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Comic

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GRAPHIC MEDICINE REVIEW

The Alcohol Flush Response

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Abstract

Nearly 540 million people world-wide have facial flushing and an increased heart rate after consuming alcohol. Known as the alcohol flushing response, this reaction to alcohol is a result of a genetic variant in an enzyme aldehyde dehydrogenase 2 (ALDH2), known as ALDH2*2. Mainly carried by those of East Asian descent, the genetic variant is likely the most common genetic variant carried in the world. Carrying this ALDH2*2 genetic variant has important health implications with respect cancer risk which is increased when carriers of the ALDH2*2 genetic variant frequently use of alcohol or tobacco products. This comic explains the alcohol flush response and the health risks associated with alcohol and tobacco use for those who carry an ALDH2*2 variant.

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Competing Interests: The author declares that they have no competing interests.

Background

The alcohol flush response is a reaction to alcohol that causes facial flushing and tachycardia. Mainly prevalent for those of East Asian descent (China, Japan, Korea, and Taiwan), this response to alcohol affects nearly 540 million people worldwide and is caused by an inactive genetic variant in the enzyme aldehyde dehydrogenase 2 (ALDH2) (Gross, 2015).

So why should we care whether people flush after they drink alcohol? This phenotype of flushing after consuming alcohol has important health implications. As described in this comic, the facial flushing that occurs after alcohol consumption is a warning sign that the body cannot break-down a metabolite of alcohol, called acetaldehyde. This alcohol metabolite acetaldehyde in turn accumulates within the body. This accumulation of acetaldehyde is what triggers the physiological effects that produce the phenotype of facial flushing and tachycardia (Chen, 2014).

Acetaldehyde accumulation at the cellular level can trigger DNA damage and modify protein functions by forming aldehyde-induced adducts on DNA and proteins (Heymann, 2018). These adducts that occur with alcohol exposure can lead to changes within a cell that can lead to cancer (Brooks, 2009). Since alcohol is typically a beverage we drink, the alcohol exposure is concentrated within the digestive system – leading to higher risks of cancer particularly of the upper digestive track (mouth and esophagus) due to the limited ability to metabolize the alcohol metabolite acetaldehyde to acetic acid. Importantly, there are other sources of aldehydes besides alcohol. This comic highlights that besides alcohol, another source of aldehyde exposure is cigarettes and e-cigarettes. Aldehydes, including acetaldehyde, formaldehyde, and acrolein are inhaled when using e-cigarettes (Yu, 2022). This exposure to aldehydes that are present in cigarettes or e-cigarettes, when combined with alcohol, can create an additive effect of aldehyde accumulation particularly within the upper digestive tract (Salasporo, 2004).

As aldehydes can be consumed or inhaled, besides aldehydes driving the risk for upper digestive tract cancer, aldehydes also can lead to vascular inflammation (Guo, 2023; Yu, 2022). This inflammation of the vascular system may over time potentially lead to cardiovascular and neurovascular disease (Zhang, 2023).

Due to these health reasons, it is important to relay to the public the risk carried by people that flush after drinking alcohol. We hope that relaying this information through a comic presenting the alcohol flushing response is an additional avenue to reach people about this health risk. Part of our future plans include additional public outreach relaying the health risks associated with the alcohol flushing response.

Conclusion

The alcohol flushing response is not benign. Frequent exposure to aldehydes, especially when alcohol is combined with aldehyde exposures from sources such as cigarettes or e-cigarettes may increase the risk of developing cancer.

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The Alcohol Flush Response

WHEN DRINKING ALCOHOL OR USING NICOTINE PRODUCTS (CIGARETTES OR E-CIGARETTES), OUR BODIES ARE EXPOSED TO ALDEHYDES.

THESE ALDEHYDES CAN BE TOXIC TO OUR BODIES; PARTICULARLY IF THEY CAUSE FACIAL FLUSHING AND AN INCREASED HEART RATE.

