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Proceedings Paper:

Newton, H, Friend, A, Cotterill, M et al. (2019) Risks of Azoospermia in Teenagers Following Chemotherapy: A Comparison of Pre- and Post-Treatment Semen Analysis. In: Pediatric Blood and Cancer. International Society for Paediatric Oncology Annual Congress, 23-26 Oct 2019, Lyon, France. Wiley-Blackwell. Article no: V513 SIOP19-0732. ISSN: 1545-5009. EISSN: 1545-5017.

<https://doi.org/10.1002/psc.27989>

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Risks of Azoospermia in Teenagers Following Chemotherapy: A Comparison of Pre- and Post-Treatment Semen Analysis.

BACKGROUND Infertility is a late effect of treatment with cytotoxic drugs. Little is known about the true extent of the risk.

METHODS 43 males aged ≤ 18 years stored sperm at our unit between 2008 and 2017 prior to potentially gonadotoxic treatment and subsequently provided follow-up semen analysis (89 cases in total provided pre-treatment samples). Data on cancer diagnosis, chemotherapy exposure and sperm quality at initial storage and at follow-up was collected for those with follow-up samples available. Validated parameters for semen quality in males < 17 years old is not available, consequently we report azoospermia as the single outcome. To avoid overestimating subtle changes, azoospermia was defined as a sample with < 100 sperm/ejaculate.

RESULTS Mean age at storage was 16.4 ± 0.2 years (Range 13-18) and follow-up 19.9 ± 0.4 years (Range 14-25). Mean time to follow-up sample was 4 (Range 1-8). The commonest indication for storage was cancer (88.0%), primarily lymphoma (31.5%). 81.4% of the 43 received chemotherapy.

4.7% of all initial samples and 30.3% at follow-up contained < 100 sperm/ejaculate ($p=0.0034$, RR 1.36 95%CI 1.11-1.62). Of those receiving chemotherapy: 5.7% initial samples contained < 100 sperm, versus 45.8% at follow-up ($p=0.0118$, RR 1.38 95%CI 1.08-1.75). Of those receiving an alkylating agent: 4.2% initial samples contained < 100 sperm/ejaculate, versus 32.0% at follow-up ($p=0.0232$, RR 1.41 95%CI 1.07 -1.87). Of those receiving platinum-based chemotherapy: 0% initial samples had < 100 sperm/ejaculate, versus 14.3% at follow-up. ($p=1.00$, RR 1.17 95%CI 0.86-1.58).

CONCLUSION Elevated risk of azoospermia post chemotherapy is confirmed, the highest risk being receipt of alkylating agents. Reassuringly, 70% were able to produce some sperm 4 years after treatment and consequently may be suitable for assisted reproductive support if natural conception is not feasible. Prediction of the precise response to treatment in an individual remains difficult and will require very large studies to formally evaluate.