

7th **EYES** Meeting Athens, Greece

13-15 September 2019
Royal Olympic Hotel

Under the Auspices of



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FINAL PROGRAM - ABSTRACTS BOOK



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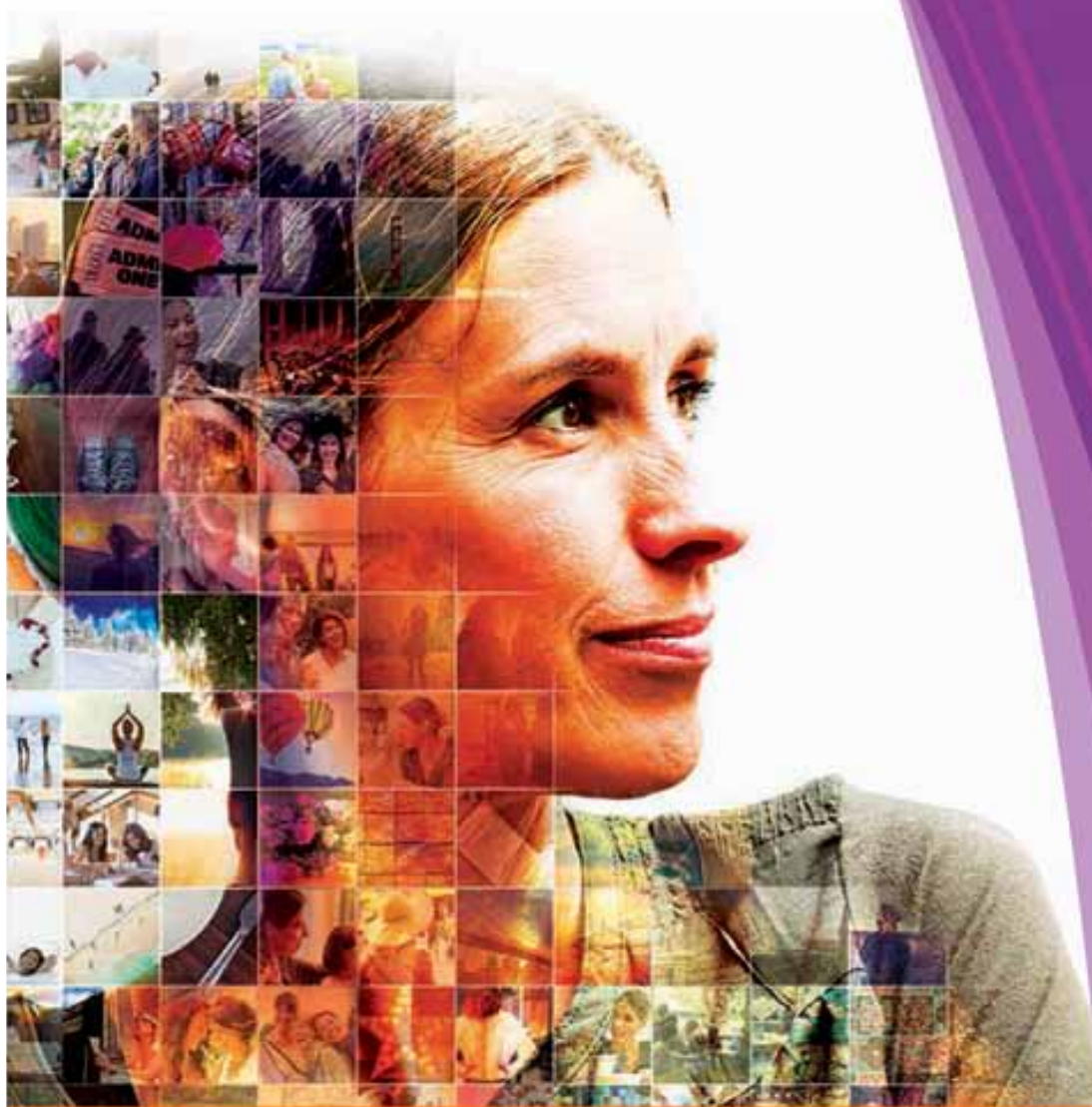
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†ΤΣε άτομα με σακχαρώδη διαβήτη τύπου 2 και υψηλό καρδιαγγειακό κίνδυνο. †Δευτερεύον καταληκτικό σημείο. Πρωτεύον καταληκτικό σημείο ήταν ο χρόνος για την έλευση του σύνθετου MACE (θάνατος οποιαδήποτε αιτιολογίας, μη θανατηφόρο έμφραγμα μυοκαρδίου και μη θανατηφόρο εγκεφαλικό). Αναλογία κινδύνου: 0,87, 95% CI, 0,79-0,97, P<0,0001 για τη μη κατωτέροτητα, P=0,01 για ανωτέροτητα.

Σύντομη Περίληψη Χαρακτηριστικών του Προϊόντος

ΟΝΟΜΑΣΙΑ ΤΟΥ ΦΑΡΜΑΚΕΥΤΙΚΟΥ ΠΡΟΪΟΝΤΟΣ Victoza 5 mg/ml ενέσιμο διάλυμα σε προγεμισμένη συσκευή τύπου πένος **ΠΟΙΟΤΙΚΗ ΚΑΙ ΠΟΣΟΤΙΚΗ ΣΥΝΘΕΣΗ** 1 ml διαλύματος περιέχει 6 mg liraglutide. Μία προγεμισμένη συσκευή τύπου πένος περιέχει 18 mg liraglutide σε 3 ml. * ανάλογα της ανθρώπινης ορμόνης γλυκαγόνη-γλυκογόνο πεπτιδ-1 (GLP-1) που παρασκευάζεται με χρήση της τεχνολογίας ανασυνδυασμένου DNA σε *Saccharomyces cerevisiae*. **Θεραπευτικές ενδείξεις** Το Victoza ενδείκνυται για τη θεραπεία ενηλίκων, εφήβων και παιδιών ηλικίας 10 ετών και άνω με σακχαρώδη διαβήτη τύπου 2 που δεν ελέγχεται επαρκώς σε συνδυασμό με διαίτα και άσκηση + ως μονοθεραπεία όταν η μεταφορμική θεωρείται ακατάλληλη εξαιτίας δυσανεξίας ή αντενδείξεων σε συνδυασμό με άλλα φαρμακευτικά προϊόντα για τη θεραπεία του διαβήτη. **Δοσολογία και τρόπος χορήγησης** Προκειμένου να βελτιωθεί η γαστρεντερική άνεση, η αρχική δόση είναι 0,6 mg liraglutide ημερησίως. Μετά από μία εβδομάδα τουλάχιστον, η δόση πρέπει να αυξάνεται στα 1,2 mg. Ορισμένοι ασθενείς αναμένεται να ωφεληθούν από μια αύξηση της δόσης από τα 1,2 mg στα 1,8 mg στα 1,8 mg με βάση την κλινική ανταπόκριση, μετά από μία εβδομάδα τουλάχιστον, η δόση μπορεί να αυξηθεί στα 1,8 mg προκειμένου να βελτιωθεί περαιτέρω ο γλυκαιμικός έλεγχος. Ημερήσιες δόσεις μεγαλύτερες των 1,8 mg δε συνιστώνται. Το Victoza μπορεί να χρησιμοποιηθεί σε συνδυασμό με άλλους υπογλυκαιμικούς παράγοντες και δεν απαιτούνται προσαρμογές της δόσης για τη μεταβολή της θεαδρενικονιδόνης και τον αναστολέα 2 του συμπαγορμικού νωτρίου-γλυκοζίνης (SGLT2). Η συνδυαστική θεραπεία με σουλφονουρία ή θιαζολιδινεδιόνη ισχύει μόνο για ενήλικες ασθενείς. Όταν το Victoza προστίθεται σε μια σουλφονουρία ή σουλινίνη, πρέπει να εξετάζεται το ενδεχόμενο μείωσης της δόσης της σουλφονουρίας ή της σουλινίνης για τη μείωση του κινδύνου υπογλυκαιμίας. Δεν είναι αναγκαία η αυτοπαρakoλούθηση των επιπέδων γλυκόζης στο αίμα για τη ρύθμιση της δόσης του Victoza. Η αυτοπαρakoλούθηση των επιπέδων γλυκόζης στο αίμα είναι αναγκαία για τη ρύθμιση της δόσης της σουλφονουρίας και της σουλινίνης, ιδίως όταν έχουν ήδη αρχίσει να μειώνονται και μειώνεται η δόση της σουλινίνης. Συνιστάται η μείωση της δόσης της σουλινίνης βάσει σταδιακής προσαρμογής. Ηλικιωμένοι ασθενείς (>65 ετών) δεν απαιτείται προσαρμογή της δόσης βάσει της ηλικίας. Παιδική δυσανεμία δεν απαιτείται προσαρμογή της δόσης σε ασθενείς με ήπια, μέτρια ή σοβαρή νεφρική δυσλειτουργία. Δεν υπάρχει καμία θεραπευτική εμπειρία σε ασθενείς με νεφροσάκχα τετακτού σταδίου και επομένως το Victoza δε συνιστάται για χρήση σε αυτούς τους ασθενείς. Ηπατική δυσλειτουργία δε συνιστάται καμία προσαρμογή της δόσης σε ασθενείς με ήπια ή μέτρια ηπατική δυσλειτουργία. Το Victoza δε συνιστάται για χρήση σε ασθενείς με σοβαρή ηπατική δυσλειτουργία. Παιδιατρικός πληθυσμός δεν απαιτείται προσαρμογή της δόσης για παιδιά ηλικίας 10 ετών και άνω. Δεν υπάρχουν διαθέσιμα δεδομένα για παιδιά ηλικίας κάτω των 10 ετών. Τρόπος χορήγησης Το Victoza δεν πρέπει να χορηγείται ενδοφλέβια ή ενδομυϊκά. Το Victoza χορηγείται μία φορά ημερησίως υποδόνηση, ανεξάρτητα από τα γεύματα, και μπορεί να ενταχθεί υποδόνηση στην καύλα, στο μηρό ή στο βραχίονα. Η θέση και η ώρα της ένεσης μπορούν να αλλάξουν χωρίς προσαρμογή της δόσης. Παρόλο αυτά, είναι προτιμότερο το Victoza να χορηγείται περίπου την ίδια ώρα της ημέρας, όταν έχει επιλεγεί η πιο εξυπηρετική ώρα. **Αντενδείξεις** Υπερσυστάθεια στη δραστηριότητα ή σε κάποιο από τα ένδοξα. **Ειδικές προειδοποιήσεις και προφυλάξεις κατά τη χρήση** Η liraglutide δεν πρέπει να χρησιμοποιείται σε ασθενείς με σακχαρώδη διαβήτη τύπου 1 ή για τη θεραπεία της διαβητικής κετοξέωσης. Η liraglutide δεν είναι υποκατάστατο της ινσουλίνης. Έχει αναφερθεί η εμφάνιση διαβητικής κετοξέωσης σε νοσηλευόμενους ασθενείς μετά από ταχεία διακοπή ή μείωση της ινσουλίνης, δεν υπάρχει θεραπευτική εμπειρία σε ασθενείς με συμφορητική καρδιακή ανεπάρκεια κατηγορίας IV σύμφωνα με την ταξινόμηση κατά New York Heart Association (NYHA) και επομένως η liraglutide δε συνιστάται για χρήση σε αυτούς τους ασθενείς. Υπάρχει περιορισμένη εμπειρία σε ασθενείς με φλεγμονώδη εντερικό νόσο και διαβητική γαστροπάρεση. Η χρήση της liraglutide δε συνιστάται σε αυτούς τους ασθενείς καθώς συσχετίζεται με παροδικές ανεπιθύμητες ενέργειες του γαστρεντερικού, συμπεριλαμβανομένων ναυτίας, εμέτου και διάρροιας. Έχει παρατηρηθεί οξεία παγκρεατίτιδα κατά τη χρήση αγωνιστών του υποδοχέα GLP-1. Οι ασθενείς