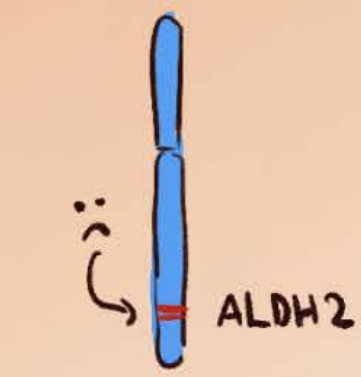
WHY DOES ALCOHOL FLUSHING OCCUR MORE OFTEN IN THE EAST ASIAN POPULATION AND WHAT ARE THE HEALTH RISKS?

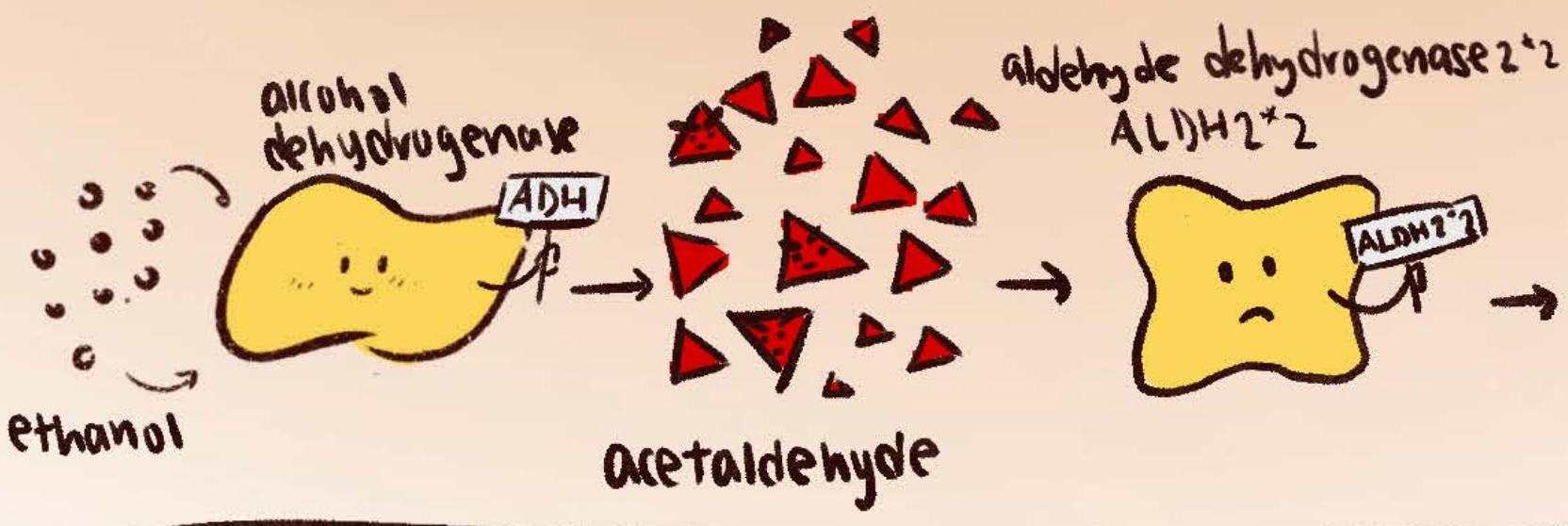
SOCIAL GATHERINGS ARE OFTEN PAIRED WITH DRINKING OR SMOKING. SOME PEOPLE, WHEN DRINKING ALCOHOL, SHOW A PHENOTYPE OF FACIAL FLUSHING; DUE TO THE ACCUMULATION OF THE ALCOHOL METABOLITE, ACETALDEHYDE.

NEARLY 20% OF PEOPLE USE ALCOHOL AND CIGARETTES TOGETHER[1]. NICOTINE PRODUCTS (CIGARETTES AND E-CIGARETTES) ALSO CONTAIN ALDEHYDES, INCLUDING ACETALDEHYDE[2,3].

