Okay. Eight. The majority
10833 seems to feel that nine would be appropriate at the
10834 moment.

10835 DR. CARLOS: Could we pin down the point
10836 Steve makes? You talked about two times optimum. It
10837 acknowledges that it depends on consumption, not on
10838 presence in the water supply. Furthermore, all recent
10839 fluorosis data are reported in terms of multiples.

10840 DR. SHAPIRO: So, you are suggesting two is
10841 a multiple?

10842 DR. CARLOS: Rather than two milligrams per
10843 liter. Also, it allows a little enabling of the
10844 optimum should that become necessary in the future.

10845 DR. KLEEREKOPER: I am not sure I follow
10846 you.

10847 DR. SHAPIRO: You are saying that two is
10848 the absolute upper limit?

10849 DR. MECKLENBURG: No, no. In dental terms,
10850 if you were talking about two times optimal, because
10851 we know a range, depending upon temperature, would be
10852 .8 or 1.2. Generally, we are always talking in terms
10853 of times the optimum. Instead of saying two parts per

10854 million, it is more sophisticated—

10855 DR. KLEEREKOPER: That is daily ingestion
10856 of fluoride in drinking water.

10857 DR. WALLACH: You are saying four times
10858 optimal.

10859 DR. MECKLENBURG: You are saying two times
10860 optimal. It could be as low as 1.3.

10861 DR. CARLOS: Not ingestion; presence.

10862 DR. SHAPIRO: What we are saying is that we

10863 DR. MARX: What we are saying is that we
10864 want to enforce the current regulation that is the
10865 primary regulation.

10866 DR. SHAPIRO: You say enforce the current
10867 regulation of .7 to 1.2 up to age nine, two times
10868 that, up to age nine and then in comparable terms for
10869 adults over 50. You are talking two times the level
10870 of an upper limit of two.

10871 DR. KLEEREKOPER: Why are we not saying
10872 four times?

10873 DR. SHAPIRO: Four times the optimal.

10874 DR. CARLOS: It doesn't really matter
10875 because we don't know what the sensitive level is
10876 there.

10877 DR. MECKLENBURG: Once you establish that,
10878 then the next thing you do is you are in that guarded

10879 range until you get to a point where you see things
10880 that are an adverse health effect. Then, you are
10881 either talking about ten milligrams per day or 20
10882 milligrams a day or something like that, depending on
10883 what studies you cite. Everything else is in doubt.

10884 DR. KLEEREKOPER: Say that again, Bob?

10885 DR. MECKLENBURG: Isn't your range of
10886 caution then above this two times optimum up to the
10887 point where you actually have evidence?

10888 DR. KLEEREKOPER: Four times optimum up
10889 to--you want us to give--

10890 DR. MECKLENBURG: Your evidence of health
10891 effect begins at ten or eight to ten or 20 to 80,
10892 depending on which studies you are citing. There is
10893 your health effects.

10894 DR. MARX: So, what is the question?

10895 DR. KLEEREKOPER: What margin of safety is
10896 appropriate?

10897 DR. MECKLENBURG: Well, the margin of
10898 safety is essentially above what you just agreed upon
10899 to whatever point you have evidence.

10900 DR. MARCUS: You want us to establish the
10901 grey zone?

10902 DR. MECKLENBURG: That is what you are
10903 doing by establishing those two limits. You have a

10904 grey zone.

10905 DR. KLEEREKOPER: Four to ten.

10906 DR. SHAPIRO: Well, ten times optimal could
10907 clearly--I think everyone would agree--be a hazard.

10908 DR. MECKLENBURG: Ten times the optimal or
10909 ten milligrams per liter?

10910 DR. WALLACH: Ten times optimal. That is
10911 what we treat osteoporosis with. I have to define the
10912 margin of safety, not in terms of dose alone, but in
10913 terms of age at which ingestion begins at a given
10914 level. I don't think that you--I mean, as an example,
10915 older patients are being given ten times optimal now
10916 year in and year out and no one brings us adverse
10917 effects. But I don't think I would then try this in a
10918 five year old, a nine year old or even a 12 year old.

10919 DR. KLEEREKOPER: Or even a healthy person
10920 age 50.

10921 MR. SMALL: I was going to ask you what
10922 would be the effect of that regimen on a normal
10923 healthy person?

10924 DR. KLEEREKOPER: We don't know. We can't
10925 talk to that.

10926 DR. SHAPIRO: What you are going at is that
10927 I think we would say above eight parts per million is
10928 the area in which we cannot protect against an

10954 DR. WALLACH: I think we have already set
10955 the limits.

10956 DR. COTRUVO: I will just read that section
10957 again.

10958 DR. SHAPIRO: Margin of safety.

10959 DR. COTRUVO: "First, known adverse health
10960 effects are compiled; second, whether any adverse
10961 effects can reasonably be anticipated, although not
10962 proven." And then, considering factors of synergism,
10963 exposure, et cetera, et cetera, et cetera.

10964 So, if you can say firmly that the effect
10965 level for the general population is X and then, in
10966 order to extrapolate that, to take into consideration
10967 the possibility that there are higher risk
10968 individuals in the population, the safety factor
10969 should be Y. Then that leads to the final recommended
10970 number for the general population.