θα πρέπει να ενημερώνονται για τα χαρακτηριστικά συμπτώματα της οξείας παγκρεατίτιδας. Εάν υπάρχει υποψία παγκρεατίτιδας, η liraglutide πρέπει να διακοπεί. Εάν επιβεβαιωθεί η οξεία παγκρεατίτιδα, η liraglutide δε θα πρέπει να χρησιμοποιείται ξανά. Κατά τη διεξαγωγή κλινικών δοκιμών αναφέρθηκαν ανεπιθύμητες ενέργειες στο θυρεοειδή αδένα, όπως βρογχίτιδα και ειδικά σε ασθενείς με προπάρκοντα θυρεοειδική νόσο. Επομένως, η liraglutide πρέπει να χρησιμοποιείται με προσοχή σε αυτούς τους ασθενείς. Οι ασθενείς που λαμβάνουν liraglutide σε συνδυασμό με σουλφονουρία ή με σουλινίνη ενδέχεται να έχουν αυξημένο κίνδυνο υπογλυκαιμίας. Ο κίνδυνος της υπογλυκαιμίας μπορεί να ελαττωθεί με μείωση της δόσης της σουλφονουρίας ή της σουλινίνης. Σε ασθενείς που λαμβάνουν ως θεραπεία liraglutide, έχουν αναφερθεί σημεία και συμπτώματα αφυδάτωσης, τα οποία περιλαμβάνουν νεφρική δυσλειτουργία και οξεία νεφρική ανεπάρκεια. Οι ασθενείς που λαμβάνουν ως θεραπεία liraglutide πρέπει να ενημερώνονται για ενδεχόμενο κίνδυνο αφυδάτωσης, ο οποίος σχετίζεται με τις ανεπιθύμητες ενέργειες του γαστρεντερικού συστήματος και να λαμβάνουν προληπτικά μέτρα για την αποφυγή της έλλειψης υγρών. Το Victoza περιέχει λιγότερο από 1 mmol νατρίου (23 mg) ανά δόση, επομένως το φαρμακευτικό προϊόν είναι ισοαξιακό «ελεύθερο νατρίου». **Γονιμότητα, κύηση και γαλουχία** Η liraglutide δεν πρέπει να χρησιμοποιείται κατά τη διάρκεια της εγκυμοσύνης και αν/ή αυτοί συνιστάται η χρήση ινσουλίνης. Εάν μια ασθενής προγραμματίζει εγκυμοσύνη ή εάν προκύψει εγκυμοσύνη, η θεραπεία με Victoza πρέπει να διακοπεί. Λόγω έλλειψης εμπειρίας, το Victoza δεν πρέπει να χρησιμοποιείται κατά τη διάρκεια του θηλασμού. Εκτός από μία μικρή μείωση στον αριθμό των ζωντανών εμφυτευμένων εμβρύων μελέτες σε ζώα δεν υποδεικνύουν άμεσες επιβλαβείς επιπτώσεις σε σχέση με τη γονιμότητα. **Ανεπιθύμητες ενέργειες** Λοιμώξεις και παρασιτώσεις: Συχνές: Φυγοσυσπλινίτιδα, βρογχίτιδα. Διαταραχές του ανοσοποιητικού συστήματος: Σπάνιες: Ανοσολογικές αντιδράσεις, διαταραχές του μεταβολισμού και της θρέψης: Συχνές: Υπογλυκαιμία, Ανορεξία, Μεταμεινόμενη όρεξη. Όχι συχνές: Αφυδάτωση, Διαταραχές του νεφρικού συστήματος: Συχνές: Κεφαλαλγία, Ζάλη, Καρδιακές διαταραχές: Συχνές: Αιχμηρό καρδιακό ρυθμό, Διαταραχές του γαστρεντερικού: Πολύ συχνές: Ναυτία, Διάρροια, Συχνές: Έμετος, Δυσπεψία, Άλγος άνω κοιλιακής χώρας, Δυσκοιλιότητα, Γαστρίτιδα, Μεταωρικός, Δυσπορία της κοιλίας, Γαστροοισοφαγική παλινδρομηση, Καούρα, Δυσφορία, Οδοντοαλγία, Σπάνιες: Εντερική απόφραξη, Πολύ σπάνιες: Παγκρεατίτιδα (συμπεριλαμβανομένης νεκρωτικής παγκρεατίτιδας), Διαταραχές του ήπατος και των χοληφόρων: Όχι συχνές: Χολοκυστίτις, Χολοκυστίτις, Διαταραχές του δέρματος και του υποδόριου ιστού: Συχνές: Εξάνθημα. Όχι συχνές: Κνίδωση, Κνησμός, Διαταραχές των νεφρών και των ουροφόρων οδών: Όχι συχνές: Νεφρική δυσλειτουργία, Οξεία νεφρική ανεπάρκεια. Γενικές διαταραχές και καταστάσεις της οδού χορήγησης: Συχνές: Κούραση, Απώλεια όρεξης, Δυσφορία, Όχι συχνές: Αίσθημα κακουχίας, Παροδικές εξετάσεις: Συχνές: Αυξημένη λιπώδη, Αυξημένη αμυλάση. **Αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών** Η αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών μετά από τη χορήγηση οφείλει να αφορά προϊόντα του φαρμακευτικού προϊόντος είναι σημαντική. Επιπλέον, η συλλογή παρακολούθηση της σχέσης οφέλους-κινδύνου του φαρμακευτικού προϊόντος. Ζητείται από τους επαγγελματίες που ταμά υγείας να αναφέρουν οποιαδήποτε πιθανολογούμενη ανεπιθύμητες ενέργειες στον Εθνικό Οργανισμό Φαρμάκων (Μεσογείων 284, GR-15562 Κολακός, Αθήνα, Τηλ: + 30 21 3204038/337, Φαξ: + 30 21 6549585, Ιστοσελίδα: <http://www.eof.gr>), για την Ελλάδα, ή στις Φαρμακευτικές Υπηρεσίες, Υπουργείο Υγείας, CY-1475, www.moh.gov.cy/cypha, Fax: + 357 22608649, για την Κύπρο. **ΚΑΤΟΧΟΣ ΤΗΣ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ** Novo Nordisk A/S, Novo Allé, DK-2880 Bagsvaerd, Δανία. **ΑΡΙΘΜΟΣ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ** EU/1/09/529/001-005 **ΗΜΕΡΟΜΗΝΙΑ ΠΡΩΤΗΣ ΕΓΚΡΙΣΗΣ/ΑΝΑΘΕΩΡΗΣΗΣ ΤΗΣ ΑΔΕΙΑΣ** Ημερομηνία πρώτης έγκρισης: 30 Ιουνίου 2009. Ημερομηνία τελευταίας ανανέωσης: 11 Απριλίου 2014. **ΗΜΕΡΟΜΗΝΙΑ ΑΝΑΘΕΩΡΗΣΗΣ ΤΟΥ ΚΕΙΜΕΝΟΥ** 08/2019. Λειτουργία πληροφοριακού στοιχείου για το παρόν φαρμακευτικό προϊόν είναι διαθέσιμα στον διαδικτυακό τόπο του Ευρωπαϊκού Οργανισμού Φαρμάκων: <http://www.ema.europa.eu/>. Περισσότερες πληροφορίες παρέχονται στην πλήρη Περίληψη Χαρακτηριστικών του Προϊόντος. Χορηγείται με ιατρική συνταγή. Α.Τ.: 108.08E

Βιβλιογραφία: 1. Fien SD, Gardin JM, Abrams J, et al. Circulation 2012;126:354-4471. 2. IDF diabetes atlas 7th edition, 2015. Available at: <http://www.idf.org/diabetesatlas/>. Last accessed: June 2017. 3. Weng K, et al. J Diabetes Complications 2012;26:169-174. 4. American Diabetes Association. Standard of medical care in diabetes - 2017. Diabetes Care. 2017;40(suppl1):S1-S135. 5. Ryden L, Guller PI, Anker SD et al. ESC guidelines on diabetes, pre-diabetes and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2013;34:3035-3087. 6. VICTOZA®, Περίληψη Χαρακτηριστικών Προϊόντος (08/2019). 7. Marso SP, et al. N Engl J Med. 2016;375(4):311-322. 8. Pratley RE, et al. Int J Clin Pract. 2011;65(4):397-407. 9. Nauck M, et al. Diabetes Care. 2016;39(9):1501-1509. 10. Buse JB, et al. Lancet. 2013;381(9861):117-124. 11. Pratley RE, et al. Lancet Diabetes Endocrinol. 2014;2(4):289-297. 12. Buse JB, et al. Lancet. 2009;374(9683):39-47. 13. Dungan KM, et al. Lancet. 2014;384(9951):1349-1357. 14. Marso M, et al. Diabet Med. 2009;26(3):268-278. 15. Nauck M, et al. Diabetes Care. 2009;32(1):84-90. 16. Russell-Jones D, et al. Diabetologia. 2009;52(10):2046-2055. 17. D'Alessio D, et al. Diabetes Obes Metab. 2015;17(2):170-178. 18. Kapitza C, et al. Diabetes Obes Metab. 2013;15(7):642-649. 19. Meier JJ, et al. Diabetologia. 2015;58(7):1263-1273. 20. Mathieu C, et al. Diabetes Obes Metab. 2014;16(7):636-644. 21. Charbonnel B, et al. Diabetologia. 2013;56(7):1503-1511.

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Welcome

Dear Colleagues and Friends,

It is my great honour and pleasure to invite you to attend the 7th ESE Young Endocrinologists and Scientists (EYES) Meeting in Athens, Greece. EYES Meetings are designed to support scientific and professional interaction among Young Scientists interested in Endocrinology from all around the World. They aim at the advance of knowledge, the sharing of experience and the promotion of future clinical and research collaborations.

Athens represents a crossroad of people and civilizations at the heart of the Mediterranean. The city's history begins in the 13th century BC. It flourished as the most important economic and cultural centre of the classical era, producing monuments of global stature and countless archaeological treasures. Modern Athens is a major city, buzzing with life and offering cultural events and activities during every season of the year. It is an appealing destination, not only because of its antiquities, but also of its beautiful neighbourhoods, its immaculately clean beaches and its excellent cuisine and famous nightlife.

The 7th EYES Meeting will take place at the Royal Olympic Hotel in the historical centre of Athens. The venue lays just in front of the famous Temple of Zeus and the National Garden, underneath the Acropolis sacred rock and only two minutes' walk to the new Acropolis Museum. The Meeting will commence on Friday afternoon 13 September 2019 and will end on Sunday afternoon 15 September 2019.

I look forward to welcoming you in Athens, where you will have the opportunity to enjoy an exciting scientific Meeting in a rich cultural and historical setting.

Dr. Stavroula A. Paschou, MD, PhD

Endocrinologist - Diabetologist

On behalf of the Athens 2019 EYES Team

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GENERAL INFORMATION

7th EYES MEETING VENUE

Royal Olympic Hotel
28-34 Ath. Diakou street, 117 43 Athens, Greece
T: (+30) 210 9288400
<https://www.royalolympic.com/>

The Meeting will be held in KALLIROE Hall of the Royal Olympic Hotel.

ACCOMMODATION

Accommodation will be offered at Royal Olympic Hotel for participants outside from Athens.

LANGUAGE

The official language is English. No simultaneous interpretation in other languages will be provided.

INTERNET ACCESS

Wireless Internet connection is available and accessible to all participants in the Hotel's premises, without any additional charge.

ORAL PRESENTATIONS

Speakers are kindly requested to hand in the PowerPoint file of their talk or oral presentation to the Meeting's Technical Secretariat, at least 1 hour before the presentation time.

POSTERS

Poster presenting authors are required to bring along their printed poster, paying particular attention to size: *Height: 1.20 m x Width: 0.80 m*. Posters should be displayed during all days of the Meeting at the designated Poster Area of KALLIROE Hall. Poster hanging tape will be provided by the Meeting's Secretariat.

PUBLICATIONS

All Abstracts of the 7th EYES Meeting will be published in *Endocrine Abstracts*.

AWARDS

The best two Oral Presentations will be awarded during the Closing session.

CERTIFICATES

Certificates of Attendance will be electronically sent to all registered delegates attending the 7th EYES Meeting, once the Meeting is over.

GENERAL INFORMATION

SOCIAL EVENTS

Offered to all registered participants:

Coffee Breaks

Coffee will be offered at a designated area of the Royal Olympic Hotel, during the official breaks of the Meeting.

Lunch Break

Standing lunch will be offered at a designated area of the Royal Olympic Hotel on Saturday 14 September 2019, 14.30-15.30.

Dinner at Plaka, Friday 13 September 2019

It will take place at the "Stamatopoulos Tavern" (Lisiou 26, Plaka, Athens 105 58, tel +30 210 3228722) on Friday 13 September 2019, 20.30. The tavern is in 12 min walking distance from Royal Olympic Hotel. The departure from the Hotel entrance will be at 20.00.

Dinner by the Sea, Saturday 14 September 2019

It will take place at the "Agora Riviera Restaurant" (Iliou 8, Vouliagmeni 166 71, tel +30 210 8961191) on Saturday 14 September 2019, 20.30. Shuttle buses will be departing from Royal Olympic Hotel entrance at 20.00.

Visit to the Acropolis Museum, Sunday 15 September 2019

An organized guided tour of the Acropolis Museum (Dionysiou Areopagitou 15, Athens 117 42) will take place on Sunday 15 September 2019, 15.00. The Museum is in 8 min walking distance from Royal Olympic Hotel. The departure from the Hotel entrance will be at 14.30.

7th EYES MEETING SECRETARIAT DESK

Friday 13 September 2019, 12.00-20:00

Saturday 14 September 2019, 08.00-20.00

Sunday 15 September 2019, 08.30-14.30

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Οκτώβριος 2018. Κωδικός: L.GR.ADC.10.2018.52590





SCIENTIFIC PROGRAM

Friday 13 September 2019

12.00-14.00 **Arrival and Registration**

14.00-14.30 **Opening**

Stavroula A. Paschou, LOC Chair

Ljiljana Marina, EYES Co-Chair

Ayse Zengin, EYES Co-Chair

Helen Gregson, ESE CEO

14.30-16.30 **Oral Presentations**

THYROID

Chairs: **Maria Prokopiou, George Simeakis, Eleftherios Spartalīs**

O 1 Prevalence of thyroid dysfunctions in a large cohort of Human Immunodeficiency Virus (HIV)-Infected Patients

Giulia Tartaro^{1,2}, Sara De Vincentis^{1,2}, Giulia Brigante^{1,2}, Chiara Diazzi², Andrea Malagoli³, Giovanni Guaraldi⁴, Vincenzo Rochira^{1,2}

¹Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy, ²Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Italy, ³Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy, ⁴Multidisciplinary Metabolic Clinic, Unit of Infectious Diseases, University of Modena and Reggio Emilia, Italy

O 2 Occurrence of second primary malignancy in Medullary Thyroid Cancer (MTC) patients

George Simeakis, Katerina Saltiki, Evangelia Zapanti, Evanthia Kassis, Maria Alevizaki

Endocrine Unit, Dept Clinical Therapeutics, Medical School National Kapodistrian University, Athens, Greece

O 3 The effectiveness of different treatment regimens in patients with Graves' ophthalmopathy

Fomina Daria

Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University

O 4 Thyroid lymphoma in a patient presenting with severe airway compromise

Maria Stamou, Chris Richey, Joseph Watson, Chaim Rube, Andy Nguyen, Brenda Garcia, Daniel Roberts, Prudence Lam, Jeffrey Roach, Sara Barcia, Christine McLaughlin, Jessica McCannon.

