KI and Thyroid Cancer
What we’ve learned since 2001

Patricia A. Milligan, CHP, RPh
Senior Technical Advisor
Division of Preparedness & Response
Office of Nuclear Security and Incident Response
US Nuclear Regulatory Commission
KI & Thyroid Cancer

• We’ve learned a lot…
  – Radiation induced thyroid cancers have distinct genetic fingerprints
  – Ingestion was the important route of exposure at Chernobyl
  – Iodine sufficiency status of thyroid gland is significant in development of thyroid disease
  – Thyroid cancer incidence appears to be increasing world wide
• And we still have a lot of questions…
Reactor Accidents

- Windscale 1957
- TMI Unit 2 1979
- Chernobyl 1986
- Fukushima 2011
Windscale 1957

- Nuclear reactor fire at Sellafield, UK
  - October 1957
  - 20,000 Ci of $^{131}$I released
  - Impacted counties in northwest England (Cumbria, Lancashire)

- **Prompt ban of milk** originating in an area of about 200 square miles for over a month
  - Reduced risk to population of thyroid cancer

- **Predicted ~260 excess thyroid cancers**, no significant increase has been observed
  - excess cases were predicted to occur at ~6.5 per year
  - expected natural incidence in UK > 600 per year
Three Mile Island
Unit 2

• March 1979 reactor was operating at 97% power
• Noble gases released ~10 million curies
• Iodine releases virtually nonexistent
  – estimated to be about 15 curies
  – no iodine found in environment
• Maximum dose to member of public closest to site ~85 mrem
• No thyroid doses
Chernobyl

- Reactor accident April 1986
- ~46 million curies of I-131 released from Chernobyl
- Limited protective measures were taken for population
  - Towns closest to reactor were evacuated
  - No protective actions implemented for milk, food in the days following the accident
Chernobyl

• Unexpected rise in thyroid cancers occurred about 5 years after the accident
  – Expected latency period ~30 years
  – Challenged the understanding of radioactive iodine and thyroid cancer

• ~6,000 cases of thyroid cancers in people who were under the age of 18 at the time of the accident
  – 15 fatal thyroid cancers (as of 2010)
Chernobyl

• Thyroid cancers attributed to ingestion of contaminated milk for days/weeks after the accident and iodine insufficiency of the pediatric population
  – World Health Organization
    • “Since radioactive iodine is short lived, if people had stopped giving locally supplied contaminated milk to children for a few months following the accident, it is likely that most of the increase in radiation-induced thyroid cancer would not have resulted”
World Health Organization

- Updated iodine prophylaxis guidelines in 1999 to reflect the state of knowledge to date regarding thyroid cancer and radioactive iodine based on Chernobyl
  - 10 mGy (1 rad) avertable thyroid dose up to 18 years old, pregnant & lactating women
  - 100 mGy (10 rad) avertable thyroid dose under 40 years of age
  - 5 Gy (500 rad) projected thyroid dose over 40
- Short latency time and number of children impacted suggested the understanding of thyroid sensitivity/biological models of cancer induction not well understood
World Health Organization

• After Chernobyl accident thyroid doses to thousands of children were several Gy (1 Gy = 100 Rad)
• However most of the children who developed thyroid cancer had estimated thyroid dose of less than 300 mGy (30 Rad)
• Excess thyroid cancer incidence seen in areas where dose to the thyroid in children was estimated at 50–100 mGy (5-10 Rad)
• Intense medical monitoring resulted in detection of thyroid cancers at a sub-clinical level; added to the overall increase of thyroid cancer numbers
Food and Drug Administration

• Issued updated iodine prophylaxis guidelines in 2001
  – 5 rad projected thyroid dose up to 18 years old, pregnant and lactating women
  – 10 rad projected thyroid dose 18-40 years old
  – 500 rad projected thyroid dose over 40
NRC KI Program

• Rule change in Jan 2001 based on Chernobyl data
• Over 48 million tablets distributed to requesting states to date
Chernobyl
20+ years later

• Ongoing studies point to serious iodine deficiency and failure of protective actions for ingestion as the cause of the increased thyroid cancers in children

• Genomic changes in DNA identified in tumors of 26 children with thyroid cancer from Chernobyl
  – “What’s really remarkable is that in every single one of these cases, we were able to find the driver mutation — the actual genetic change that caused the cancer,”
    Dr. James Fagin, Memorial Sloan Kettering Cancer Center
Fukushima