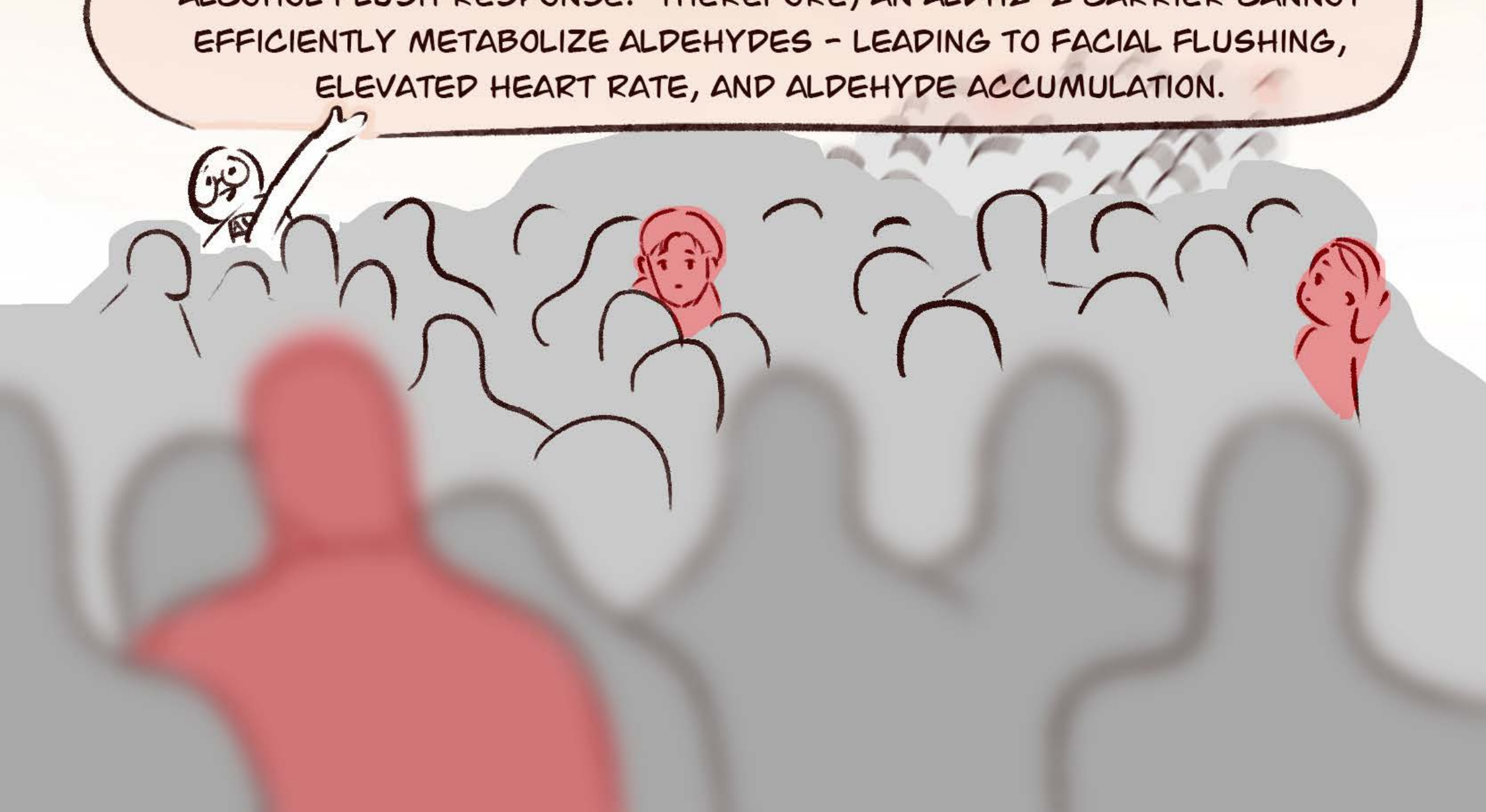
PEOPLE WITH GENETIC DEFICIENCIES FOR METABOLIZING ALDEHYDES CAUSED BY ALDH2 VARIANTS EXPERIENCE FACIAL FLUSHING AND AN INCREASED HEART RATE

THE ALDH2*2 GENETIC VARIANT IS ONE OF THE MOST COMMON GENETIC VARIANTS IN THE WORLD, AFFECTING ABOUT 560 MILLION (8% OF THE WORLD POPULATION) MAINLY OF EAST ASIAN DESCENT.

