

# **Scottish Hydatidiform Mole Follow-up**

## **Annual Report**

**2009-2010**

Immunodiagnosics Group  
Department of Immunology  
Ninewells Hospital  
DUNDEE

This is the annual report of the Scottish Hydatidiform Mole Service 2009/2010.

## **Staffing**

Dr Patrick Chien has been appointed Clinical Director of the Group, replacing Dr Maggie Thomson who retired in August 2009.

Mrs Vicky Queen has been appointed to the Assistant Co-ordinator post from 1<sup>st</sup> January 2010.

The post of temporary research assistant, which was funded by NSD to assist with the participation in the International ISOBM Workshop, came to an end in January 2010.

The Scottish Hydatidiform Mole team comprises 1.0 WTE Clinical Scientist, 2.0 WTE Healthcare Scientists, 0.2 WTE Clinical (Gynaecologist+ Pathologist), 1.7 WTE Administration and Records.

## **Background**

The Scottish hydatidiform mole follow-up service is performed by the Immunodiagnostics Group and is based in the Department of Immunology, Ninewells Hospital, Dundee. It is the Scottish centre for the UK hydatidiform mole follow-up service, the other centres being in London's Charing Cross Hospital and Sheffield's Royal Hallamshire.

The follow-up involves the diagnosis and registration of women in Scotland presenting with a molar pregnancy. Monitoring of these women involves measurement of human chorionic gonadotrophin (hCG) concentration in sequential urine samples until normal levels are reached. Continued raised levels of hCG in 'non-pregnant' samples suggest a disease recurrence or the development of choriocarcinoma. Such measurement therefore provides a unique assay for cancer.

The Immunodiagnostics Group also manufacture and distribute iodinated hCG to the other two UK hydatidiform mole follow-up centres every four weeks. This activity is vital to the continuity of the UK hydatidiform mole follow-up service which employs a unique radioimmunoassay for hCG which is internationally recognised as the 'gold standard'.

## **Activity**

1 Production of Iodinated hCG (April 2009 – March 2010).

The amount of <sup>125</sup>I-hCG was as predicted. <sup>125</sup>I-hCG was prepared at four-weekly intervals during this period (13 production runs in total). Each run produced 20µg of <sup>125</sup>I-hCG therefore we have produced a total of 260µg.

Each batch of iodinated hCG was CE marked in accordance with the supply of medical devices. Each preparation of iodinated protein passed the internal and

external QC controls, which have been established by Immunodiagnostics Group and written into the ISO 9001 quality system.

Each batch of iodinated hCG was distributed, free of charge, to the UK Hydatidiform Mole follow-up centres at London's Charing Cross (65µg) and Royal Hallamshire in Sheffield (39µg). We have also used 30µg in Dundee to perform the annual Scottish follow-up service and service developments.

Due to problems we were experiencing with the quality of supplied <sup>125</sup>iodine, it was necessary to perform an additional 2 iodinations to investigate the problems. This additional material was never used and was disposed of in the appropriate manner.

## 2 Hydatidiform Mole Registrations (April 2009 – March 2010)

The number of new registrations for this period was 137.

The annual figures broken down by referring Health Board are:

Health Board	Pregnancies Registered (molar)	Non-molar Pregnancies Referred	Non-molar Pregnancies Registered
Tayside	13(12)	5	1
Grampian	30(23)	21	7
Lothian	14(11)	5	3
Highland	12(12)	1	0
Lanarkshire	10(10)	8	0
Ayrshire	13(13)	0	0
Greater Glasgow and Clyde	24(22)	9	2
Fife	11(8)	12	3
Forth Valley	7(7)	1	0
Dumfries & Galloway	3(2)	2	1
Borders	0	0	0
Western Isles	0	0	0
Orkney	0	0	0
Shetland	0	0	1
<b>TOTAL</b>	<b>137 (120)</b>	<b>64</b>	<b>17</b>

## **Mole Classification (pathology and ploidy)**

During this period the number of tissue blocks referred to the service for ploidy analysis to assist in reclassification of the pregnancy was 205. Further laboratory testing comprising CISH and p57 analysis was performed on 12 of the more ambiguous tissue samples to assist in the pathological classification.

There was excellent agreement between histological classification of moles and the ploidy analysis of the tissue as measured by flow cytometry. The determination of ploidy consistently gives 99% agreement with pathological classification of moles, up from 95% in 2008-2009.

The timely classification of referred cases enabled us to prevent the registration and hence follow-up of 47 women with non-molar pregnancies (73% of non-molar pregnancies referred). This is an improvement on last year when 61% of non-molar pregnancies referred were reclassified before registration.

Unfortunately, due to the high referral rate of non-molar pregnancies some 17 were still registered before re-classification.

## **Trends, Demand and Referral Patterns**

### 1 <sup>125</sup>I-hCG production

We are predicting that the level of production of iodinated hCG will remain at the same for the period 2010-2011. We have developed a new assay for urinary hCG and this requires validation before it can replace the existing immunoassay format. This will be achieved by running it in parallel with our existing assay for at least 6 months. We have recently started performing this new assay alongside the routine assay used for measuring hCG in patient urine. We expect the production of <sup>125</sup>I-hCG to be less in 2011.