Mount Auburn Hospital, Harvard Medical School, Cambridge, USA

O 5 Caprini score is not reliable in predicting the preoperative risk of thromboembolism in thyroid and parathyroid surgery

Konstantinos Iliakopoulos¹, Eirini Pantiora¹, Ourania Preza², Christos Psychogios², Chara Bourgioti², Aristides Antoniou², Dionysis Dellaportas¹, Nikolaos Dafnios¹, Thomas Kotsis¹, Constantinos Nastos¹

¹2nd Department of Surgery, Aretaieion Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, ²1st Department of

Radiology Aretaieion Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

O 6 Local hypothyroidism in brain cortex leads to diminished glucose metabolism in Alzheimer's disease animal model

Tetiana Shcholok, Tetiana Gorbach

Department of Biochemistry, Kharkiv National Medical University, Kharkiv, Ukraine

O 7 Coexistence of medullary carcinoma and papillary carcinoma of the thyroid in a 35 year old patient with RET protooncogene mutation

Flavia Giselle Nuțu², Roxana Dușceac^{1,2}, Cătălina Poiană^{1,2}

¹Carol Davila University of Medicine and Pharmacy Bucharest, Romania,

²National Institute of Endocrinology C.I.Parhon, Bucharest, Romania

O 8 Toxic adenoma as a rare cause of hyperthyroidism in a prepubertal boy.

Ioanna Kosteria, Ioannis-Anargyros Vassilakis, Marina Koulenti, Antonios Voutetakis, Christina Kanaka-Gantenbein

Division of Endocrinology, Diabetes and Metabolism, First Department of Pediatrics, National and Kapodistrian University of Athens Medical School, Aglia Sophia Children's Hospital, Athens, Greece

O 9 Comparison of thyroglobulin levels on the third and fifth day after rhTSH injection in patients with differentiated thyroid cancer

Kogia Christina, Drakou Maria, Lilis Dimitrios, Ioannidis Dimitrios, Polymeris Antonis

Department of Endocrinology, Metabolism and Diabetes Mellitus, Sismanogleio-Amalia Fleming General Hospital, Melissia Greece

O 10 The genetic landscape of indeterminate thyroid nodules

Martyna Borowczyk¹, Ewelina Szczepanek-Parulska¹, Szymon Dębicki¹, Bartłomiej Budny¹, Frederik A. Verburg², Dorota Filipowicz¹, Elżbieta Wrotkowska¹, Małgorzata Janicka-Jedyńska³, Barbara Więckowska⁴, Lidia Gil⁵, Katarzyna Ziemnicka¹, Marek Ruchała¹

¹Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poland, ²Department of Nuclear Medicine, University Hospital Marburg, Marburg, Germany, ³Department of Clinical Pathology, Poznan University of Medical Sciences, Poznan, Poland, ⁴Department of Computer Science and Statistics, Poznan University of Medical Sciences, Poznan, Poland, ⁵Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poland

O 11 Role of SIX1 homeoprotein in the regulation of TGFβ pathway in anaplastic thyroid cancer

Adrián Acuña-Ruiz¹, Garcilaso Riesco-Eizaguirre^{2,3}, Pilar Santisteban^{1,3}

¹Departamento de Biología del Cáncer, Instituto de Investigaciones Biomédicas "Alberto Sols", Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain, ²Hospital Universitario de Móstoles, Madrid, Spain, ³Centro de Investigación Biomédica en Red de Cáncer (CIBERONC) Instituto de Salud Carlos III (ISCIII), Madrid, Spain

O 12 Brain energy metabolism in an animal model of the co-occurrence of depression and hypothyroidism

Katarzyna Głombik, Jan Detka, Anna Kurek, Bogusława Budziszewska
Department of Experimental Neuroendocrinology, Maj Institute of Pharmacology, Polish Academy of Sciences, Cracow, Poland

O 13 Early onset thyroiditis and late onset Fulminant Type 1 Diabetes Mellitus following Pembrolizumab therapy

Angelos Kyriacou^{1,2}, Eka Melson^{3,4}, Punith Kempegowda^{3,4}

¹*CEDM Centre of Endocrinology, Diabetes and Metabolism, Limassol, Cyprus,*

²*Department of Endocrinology, Salford NHS Foundation Trust, Salford, UK,*

³*Institute of Metabolism and Systems Research, University of Birmingham, UK,*

⁴*Health Education West Midlands, Birmingham, UK*

O 14 Effects of thyroid function on peripheral serum markers: results from a cohort of thyroid cancer patients

Maria Laura Monzani^{1,2}, Sara De Vincentis^{1,2}, Francesca Della Casa Venturelli¹,
Francesca Piccinini^{1,2}, Simonetta Tagliavini³, Robin P. Peeters⁴, Manuela Simoni^{1,2}, Giulia Brigante^{1,2}

¹*Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy,* ²*Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy,* ³*Department of Laboratory Medicine and Pathology, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy,* ⁴*Department of Internal Medicine, Academic Center for Thyroid Diseases, Erasmus Medical Center, Rotterdam, the Netherlands*

16.30-17.00

Lecture

Chairs: **George Boutsios, Constantinos Nastos**

Thyroid cancer: from genetics to current management

Maria Alevizaki

17.00-17.30

Coffee Break

17.30-18.30

Oral Presentations

ADRENALS

Chairs: **Giuseppe Defeudis, Ioanna Mavroeidi, Nikolaos Voulgaris**

O 15 Aldosterone-to-renin ratio as an accurate diagnostic tool in patients on antihypertensive therapy

Agnieszka Łebek-Szatańska, Piotr Glinicki, Karolina M. Nowak, Monika Rdzanek, Wojciech Zgliczyński, Lucyna Papierska
Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland

O 16 hCG stimulation induces cortisol secretion in menopausal patients with adrenal incidentalomas

Antoan Stefan Sojat¹, Ljiljana Marina¹, Miomira Ivovic¹, Milina Tancic Gajic¹,

Zorana Arizanovic¹, Jelena Milin Lazovic², Aleksandra Kendereski¹, Svetlana Vujovic¹

¹Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Serbia, ²Institute of Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Serbia

O 17 Impact of glucocorticoid receptor gene polymorphisms on occurrence of steroid-induced adverse events

Karolina M. Nowak¹, Marta Sobalska – Kwapis², Monika Rdzanek¹, Katarzyna Romanowska-Próchnicka³, Anna Nowakowska-Płaza⁴, Lucyna Papierska¹

¹Department of Endocrinology, Centre of Postgraduate Medical Education, Bielanski Hospital, Warsaw, Poland, ²Biobank Lab, Department of Molecular Biophysics, University of Lodz, Lodz, Poland, ³Department of Systemic Connective Tissue Diseases, Eleonora Reicher National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland, ⁴Department of Rheumatology, Eleonora Reicher National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland

O 18 Transcriptome profiling explains clinical characteristics of *PRKACA* mutant cortisol-producing adenomas

Jung Hee Kim^{1,5}, Insoon Jang², Su-Jin Kim³, Ra-Young Song³, Kwang Soo Kim², Hyun-Seob Lee², Moon Woo Seong⁴, Chan Soo Shin¹, Kyu Eun Lee³

¹Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea, ²Translational Research Institute, Biomedical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea, ³Department of Surgery, Seoul National University College of Medicine, Seoul, Republic of Korea, ⁴Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea, ⁵Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University College of Medicine, Seoul, Republic of Korea

O 19 Partially successful adrenal vein sampling can in some cases reveal the etiology of primary aldosteronism

Karin Zibar Tomšić¹, Vilim Molnar², Tina Dušek^{1,2}, Ivana Kraljević¹, Tanja Škorić Polovina¹, Annemarie Balaško¹, Mirsala Solak¹, Darko Kaštelan^{1,2}

¹Department of Endocrinology, University Clinical Hospital Center, Zagreb, Croatia, ²School of Medicine, University of Zagreb, Croatia

O 20 Phenotype of patients carrying the c.709(-7-2)del *PRKAR1A* mutation in a large cohort of 40 patients

Fatimetou Abderrahmane¹, Gerald Raverot², Hervé Lefebvre³, Catherine Cardot-Bauters¹, Marie-Christine Vantyghem¹, Jérôme Bertherat^{*4}, Stéphanie Espiard^{*1}

¹Service d'endocrinologie, diabétologie, métabolisme et nutrition, CHR-U de Lille, Hôpital Huriez, France, ²Fédération d'endocrinologie, groupement Hospitalier Est, Hospices Civils de Lyon, France, ³Service d'endocrinologie, diabète et maladies métaboliques, CHU de Rouen, France, ⁴Service d'endocrinologie, Centre de

référence des maladies surrénaliennes rares, Assistance Publique Hôpitaux de Paris, Hôpital Cochin, Paris, France

**co-last authors*

O 21 Urine steroid metabolomics as a novel diagnostic tool for recurrent adrenocortical carcinoma detection

Vasileios Chortis^{1,2,3}, Irina Bancos^{1,4}, Thomas Nijman⁵, Lorna C. Gilligan¹, Angela E. Taylor¹, Cristina L. Ronchi^{1,2,3,6}, Michael W. O'Reilly^{1,2,3}, Jochen Schreiner⁶, Miriam Asia^{2,3}, Anna Riester⁷, Massimo Terzolo⁸, Rosella Libé⁹, Marcus Quinkler¹⁰, Letizia Canu¹¹, Isabel Paiva¹², Maria J. Bugalho¹³, Darko Kastelan¹⁴, M. Conall Dennedy¹⁵, Mark Sherlock¹⁶, Urszula Ambroziak¹⁷, Dimitra Vassiliadi¹⁸, Jerome Bertherat⁹, Felix Beuschlein^{7,19}, Martin Fassnacht^{6,20,21}, Jonathan J. Deeks^{22,23}, Michael Biehl⁵, and Wiebke Arlt^{1,2,3,23}

¹Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK, ²Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK, ³Department of Endocrinology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, ⁴Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, USA, ⁵Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligence, University of Groningen, Groningen, The Netherlands, ⁶Division of Endocrinology and Diabetes, Department of Internal Medicine I, University Hospital, University of Würzburg, Germany, ⁷Medizinische Klinik and Poliklinik IV, Ludwig-Maximilians-Universität München, Munich, Germany, ⁸University of Turin, Turin, Italy, ⁹INCa- COMETE, Cochin Hospital, Institut Cochin, Institut National de la Santé et de la Recherche Médicale Unite 1016, René Descartes University, Paris, ¹⁰Endocrinology in Charlottenburg, Berlin, Germany, ¹¹Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence, Italy, ¹²University Hospital of Coimbra, Portugal, ¹³Serviço de Endocrinologia Diabetes e Metabolismo, Hospital de Santa Maria, Lisbon, Portugal, ¹⁴Department of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia, ¹⁵National University of Ireland Galway (NUIG), Galway, Republic of Ireland, ¹⁶Department of Endocrinology, Beaumont Hospital, Dublin and the Royal College of Surgeons, Republic of Ireland, ¹⁷Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland, ¹⁸Evangelismos Hospital, Athens, Greece, ¹⁹Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, Universitäts-Spital Zürich, Zürich, Switzerland, ²⁰Comprehensive Cancer Center Mainfranken, University of Würzburg, Würzburg, Germany, ²¹Central Laboratory, University Hospital of Würzburg, Würzburg, Germany, ²²Institute of Applied Health Research, University of Birmingham, Birmingham, UK, ²³NIHR Birmingham Biomedical Research Centre, University Birmingham NHS Hospital Trusts and University of Birmingham, Birmingham, UK

Friday 13 September 2019

- 18:30-19:00 **Lecture**
Chairs: **Vasiliki Bravi, Ljiljana Marina**
Stress: Endocrine physiology and pathophysiology
George P. Chrousos
- 20.00 **Dinner at Plaka**

09.00-10.30 **Oral Presentations**

OBESITY AND LIPIDS

Chairs: Despina Avramidou, Maria Barmpari, Kostis Michalakis

O 22 Anthropometric and hormonal predictors of metabolic obesity phenotypes in menopause

Eleni Armeni¹, Areti Augoulea¹, Demetrios Rizos², George Kaparos², Anastasia Soureti¹, Iliana Karagouni¹, Michail Apostolakis¹, Irene Lambrinoudaki¹

¹Second department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece, ²Hormonal and Biochemical Laboratory, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece

O 23 Sarcopenia and sarcopenic obesity in liver transplantation population

C.M. Peteiro Miranda, J.J. Orteza Toro, B. Sanz Martín, S. Roman Gimeno, J.A. Gimeno Orna, M.J. Ocón Bretón

Endocrinology and nutrition, Hcu Lozano Blesa, Zaragoza, Spain

O 24 Proglucagon peptide family responses after RYGB surgery in obese patients with type 2 diabetes

Kleopatra Alexiadou¹, Joyceline Cuenco¹, James W. Howard², Matthieu Fleuret², Preeshila Behary¹, George Tharakan¹, Nicolai J. Wewer Albrechtsen³, Jens Juul Holst⁴, Jason Pembroke², Robert Wheller², Ahmed R. Ahmed¹, Steve R Bloom¹, Tricia M. Tan¹

¹Section of Investigative Medicine, Imperial College London, London, U.K., ²LGC Limited, Fordham, Cambridgeshire, U.K., ³Department of Clinical Biochemistry, Rigshospitalet, Copenhagen, Denmark, ⁴Panum Institute, Department of Biomedical Sciences and the Novo Nordisk Foundation Centre for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark

O 25 Evaluation of microRNA in patients with obesity: association with coronary artery disease

Teona A. Shvangiradze, Irina Z. Bondarenko, Ekatreina A. Troshina

Endocrinology Research Centre, Moscow, Russia

O 26 Associations between FSH levels and indices of regional and total obesity in women after menopause