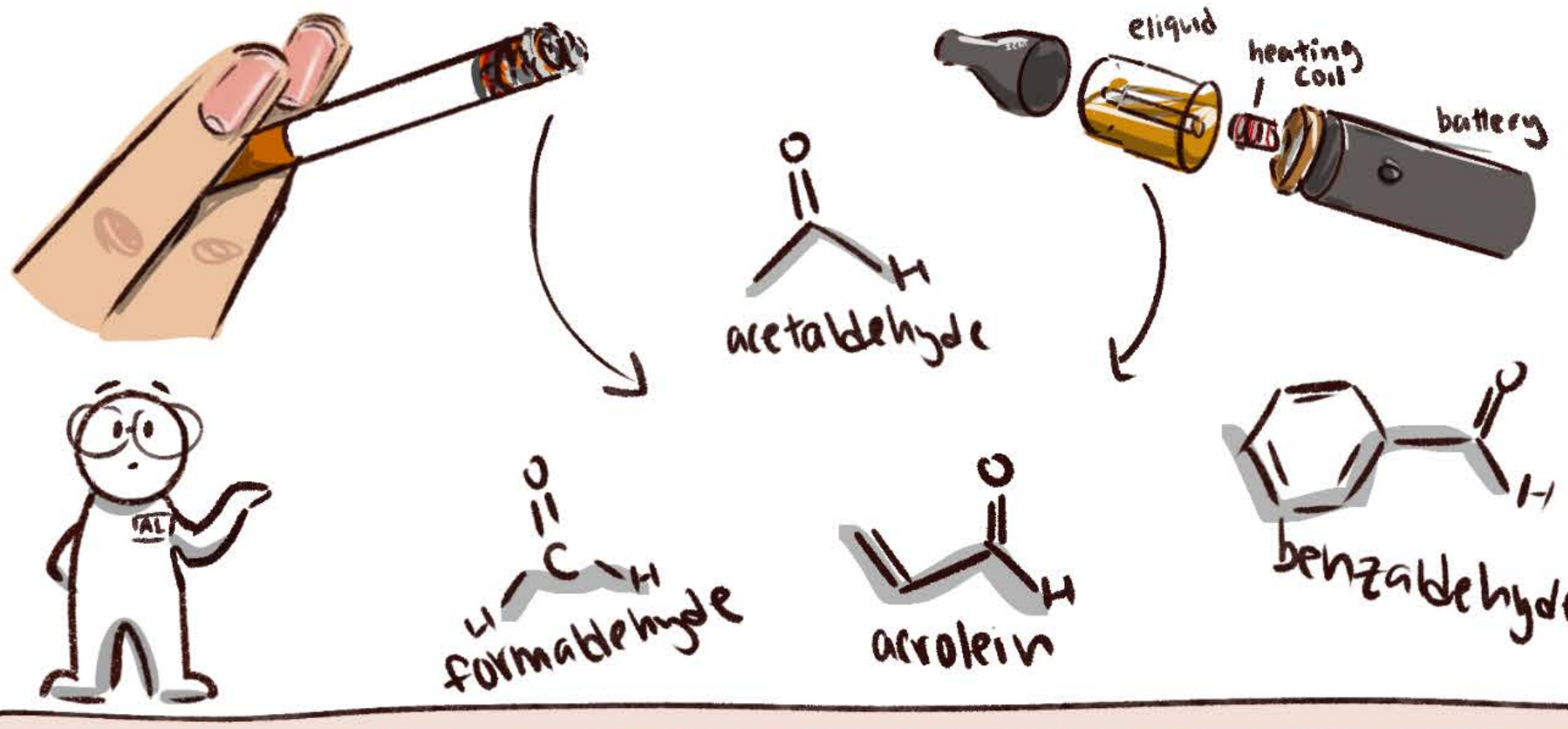




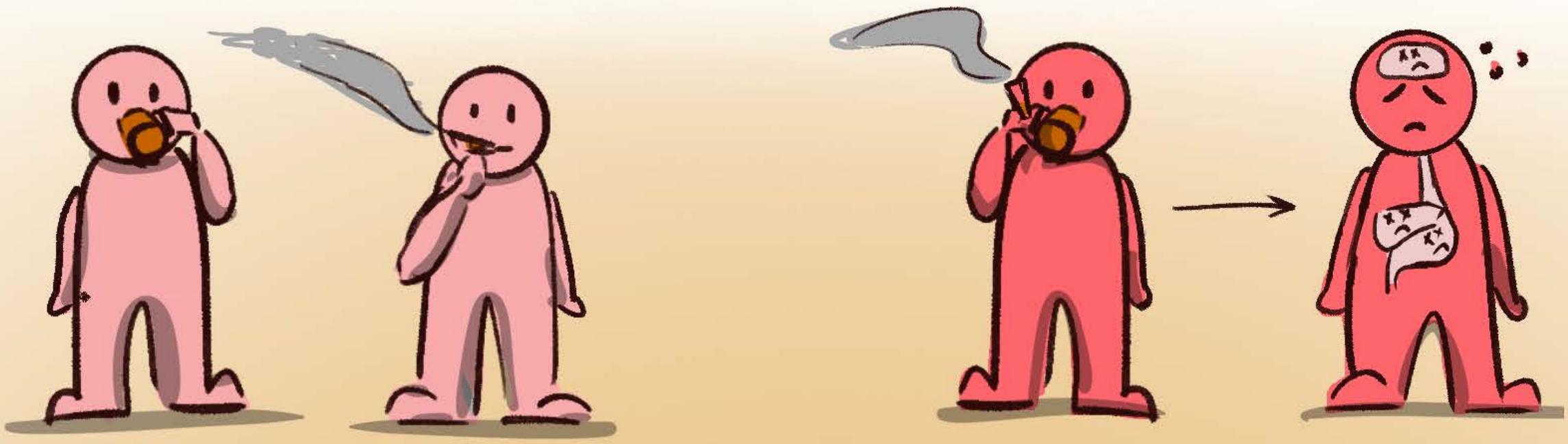
ONE COPY OF AN ALDH2*2 GENETIC VARIANT IS NEEDED TO CAUSE AN ALCOHOL FLUSH RESPONSE. THEREFORE, AN ALDH2*2 CARRIER CANNOT EFFICIENTLY METABOLIZE ALDEHYDES - LEADING TO FACIAL FLUSHING, ELEVATED