– Reactor accident March 2011
– ~4.5 million curies of I-131 released
– **Protective measures** were promptly implemented for population
  • Populations were evacuated and sheltered in place based on risk
  • Environmental sampling and subsequent food restrictions implemented in the days following the accident
Lessons from Fukushima
KI Use

• Use of KI was not implemented uniformly
• Most, if not all, areas populations were already evacuated when KI decisions were made
  – Very little KI was administered to the population- anecdotal use of KI
• Prompt interdiction of food/milk/water prevented uptakes
Lessons from Fukushima

**KI Use**

- Thyroid doses very low amongst the pediatric population
  - <0.1 rad - ~10 rad upper bound
  - No increases in thyroid nodules or other evidence of thyroid disease
  - Extensive testing has revealed a higher rate of thyroid nodules in the pediatric population of Japan than expected
    - Control prefectures have similar rates as exposed prefectures
Claims of thyroid cancer after Fukushima

- Some researchers claiming increases in thyroid cancer in children exposed to Fukushima radiation
- Comparisons with control populations show that the Fukushima child thyroid cancer frequencies are consistent
  - 41.2% Fukushima children with detectible nodules/cysts; the combined percentage found in the three control prefectures was 56.6%.
  - 0.6% Fukushima children with the anomalies met additional testing criteria, other prefectures had a rate of over 1%. 
Claims of thyroid cancer after Fukushima

• Important study findings:
  – Child thyroid anomalies first detected in Fukushima Prefecture have been occurring quite normally across the entire country, but had gone largely unnoticed before the national screenings of 2102-13.
  – Tumor biopsies have found no indication of radiogenic origins and most have indications of adult thyroid tumors.
Are Thyroid Cancer Rates Increasing World-Wide?

• In the last decades thyroid cancer incidence has continuously and sharply increased all over the world
  – Some experts attribute increased incidence of thyroid cancer to the increased detection of small cancers in the preclinical stage
  – Some experts believe the data suggests a true increase above the increased detection
  – Some “experts” attribute increase to nuclear power
  – Mostly likely due to a combination of more sensitive diagnostic procedures and of a true increase due to increased exposure to medical radiation, increase in stable iodine uptake and possible other environmental factors
World Health Organization

- Updating the 1999 guidelines on iodine blocking therapy
- Considering health data from Chernobyl and Fukushima
- Conducted a survey of member countries on iodine blocking therapy for public health uses
- Extensive literature search
ITB Evidence-to-Recommendation matrix

Evidence to Recommendation framework

Should KI be administered vs. not administered to people exposed to radionuclide release in the environment in the setting of radiological or nuclear emergency?

Population: People exposed to radionuclide release in the environment
Intervention: KI administration
Comparison: No KI administration
Setting: radiological or nuclear emergency
Perspective: public health

Subgroup considerations: children and adolescents 0-18, pregnant and breast-feeding women, elderly

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>JUDGEMENTS</th>
<th>RESEARCH EVIDENCE</th>
<th>ADDITIONAL CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the problem a priority?</td>
<td>No</td>
<td>Probably No</td>
<td>Uncertain</td>
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Factors determining strength of recommendation

• Priority of the problem
• Quality of evidence
• Balance of benefits and harms
• Values and preferences
• Resource use
• Equity
• Feasibility
• Acceptability