Eleni Armeni¹, Stavroula A. Paschou¹, Areti Augoulea¹, Stefanos Stergiotis¹, Panagiota Chatzivasilou¹, Dimitrios Rizos², George Kaparos², Konstantinos Panoulis¹, Anastasia Palaiologou¹, Irene Lambrinoudaki¹

¹Second Department of Obstetrics and Gynecology, Aretaieio Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece, ²Hormonal and Biochemical Laboratory, Aretaieio Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece

O 27 Subcutaneous white adipocytes histological evaluation in obese bariatric patients: size matters

Ioana Hristov¹, Daniel Timofte², Andrei Hristov⁴, Adrian Tiron⁵, Crina Tiron⁵, Teodor Oboroceanu¹, Veronica Mocanu¹

¹University of Medicine and Pharmacy "Gr. T.Popa" Iași, Department of Morpho-Functional Sciences II, ²University of Medicine and Pharmacy "Gr. T.Popa" Iași, Department of Surgical Sciences I, ³University of Medicine and Pharmacy "Gr. T.Popa" Iași, Department of Medical Sciences II, ⁴Surgery Department, Emergency Hospital Vaslui, Romania, ⁵TRANSCEND Research Institute, Regional Oncology Institute, Iasi, Romania

O 28 Hypoxia modulates effects of fatty acids on human pancreatic β -cells

Jan Šrámek¹, Vlasta Němcová-Fürstová¹, Jan Polák², Jan Kovář¹

¹Department of Biochemistry, Cell and Molecular Biology and Center for Research of Diabetes, Metabolism and Nutrition, Third Faculty of Medicine, Charles University, Prague, Czech Republic, ²Department of Pathophysiology, Third Faculty of Medicine, Charles University, Prague, Czech Republic

O 29 MTHFR polymorphic variants are associated with the predisposition of weight loss in girls with anorexia nervosa

Areti Augoulea¹, Eleni Armeni¹, Evangelia Deligeoroglou¹, Emmanuel Economou², Georgios Papadimitriou¹, Evgenia Stergioti¹, Vassilios Karountzos¹, Artemis Tsitsika³, Konstantinos Panoulis¹, Irene Lambrinoudaki¹

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²Clinical Laboratory of Therapeutic Individualization, National and Kapodistrian University of Athens, School of Medicine, Aretaieio Hospital, Athens, Greece,

³Adolescent Health Unit, Second Department of Pediatrics, P. and A. Kyriakou Children's Hospital, University of Athens, Leoforos Mesogeion 24, Athens, Greece

O 30 AKR1D1 is a novel regulator of metabolic phenotype in human hepatocytes and is dysregulated in non-alcoholic fatty liver disease

Nikolaos Nikolaou¹, Laura L. Gathercole^{1,2}, Lea Marchand¹, Sara Althari¹, Niall J. Dempster¹, Charlotte J. Green¹, Martijn van de Bunt¹, Catriona McNeil¹, Anastasia Arvaniti^{1,2}, Beverly A. Hughes⁴, Bruno Sgromo⁵, Richard S. Gillies⁵, John Ryan³, Wiebke Arlt⁴, Leanne Hodson¹, Jeremy W. Tomlinson¹

¹Oxford Centre for Diabetes, Endocrinology and Metabolism, NIHR Oxford Biomedical Research Centre, University of Oxford, Churchill Hospital, Oxford, UK, OX3 7LE, UK, ²Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, OX3 0BP, UK, ³Translational Gastroenterology Unit, University of Oxford, Oxford, UK, ⁴Institute of Metabolism and Systems Research, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK,

⁵Department of Upper GI Surgery, Churchill Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Saturday 14 September 2019

10.30-10.35 **Introducing the Bioscientifica Trust**
Stavroula A. Paschou

10.35-11.30 **Clinical Workshop**
Chairs: Christina Kogia, Ioanna Kosteria
Transition clinics from pediatric to adult Endocrinologist
Christina Kanaka-Gantenbein and Andromachi Vryonidou

11.30-12.00 **Coffee Break**

12.00-13.30 **Oral Presentations**
PITUITARY

Chairs: Dimitrios Askitis, Nektaria Papadopoulou, Dorina Ylli

O 31 Onset of radiation-induced hypopituitarism in pituitary adenomas
K. Seejore¹, G. Tudawe², T. Mansoor², J.M. Lynch¹, S.M. Orme¹, N. Phillips³,
C. Loughrey⁴, R.D. Murray^{1,5}

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O32 PITUITARY APOPLEXY CLINICAL PRESENTATION AND MANAGEMENT: THE EXPERIENCE OF A SINGLE CENTER

S. Dalakoura¹, N. Kalogeris¹, R. Gyftaki¹, E. Herolidi¹, A. Dermentzoglou¹,
V. Loi¹, S. Paschou¹, K. Barkas², A. Vryonidou¹

¹Department of Endocrinology, Diabetes Mellitus and Metabolism, ²Neurosurgery Clinic General Hospital of Athens "Korgialenio-Benakio", Hellenic Red Cross

O 33 Bone health and final height in craniopharyngioma patients

Selveta S. van Santen^{1,4}, Daniel S. Olsson^{2,3}, Casper Hammarstrand^{2,3}, Mark Wijnen¹, Gudmundur Johannsson^{2,3}, Aart J van der Lely¹, MM van den Heuvel-Eibrink⁴, Sebastian JCMM Neggers^{1,4}

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O 34 Splicing machinery is dysregulated in pituitary neuroendocrine tumors (PitNETs) and associated with aggressiveness features

Juan M. Jiménez-Vacas^{1,2,3,4}, Mari C. Vázquez-Borrego^{1,2,3,4}, Antonio C. Fuentes-Fayos^{1,2,3,4}, Eva Venegas-Moreno⁵, Mônica R. Gadelha^{6,7}, María A.

Gálvez-Moreno^{1,3,8}, Alfonso Soto-Moreno⁵, Manuel D. Gahete^{1,2,3,4}, Justo P. Castaño^{1,2,3,4}, Raúl M. Luque^{1,2,3,4}

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O 35 Somatostatin analogues in the therapy of clinically non-functioning pituitary adenomas- do they decrease the risk of tumour progression?

Natalia Bozeana Zawada

Department of Clinical Endocrinology, Medical University of Lodz

O 36 Unusual cause of gigantism - Growth hormone releasing hormone (GHRH)-secreting pancreatic neuroendocrine tumour in a patient with multiple endocrine neoplasia type 1 (MEN1)

Vinaya Srirangam Nadhamuni¹, Donato Iacovazzo¹, Jane Evanson², Jacqueline Trouillas³, Tom Kurzawinski⁴, Satya Bhattacharya², Márta Korbonits¹

¹Department of Endocrinology, William Harvey Research Institute, Bart's and the London School of Medicine and Dentistry, Queen Mary, University of London, Mile End Rd, Bethnal Green, London, UK, ²St Bartholomew's Hospital, W Smithfield, London, UK, ³Department of Pathology, Groupement Hospitalier Est, Hospices Civils de Lyon, Bron, France, ⁴Division of Endocrine Surgery, University College Hospital, Bloomsbury, London, UK

O 37 Sparsely and densely granulated growth hormone-secreting pituitary tumours (somatotropinomas): from histopathology to epigenomics

Vinaya Srirangam Nadhamuni, Sayka Barry, Márta Korbonits

Department of Endocrinology, William Harvey Research Institute, Queen Mary University of London

O 38 Non-functioning pituitary adenomas experience of a reference center

Clara Cunha¹, Cátia Ferrinho¹, Eugénia Silva¹, Lúcia Dias², Conceição Marques², Martinha Choroão³, Catarina Saraiva¹, João Sequeira Duarte¹

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O 39 The role of microRNAs and its targeted genes in development of ACTH-dependent hypercortisolism

Khandaeva P.M., Belaya Zh.E., Nikitin A.G., Solodovnikov A.S., Lutsenko A.S. Endocrinology Research Centre, Moscow

Saturday 14 September 2019

O 40 T2-signal intensity, SST receptor expression and first-generation somatostatin analogs efficacy predict hormone and tumor responses to pasireotide in acromegaly

Eva C. Coopmans¹, Joppe J. Schneiders², Nour El-Sayed¹, Nicole S. Erler³, Leo J. Hofland¹, Patrick Petrossians⁴, Sjoerd van den Berg⁵, Aart-Jan van der Lely¹, Ammar Muhammad¹, Sebastian J.C.M.M. Neggers¹

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13.30-14.30 Parallel Guided Poster Sessions

Session A: GP1-GP10

Chairs: Liubov Matcekhina, Spiros Sapounas

Session B: GP11-GP20

Chairs: Vasileios Chortis, Andreas Rizoulis

Session C: GP21-GP28

Chairs: Punith Kempegowda, Dimitris Margaritopoulos

Session D: GP29-GP37

Chairs: Vasiliki Antonopoulou, Maria Stamou

Session E: GP38-GP46

Chairs: Maria Christou, Nikos Kalogeris

14.30-15.30 Lunch Break

15.30-16.30 Oral Presentations

CALCIUM AND BONE

Chairs: Anastasia Dede, Maria Mizamtsidi, Ayse Zengin

O 41 Clinical features of primary hyperparathyroidism in women of different age groups according to the Russian Online Register database

Mirnaya S.S., Volodicheva V.L., Bibik E.E., Mokrysheva N.G.

Endocrinology Research Centre, Moscow, Russian Federation

O 42 Osteoprotegerin and receptor activator of nuclear factor kappa-B ligand levels and their association with BMD in acromegaly

Jowita Halupczok-Żyła, Aleksandra Jawiarczyk-Przybyłowska, Marek Bolanowski

Department and Clinic of Endocrinology, Diabetes and Isotope Therapy, Wrocław Medical University, Wrocław, Poland

O 43 Vitamin D deficiency in pregnant women in Russia Federation

Anastasia Rybakova, Nadezhda Platonova, Ekaterina Troshina, Larisa Nikankina

Endocrinology Research Centre, Moscow, Russia

Saturday 14 September 2019

O 44 Quality of Life in Chronic Hypoparathyroidism

Elena V. Kovaleva, Natalia G. Mokrysheva

Endocrinology Research Centre, Moscow, Russian Federation

O 45 Antiosteoporotic drugs effectiveness and Ca/Vit D supplementations intake in elder patients with osteoporosis

L. Machekhina, Yu. Onuchina, E. Dudinskaya, N. Brailova, K. Eruslanova, O. Tkacheva

Russian Gerontology Research and Clinical Centre, Moscow

O 46 Effect of treatment with Cinacalcet on TBS and BMD in patients with chronic renal failure with secondary hyperparathyroidism in hemodialysis

Mola Reyes Laura¹, Librizzi María Soledad¹, Hernández Martínez Eduardo², Mérida Herrero Eva², Trujillo Cuéllar Hernando², Martín Arriscado Cristina³, Hawkins Carranza Federico¹

¹Endocrinology and Nutrition Department. Hospital 12 de Octubre, Madrid. Spain, ²Nephrology Department. Hospital 12 de Octubre, Madrid. Spain,

³Research Assistance Department. Hospital 12 de Octubre, Madrid. Spain

16.30-17.00 **Lecture**

Chairs: Luis Cardoso, Athanasios Fountas

Ultradian system as an “endocrine holter”: evidence and perspectives

Marinella Tzanela

17.00-17.30 **Coffee Break**

17.30-18.30 **Oral Presentations**

REPRODUCTIVE ENDOCRINOLOGY

Chairs: Adam Czyzyk, Filio Spanoudi, Agathi Vasileiou

O 47 Efficacy of sex hormone replacement and growth hormone therapy on bone mineral density in patients with Turner syndrome

Tvarijonaviciute Laura¹, Donielaite Gyte¹, Kriksciuniene Ruta^{1,2}

¹Lithuanian University of Health Sciences, Kaunas, Lithuania, ²The Hospital of Lithuanian University of Health Sciences Kauno Klinikos, Department of Endocrinology, Kaunas, Lithuania

O 48 Real-world management of male idiopathic infertility in indication for FSH treatment: a multicenter, longitudinal, observational cohort study (open registry)

Sara De Vincentis^{1,2}, Rocco Rago³, Alessandro Dal Lago³, Francesco Lombardo⁴, Francesco Pallotti⁴, Francesco Cargnelutti⁴, Rosario Pivonello⁵, Marco Mazzella⁵, Cristina De Angelis⁵, Mariarita Rampini⁶, Patrizia Alfano⁶, Giancarlo Balercia⁷, Gianmaria Salvio⁷, Melissa Cutini⁷, Maria Elisabetta Coccia⁸, Laura Badolato⁸, Giulia Orlandi⁸, Aldo E. Calogero⁹, Rosita A. Condorelli⁹, Laura M. Mongioi⁹, Adolfo Allegra¹⁰, Angelo Marino¹⁰, Nicola Iannantuoni¹¹, Clelia Zullo¹¹, Caterina Capuozzo¹¹, Manuela Simoni^{1,2}, Daniele Santi^{1,2}

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O 49 Genetic background predicts the presence of oligo- or amenorrhea in girls with anorexia nervosa

Areti Augoulea¹, Eleni Armeni¹, Stavroula A. Paschou¹, Evangelia Deligeoroglou¹, Emmanuel Economou², Georgios Papadimitriou¹, Evgenia Stergioti¹, Vassilios Karountzos¹, Artemis Tsitsika³, Konstantinos Panoulis¹, Irene Lambrinoudaki¹

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O 50 Polycystic ovary syndrome: inositol vs. Metformin vs. Oral contraceptives – a prospective study

Borlea Andreea¹, Cotoi Laura¹, Deharde Lisa Katharina², Petre Izabela³, Navolan Dan Bogdan³, Stoian Dana⁴

¹PhD Student, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania, ²"Victor Babes" University of Medicine and Pharmacy Timisoara, Romania, ³Department of Obstetrics Gynecology, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania, ⁴Department of Internal Medicine II, "Victor Babes" University of Medicine and Pharmacy Timisoara, Romania