10971 DR. SHAPIRO: Well, you don't pull a number
10972 out of the air, say six times the optimal level. Four
10973 times the optimal level is what we would recommend
10974 for adults and six times the optimal level might
10975 bring you into an area where you--

10976 DR. WALLACH: Why don't we say anything
10977 greater than four because we are setting that level
10978 for all other individuals, except under age nine.

10979 DR. SHAPIRO: We could cut it that close. I
10980 just don't know where the truth is. That is what I
10981 don't know.

10982 DR. CARLOS: When you talk about dose, it
10983 would probably make more sense to use milligrams per
10984 liter because "optimal" has no meaning except in the
10985 case of dental fluorosis.

10986 DR. MARX: But the multiplication of
10987 optimal is adjusted for climate and that is why it
10988 would be useful.

10989 DR. CARLOS: Yes, but it only pertains to
10990 dental.

10991 DR. COTRUVO: I think one way around
10992 it--first of all, there are uncertainties on
10993 determining just how much water consumption--you
10994 know, what the average water consumption is in a
10995 particular community.

10996 Now, I am told that diabetics drinks two or
10997 three or four times as much water as the average
10998 person. They are not taken into consideration here.
10999 That is why the uncertainty factor.

11000 So, I would say it is simpler to make your
11001 recommendation based on daily dose and then say in
11002 the application of this it can be considered, the
11003 climate, et cetera, et cetera, can be considered in

11004 the application of this.

11005 DR. SHAPIRO: Were that the case, we would
11006 talk about the four parts per million, four
11007 milligrams per liter and the two and phrase it as you
11008 say which I think is very helpful, that there is an
11009 optimal.

11010 DR. MARX: I think we have a problem with
11011 the lower age range because there we can't say that
11012 we want to have the margin of safety of, say, two to
11013 four-fold because then we get into the range in which
11014 you have therapeutic effects of fluoride for
11015 prophylaxis and dental care. If we were just
11016 handling this as an environmental contaminant, we
11017 could say we begin to see fluorosis at two parts per
11018 million. So, we want a safety factor of four. We
11019 recommend that it be kept below a half a part per
11020 million.

11021 Clearly, we have to make an allowance
11022 there. We can't just talk about safety.

11023 DR. MECKLENBURG: This is inconsistent with
11024 the Surgeon General because, between that two and
11025 four times optimum, we do have a 50 percent increase
11026 in caries protection.

11027 DR. KLEEREKOPER: Do we have to define
11028 "optimum"?

11029 DR. WALLACH: I don't think we are being
11030 asked to give a figure as a multiple for a safety
11031 factor as in radiation doses. I don't think we are
11032 being asked to do that. I think we can define it in
11033 an absolute unit, milligrams per day or parts per
11034 million in drinking water and not say it has to be
11035 ten times this or five times that.

11036 DR. KLEEREKOPER: Could you just clarify
11037 what "optimum" means to you?

11038 DR. MECKLENBURG: "Optimum" means the
11039 protection against caries that doesn't really run any
11040 risk of showing the slightest amount of fluorosis.

11041 DR. KLEEREKOPER: So, our recommendation
11042 for children is twice the optimum.

11043 DR. MECKLENBURG: A lay person generally
11044 wouldn't take a lower range.

11045 DR. KLEEREKOPER: And those optimum levels
11046 have been determined individually for each water
11047 supplier in the United States based on temperature
11048 and climate.

11049 DR. MECKLENBURG: Right.

11050 DR. SHAPIRO: And at twice that optimal
11051 level, you are running morbidity on the order of a
11052 couple percent.

11053 DR. MECKLENBURG: Yes, you are just

11054 beginning to find some clinical fluorosis.

11055 DR. KLEEREKOPER: So, the margin of safety
11056 for—

11057 DR. MECKLENBURG: Four times is where you
11058 would begin to see it.

11059 DR. KLEEREKOPER: So, for children, it
11060 would be four times that and you still allow that you
11061 might have 15 percent, you are saying?

11062 DR. MECKLENBURG: No. I think it is the
11063 other way around. I think optimal is one time. Two
11064 times is the standard and that is where you begin to
11065 see some evidence. Four times, you run a reasonably
11066 strong risk of starting to get into brown stains.

11067 DR. KLEEREKOPER: So, tell me again what
11068 the margin of safety should be for a child up to age
11069 nine?

11070 DR. MECKLENBURG: To avoid any reasonable
11071 chance of fluorosis at all, two times.

11072 DR. SHAPIRO: Why can't we say we see that,
11073 in terms of the available information, as the upper
11074 limit and we don't necessarily think there should be
11075 a margin of safety because we don't know what happens
11076 after that point.

11077 DR. COTRUVO: I think we are interpreting
11078 margin of safety differently. To our mind, a margin

no effect level

11079 of safety is the uncertainty range which one adds on
11080 in the lower direction to insure against the effect
11081 occurring. I mean, you have identified the effect in
11082 an animal population. You add a margin of safety and
11083 say we are going to one-half that or one-tenth that.

11084 DR. HUGHES: We haven't considered renal
11085 failure, for example. That would be something to
11086 consider.

11087 DR. SHAPIRO: I would like to consider that
11088 after lunch. I just want to end this issue and we can
11089 talk about special populations after lunch.

