

April 2005

To members of the SAMSAS Advisory Group

Please find attached a discussion paper on Trisomy 18, on which we would greatly appreciate your opinion.

The last review on T18 was conducted in 1996, well before 1st trimester combined screening being introduced in 2000/2001.

After your consideration of the data presented in the discussion paper, could you please indicate whether you are for or against the reporting of Trisomy 18 risks by the SAMSAS program, and reply on the attached form.

A clear majority in favour of reporting will be required to effect the change. If the issue is unclear, a meeting of the SAMSAS advisory group will be convened to discuss the issue.

If a majority in favour of risk reporting is reached then notification to SAMSAS customers will occur via a bolded footnote on SAMSAS reports for 30 days prior to implementation.

T18 risk reports will be of the same format as currently used for T21 and NTD's see examples attached.

Professor Eric Haan, Dr Janice Fletcher and myself will not be casting a vote.

You will be notified by letter of the outcome.

With kind thanks,



Robert Coccione, Head, Antenatal Screening (SAMSAS) Program.

cocciolonr@wch.sa.gov.au phone 8161 7296, fax 8161 8085

Circulation

Professor Eric Haan
Dr Janice Fletcher
Dr Brian Peat
Dr David Morris
Dr Chris Wilkinson
Dr Peter Muller

Professor Robert Bryce
Dr Robert Graham Jones
Dr Christopher Verco
Dr Geoff Mathews
Dr Karen Shand
Sr Lyn Langley

Professor G Dekker
Dr Sue Kennedy-Andrews
Dr Amita Singla
Dr Kelton Tremellen
Sr Jenny Miller

Dr Shelby Jarell
Ms Joanne Burke
Dr Henry Cho
Dr Neil Tamlin

Discussion Paper Trisomy 18 (T18)

The South Australian Maternal Serum Antenatal Screening (SAMSAS) Program introduced 2nd trimester multi-analyte maternal serum screening for Down syndrome in 1990/91. At that time SAMSAS was requested by the obstetric community not to issue risks for T18.

The recent shift to 1st trimester screening and the use of “soft markers” in management protocols suggest a review of whether T18 risks should be reported.

The following information is presented for your consideration.

The 1st trimester screening risk incorporates maternal age at delivery, nuchal translucency thickness, maternal serum free beta hCG and Pregnancy Associated Plasma Protein-A. The 2nd trimester screening risk incorporates maternal age at delivery, maternal serum alpha fetoprotein, free beta hCG and unconjugated estriol.

Tables 1 and 2 on page 3, represent known T18 cases in the SAMSAS database that have been screened in 1st or 2nd trimester. For each case, a T18 and T21 risk is shown as being either high or low based on a risk cut off of 1:300.

All cases were screened prospectively.

Our data shows:

- 11/12 or 91.7% of T18 cases from 1st trimester would have been detected if T18 risks were reported, because they would have screened high risk for either T18 or T21. 9/12 or 75% of T18 cases were detected in the absence of T18 risk reporting because they screened high risk for T21.
- 19/20 or 95% of T18 cases from 2nd trimester would have been detected if T18 risks were reported because they would have screened high risk for either T18 or T21. 9/20 or 45% of T18 cases were detected in the absence of T18 risk reporting because they screened high risk for T21.
- The additional increase in the overall recall rate (or the % of pregnancies which would be screened at increased risk), adjusting for high risk T18 pregnancies also screened high risk for T21, would be <0.1% for 1st trimester and <0.5% for 2nd trimester screen. If women currently accepting screening were all screened in 1st trimester, an additional 13 pregnancies would need counselling for a high risk report. From this 13, we would expect to find at least two cases with an abnormal karyotype.
- 2002 audits of 1st trimester screened pregnancies show that 1 in 4 pregnancies screened at increased risk for T18 will be affected. This is 4 times the specificity for T21. 1 in 2 pregnancies screened at increased risk for T18 will have an abnormal karyotype.

Currently, T18 pregnancies are in effect being screened for by ultrasonography (in 1st trimester with nuchal translucency measurements and in 2nd trimester with the morphology scan) and the information available from the maternal serum screen is not being reported.

An earlier T18 study conducted by the SAMSAS program and the Medical Imaging Department of the WCH in 1999, showed that for 2nd trimester pregnancies the combination of the biochemical risk and ultrasound markers was very powerful, leading to a predictive value of 1 in 2. Practically, if we report cases as low risk in 1st trimester, but soft markers are noted during the morphology scan, then 2nd trimester biochemistry has a place in management.

The biochemical pattern seen in T18 affected pregnancies is quite distinct in both 1st and 2nd trimester with at least one, but mostly all, markers being significantly low. Consequently, the resulting risks are very high with 90% of affected pregnancies having T18 risks of $\geq 1:50$ (and 75% having T18 risks of $\geq 1:10$). Effectively what this means is that the maternal age risk bears little weight; the resulting risk is driven by the strength of the biochemical pattern.

Summary

- The majority of pregnancies affected with T18 are currently being offered diagnostic testing as they also screen at increased risk for T21.
- If T18 risks were reported, 13 additional pregnancies per annum would be offered diagnostic testing, with negligible change to the overall false positive rate of the screening program.
- Not reporting T18 risks is denying obstetricians and ultrasonographers information.
- The specificity of screening for T18 is four times that of Down syndrome.

Yours sincerely,



Robert Cocciolone, BAppSc (Med Lab Sc), Head, Antenatal Screening (SAMSAS) Program

April 2005

Table 1 First Trimester T18 Known Cases

| CASE | T21 Risk | T18 Risk |
|------|------------|------------|
| 1 | High | High |
| 2 | High | High |
| 3 | Low | High |
| 4 | High | High |
| 5 | Low | High |
| 6 | High | High |
| 7 | High | Low |
| 8 | High | High |
| 9 | High | High |
| 10 | High | High |
| 11 | Low | Low |
| 12 | High | High |

Table 2 Second Trimester T18 Known Cases

| CASE | T21 Risk | T18 Risk |
|------|------------|------------|
| 1 | High | High |
| 2 | High | High |
| 3 | High | High |
| 4 | High | Low |
| 5 | High | High |
| 6 | High | High |
| 7 | Low | High |
| 8 | High | High |
| 9 | High | High |
| 10 | Low | High |
| 11 | Low | High |
| 12 | Low | High |
| 13 | Low | High |
| 14 | High | High |
| 15 | Low | High |
| 16 | Low | High |
| 17 | Low | Low |
| 18 | Low | High |
| 19 | Low | High |
| 20 | Low | High |

SAMSAS Trisomy 18 Discussion Paper

Response Form

Please tick your preference.

[] I **am** in favour of SAMSAS reporting Trisomy 18 risks.

[] I am **not** in favour of SAMSAS reporting Trisomy 18 risks.

Signed: Print Name:

Date:.....

Please send this response in the envelope provided. Comments welcomed.