O 51 THE INFLUENCE OF SEX ON THE EVOLUTION OF MESENTERIC METASTASIS IN SMALL INTESTINAL NEUROENDOCRINE TUMOURS

Anela Blažević¹, Wouter Zandee¹, Johannes Hofland¹, Anand Iyer¹, Gaston J. H. Franssen², Marie-Louise F. van Velthuysen³, Tessa Brabander⁴, Richard A. Feelders¹, Leo J. Hofland¹, Wouter W. de Herder¹

¹Department of Internal Medicine, Section Endocrinology, ²Department of Surgery, ³Department of Pathology, ⁴Department of Radiology and Nuclear

Saturday 14 September 2019

Medicine, ENETS Centre of Excellence, Erasmus University Medical Center and Erasmus MC Cancer Institute

O 52 Defining molecular mechanisms regulating SIRT1 expression and its roles in human granulosa-lutein cells

Magdalena Szymanska^{1*}, Sarah Manthe¹, Ketan Shrestha¹, Eliezer Girsh², Shevach Friedler², Rina Meidan¹

¹*Department of Animal Sciences, The Robert H. Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Rehovot, Israel,*

²*IVF unit, Barzilai University Medical Center, Ashqelon, Israel*

**supported by The Robert H. Smith Faculty of Agriculture, Food and Environment Research, Fund for International Cooperation.*

O 53 Seasonal changes of serum gonadotropins and testosterone in men: a reappraisal from a large data set of real-world observations over eight years

Giorgia Spaggiari¹, Antonio R. M. Granata¹, Monica Setti², Simonetta Tagliavini³, Tommaso Trenti³, Manuela Simoni^{1,4}, Daniele Santi^{1,4}

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18.30-19.00

Lecture

Chairs: Eva Coopmans, Antonios Voutetakis

Endocrinology in the Greek Mythology

Neoklis Georgopoulos

20.00

Dinner by the Sea

09.00-11.00 Oral Presentations

DIABETES MELLITUS

Chairs: Kleopatra Alexiadou, Maria Andrikoula, Sofia Antoniou

O 54 Sarcopenia is associated with poor glycemic control and peripheral neuropathy in elderly women with type 2 diabetes mellitus

Y.S. Onuchina^{1,2}, I.V. Gurieva^{1,3}

¹Federal State Budgetary Institution «The Federal Bureau for Medical-social Expertise» of Ministry of Labor and Social Protection of the Russian Federation, Moscow, Russia, ²Pirogov Russian National Medical University, The Russian Clinical and Research Center for Gerontology, Moscow, Russia ³Federal State Budgetary Educational Institution of Further Professional Education «Russian Medical Academy of Continuous Professional Education» of the Ministry of Healthcare of the Russian Federation, Moscow, Russia

O 55 Glucocorticoid treatment is associated with dose-dependent insulin resistance in healthy male volunteers

Riccardo Pofi^{1,2}, Ilaria Bonaventura^{1,2}, Nanthia Othonos¹, Thomas Marjot¹, Ahmed Moolla¹, Andrea M. Isidori², Leanne Hodson¹, Jeremy W. Tomlinson¹

¹Department of Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM) and NIHR Oxford Biomedical Research Centre, Churchill Hospital, University of Oxford, Oxford, UK, ²Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy

O 56 Effects of novel antidiabetic agents on the arterial wall elastic properties as a marker of vascular function in patients with type 2 diabetes mellitus

Panagiota Stampoulou¹, Gerasimos Siasos¹, Evanthia Bletsas¹, Konstantinos Batzias¹, Stavroula A. Paschou¹, Alexis Antonopoulos¹, Vasiliki Tsigkou¹, Evangelos Oikonomou¹, Nikolaos Gouliopoulos¹, Anastasia Thanopoulou², Marina Noutsou², Andromahi Vryonidou³, Nikolaos Tentolouris⁴, Dimitris Tousoulis¹

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O 57 β -hydroxybutyrate and risk for incident type 2 diabetes: results from the prevend prospective cohort study

Jose L. Flores-Guerrero¹, Margery A. Connelly², Dion Groothof¹, Eke G. Gruppen¹, Stephan J.L. Bakker¹, Robin P.F. Dullaart³

¹Department of Internal Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, ²Laboratory Corporation of America Holdings (LabCorp), Morrisville, North

Carolina, USA, ³Department of Internal Medicine, Division of Endocrinology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

O 58 Arterial stiffness is an independent predictor for risk of mortality in patients with type 2 diabetes mellitus: the REBOUND study

Jeong Mi Kim^{1,2}, Sang Soo Kim^{1,2*}, In Joo Kim^{1,2*}, Mi Kyung Kim³, Soon Hee Lee⁴, Chang Won Lee⁵, Min Chul Kim⁶, Jun Hyeob Ahn⁷, and for the Relationship between Cardiovascular disease and Brachial-ankle Pulse Wave Velocity (baPWV) in Patients with Type 2 Diabetes (REBOUND) Study Group
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*These authors have contributed equally to this work reported, thus both should be considered as the corresponding-authors

O 59 Reduced insulin clearance relates to increased liver fat content in recent-onset type 2 diabetes and to impaired glucose control in recent-onset type 1 diabetes

Sofia Antoniou^{2,3}, Oana P. Zaharia^{2,3}, Pavel Bobrov^{3,4}, Klaus Strassburger^{3,4}, Yanislava Karusheva^{2,3}, Kálmán Bódis^{1,2,3}, Yuliya Kupriyanova^{2,3}, Volker Burkart^{2,3}, Jong-Hee Hwang^{2,3}, Karsten Müssig^{1,2,3}, Amalia Gastaldelli^{5,6}, Michael Roden^{1,2,3}, Julia Szendroedi^{1,2,3}

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O 60 Increased risk of site-specific cancer in people with type 2 diabetes: a national cohort study

Linkeviciute-Ulinskiene Donata¹, Patasius Ausvydas^{2,3}, Zabuliene Lina⁴, Smailyte Giedre^{2,3}

¹Institute of Biomedical Sciences, Department of Pathology, Forensic Medicine and Pharmacology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania,

²Laboratory of Cancer Epidemiology, National Cancer Institute, Vilnius, Lithuania, ³Institute of Health Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania, ⁴Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

O 61 Relationship between hematological and glycemic parameters and degenerative complications in type 2 diabetes mellitus in a prospective study

Dragana Milosevic¹, Violeta Lukic-Panin^{2,3}

¹Health Care Center Indjija, Department of Laboratory Medicine, Indjija, Serbia,

²Faculty of Medicine Novi Sad, Department of Science, Novi Sad, Serbia, ³Sana Clinic Cham, Roding, Germany

O 62 Serum metabolomic fingerprinting of diabetes reveals persistent changes 3 days after the episode

Beata Małachowska¹, Michał Ciborowski², Karolina Pietrowska², Adam Krętowski², Wojciech Młynarski³, Wojciech Fendler^{1,4}

¹Department of Biostatistics and Translational Medicine, Medical University of Lodz, Lodz, Poland, ²Clinical Research Centre, Medical University of Bialystok, Bialystok, Poland, ³Department of Pediatrics, Oncology and Hematology, Medical University of Lodz, Lodz, Poland

O 63 Flash Glucose Monitoring technology in the management of children and adolescents with type 1 Diabetes leads to improved glycemic control

Ioanna Kosteria, Maira Arkoumani, Stavroula A. Paschou, Ioannis-Anargyros Vassilakis, Christina Kanaka-Gantenbein

Diabetes Centre, Division of Endocrinology, Diabetes and Metabolism, First Department of Pediatrics, National and Kapodistrian University of Athens Medical School, Aghia Sophia Children's Hospital, Athens, Greece

O 64 Conservative management of diabetic foot ulceration complicated by underlying osteomyelitis

E. Dorman¹, V. Salem^{1,2}, J. Valabhji¹, V. Bravis^{1,2}

¹Department of Diabetes and Endocrinology, St Mary's Hospital, Imperial College Healthcare Trust, London, UK, ²Department of Endocrinology, Diabetes and Metabolism, Imperial College, London, UK

O 65 Endothelial function and arterial stiffness indices remain unchanged following intensification of glycemic control in poorly controlled patients with long-standing type 2 diabetes mellitus

Sofia Antoniou¹, Katerina K. Naka², Aris Bechlioulis², Dimitrios Makriyiannis³, Marios Papadakis⁴, Agathocles Tsatsoulis¹, Lampros K. Michalis², Stelios Tigas¹

¹Department of Endocrinology, University Hospital of Ioannina, Ioannina, Greece, ²2nd Department of Cardiology and Michaelidion Cardiac Center, University of Ioannina, Ioannina, Greece, ³Department of Medicine, Hatzikosta General Hospital, Ioannina, Greece, ⁴Department of Surgery, Helios Clinic, University Hospital Witten-Herdecke, Germany

O 66 Influence of empagliflozin on serum calcium and phosphorus concentrations in patients with type 2 diabetes

D. Lebedev, A. Babenko

Institute of Endocrinology, Almazov National Medical Research Centre, Saint Petersburg, Russian Federation

O 67 Treatment intensification with novel antidiabetic agents alters platelet function parameters in patients with type 2 diabetes

Evanthia Bletsa¹, Gerasimos Siasos¹, Panagiota K. Stampoulou¹, Stavroula A. Paschou¹, Alexios Antonopoulos¹, Konstantinos Batzias¹, Nikolaos Gouliopoulos¹, Marina Zaromytidou¹, Evangelos Oikonomou¹, Vasiliki Tsigkou¹, Konstantinos Mourouzis¹, Efthimia Pavlou², Maria Kozanitou³, Anastasia Thanopoulou⁴, Andromachi Vryonidou⁵, Eva Kassi⁶, Nikolaos Tentolouris⁷, Zoi Pallantza³, Dimitris Tousoulis¹

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11.00-11.30

Lecture

Chairs: Elena Armeni, Daniele Santi

Hormone replacement therapy in premature ovarian insufficiency and menopause

Irene Lambrinoudaki

11.30-12.00

Coffee Break

12.00-12.45

Research Workshop

Chairs: Gefsi Mintziori, Damianos Tsitlakidis

How to write a paper: tips and tricks

Dimitrios G. Goulis

12.45-13.15

Lecture

Chairs: Peter Aldiss, Paraskevi Mentzelopoulou

Exercise is Medicine

Anastassios Philippou



Sunday 15 September 2019

- 13.15-14.00 **EYES General Assembly - Interactive Discussion**
Moderators: Ljiljana Marina, Ayse Zengin
Young Endocrinologists and Scientists in Europe: challenges and perspectives
- 14.00-14.30 **Awards and 8th EYES Meeting Announcement - Closing**
Ljiljana Marina, EYES Co-Chair
Ayse Zengin, EYES Co-Chair
Invitation to 8th EYES Meeting, 2020 LOC Representative
Stavroula A. Paschou, LOC Chair
- 14.30 **Visit to Acropolis Museum**



INVITED SPEAKERS



Maria Alevizaki

Professor of Endocrinology, Kapodistrian University School of Medicine, Athens. PhD thesis, London University. Clinical Specialty in Internal Medicine and Endocrinology. She has served as an Officer in the ExCo of the European Society of Endocrinology (ESE) and in the ExCo of the European Thyroid Association (ETA). She has served as chair of the Congress subcommittee and member of the Publication subcommittee of ESE and as chair of the Educational Committee of ETA. She has served in many POCs for European Congresses. Editorial board member of several international journals (ETJ, ECED, Thyroid Research, Endocrine, Hormones, EJE). Until recently deputy Chief Editor of EJE. She has 180 publications in peer reviewed medical journals. Her work has been cited >4000 times. Clinical and Research Interests: Thyroid carcinoma. Medullary thyroid carcinoma. Familial thyroid disease. Subclinical thyroid disease. Endocrine tumours.



George P. Chrousos

Professor George Chrousos was born in Patras, Greece, in 1951. He completed his MD studies at the National and Kapodistrian University of Athens (NKUA) as the valedictorian of his class in 1975. He obtained his Sciences Doctorate from NKUA, and did his residency in Medicine, NKUA, and Pediatrics, New York University, and his fellowship in Endocrinology, Metabolism and Diabetes at the National Institute of Child Health and Human Development (NICHD), National Institutes of Health (NIH), Bethesda, MD. He was Chief of the Pediatric and Reproductive Endocrinology Branch, NICHD, NIH, and subsequently Chairman, First Department of Pediatrics, NKUA, Athens, Greece, until 2018. Currently, he is Professor Emeritus of Pediatrics and Endocrinology, Holder, UNESCO Chair on Adolescent Health Care, Director of the University Research Institute on Maternal and Child Health and Precision Medicine at the NKUA, and Senior Investigator at the Biomedical Research Foundation of the Academy of Athens. Professor Chrousos pioneered studies that elucidated the effects of stress on the organism at the behavioral, neuroendocrine, cellular and molecular levels and made fundamental contributions to the understanding, diagnosis and treatment of pituitary, adrenal and stress-related complex pathologies, i.e., major depression, obesity/metabolic syndrome, and autoimmune/inflammatory, reproductive and sleep disorders. He made seminal observations in the glucocorticoid signaling system of the cell and deciphered some of its key clinical implications. Professor Chrousos's work has been cited over 144,000 times (H-index 185) making him one of the top 100 cited authors (Google Scholar) and physician-scientists (ISI) in both Clinical Medicine and Biology and Biochemistry, and the top cited clinical pediatrician or endocrinologist in the world. He has received numerous major awards, including the Fred Conrad Koch Award, the highest honor of the US Endocrine Society. He is a Doctor Honoris Causa of the Universities of Liege, Belgium, Universita Politecnica delle Marche, Ancona, Italy, and University of Patras, Greece, and an honorary professor of the Universities of Warwick, UK, St. Petersburg State Pediatric Medical University, Russia, and Xi'an Medical University, China. He is an elected member of the American Society for Clinical Research, the Association of American Physicians, the Academia Europaea and the US National Academy of Medicine.