All these factors must be included in the process of deriving recommendations
<table>
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<tr>
<td>How large are the resource requirements?</td>
<td>Large costs</td>
<td>Kenigsberg's paper on Chemobyl KI costs – in Russian (ZC to check)</td>
<td>Resources: KI stockpile acquisition, disposal and renewal, storage, education for public and healthcare providers, communication campaign, logistics of distribution/pre-distribution. Saved costs: thyca management.</td>
</tr>
<tr>
<td>How large is the incremental cost relative to the net benefit?</td>
<td>Very large</td>
<td>No actual evidence (check Kenigsberg paper)</td>
<td>Here judgement applies to the stockpiling/supply of KI, rather than administering KI, as latter requires to have a stockpile in place. Considering risk of a severe nuclear accident 1 in 10,000 reactor-year (LvB – ref), the cost-effectiveness of KITB may be low. From a health policy maker's perspective, KITB cost-effectiveness may be higher, since KI costs is low.</td>
</tr>
<tr>
<td>What would be the impact on health inequities?</td>
<td>Increased</td>
<td>No actual evidence</td>
<td>The issue relates to pre-distribution choice, which varies from country to country. Pre-distribution is not explicitly included in the scope of this guideline, however, having a comprehensive national program on EPR planning would lead to increased equity.</td>
</tr>
<tr>
<td>Is the option acceptable to key stakeholders?</td>
<td>No</td>
<td>No actual evidence</td>
<td>Stakeholders: policymakers, emergency response agencies, public, healthcare professionals, nuclear operators, nuclear safety authorities, radiation protection authorities, researchers, academia, KI manufacturers, risk communicators, etc.</td>
</tr>
<tr>
<td>Is the option feasible to implement?</td>
<td>No</td>
<td>Polish evidence Fukushima experience?</td>
<td>In general, KI is easy available, has a low cost, long shelf life, and national KITB policies/programs already established in many countries. However, variation in national policies on KI stockpiling and distribution represent a challenge.</td>
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</tbody>
</table>
### Recommendation

The panel suggests to administer KI over not administer KI to people exposed to radiiodine release in the environment in the setting of radiological or nuclear emergency (Conditional recommendation; Very low quality)

#### Key considerations:
- KITB should be implemented as a component of comprehensive public health approach in combination with other protection actions (evacuation and sheltering, restriction of contaminated food and drinking water consumption). KITB should not be considered as a single alternative.
- Provisions for KITB implementation need to be carefully considered at the planning stage (see implementation considerations below).
- Optimal timing of administration starts 24 hours prior to, and up to 2 hours after the expected onset of exposure. It would still be reasonable to administer KITB up to 8 hours after the estimated onset of exposure.
- Starting KITB later than 24 hours following the exposure may carry more harms then benefit (by prolonging the biological half-life of radioactive iodine in the thyroid).
- Single KI administration is typically sufficient. However, in the case of prolonged (beyond 24 hours) or repeated exposure, and unavoidable ingestion of contaminated food and water, and when evacuation is not feasible, consider repeated administration of KI. Neonates should not receive repeated KI.

#### Justification

There is well-documented evidence from various sources (epidemiological, experimental, pathophysiological, clinical, etc.) pointing to more benefits than harms of KITB.

#### Subgroup considerations
- Individuals most likely to benefit include children, adolescents, pregnant and breastfeeding women, and those living in iodine deficiency areas.
- Individuals older than 40, are less likely to benefit from KITB.
- Neonates and elderly are at higher risk of adverse health effects of KI.
- Individuals exposed to high dose (e.g., emergency workers) are likely to benefit from KITB irrespective of age.
Key considerations for the recommendation on ITB

- ITB should be implemented as a component of comprehensive public health approach in combination with other protection actions (evacuation and sheltering, restriction of contaminated food and drinking water consumption). ITB should not be considered as a single alternative.

- Provisions for ITB implementation need to be carefully considered at the planning stage (see implementation considerations below).

- Optimal timing of administration starts 24 hours prior to, and up to 2 hours after the expected onset of exposure. It would still be reasonable to administer KITB up to 8 hours after the estimated onset of exposure.

- Starting ITB later than 24 hours following the exposure may carry more harms then benefit (by prolonging the biological half-life of radioactive iodine in the thyroid).

- Single KI administration is typically sufficient. However, in the case of prolonged (beyond 24 hours) or repeated exposure, and unavoidable ingestion of contaminated food and water, and when evacuation is not feasible, consider repeated administration of KI. Neonates should not receive repeated KI.
Key considerations for the recommendation on ITB

Sensitive subgroups:

• Individuals most likely to benefit include children, adolescents, pregnant and breast-feeding women, and those living in iodine deficiency areas.
• Individuals older than 40, are less likely to benefit from ITB.
• Neonates and elderly are at higher risk of adverse health effects of KI
• Individuals exposed to high dose (e.g., emergency workers) are likely to benefit from ITB irrespective of age.
KI

- KI is part of the range of protective actions in most countries
- Distribution plans vary widely; some countries have limited distribution (within plume exposure pathway) and other countries distribute at great distances from nuclear power plants
- Challenges to public health officials to get KI distributed in timely manner
Question

What is the right role for KI to play as part of nuclear power plant protective actions?
Thank you

Questions?

Contact information:
Patricia Milligan
301-287-3739
Patricia.milligan@nrc.gov