HEART RATE, AND ALDEHYDE ACCUMULATION.



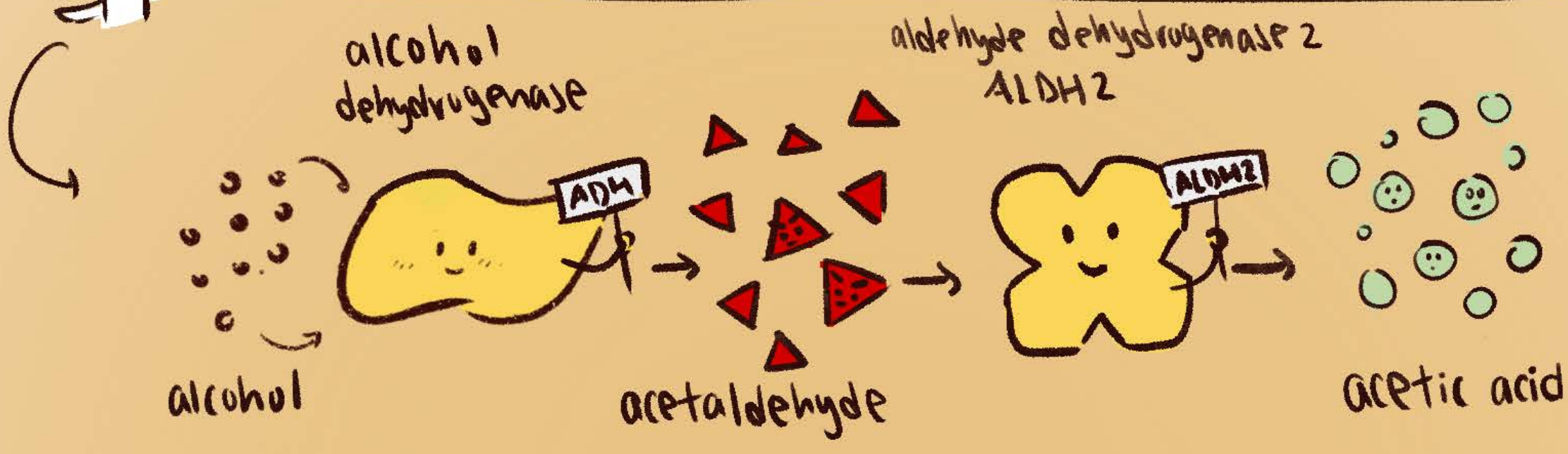
IMPRORTANTLY, NICOTINE PRODUCTS (TOBACCO AND E-LIQUIDS) RELEASE ALDEHYDES INCLUDING ACETALDEHYDE, FORMALDEHYDE, AND ACROLEIN. FLAVORINGS, SUCH AS BENZALDEHYDE OR VANILLIN ARE ALSO ALDEHYDES.