Neoklis Georgopoulos

Neoklis Georgopoulos is an Endocrinologist, Professor of Endocrinology, Reproductive Endocrinology of Patras Medical School. He is married, he has two daughters, he lives constantly in Patras, Greece and he is an amateur collector of wild mushrooms. Trained in Reproductive Endocrinology in Harvard Medical School he is constantly involved in the diagnosis, treatment and research of hypothalamic-pituitary disorders, namely GnRH deficiency, hypothalamic amenorrhea (anorexia nervosa, athletic and stress amenorrhea), PCOS, etc. He has over 100 international publications, based on his clinical and basic molecular research work. Over the last years part of his research work is devoted to the clinical and molecular basis of female sexuality. His work has gained worldwide recognition with more than 15 research awards, reviewer invitations in more than 40 international medical journals and more than 200 lectures in national and international medical meetings. As an amateur of history and philosophy, with a special interest in Greek literature, he has published more than 10 papers in international medical journals on a modern medical interpretation of ancient Greek myths and classical reports of disorders of sexual development and ambiguous genitalia.



Dimitrios G. Goulis

Professor Dimitrios G. Goulis completed his medical training (MD) and received his Doctor of Philosophy (PhD) degree from the Aristotle University of Thessaloniki. Having a scholarship from the European Union, he worked as clinical research fellow at St. Mary's Hospital, London, acquiring the specialty of Endocrinology, Diabetes and Metabolism. He is currently professor of Reproductive Endocrinology in the 1st Department of Obstetrics and Gynecology, Aristotle University. Prof. Goulis has published 270 full papers in peer-review international journals. He was an invited speaker in more than 380 international and Greek congresses. He is currently or had been Head of the Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology; Director of the training center in Andrology of the European Academy of Andrology; Vice-President and Secretary general of the European Menopause and Andropause Society (EMAS); Secretary general of the European Academy of Andrology (EAA); member of the executive committees for the postgraduate training programs (MSc) in "Medical Research Methodology" and "Human Reproduction" (Aristotle University of Thessaloniki) and associate editor of "Human Reproduction", "Andrology", "Metabolism", "Journal of Endocrinological Investigation", "Hormones", "Anir" and "Human Reproduction Open". Prof. Goulis' main research interests include Andrology, menopausal transition, endocrine complications of pregnancy, polycystic ovary syndrome and research methodology.



Christina Kanaka-Gantenbein

Professor Christina Kanaka-Gantenbein, MD, PhD, FMH (CH) is Professor of Pediatrics and Pediatric Endocrinology, Director of the First Department of Pediatrics of the Medical School of the National and Kapodistrian University of Athens. She graduated from the Medical School of the National Kapodistrian University of Athens as a top grade student with Distinction. As a scholarship recipient she trained in Pediatrics in Germany and Switzerland and subsequently subspecialized in Pediatric Endocrinology in Switzerland and France having worked near well-known founders of the European Society for Pediatric Endocrinology. After a 10year training in Pediatrics and Pediatric Endocrinology abroad, she returned in Athens, where she was elected as Assistant Professor for Pediatric Endocrinology and Juvenile Diabetes of the Medical School of the National and Kapodistrian University of Athens in December 2004. In February 2011 she was promoted as Associate Professor for Pediatric Endocrinology and Juvenile Diabetology and finally in June 2016 as Full Professor of Pediatric Endocrinology of the same University. She has hold numerous lectures in several National and International Congresses, has published over 130 peer-reviewed papers in Pediatrics and Pediatric Endocrinology, is a reviewer of several international journals and is an active member of several Endocrine Societies worldwide. Her main research topics of interest are diabetes, the health of children born after assisted reproduction, the intrauterine origin of adult diseases and the transition of children with chronic endocrine disorders to adult health care settings. In June 2018 Professor Christina Kanaka-Gantenbein has been elected Director of the first Department of Pediatrics of the Medical School of the National and Kapodistrian University of Athens and is now leading the biggest University Children's Hospital in Greece, deeply interested in providing high standard education to the medical students, to the Fellows and Residents in Pediatrics as well as the best care to the young pediatric patients.



Irene Lambrinoudaki

Dr. Lambrinoudaki was born in Athens and graduated from Athens University Medical School. She conducted her Doctoral Thesis in Ruprecht Karls University in Heidelberg, Germany on the Epidemiology of osteoporosis in association with endogenous sex hormones. She was trained in Clinical Endocrinology in the Department of Pathophysiology, Athens University Medical School and in the Departments of Endocrinology and Metabolism, in Ruprecht Karls University, Heidelberg, Germany, in Nikaia General District Hospital, Piraeus, Greece and in Queen Mary Hospital, University of Hong Kong. Currently she is Professor of Endocrinology in the 2nd Department of Obstetrics and Gynecology, Medical School, University of Athens, Greece. She has been responsible for educational, clinical and research activities in her Department since 2000. She has authored 198 publications in peer-reviewed international journals, mainly on gynecological endocrinology, menopause, hormone therapy and osteoporosis. She is President of the Hellenic Society of Climacterium and Menopause, Past President of the European Menopause and Andropause Society (EMAS, 2015-2017), Scientific Director of EMAS (2017-today) and Editor of the journal MATURITAS, official journal of EMAS. She is the recipient of the 2018 Henry Burger Prize which is awarded by the International Menopause Society to the Scientist with the most significant contributions in the field of menopause in the previous five years of a World Congress.



Anastassios Philippou

Dr. Anastassios Philippou is Associate Professor of Experimental Physiology-Exercise Physiology at the Medical School of the National and Kapodistrian University of Athens, Greece. He is a graduate of Exercise Science (1992) and Physical Therapy (1997) with postgraduate (2002), doctoral (2009) and postdoctoral (2011) studies in the Biology and Physiology of Exercise and Skeletal Muscle. He has more than 70 publications in international scientific journals and has been involved in the translation and scientific editing of books as well as the writing of (Greek and English) book chapters. He is the General Secretary of the "Institute of Applied Physiology & Exercise in Medicine", Founding Member of the Greek National Center "Exercise Is Medicine - Greece" and a member of 8 scientific societies. His scientific work covers a wide field in the Physiology of Exercise and in particular the skeletal muscle, for which he has received international and national awards. As part of his postdoctoral studies (UPENN, USA) and cooperation / funding from NASA, he participated in the study of the muscle atrophy of experimental animals in the latest space mission of NASA (STS-135).



Marinella Tzanela

Dr. Tzanela is born in 1957 in Athens, Greece completed her medical studies in 1981 in the University of Athens, and defended her medical thesis in 1985 in the same University. She did her fellowship in endocrinology at Evaggelismos Hospital in Athens and got her boards certification in 1990. She participated in many research programs both in Greece and USA (Department of Pharmacology, University of Athens Under prof M. Batrinos, Department of Pathophysiology University of Athens under prof M. Anapliotou, department of Reproductive Endocrinology Medical College of Georgia, under prof P.McDonough, Department of Pediatric Endocrinology under Prof H. Gayda, and Department of neuroscience under prof G. Tannenbaum at McGill university in Montreal Canada). At 1998 she joined the department of Endocrinology at Evagelismos, where is currently senior consultant in endocrinology and responsible for the pituitary clinic. The last year by her efforts together with the rest of the endocrine team, the department of Evaggelismos was approved the first center of excellence for pituitary, adrenals, and thyroid cancer by the Greek Ministry of Health Her main research interests focus in neuroendocrinology and she has published mores than 70 papers in peer reviewed journals. She has trained more than 50 fellows in endocrinology.



Andromachi Vryonidou

Andromachi Vryonidou MD, PhD. Head of Department of Endocrinology, Diabetes and Metabolism, General Hospital “Korgialenio – Benakio”, Athens. PhD thesis, Kapodistrian University School of Medicine, Athens. Clinical Specialty in Endocrinology, Diabetes and Metabolism. She participated in many multicentre studies as co- and principal investigator, in the field of type 2 diabetes mellitus. She has served as treasurer, vice-president and present president of the Hellenic Endocrine Society. She has 50 publications in peer reviewed medical journals. Her work has been cited >2000 times. Clinical and Research Interests: Reproductive Endocrinology. Polycystic Ovary Syndrome. Insulin resistance and Diabetes Mellitus. Adrenal tumours.

The background of the page features a soft, watercolor-style illustration of a bright sun in the upper left, casting a warm glow across the sky. On the right side, there is a faint, sketchy drawing of a classical building with columns and a pediment.

ABSTRACTS

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Prevalence of thyroid dysfunctions in a large cohort of Human Immunodeficiency Virus (HIV)-Infected Patients

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Objective: Highly Active Antiretroviral therapy (HAART) has been associated with several endocrine abnormalities. Data concerning thyroid dysfunction in HIV are still controversial. The aim of this study was to investigate the prevalence of thyroid dysfunctions and their association with HAART and HIV-infection in a large cohort of HIV-infected patients.

Methods: A retrospective cross-sectional study was carried out involving HIV-infected patients whose thyroid-stimulating hormone (TSH) and thyroid hormones (fT3, fT4) were evaluated from 2007 to 2017. A large database containing clinical information was approved by the local ethical committee. Laboratory ranges were used to identify hypothyroid (TSH above the upper limit) and hyperthyroid patients (TSH below the lower limit). Age, sex, CD4 nadir and count, HAART and sodium levels were collected.

Results: Data from 1966 HIV-infected patients (69% males, 31% females; age 46±8 years; HIV-infection duration 31±9 years) were retrospectively analysed. Total hypothyroidism prevalence, including 70 patients already on levothyroxine therapy (3.6%), was 3.9%. Undiagnosed hypothyroidism was found in 89 (4.7%) patients (4.4% subclinical, 0.3% overt). Only 6 patients (0.4%) were hyperthyroid (0.3% subclinical, 0.1% overt). Hypothyroid subjects had been exposed to significantly longer HAART duration ($p=0.02$). TSH did not correlate with any of measured parameters.

Conclusions: Prevalence of undiagnosed thyroid dysfunctions in our cohort of HIV-infected patients seems to be lower compared to general population, except for subclinical hypothyroidism which is similar. Only HAART seems to be related to hypothyroidism even though TSH levels did not correlate with HAART duration. We speculate that disrupted immune competence can explain the reduced prevalence of thyroid dysfunctions, which are mainly due to autoimmune disease.

Occurrence of second primary malignancy in Medullary Thyroid Cancer (MTC) patients

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Objectives: Coexistence of two different malignancies is frequently reported. Sometimes occurs in the context of well-established syndromes like MEN2. Rearranged during transfection (*RET*), is an oncogenic driver activated in different kinds of neoplasias such as: MTC, Differentiated Thyroid Cancer (DTC), Non-Small Cell Lung Cancer (NSCLC). We have previously reported an increased prevalence of DTC in familial MTC patients carrying the *RET* (G533C) mutation. Aim of this study was to record the extrathyroidal malignancies in MTC patients of our Unit.

Methods: 57/297 patients presented with second malignancy during a follow-up of 1-15yrs. They were classified in 3 groups; Group 1: MTC+Extrathyroidal malignancy, Group 2: MTC+DTC, Group 3: MTC-alone.

Results: 19/57pts (Group1) were diagnosed with an extrathyroidal malignancy 2-10yrs after MTC; location-type: Breast (5/19), Kidney-Bladder (3/19), Sarcoma (2/19), Lung-NSCLC (2/19), Prostate (1/19), Colon (1/19), Chronic Myeloid Leukemia (1/19). Prior to MTC, 4 patients were diagnosed with Head & Neck cancer and Melanoma. Group 2 (Concomitant MTC+DTC): 38/57pts. Group 1 patients vs Group 2 & 3 presented with worse disease stage at diagnosis ($p=0.006$). Accordingly they had more frequently lymph node infiltration ($p=0.007$), capsular & soft tissue invasion ($p=0.001$); higher pre- and post-operative Calcitonin levels were recorded in them ($p=0.028$). Tumor size was larger in Group 1 pts ($p=0.003$). C-cell hyperplasia was more frequent in Group 2 ($p=0.003$). No differences were found regarding sex, family history, multifocality or distant metastases.

Conclusions: Synchronous or asynchronous primary malignancies may occur with MTC. *RET* oncogenicity through several mechanisms (activating mutations, increased expression, risk-associated SNPs) has been proposed as a possible shared aetiopathogenic mechanism. Elucidation of the common genetic pathways possibly involved in coexistence of two phenotypically different types of malignancy could be crucial for precision medicine and tailor-made therapy.

O 3

The effectiveness of different treatment regimens in patients with Graves' ophthalmopathy

Fomina Daria

Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University

According to the recommendations of the European Group for the study of Graves' orbitopathy (EUGOGO), pulse therapy with glucocorticosteroids, is the method of choice in active EOP of moderate severity or severe course. The choice of scheme depends largely on the doctor's preferences, as the comparative effectiveness of many of them remains uncertain.

Objective: to evaluate the effectiveness of various schemes of pulse therapy with methylprednisolone in patients with EOP.

Methods: the study included 48 patients with moderate and severe forms of EOP in the active stage ($CAS \geq 3$), the average age $54,77 \pm 13.78$ years. Patients of the 1st group ($n=4$) received methylprednisolone acetate (MP) at a dose of 1,000 mg intravenously daily for 3 days. Patients of group 2 ($n=36$) received MP continuously for 5-7 days, at a dose of 1000 mg intravenously. Patients of group 3 ($n=8$) received MP at a dose of 1000 mg intravenously for 3 days, after 3 days – a repeated cycle of triple daily administration of MP at a dose of 1000 mg intravenously. The total dose of GCS in all groups did not exceed 8 grams. Assessment of the degree of EOP activity was carried out on the CAS scale. Clinically significant effect was considered to be a decrease in activity on the CAS scale > 2 points. The severity of ophthalmopathy was assessed according to the EUGOGO classification.