11090 Is it necessary to consider a safety
11091 factor? Can we recommend it as a primary level that
11092 in children up to age nine go no higher than twice
11093 the current recommended level of .7 to 1.2, not
11094 talking about total intake, and for adults four times
11095 the optimal level of .7 to 1.2. That is, everybody
11096 above the age of nine has primary regulations. This
11097 is because of the uncertainties of exceeding those
11098 levels.

11099 DR. COTRUVO: Joe is suggesting that we
11100 give an absolute number rather than four times the
11101 range.

11102 DR. KLEEREKOPER: For adults?

11103 DR. COTRUVO: For all of them.

11104 DR. SHAPIRO: See, the thing you are
11105 getting into is that you are not improving your
11106 accuracy any at that point. You are not making the
11107 statement any firmer. You are just coming up with a
11108 number and you take some prerogative from the local
11109 area, I think, in dealing with it.

11110 DR. COTRUVO: I think it would work the
11111 other way. I think, if there were a number that was
11112 based on daily dose--

11113 DR. SHAPIRO: All right. That number of
11114 2.4--

11115 DR. COTRUVO: Well, whatever the number is.

11116 DR. SHAPIRO: 2.4 as a maximum up to age
11117 nine, right? And then it would go as high as 4.8 up
11118 to a maximum for anyone above the age of nine.

11119 DR. COTRUVO: For adults. Okay, but that is
11120 a very fixed range.

11121 DR. KLEEREKOPER: If you say 2.4 parts per
11122 million as a maximum allowable level, that could
11123 occur in a very hot area with a high level of fluid
11124 intake. Then you have really exceeded what you wanted
11125 to do.

11126 DR. WALLACH: That is what I just said.
11127 That is why I wanted to stay away from the number.

11128 DR. MARX: What Joe asked us to do is give

11129 an absolute number and put in a statement that it
11130 should be adjusted depending on local conditions.

11131 DR. SHAPIRO: Then you can say that
11132 absolute number is one.

11133 MR. SMALL: Why do we want to lose
11134 accuracy?

11135 DR. KLEEREKOPER: What I was saying is you
11136 give an absolute number and then we said the number
11137 is twice currently 1.2. So that is 2.4 and you could
11138 have communities where there is very high
11139 temperature, high humidity and a high fluoride
11140 content with a high water consumption getting much
11141 more fluoride than you want. We are concerned about
11142 total daily fluoride consumption.

11143 DR. SHAPIRO: Mike, they have presumably
11144 calculated that optimal number.

11145 DR. MECKLENBURG: That table has been
11146 accepted for 20 years.

11147 DR. SHAPIRO: Everybody knows that. If you
11148 say twice that, then that is the number, but don't
11149 fix it for everyone.

11150 DR. MARX: If we are going to set the age
11151 zero to nine based on the issue of dental fluorosis,
11152 I don't see any reason why we shouldn't take the
11153 recommendations of the dental panel. What is wrong

11154 with that?

11155 DR. SHAPIRO: That is what we are doing.

11156 DR. MARX: We are discussing whether we
11157 should give an absolute.

11158 DR. WALLACH: There is a well-determined
11159 standard in well-defined terms now. Why don't we just
11160 leave it the way it is and say we are sticking with
11161 the current standard up to age nine and we are
11162 willing to see that standard doubled after that age
11163 and just not change any of the terminology. Every
11164 time you change it you confuse people.

11165 DR. MECKLENBURG: I would like, if you
11166 could, review the statement that we have already have
11167 Dr. Koop sign on page one and two and see if you can
11168 live with that from your knowledge and what you have
11169 heard medically where he recommends an optimal, where
11170 he doesn't recommend over two times optimum and where
11171 he does say that there is no evidence of adverse
11172 health effects in drinking water supplies and then
11173 work out the health effects after lunch.

11174 DR. SHAPIRO: We are saying that up to age
11175 nine.

11176 DR. MARX: No, we are not. The panel is
11177 saying the dental effects are adverse health effects.
11178 The panel right now is saying this should be an

This statement refers to the 1982 S.G. ad hoc comm on dental fluorosis (Albertini, et al) and the NDWAC (Natl. Drinking Water Advisory Council to the EPA). The NDWA had several meetings after 1982.

11179 primary regulation.

11180 DR. SHAPIRO: As far as I can see, we are
11181 saying something very different from what everyone
11182 else has said. In fact, I think we are taking a
11183 somewhat more stringent approach to this.

11184 DR. MARCUS: Dr. Koop says he encourages
11185 communities. That doesn't sound like primary
11186 regulation.

11187 DR. MARX: Because the Dental Panel said it
11188 should not be a primary regulation.

11189 DR. MECKLENBURG: Not on the basis of
11190 dental. Now, if you have evidence in medical--so far,
11191 what I thought you were doing was not trying to make
11192 a dental judgment. I thought you were making a
11193 medical judgment which was fairly consistent with the
11194 dental judgment.

11195 DR. SHAPIRO: We are making a medical
11196 judgment. The medical judgment is that twice the
11197 optimum of .7 to 1.2 for children up to the age of
11198 nine and four times the optimum for individuals above
11199 the age of nine as primary regulation and don't go to
11200 South Carolina.