USING ALCOHOL AND NICOTINE TOGETHER CAN RAISE ALDEHYDE LEVELS IN THE BODY TO A HIGHER LEVEL THAN USING EITHER ALONE[4]. ELEVATED ALDEHYDE LEVELS CAN HAVE ADVERSE EFFECTS IN PEOPLE WITH GENETIC DEFICIENCIES FOR METABOLIZING ALDEHYDES.



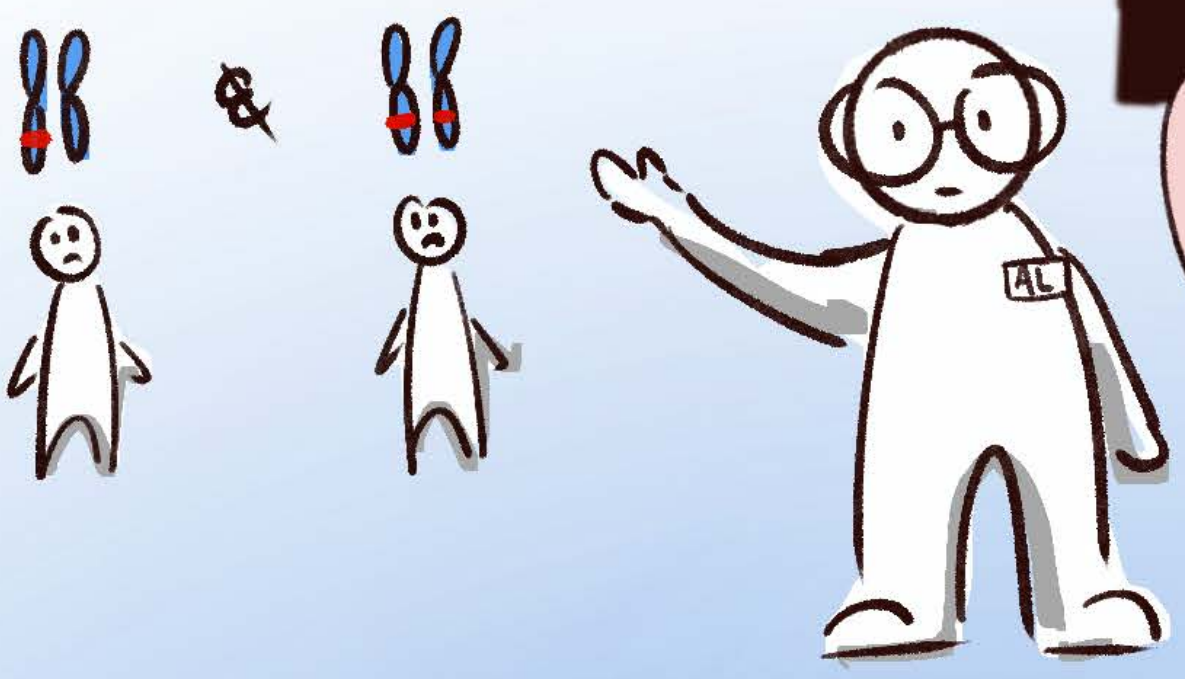
OUR BODIES BREAK DOWN ALDEHYDES USING THE ENZYME, ALDEHYDE DEHYDROGENASE 2 (ALDH2), WHICH CONVERTS ALDEHYDES TO LESS TOXIC COMPOUNDS. THIS PREVENTS ALDEHYDES FROM CAUSING DNA DAMAGE WHICH CAN LEAD TO CANCER.