Results: Before therapy, the median CAS in the 1st group was 5.5 points [3,5;6,75], in the 2nd group 5 points [4,2;6,1], in the 3rd group 6.5 points [6,3;9,5]. 1 week after the end of pulse therapy, the median score on the CAS scale in patients of group 1 was 3.5 [2.25;4.75], and in group 2 and 3 3.3 [2.2;4.1] and 3.1 [2.3;5.25], respectively. Significant effect was recorded in the 2nd ($p < 0.05$) and 3rd ($p < 0.01$) groups.

Conclusions: There was no significant effect in patients who received intravenous injections of MP daily for three days. In the group with continuous administration of MP in a total dose of 5-7 grams there was a decrease in the activity of EOP a week after the end of therapy. In patients with high activity using of MP in intermittent mode, in a total dose of 6 grams, leads to a decrease in the activity of ophthalmopathy within a week after the end of therapy.

Thyroid lymphoma in a patient presenting with severe airway compromise

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Background: Preexisting chronic autoimmune thyroiditis is the only known risk factor for thyroid lymphomas, a rare variant of thyroid cancer. Here, we describe a male patient with previously undiagnosed Hashimoto's thyroiditis who presented with severe airway compromise due to a thyroid lymphoma.

Case report: 60 y/o, former smoker, presented with 2 month neck fullness and dyspnea that awakened him throughout the night due to malpositioning of his neck. He had no other symptoms. A neck and head CT demonstrated a thyroid goiter, with each thyroid lobe measuring 11.0 cm x 4.0 cm with mass effect on the airway, hypopharynx, and esophagus. The patient was emergently intubated for airway protection. Thyroid studies were significant for subclinical hypothyroidism (TSH of 9.7 uIU/ml and fT4 of 0.85ng/dL) with positive anti-tPO antibodies (2030 uIU/mL) consistent with Hashimoto's thyroiditis. Thyroid ultrasound showed diffuse heterogeneous texture and biopsy showed plasmacytoid cells and lymphoplasmacytic infiltrate involving fibrous tissue. Flow cytometry confirmed a B- cell lymphoma with plasmacytic differentiation. The patient was started on chemoradiation.

Conclusions: Severe airway compromise may occur in up to 25% of patients with thyroid lymphoma. Given the dramatic clinical presentation of rapid growth and airway compromise, the clinical impulse is to treat surgically with a total thyroidectomy. However, the differential diagnosis of a rapidly growing goiter includes lymphoma, which can be quickly diagnosed with a core biopsy and flow cytometry. Such lymphomas respond quickly to the combination of chemotherapy (with steroid component) and local radiation, potentially obviating the need for tracheotomy.

Caprini score is not reliable in predicting the preoperative risk of thromboembolism in thyroid and parathyroid surgery

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Objective: Bleeding is one of the most dangerous complications following thyroid and parathyroid surgery. For this reason prophylactic perioperative thromboprophylaxis is not routinely use. The aim of this study is to investigate the incidence of clinical and subclinical deep vein thrombosis (DVT) and to validate the Caprini score as a predictive factor of high risk patients after these operations.

Material and Method: This is a prospective study involving patients who have undergone thyroid and parathyroid operations in our department. Preoperatively D-dimers level and ultrasonography of the lower extremity veins were used to exclude the pre-operative presence of DVT. Patients were scored using the Caprini criteria. None of them received thromboprophylaxis. Postoperatively, they were clinically evaluated for the presence of DVT, in addition to D-dimers level and color Doppler on the 7th post-operative day. The incidence of clinical and subclinical DVT was recorded.

Results: Data included 103 patients 17-78 years (average 53.3) and body mass index 16-48 (average 26.8). 94% of the patients were at higher and highest risk of developing DVT according to Caprini and should have received thromboprophylaxis. The mean D-dimers concentration was 1.1 ± 0.8 , while no patient developed clinical DVT postoperatively and had no subclinical DVT findings in the Doppler ultrasound the 7th post-operative day.

Conclusions: The risk of thromboembolic disease in patients undergoing thyroid and parathyroid operation cannot be reliably assessed with the Caprini system. Despite the risk factors, rapid post-operative mobilization of patients leads to the near zero incidence of DVT and therefore it seems that perioperative anticoagulation treatment is not necessary, possibly increasing the possibility of post-operative bleeding.

Local hypothyroidism in brain cortex leads to diminished glucose metabolism in Alzheimer's disease animal model

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Objective: This study analyzes impairments occurred in local thyroid hormones metabolism and their connection to decreased glucose uptake, amyloid- β accumulation and apoptosis of neurons in pharmacologically induced animal model of Alzheimer's disease.

Methods: Spectrophotometry, immunoassay, morphological studies including immunohistochemistry, rat Scopolamine-induced Alzheimer's disease model (WAG male rats).

Results: The conducted study showed that local hypothyroidism in brain cortex is observed despite euthyroid status of the organism. We believe that abnormal thyroxine deiodination can be the reason of these impairments due to increased glutamate content and its excitotoxic properties.

It was reported that thyroid hormones determine basal metabolic rate due to their influence on mRNA synthesis. Hypothyroidism, as observed in our study, could influence both amount and activity of enzymes that take part in glucose metabolism. We have observed significant increase in pyruvate dehydrogenase activity and decrease in the citric acid cycle key enzymes. These changes indicate diminished glucose metabolism in brain cortex tissue.

Another aspect of local hypothyroidism is that thyroid hormones are known to potentiate the impact of catecholamines on heat shock proteins synthesis which play a pivotal role in cell reparation. Thus, lipid peroxidation activation can lead to apoptosis activation.

Conclusion: As a consequence of local hypothyroidism, glucose utilization was diminished and this led to decreased ATP content, amyloid- β accumulation in brain cortex tissue and cell death.

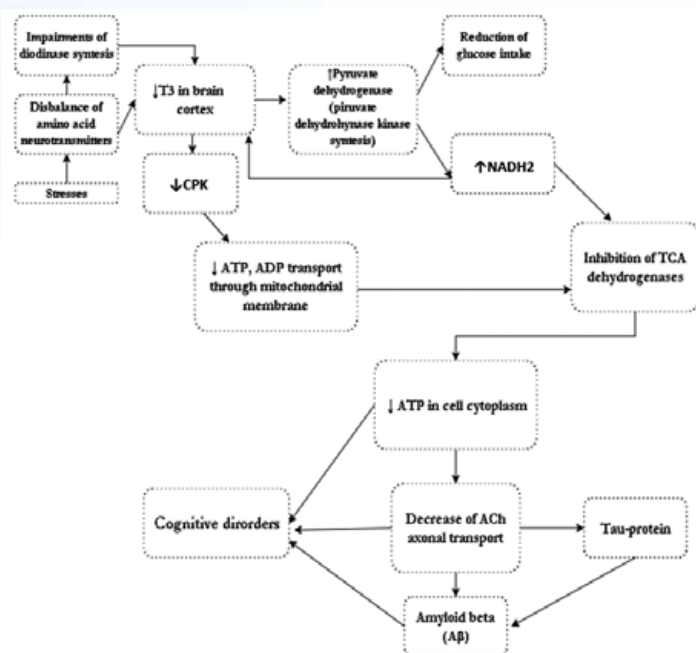


Fig. 1 The role of neurotransmitting, endocrine and metabolic factors in Alzheimer's disease development in rats

Coexistence of medullary carcinoma and papillary carcinoma of the thyroid in a 35 year old patient with RET protooncogene mutation

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Background: Medullary and papillary thyroid carcinomas are distinct entities, regarding their incidence, cellular and genetic origin, histopathological features and prognosis, but there have been described a few cases of the two occurring simultaneously in the same patient. Medullary thyroid carcinoma represents between 1-5% of all thyroid malignancies and it is responsible for 12-13% of all cancer related deaths. The familial form (10-20% of the cases) is caused by a RET protooncogene germline mutation and it can also be found in multiple endocrine neoplasia patterns (2A and 2B). Medullary carcinoma arises from the C-parafollicular cells and it usually metastasize to cervical lymphatic nodes and surrounding tissues. The therapeutic approach should always include total thyroidectomy, lymphadenectomy and genetic testing for RET mutations.

Case presentation: We will report the case of a 35 year old female patient with family history of medullary thyroid carcinoma, who has tested positive for RET protooncogene mutation. Patient had no symptoms, serum calcitonin was elevated preoperative and neck ultrasound showed a hypoechogenic, unprecise delimited area of 3/3 mm in the left thyroid lobe. She underwent prophylactic total thyroidectomy and histopathology examination showed presence of both medullary bilateral microcarcinoma and papillary microcarcinoma, follicular variant. We will also present the genealogical tree of the RET mutation in the patient's family along with some distinctive details of their disease.

Conclusion: We reported a case with a rare finding, coexistence medullary and papillary carcinoma of the thyroid, in a patient with family history of medullary carcinoma of the thyroid with RET protooncogene mutation.

Toxic adenoma as a rare cause of hyperthyroidism in a prepubertal boy

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Background: Toxic adenoma (TA) is a rare cause of hyperthyroidism in children, representing less than 3% of cases, more frequently affecting girls. The risk of malignancy in pediatric autonomous nodules is unknown. Despite current guidelines on the management of TA, published case series reveal discrepancies in medical practice.

Case presentation: We report a case of TA in a 7-year old boy, incidentally detected as a palpable mass during examination for laryngitis. Initial laboratory findings depicted TSH < 0.005 μU/ml (0.4-4.14), fT4: 2.85 ng/dl (0.8-1.8) and negative thyroid autoantibodies, including Anti-TGs, Anti-TPOs and TRAbs. The child had no symptoms of hyperthyroidism. Thyroid ultrasound revealed a thyroid nodule of 3.26x2.5x1.8 cm, with no signs suggestive of malignancy. Treatment with carbimazole was initiated promptly. Scintigraphy with ⁹⁹Tc confirmed the diagnosis of TA, with increased focal uptake and peripheral suppression. Surgical resection was scheduled and, in the meantime, propranolol was added to treatment due to tachycardia. Gradually euthyroidism was achieved. On surgeon's request, the child received potassium iodine 4 days prior to surgery, as well as vitamin D and calcium. Histologic examination was negative for malignancy. Carbimazole, propranolol and calcium were discontinued on the 2nd, 5th and 10th post-operative day, respectively. Treatment with thyroxine was initiated on the 6th post-op day.

Conclusions: This is a rare case of TA in a prepubertal boy. Despite guidelines, highly experienced surgeons on such rare entities are not broadly available. More case reports are necessary in order to validate best management strategies.

Comparison of thyroglobulin levels on the third and fifth day after rhTSH injection in patients with differentiated thyroid cancer

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Objective: Thyroglobulin (Tg) production by normal or malignant thyroidal cells is TSH dependent. The rhTSH administration for Tg stimulation in patients with differentiated thyroid cancer (DTC), after thyroidectomy and eradication of thyroid remnants with I-131, offers an alternative to thyroid hormone withdrawal preventing the progressive morbidity of hypothyroidism. Tg measurement is usually obtained on the 3rd and 5th day after the first rhTSH injection. Our study's aim is to evaluate the stimulated Tg on the third and fifth day after rhTSH administration.

Methods: Thirty-three DTC patients (9 men, 24 women) with negative antiTg antibodies and a mean age of 41.2 ± 13.4 years were included. rhTSH was injected twice on two consecutive days. Tg and TSH were measured at baseline and on day 3 and 5 after the first injection. Tg was measured by chemiluminescence (inter assay variation 4%, functional sensitivity 0.9 ng/ml).

Results: At baseline TSH was undetectable up to $0.96 \mu\text{IU/ml}$ (mean \pm SD, $0.21 \pm 0.3 \mu\text{IU/ml}$) and Tg was also undetectable up to 3.53 ng/ml ($0.98 \pm 3.4 \text{ ng/ml}$). TSH increased above 65 ng/ml in all patients and was higher on day 3 (mean \pm SD, $101.8 \pm 25.2 \text{ ng/ml}$) than on day 5 (20.2 ± 11.1) compared with baseline ($p < 0.001$), as expected. Tg increased in 7 patients (21.2%), being unchangeable in the rest 26. In these 7 responders mean Tg levels \pm SD were $1.53 \pm 1.1 \text{ ng/ml}$ at baseline, $8.5 \pm 7.7 \text{ ng/ml}$ on day 3 and $15.8 \pm 21.3 \text{ ng/ml}$ on day 5.

Conclusions: In conclusion, after rhTSH injection in differentiated thyroid cancer patients, thyroglobulin measurement only on day 5 is quite enough and seems to be superior than that on day 3.

The genetic landscape of indeterminate thyroid nodules

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Objective: The thyroid fine needle aspiration biopsy (FNAB) may bring inconclusive cytological results of atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) or follicular neoplasm/suspicious for follicular neoplasm (FN/SFN). The objective of the study was to describe the genetic landscape of indeterminate thyroid nodules to better understand this phenomenon and identify genetic markers potentially differentiating benign and malignant lesions.

Methods: FNAB samples were acquired from 25 (2 men and 23 women) Caucasians patients diagnosed preoperatively with FLUS (16) and SFN (9). Genomic DNA was isolated and the 50-gene Ion AmpliSeq Cancer Hotspot Panel v2 was used to perform next-generation sequencing (NGS). The obtained data were analyzed and compared with clinical data including final post-surgical diagnoses.