11201 DR. MARCUS: They will tar and feather you.

11202 DR. SHAPIRO: That is right. Is there any
11203 question about that?

Crippling bone fluorosis

11204 MR. SMALL: Would you review up to age
11205 nine, twice the optimal is guarding against some
11206 adverse health effects? Is that potential or what?

11207 DR. SHAPIRO: Is guarding against an
11208 adverse effect of fluoride up to nine.

11209 MR. SMALL: The law says to be a regulation
11210 it has to be against an adverse health effect,
11211 doesn't it, Jim?

11212 DR. MARX: The adverse effect that we are
11213 concerned with is crippling bone fluorosis.

11214 MR. SMALL: We can't change the law, can
11215 we?

11216 DR. MARX: That is what we voted on. I
11217 thought we voted on that. I think that is what the
11218 vote was that we considered it an adverse health
11219 effect. But I think there is some disagreement on the
11220 panel. Some people think that the childhood level
11221 should be brought up to 18. That is not unanimous.

11222 DR. MARCUS: That is correct.

11223 MR. SMALL: What is the adverse health
11224 effect?

11225 DR. MARCUS: Well, there were several under
11226 consideration, but I think the most powerful ones
11227 were Dr. Wallach's consideration of skeletal
11228 maturation and retention of potential toxicity from

*Cited: Fluoride binding
Plutonium
lead
radiation,
smoke
detectors*

osteosarcoma

11229 the environment.

11230 DR. MARX: That is potential. The adverse
11231 effect is crippling fluorosis and arthralgia. Those
11232 are the things we agreed on.

11233 DR. MARCUS: Maybe we agreed for different
11234 reasons. My vote for that was based on Dr. Wallach's.
11235 Yours may have been based on others, but we all agree
11236 that we voted on that for adverse health reasons.

11237 DR. SHAPIRO: The fact of the matter is
11238 that you included dental disease in your
11239 consideration.

11240 DR. WALLACH: It is also the period of
11241 greatest skeletal turn-over and maturation.

11242 DR. SHAPIRO: John, to answer your
11243 question, the panel understands that there are too
11244 many uncertainties here and, from the available data
11245 and understanding the bone turn-over is not only more
11246 rapid, but that the younger individual is perhaps
11247 more sensitive to the effects of fluoride, it says,
11248 with this uncertainty, we cannot go up to the level
11249 in the adult where we are reasonably certain that, in
11250 an adult bone with slower turn-over, there could be
11251 an adverse effect.

11252 So, in a sense, you are exerting a margin
11253 of safety for the child.

They are arguing as if there were 2
different sets of people - one for children - 9 and
the other for adults. They should be arguing
here

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11254 DR. MARX: I don't agree with that.
11255 DR. MARCUS: Well, we voted on this.
11256 DR. MARX: No, we voted on the margin, but
11257 the reason--

11258 DR. MARCUS: So we had different reasons?

11259 DR. MARX: My reason for voting on the low
11260 margin for age zero to nine is because I accept the
11261 cosmetic effects of dental fluorosis as an adverse
11262 health effect. My reason for taking nine as the
11263 cut-off is because I don't see the skeletal
11264 maturational thing as a recognized adverse effect.

11265 The panel was clearly divided on that
11266 issue. I think there were five people who were not
11267 concerned about the levels we are talking about
11268 causing adverse effects on the skeleton and there
11269 were three people who thought that that was a
11270 problem.

11271 DR. COTRUVO: That may fit into the
11272 sentence which says "must decide whether the effects
11273 may be reasonably anticipated, even though not proven
11274 to occur."

11275 DR. MARCUS: Also, I think it is fairly
11276 close to unanimous that we all agreed that dental
11277 fluorosis problem is, in fact, has medical
11278 ramifications. Almost everybody agreed on that. Not

11279 knowing where bone disease begins at any age, what
11280 you are saying is that ^{if} there is something going on in
11281 the teeth, then the likelihood is that there is
11282 something going on in the bone. You don't know that
11283 it is there; you don't know that it is not there.

11284 DR. MARX: Make a proposal so that we can
11285 vote on it.

11286 DR. SHAPIRO: Let's finalize this by asking
11287 for a vote that, up to age nine, we accept twice the
11288 current recommended levels of .7 to 1.2 and that,
11289 above that age, we accept four times the recommended
11290 level as preventing against adverse effects.

11291 Is there any further discussion?

11292 (No response.)

11293 DR. SHAPIRO: All right. All those in
11294 favor?

11295 (There was a show of hands.)

11296 DR. SHAPIRO: All those opposed?

11297 (There was a show of hands.)

11298 DR. SHAPIRO: Two are opposed. Now, let's
11299 have lunch. It is twenty after. I would like to talk
11300 some more about special groups and then extent to
11301 which we can include in our proposal to the PHS and
11302 the EPA a very strong interest in expanding the
11303 amount of data that is available.

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11304 (Whereupon, the conference adjourned for
11305 lunch, to reconvene at 1:45 p.m..)

11306 * * * AFTERNOON SESSION * * *

11307 - - -

11308 1:45 p.m.

11309 - - -

11310

11311

11312 DR. SHAPIRO: The process, as Joe explains
11313 to me, if we develop a paper--the transcript will be
11314 available in eight days.