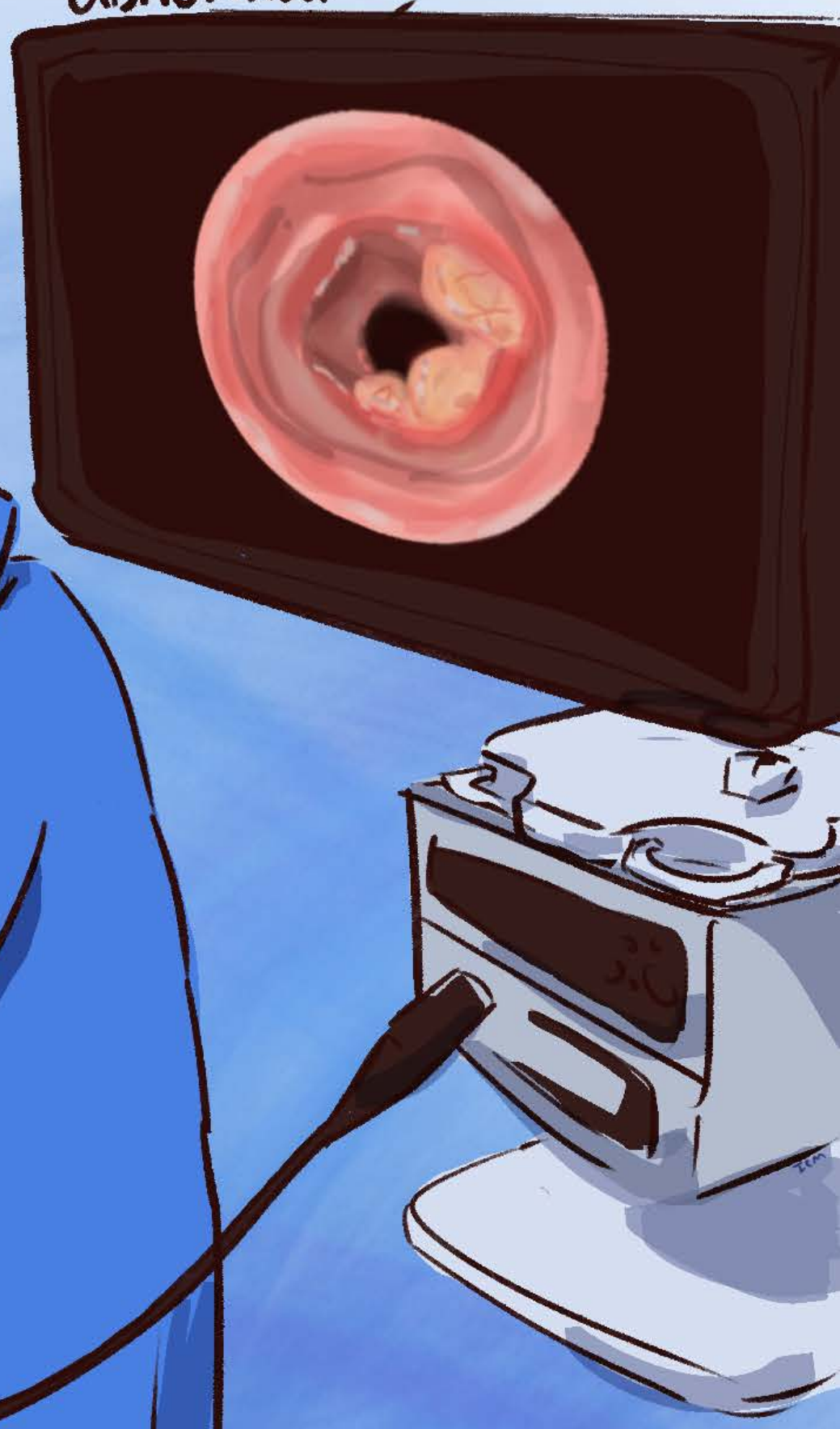
PEOPLE WHO CARRY AN ALDH2*2 VARIANT ARE AT HIGHER RISK FOR SEVERAL CANCERS, IN PARTICULAR ORAL, PHARYNGOLARYNGEAL, AND ESOPHAGEAL CANCERS[5, 6, 7].