### 2 Patient Referrals and Registration Patterns

- The number of referrals for mole follow-up this period was slightly less than last year and this is reflected in the number of registrations, 137 compared to 171 for 2008-2009. Out of these, 120 were true moles (87.5%) compared to 149 true moles last year (87.1%).
- A large number of referrals were non-molar (64), slightly up on last year (56). We were successful in preventing the registration of 47 of these (73%) resulting in 17 non-molars being registered. This is an improvement on last year when 61% non-molars were reclassified before registration. As in previous years, we prefer to see this cautious attitude being taken, where a suspected case is referred, rather than risk the possibility of missing a true molar pregnancy.
- The number of referrals from Grampian was significantly higher than last year however these numbers do fall in line with previous years perhaps, reflecting natural fluctuation in referral pattern. Greater Glasgow and Clyde show a decrease in the number of referrals having displayed an increase in numbers

last year. Again the numbers fall in line with those reported in previous years and reflect natural fluctuation in referral patterns.

- The number of referrals by the other Health Boards was comparable to last year's figures.
- There were 7 patients referred to Charing Cross for treatment.

### **Quality and Accreditation**

All batches of iodinated hCG were CE marked in accordance with the supply of medical devices with each batch passing internal and external QC controls which have been established by Immunodiagnostics Group and written into the ISO 9001 quality system.

Our routine radioimmunoassay has performed well in the external NEQAS scheme for measurement of hCG both in serum and urine.

We have successfully maintained our level of BSI accreditation during this period having been successfully audited by internal auditors in 2009.

### **Clinical Audit and Response Times**

Turnaround time for pathology has continued at around 14 days from receipt of pathology sample to reviewed diagnosis. As in previous years this has allowed us to prevent the unnecessary registration of a significant number of women who are referred to us with a non-molar pregnancy (see above).

### **Service Developments and Future Plans**

#### **New Immunoassays for hCG**

The assay development project has resulted in the creation of several sheep monoclonal antibodies with characteristics suitable for the measurement of all forms of hCG by immunoassay. The new antibodies have been partially characterised in Dundee using immunoassay techniques and also using our BIAcore facility. We have demonstrated that the antibodies are capable of detecting all forms of hCG distributed by NIBSC as standards. They also mimic the routine radioimmunoassay when used in the same format. Development of the new assay format has been undertaken in collaboration with Mologic Ltd and Charing Cross however several problems have been found with the format which had been developed at Mologic Ltd.

The task of finding a solution to these problems was given to the team in Dundee in October 2009. Since then, extensive development work has been performed by the existing Dundee team together with the assistance of a full time research assistant funded by Mologic.

To date, we have established a new, chemiluminescence based immunoassay to measure hCG in urine. This is currently being run in parallel with the routine hCG

RIA. Correlation between the two assays has been excellent. A major advantage of this new assay is that it takes only 3 hours to complete compared to the current 24 hour routine radioimmunoassay. This will result in a results being available on the same day a sample is received.

We are now trying to resolve problems associated with the measurement of hCG in serum. This is particularly difficult due to the complex matrix of serum. Progress has been good and we have several assay formats nearing completion. We hope to have the final format before June 2010.

### **Precise DNA Genotyping Analysis**

We are currently exploring the feasibility to setting up this service in addition to the histological and ploidy analysis in collaboration with the Department of Pathology at Ninewells Hospital, Dundee to further improve on the confidence of diagnosis of non-molar hydropic pregnancies, complete and partial molar pregnancies. Discussions with the relevant parties are still on-going and it is hoped that we may be able to report to the next annual meeting with NSD later on this year as to whether a full business plan will be submitted to be considered for this service to be implemented.

### **Provision of Counselling Service**

It is evident that our sister organisations in England at both Sheffield and London are now providing qualified counselling service for patients who are under hCG surveillance following the diagnosis of molar pregnancy as well as those who are undergoing chemotherapy using the telephone or Skype video-conferencing. We would like to discuss the possibility of submitting a business plan for this service for Scottish patients at the next annual meeting with NSD later on this year.

### **Participation in the ISOBM hCG workshop**

The work carried out in Dundee is being compiled into a final report, which will be submitted to the workshop co-ordinator before June 2010. This will be combined with reports from the other investigation groups before the complete findings are submitted for publication. It has been proposed that additional work is required to complete the study and unfortunately we may have to decline further participation if this proves to be extensive.

### **Assistant Co-ordinator**

Vicky Queen was appointed to the post of assistant co-ordinator in January 2010. This has provided much needed support to the day to day running of the service.

### **Annual Meeting**

The annual meeting of the UK Hydatidiform Mole Follow-up Service was scheduled to be held at Charing Cross, London in January 2010 however, due to weather conditions at the time this was rescheduled for May 2010.

## **Summary and Conclusions**

- The level of activity for 2009-2010 was as predicted for the production of iodinated hCG.
- The number of women registered for follow-up was slightly less than last year but still within natural variability observed over time.
- The turnaround time for re-classification of moles is running at 14 days, which is sufficient to prevent a significant number of women with non-molar pregnancy being registered.
- A total of seven women were referred to Charing Cross for treatment.
- A new immunoassay for urinary hCG is now running in parallel with the routine assay and is correlating well.
- New immunoassay formats are being developed for serum hCG and it is hoped these will be finalised in June 2010.
- A report on the Dundee investigation performed for the ISOBM hCG workshop is being compiled and will be submitted before June 2010. Further participation may have to be curtailed.

Prepared by Dr Stewart and Dr Chien (May 2010)