11315 DR. KLEEREKOPER: An edited transcript.

11316 DR. SHAPIRO: Yes, sort of. It depends on
11317 how much time I have, but I will certainly distribute
11318 that to anyone or all. It takes a few days to make
11319 sufficient copies. I guess we would have to develop a
11320 report of this to Bob. Is that right?

11321 DR. MECKLENBURG: Yes.

11322 DR. SHAPIRO: To relay to the Surgeon
11323 General who would then--

11324 DR. MECKLENBURG: The basic report will be
11325 in the form of a letter to the Environmental
11326 Protection Agency.

11327 DR. SHAPIRO: Hopefully, with his blessing.
11328 What I will do is, after we get something together, I
11329 will circulate it to all of you and ask that you make
11330 any comments you feel appropriate and then we will

11331 incorporate them. If it looks like there is anything
11332 wildly different, we will send it out again. So, when
11333 it finally goes to the Surgeon General, everyone has
11334 seen it and everyone has had a chance to make any
11335 corrections or modifications.

11336 I thought perhaps we could spend a minute
11337 in any details that you would like to discuss, but
11338 one I would like to bring up is how one includes in a
11339 way likely to be effective a request to do certain
11340 studies, to have EPA take the lead as an agency, for
11341 example, in looking at some of these concerns that we
11342 have, particularly in children or in any others at
11343 the moment.

11344 One that was discussed was the renal
11345 patient who is at risk, but I am not sure of the
11346 dimensions of that problem. But in children I think
11347 we could look at things that might be fairly easy to
11348 get ahold of like age-related height, weight, the EKG
11349 status and whatever else seems necessary.

11350 DR. KLEEREKOPER: Perhaps the best way to
11351 establish the data base would be to go specifically
11352 to those communities you identified that have had
11353 generation exposure to high endemic fluoride levels
11354 and to document what we can in that group and perhaps
11355 try to find a comparable demographic group in a

11356 non-fluoride area. But rather than take a global look
11357 at what potential effects are on kids in Chicago or
11358 Detroit or Palo Alto, I think it would be best to
11359 focus on those that we know for generations have had
11360 high exposure.

11361 DR. SHAPIRO: Clearly, I think you would do
11362 it in those areas where there was natural
11363 fluoridation and that is within the EPA's mandate or
11364 PHS, for that matter.

11365 DR. MARCUS: It would be of interest to
11366 take some modern techniques down to those areas, such
11367 as dual photon absorptometry. You can get a
11368 determination of the incidence of bone mineral
11369 density in both the vertebral spine and appendicular
11370 skeleton and get some other information on general
11371 health.

11372 DR. SHAPIRO: What other special
11373 populations should we be considering?

11374 DR. KLEEREKOPER: What other studies should
11375 be looked at?

11376 DR. SHAPIRO: What are we overlooking?

11377 DR. ROWE: Plutonium levels in the bone,
11378 these toxic things.

11379 DR. MARCUS: Certainly lead.

11380 DR. ROWE: We can make those kinds of

11381 measures now.

11382 DR. KLEEREKOPER: Can you measure total
11383 body fluoride, calcium?

11384 DR. SHAPIRO: I am not sure how you do
11385 that. I would assume you would use something like
11386 neutron activation or something.

11387 MR. SMALL: How do you look at children's
11388 cell maturation? Is this by hand x-ray or by some
11389 other method?

11390 DR. KLEEREKOPER: X-rays would be
11391 inappropriate.

11392 MR. SMALL: Epidemiologically or
11393 clinically?

11394 DR. SHAPIRO: You could look at wrist bones
11395 and measure maturation.

11396 MR. SMALL: Would this involve parental
11397 consent and all that good stuff?

11398 DR. SHAPIRO: You could get it. Usually we
11399 get it, I think.

11400 DR. SHUPE: I was going to say one thing we
11401 observed clinically in a bunch of animals in the
11402 field was that, on a given level of intake that we
11403 were measuring and knew they were taking in, we
11404 anticipated a number three tooth, but these animals
11405 that were on high molybdenum--there were some areas

11406 out there with high molybdenum--you would usually
11407 find a number four tooth with a little more
11408 deposition of fluoride in the bone. Those were some
11409 animals clinically in an area where they had elevated
11410 levels of molybdenum in the vegetation.

11411 DR. MARCUS: Would it be useful to trap
11412 small animals in various locales and examine their
11413 teeth?

11414 DR. SHUPE: Some of the animals you are
11415 thinking of, their teeth erupt continuously. They are
11416 constantly erupting. They are different than the
11417 herbivores and the horses in that.

11418 Now, there was a fellow who has since
11419 passed away that did quite a bit of trapping of
11420 animals around the country and I don't know how
11421 meaningful this information was, but anyway these
11422 animals do tell you a lot like on lead poisoning and
11423 a lot of these other different things.

11424 DR. OHANIAN: Talking about well water, it
11425 is not clear how relevant some of this was.

11426 DR. KLEEREKOPER: The dentists have done a
11427 lot of field work in several communities, looking and
11428 grading teeth. In any of those studies, did anybody
11429 look at anything else and could one identify from the
11430 work that has been done the children who have got

11431 Stage III dental fluorosis and those with Stage IV or
11432 were just numbers looked at?

11433 DR. CARLOS: Well, the various periods of
11434 dental fluorosis, of course, were, but do you mean
11435 other medical concerns?