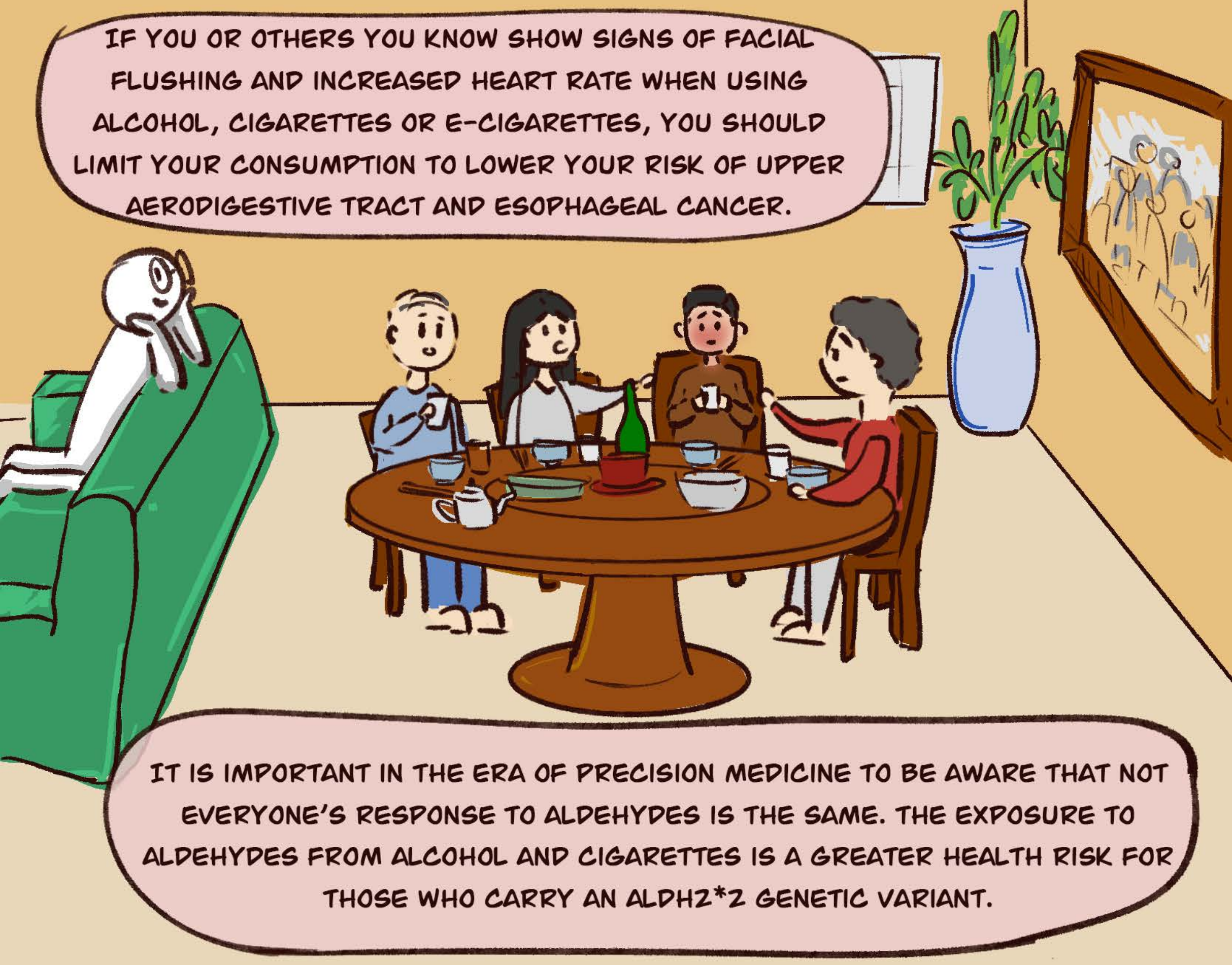
normal

ONE WAY TO LOWER THIS RISK IS TO STOP USING ALCOHOL, CIGARETTES AND E-CIGARETTES.



abnormal





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