

## What puts children at risk for secondary AML?

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Good afternoon, everybody. Welcome to *Managing AML*. My name is Andy Kolb. I'm a pediatric oncologist. I am frequently asked, "What puts children at risk for secondary AML?" The primary risk factor for secondary AML in children is exposure to chemotherapy. Chemotherapies that increase the risk for secondary AML include the epipodophyllotoxin, etoposide being the one most commonly used. Higher doses or a more frequent etoposide will increase risk for the development of secondary AML. The other are alkylators. High doses of alkylator-based therapy can certainly increase the risk for secondary AML.

The latency period for development of secondary AML, the median time is around three to four years following treatment. Though sad to say, survival is another important factor in determining risk for secondary AML. There are other therapies, so we see secondary AML in children who are exposed to drugs like azathioprine or mercaptopurine for treatment of other rheumatologic diseases. These cases are rare, but have certainly been reported, exposure to radiation may increase the risk, and just about any DNA-damaging agent can increase risk for the development of secondary AML. The risk is greatest with higher doses, longer exposure, and drugs like etoposide and alkylator-based therapies.

The other risk factor for development of secondary AML would be any underlying congenital abnormalities. There are risks from patients that have congenital P53 mutations, patients that have congenital mutations in RAS pathway in mismatch repair mechanisms. All children who are diagnosed with any malignancy should have an evaluation with the genetic counselor to determine if there are any congenital risks for the development of secondary AML. These are rare events, but still can occur, and patients who have already manifested a primary malignancy should be screened for risks for developing secondary malignancies.

Then cancer type is another risk, though I think this is a surrogate for exposure to chemotherapy. We see a lot of secondary AML in patients with sarcomas who have received high doses of alkylator therapy, exposure to drugs like etoposide, and in leukemia patients because of the combination of alkylators, etoposide-based therapy, as well as drugs like mercaptopurine. Thank you for the question.