11436 DR. KLEEREKOPER: Did anybody ask any other
11437 questions of the kids? Thousands of kids have been
11438 studied, have they not, in epidemiologic studies.

11439 DR. CARLOS: Well, there have only been a
11440 few recently. These are listed in one of the
11441 documents. So, it would be a few thousand children in
11442 Illinois and Texas mostly and Carolina.

11443 DR. KLEEREKOPER: Were there any medical
11444 questionnaires?

11445 DR. CARLOS: Not that I know of.

11446 DR. KLEEREKOPER: So it was just "show me
11447 your teeth"? Is that what it was?

11448 DR. CARLOS: As far as I know.

11449 MR. SMALL: There question was asked about
11450 whether they had used fluoride supplements or whether
11451 they took vitamins with fluoride in their early days
11452 and that sort of thing.

11453 DR. KLEEREKOPER: And those children who
11454 were identified in the Illinois study as having Stage
11455 III or IV fluorosis are they identifiable?

NTP

11456 DR. CARLOS: Yes, the children are
11457 identifiable. Yes, they could be studied.
11458 DR. SHAPIRO: Do you have rosters of those
11459 children?
11460 DR. CARLOS: Yes.
11461 DR. KLEEREKOPER: That may be something to
11462 look at.
11463 DR. CARLOS: There are very few in number,
11464 of course.
11465 DR. KELLER: The National Toxicology
11466 Program currently has sodium ^{FLUORIDE} chloride tests, chronic
11467 toxicity study phase. They are due to be sacrificed
11468 in December of this year. I just checked on this
11469 yesterday. This is rats. It may be mice.
11470 DR. MARCUS: I was afraid you meant the
11471 kids in Illinois.
11472 DR. SHAPIRO: Were there different feeding
11473 levels?
11474 DR. KELLER: They have some protocols for
11475 getting the "no effect" and "subtoxic effect."
11476 DR. KLEEREKOPER: Jim has done a superb
11477 animal toxicology study and you know what it does to
11478 animals.
11479 DR. SHAPIRO: These were cancer.
11480 DR. KELLER: That is one of the end points.

11481 of course, but I am not certain that it is the only
11482 one in this case.

11483 MR. SMALL: Mutagenesis also.

11484 DR. SPENCER: I would like to ask, in those
11485 children who develop dental fluorosis and only a
11486 certain percentage in high fluoride areas have
11487 developed it, is there anything known about their
11488 nutritional status and about their intake of calcium,
11489 phosphorus and magnesium?

11490 DR. CARLOS: We don't have that, no.

11491 DR. KLEEREKOPER: That is one of the
11492 studies we could recommend they do.

11493 DR. SHAPIRO: Well, are there any other
11494 issues that we should consider? Joe, are there things
11495 that we ought to do that we haven't done yet?

11496 DR. COTRUVO: No, I don't think so.

11497 DR. SMITH: Well, you mentioned the renal
11498 group and many causes of polydipsia ought to be
11499 looked at.

11500 DR. KLEEREKOPER: Some of the renal work
11501 has been looked at. Patients with renal disease are
11502 at risk for developing bone disease. People have done
11503 studies on the effect of fluoride in the water to
11504 bone disease that patients with renal failure get.
11505 Essentially, they came out as negative studies. There

11506 were no ill effects from adding to the water.

11507 The other question, whether fluoride causes
11508 renal disease, is not known.

11509 DR. SHAPIRO: I am talking about the
11510 progressive storage of fluoride in patients with
11511 renal disease in high fluoride areas.

11512 MR. SMALL: Well, in dealing with total
11513 renal failure and dialysis, there have been
11514 recommendations made by the national group that the
11515 water be completely de-ionized for dialysis and that
11516 a unit be included for this purpose, reverse osmosis,
11517 to complete de-ionization.

11518 In fact, I know only one, Maryland, has
11519 since issued a regulation legally requiring that
11520 procedure in dialysis. That is becoming a little moot
11521 as far as fluoride. In extracting all of the other
11522 elements, the fluoride goes out, 96 or 97 percent.

11523 DR. COTRUVO: The limit is one-tenth a
11524 milligram.

11525 MR. SMALL: .2

11526 DR. COTRUVO: Two-tenths.

11527 DR. KLEEREKOPER: But their recommendation
11528 was not based on the adverse effects of fluoride, but
11529 rather on the other elements.

11530 MR. SMALL: There was a question about

11531 fluoride, but there were other things thought more
11532 important.

11533 DR. MARCUS: In Maryland, they had that
11534 accident. That is probably what drove that.

11535 MR. SMALL: Aluminum was the first concern. →

11536 DR. HUGHES: But there are no *see insert*
11537 recommendations standing with regard to renal failure
11538 short of dialysis patients?

11539 MR. SMALL: No, not that I know of.

11540 DR. MARCUS: Well, I expressed some concern
11541 yesterday about older people who have diminishing
11542 GFR, but I am satisfied as of today that concerns
11543 about the added fluoride burden that that might
11544 potentially have in older people is really trivial.

11545 DR. ROWE: As long as you keep it at four.

11546 DR. MARCUS: Yes.

11547 DR. ROWE: In people who have polydypsⁱpsia,
11548 diabetics maybe, certainly people with DI, diabetes
11549 insipidus, again there is a very small number, though
11550 they do exist. Once in a while, you will see a whole
11551 family that has it and they don't realize it and they
11552 are drinking ten liters a day of water.

11553 DR. MARX: If they aren't diagnosed, you
11554 aren't going to be able to do anything about it.

11555 DR. ROWE: They exist, but it is very

11556 small.

11557 DR. KLEEREKOPER: There is one group of
11558 patients that I recommend and I guess most people
11559 recommend a very high fluid intake is the kidney
11560 stone population which probably has a high prevalence
11561 in the community with diabetes insipidus. It may be
11562 high in diabetes mellitus, but that is the group that
11563 maybe worth looking at.

11564 To my knowledge, all the recommendations to
11565 increase fluid intake are associated with a decrease
11566 in the incidence of nephrophthisis and I can't
11567 imagine it is going to have any adverse effect.

11568 DR. WALLACH: Right, except for the
11569 hyperoxyluric patients, it is unusual for children to
11570 form kidney stones. Most kidney stone formers are
11571 adults.

11572 DR. KLEEREKOPER: We are talking about the
11573 potential harmful effects from increasing fluid
11574 consumption.

11575 DR. WALLACH: Yes, but the point is that
11576 these are adults with dangers of high fluoride intake
11577 are smaller to begin with.

11578 DR. SHAPIRO: Well, if the adult is living
11579 in a community where fluoride level in the water is
11580 allowed to be up around four, I don't think we would

11581 want to see them taking four liters of fluid.]

11582 DR. KLEEREKOPER: That is a potential group
11583 at risk.

11584 DR. SHAPIRO: Well, if there are no other
11585 matters to discuss, I think we can adjourn the
11586 meeting, certainly with my thanks for your coming
11587 here and wrestling with this very, very difficult
11588 problem.

11589 It may be that we have helped the EPA. It
11590 may be that we will have 16 states down on our necks.
11591 Not only are we not throwing out what they wanted,
11592 but we are telling them that they have to go back and
11593 make some special arrangement for children as a
11594 matter of regulation which they didn't anticipate
11595 doing. That should set up a bit of a howl.

11596 What is your process. When should we start
11597 to get some feedback? As soon as the Surgeon General
11598 accepts what we have said? What if he doesn't accept
11599 it? Do we have to convene again?

11600 DR. MECKLENBURG: Probably.

11601 DR. KLEEREKOPER: How likely is that, Bob?

11602 DR. ROWE: He is a surgeon.

11603 DR. MECKLENBURG: I think he will very
11604 serious consider what this committee has said. You
11605 really brought in the best information available. It

11606 would have to be extremely seriously considered.

11607 DR. SHAPIRO: As a pediatrician, I don't
11608 think you could argue with tightening up the rules to
11609 protect children. I can't imagine a political
11610 question that would compromise our recommendation.

11611 DR. MARX: What are you planning to say to
11612 address this question that some people have expressed
11613 a concern about skeletal maturation?

11614 DR. SHAPIRO: What I will do is report the
11615 fact that it was not unanimous within the committee,
11616 that there would be some recommendation framed in the
11617 letter as regards to the need for additional study in
11618 populations at risk so that there is a better answer
11619 three years hence when this might again be up for
11620 consideration.

11621 DR. MARX: I have a question that, before
11622 this is in final form, that you circulate a draft.

11623 DR. SHAPIRO: Oh, I said that earlier.

11624 DR. WALLACH: You will put cardiovascular
11625 and skeletal turn-over studies in this?

11626 DR. SHAPIRO: Yes, I think there are some
11627 things we simply don't know. I think having some idea
11628 of how these things are accepted from a regulatory
11629 standpoint, the recommendation will stand alone. We
11630 can accomplish these other things. That is something

11631 else, but you are really going in with a
11632 recommendation that is not necessarily linked to have
11633 that information.

11634 DR. MARCUS: I would like to establish
11635 another point which I think is important in terms of
11636 how somebody who might be not on this committee would
11637 read the report because it would seem to me that
11638 there would be two options, depending on how the
11639 report were written.

11640 One would be that the committee was very
11641 concerned about potential hazards associated with
11642 fluoride and we singled out a group of individuals,
11643 that is children below the age of nine, for special,
11644 additional protection and I can see that somebody who
11645 might be on the outside fluoridation lobby would use
11646 that as food for his fodder.

11647 On the other hand, another interpretation
11648 could be, depending on how it was written, that this
11649 committee was by and large unimpressed by real
11650 dangers associated with fluoride. We are being fairly
11651 cautious with children, but we are actually relaxing
11652 our concerns about everybody above the age of nine or
11653 people whose teeth have already erupted.

11654 My impression from talking with most of the
11655 people around the room is that the second case is a

11656 more accurate representation of the views of this
11657 committee and I think it would be a very good idea to
11658 formulate whatever the conclusions are in a way that
11659 could not be used like what happened in that
11660 newspaper article.

11661 DR. KLEEREKOPER: One way to do that would
11662 be to say what a lot of us have said, that we regard
11663 dental fluorosis in the Stage III level as an adverse
11664 health effect and that is what the regulation has
11665 been aimed to prevent. That is really what we have
11666 done.

11667 DR. WALLACH: Not all of us are saying that
11668 age nine is a good cut-off point.

11669 DR. MARCUS: I understand that.

11670 DR. SHAPIRO: It is easier to equivocate
11671 around that than it is with what the committee that
11672 framed these options before us did. They said they
11673 couldn't choose between four and eight. I think we
11674 have made a better decision.

11675 DR. CARLOS: I think it might be well worth
11676 considering how you phrase the recommendation, the
11677 rationale for the recommendation very carefully in
11678 terms of potential adverse effect.

11679 The reason is that we have on record the
11680 Surgeon General, the American Medical Association,

11681 the American Dental Association all saying that there
11682 is no adverse health effect.

11683 I think, in the case of dental fluorosis,
11684 we can't find any data to the contrary; however, I
11685 certainly accept and I think most people do that
11686 there may well be and we just haven't found it yet
11687 and that would be true of the other things you are
11688 speaking of as well. It is potential.

11689 DR. MARCUS: I don't think that is the
11690 sense of the committee. I think that the sense of the
11691 committee is that the cosmetic effect represents an
11692 adverse health effect, that this is psychologically
11693 damaging. People walk around covering their mouths.

11694 DR. SHAPIRO: I think the Surgeon General
11695 left a big loophole, frankly, when he raised this
11696 cosmetic issue. I think he, in effect, was saying
11697 there is still some room for doubt as to whether what
11698 we are saying is the best really that can be said.

11699 DR. CARLOS: There is more study needed in
11700 the matter.

11701 DR. SHAPIRO: That is right and I would
11702 seize on that, expressing the concern of the
11703 committee that we don't have all the answers.

11704 DR. CARLOS: The concentration of research
11705 has really been around optimal levels.

11706 DR. COTRUVO: The previous Surgeon General
11707 was even stronger on that subject.

11708 DR. SHAPIRO: On what subject?

11709 DR. COTRUVO: Of the psychological effects
11710 resulting from cosmetic.

11711 DR. SHAPIRO: Did you write anything on
11712 that?

11713 DR. COTRUVO: Yes.

11714 DR. SHAPIRO: Could you get that to us so
11715 we could take a look at it?

11716 DR. COTRUVO: Yes.

11717 DR. CARLOS: It is all very well to say
11718 that you think that may be the case and I am not
11719 arguing that, but we have no data, not a shred. What
11720 I am concerned with is that we will come into
11721 conflict with statements that are already in the
11722 public record without any data on which to base the
11723 conflict.

11724 I think we can get around the whole thing
11725 by saying there is substantial belief that there are
11726 potential health effects, psychological, structural,
11727 functional, whatever and this may turn out to be the
11728 case.

11729 DR. SHAPIRO: I think everyone would agree.

11730 DR. MARCUS: The word "potential" is often

731 interpreted by lay audiences to mean "likely" or
732 "probably."

733 MR. SMALL: That is why I was saying it is
734 too strong.

735 DR. KLEEREKOPER: It is still less than
736 what I feel is going to be potentially the real
737 adverse effect.

738 MR. SMALL: I think there is a skeletal
739 maturation problem. "Potential" is a strong word for
740 that.

741 DR. KLEEREKOPER: But the skeletal
742 maturation thing is really a gut reaction. There is
743 really no evidence to support that or substantiate
744 it. I don't think.

745 MR. SMALL: You can call it potential, but
746 there is no evidence.

747 DR. MARX: This is a term that the EPA has
748 defined. They are asking what are the potential
749 effects. They have defined the term. So, we are left
750 with their terminology.

751 DR. COTRUVO: No, it is defined in the law.

752 DR. MARX: Right, it is defined in the
753 regulation.

754 DR. SHAPIRO: What is the largest city you
755 would fine--is it Bartlett or Lubbock or some place

11756 where--

11757 MR. HANSON: High levels?

11758 DR. SHAPIRO: Yes, very high levels where
11759 you could really start to look in a prospective
11760 manner at bones from a children's hospital.

11761 MR. HANSON: Myrtle Beach, South Carolina.

11762 DR. KLEEREKOPER: I will take three months
11763 sabbatical and do that.

11764 DR. MARX: If we put in the word
11765 "potential", does that take this out of the
11766 possibility of primary regulation? A primary
11767 regulation can be made for the potential?

11768 MR. SMALL: Potential adverse effect is
11769 sufficient for a primary regulation.

11770 DR. SHAPIRO: "The Administrator must
11771 decide whether any adverse effects can be reasonably
11772 anticipated even though not proved to exist."

11773 Okay. If there are no other questions.

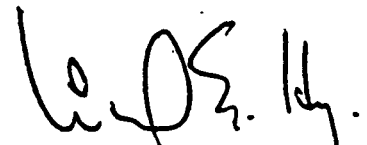
11774 Thank you.

11775 (Whereupon, at 2:45, on April 19, 1983,
11776 the hearing adjourned.)

*** C E R T I F I C A T E ***

This is to certify that this is a true and accurate verbatim transcription of the proceedings in the matter of a meeting of the Fluoride Panel which took place at 9:00 a.m., on April 18-19, 1983, in Conference Rm. 2C116 of the Clinical Center, National Institutes of Health, Main Campus, Bethesda, Maryland.

STENOTECH, INC.



Michael E. Hyer

President

ORIGINAL