Results: The overall malignancy rate was 28%. *KDR*, *RET*, and *TP53* genes mutations were the most frequent in FLUS and SFN samples finally diagnosed as cancers, whereas alterations *RET*, *TP53*, *FLT3*, *APC*, and *PDGFRA* predominated in benign tumors. Malignant samples tended to have *KDR* mutations more often (75%vs.20%, $P=0.095$). A total number of mutated genes was significantly higher in patients with benign tumors (17vs.11, $P=0.0184$) and the mean number of 4.9 mutations per patient (range: 1-9) did not differ in both groups.

Conclusions: The results show that the indeterminate thyroid nodules' genetic background heterogeneity corresponds to their histopathological diversity. The role of *KDR* as a possible malignancy marker needs to be confirmed. FNAB samples may constitute a reliable source of genetic material for NGS studies giving a better insight in thyroid nodules molecular profile.

Role of SIX1 homeoprotein in the regulation of TGF β pathway in anaplastic thyroid cancer

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Anaplastic thyroid carcinomas (ATC) are characterised by a poor prognosis, due to a highly proliferative, metastatic and undifferentiated state. Follicular thyroid cells undergo epithelial to mesenchymal transition (EMT) by the upregulation of TGF β pathway. Interestingly, in many epithelial cancer types a correlation between high levels of SIX1 expression and TGF β signaling has been described.

Objective: Study the role of SIX1 homeoprotein in thyroid cancer, as a potential marker of TGF β pathway and EMT.

Methods: Analysis of SIX1 expression in thyroid cancer cells by qPCR and western-blot. Evaluation of the effect of multiple ligands and inhibitors of TGF β and PI3K pathway in the SIX1 levels. Generation of stable cells that overexpress SIX1 or SIX1 shRNAs by lentiviral particles. Quantification of cell proliferation, migration and invasion by BrDU, cell cycle, wound-healing and matrigel invasion assays. Luciferase assays for analyzing TGF β activation.

Results: We show ATC cells present higher mRNA and protein levels of SIX1 comparing to the control cell line NThyOri and papillary thyroid cancer cells. Overexpression of SIX1 produces an increase of EMT markers, cell proliferation, migration, invasion, and amplifies TGF β pathway. Opposite results were found by loss-of-function experiments. TGF β 1 treatment has a dual effect over SIX1 expression whereas the inhibition of the PI3K pathway, mediated by the overexpression of PTEN or by using the AKTi inhibitor, reduces SIX1 expression in ATC cell lines.

Conclusions: Given that SIX1 participates in the epithelial dedifferentiation and malignant behaviour of ATC cells, we described it as a potential therapeutic marker in ATC.

Brain energy metabolism in an animal model of the co-occurrence of depression and hypothyroidism

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Objective: The association between thyroid function and mood disorders has long been recognized but little is known about the mechanisms underlying this relationship. Thyroid dysfunction often leads to the development of mental diseases and in patients with affective disorders, 1-4% suffers from hypothyroidism and 4-40% show signs of subclinical hypothyroidism. The aim of the present study was to assess the effects of hypothyroidism on metabolic processes in the brain of Wistar and Wistar-Kyoto rats (an animal model of endogenous depression).

Methods: Study was performed in an animal model of depression (Wistar-Kyoto rats) and model of coexistent depression and hypothyroidism (Wistar-Kyoto rats treated with 6-n-propyl-2-thiouracil - PTU). PTU (0.05 %) was administered in drinking water for 3 weeks. The forced swim test, ELISA tests, colorimetric assays, and Western blot were applied to investigate the changes in selected metabolic markers in the frontal cortex and hippocampus.

Results: 3-weeks of PTU administration lead to increase in TSH and decrease in fT3 and fT4 levels in the plasma of control and Wistar-Kyoto group. In the brain, we observed the diminished concentration of key glycolytic compound: pyruvate, disturbances of the linking the glycolysis metabolic pathway to the citric acid cycle and diminished levels of respiratory chain complexes. Additionally, we observed alternations in brain mitochondrial coupling efficiency.

Conclusions: Obtained results indicate an important contribution of thyroid hormones to brain metabolism in the course of depression.

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Early onset thyroiditis and late onset Fulminant Type 1 Diabetes Mellitus following Pembrolizumab therapy

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Background: Pembrolizumab is a novel anti-cancer drug that targets programmed cell death protein 1 (PD-1) receptor on lymphocytes resulting in their activation against tumor cells. PD-1 receptors are also distributed in endocrine organs and pembrolizumab use has long-been associated with hypophysitis and thyroiditis. We describe a patient with pembrolizumab-induced thyroiditis who developed an uncommon fulminant Type 1 Diabetes Mellitus (FT1D).

Case presentation: A 68-year old Phillipino woman was diagnosed with lung cancer in 2016. She had no response to chemotherapy and subsequently commenced on pembrolizumab in March 2017. There was no history of diabetes or any other endocrinopathy.

Blood tests prior to third cycle of pembrolizumab in April 2017 showed thyrotoxicosis (FT4 34pmol/L (9.0-19.0 pmol/L), TSH 0.03 mIU/L (0.35-4.94 mIU/L)). She was managed conservatively and became hypothyroid (TSH 29.4 mIU/L, FT4 9.17 pmol/L) in June 2017 and hence started on thyroxine replacement.

In early 2018, she became acutely unwell with hyperglycaemia (plasma glucose- 48.95mmol/L), ketosis (urine ketones +++) and severe metabolic acidosis (pH-7.062). She was diagnosed with diabetic ketoacidosis. Eventually, DKA resolved with appropriate treatment and she was commenced on basal-bolus insulin for newly diagnosed diabetes. Subsequent tests revealed lack of autoimmune nature (C-peptide of <33.1 pmol/L (330-1400 pmol/L), negative IA-2 (4.5%, reference<6.5%), GAD-65 (0.01 IU/ml, reference<1 IU/ml) and Zinc-transporter 8 antibodies (2.1 RU/ml, reference<15 RU/ml). Patient was hence diagnosed with pembrolizumab-induced FT1D.

Conclusion: Only recently has type 1 diabetes mellitus been acknowledged as an adverse effect of pembrolizumab. These patients need close monitoring and joint specialist follow-up to mitigate such complications.

Effects of thyroid function on peripheral serum markers: results from a cohort of thyroid cancer patients

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Objective: The aim of this study was to identify changes in thyroid hormone metabolism occurring in different thyroid functional states and to evaluate tissue response to thyroid hormone changes.

Methods: Two hundred subjects (137 F, 63 M, mean age: 50.3 ± 14.4 years) waiting to be treated or treated with total thyroidectomy for differentiated thyroid cancer were enrolled in this study. Thyroid function was investigated measuring TSH, fT4 and fT3, and total cholesterol, cholesterol HDL, triglycerides, CK and myoglobin were analyzed as serum markers of tissue thyroid state. According to time (before or after thyroidectomy) and LT4 therapy, patients were divided in 5 groups: euthyroid before total thyroidectomy (T0, n=17), hypothyroid before radioactive iodine (RAI) therapy (T1, n=69), hyperthyroid on LT4 TSH-suppressive therapy (T2, n=107), TSH-stimulated with rh-TSH (T3, n=116), euthyroid on LT4 replacement therapy (T4, n=33). The non-parametric Kruskal-Wallis test was used for comparison among 5 groups.

Results: Even though TSH, fT4 and fT3 levels were not significantly different among patients before (T0) and after thyroidectomy on LT4 replacement therapy (T4), fT3/fT4 ratio was lower in T4 than T0 patients, probably for a deranged conversion of T4-to-T3. Moreover, total cholesterol (p=0.306), calculated-LDL (p=0.463), triglycerides (p=0.318) and CK (p=1) levels did not show statistically significant differences between hypothyroid (T1) and euthyroid patients on LT4 replacement therapy (T4).

Conclusions: In thyroidectomized patients on LT4 replacement therapy, despite a biochemical restoration of euthyroidism, T3 levels in peripheral tissues are not fully normalized, with a consequent, documented worsening of lipid profile and skeletal muscle damage.

Aldosterone-to-renin ratio as an accurate diagnostic tool in patients on antihypertensive therapy

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Objective: Withdrawal of the medications prior to screening for primary aldosteronism is problematic, sometimes impossible and probably not necessary as the routine practice. The aim of this study was to evaluate diagnostic accuracy of aldosterone-to-renin ratio in hypertensive patients undergoing laboratory screening for primary aldosteronism without obligatory drug modifications.

Methods: Plasma aldosterone and direct renin concentrations from 20 patients with primary hyperaldosteronism (group 1) and 80 controls (group 2) were measured and aldosterone-to-renin ratio was calculated. Patients were taking their usual antihypertensive drugs (one third was on 4 or more drug classes), excluding only mineralocorticoid receptor blockers. In the next step, necessary drug modifications were done and diagnostic process was carried on according to the current Endocrine Society guidelines.

Results: Group 1 and 2 were comparable in terms of age (57,5 vs 55,5 yrs, accordingly), BMI (28,18 vs 29 kg/m²), severity of hypertension (refractory hypertension in 25 vs 22,5%) the number of drugs taken (2 vs 2) and differ significantly in matters of the duration of hypertension (15 vs 7 yrs, $p=0,03$) and hypokalaemia (3,8 vs 4,24 mmol/l, $p=0,0001$). Aldosterone-to-renin ratio with the best cut-off level of 2,07 ng/dl/mlU/l was characterized by 95% sensitivity, 87,5% specificity and 89% accuracy (AUROC=0,94). With the cut-off level of 1,4 ng/dl/mlU/l the sensitivity of 100% was achieved.

Conclusions: The results of our work show that aldosterone-to-renin ratio serves as an accurate and reliable diagnostic tool despite antihypertensive therapy.

hCG stimulation induces cortisol secretion in menopausal patients with adrenal incidentalomas

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Introduction: Secretory adrenal tumors sensitive to luteinizing hormone (LH) and/or human chorionic gonadotropin (hCG) are well documented in the literature. LH and hCG share a mutual LH/hCG receptor and a comparable physiological role.

Objective: The aim of our study was to evaluate the response of adrenal steroids (cortisol, aldosterone and dehydroepiandrosterone sulphate (DHEAS)) to exogenous hCG stimulation in menopausal patients with adrenal incidentalomas (AI).

Methods: The study group consisted of 14 patients with AI, average age 60.13 ± 7.28 years, average BMI 27.60 ± 4.66 kg/m² and average menopause duration 10.86 ± 7.79 years. Based on the cortisol level after 1mg dexamethasone suppression test (1mg DST), AI patients were divided in to two groups: 1st - non-functional AI (NAI) and 2nd – AI with (possible) autonomous cortisol secretion ((P)ACS). The morning after 1mg DST all patients received 10.000 IU hCG intramuscularly starting at 08.00AM with cortisol measurements every 30 minutes for 3 hours. Positive cortisol response to hCG was considered as a raise of cortisol for at least 25% of basal cortisol value (0 min).

Results: 11 patients showed positive cortisol response, 5 with NAI and 6 with (P)ACS. Maximal response in NAI group was 74%, and in (P)ACS group was 186%. The average cortisol response in group with NAI was 44%, whereas it was 98% in group with (P)ACS. Cortisol response in patients with (P)ACS was significantly higher than in patients with NAI ($p < 0.05$). There was no positive response in aldosterone or DHEAS levels.

Conclusion: Our results imply that LH could be a contributing factor to steroidogenesis in menopausal patients with AI.

Impact of glucocorticoid receptor gene polymorphisms on occurrence of steroid-induced adverse events

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Objective: Previous studies indicated that two glucocorticoid receptor gene polymorphisms *bclI* and N363S (GC-S) are associated with increased sensitivity to glucocorticoids and two other polymorphisms 9 β and ER22/23EK (GC-I) are related to decreased sensitivity to glucocorticoids. The aim of the study was to determine whether these genetic changes can effect on the occurrence of steroid-induced adverse events.

Methods: 150 patients treated with glucocorticoids for over 3 months due to connective-tissue disease underwent clinical and biochemical evaluation. Genotyping of polymorphisms was carried out using a high resolution post PCR method that analyzes High Resolution Melting profiles. Analysis was performed comparing adverse effects of GCS treatment in carriers of GC-S or GC-I polymorphisms vs noncarriers.

Results: There was no significant difference in age, time of treatment, current and cumulative dose of glucocorticoids, BMI, waist circumference, bone mineral density, lean and fat mass, HOMA-IR, HbA1c, Matsuda Index, lipid profile, insulin or glucose concentration in OGTT or presence of adverse events of glucocorticoid treatment, including arterial hypertension, CVD, diabetes, osteopenia/osteoporosis and „Cushingoid appearance” between GC-S carriers (n=74) vs noncarriers (n=76). GC-I carriers (n=46) had higher median cumulative dose of treatment (18.4 g vs 11.8 g, p=0.03) and there was higher prevalence of osteopenia/osteoporosis in this group comparing to GC-I noncarriers (n=104). There was no significance in other analyzed parameters.

Conclusions: The results of the present study show that there is no impact of glucocorticoid receptor polymorphisms on occurrence of steroid-induced adverse effects. Higher prevalence of osteopenia/osteoporosis in GC-I carriers is probably related to higher cumulative dose of glucocorticoids.

Transcriptome profiling explains clinical characteristics of *PRKACA* mutant cortisol-producing adenomas

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Objectives: The activating mutation (L206R) in *PRKACA* has been reported in more than 30-50% of cases with cortisol-producing adenomas (CPAs). We aimed to compare the clinical characteristics and gene expression profiling between *PRKACA* L206R mutant and wild type CPAs.

Methods: We included 57 subjects with CPAs who underwent adrenalectomy at Seoul National University Hospital. Sanger sequencing for *PRKACA* was conducted in 57 CPA tumor tissues. RNA sequencing was performed in 13 fresh frozen tumor tissues.

Result: The prevalence of *PRKACA* L206R mutation was 53% (30/57). The mean age of study subjects was 42 ± 12 years and female was 89.5% (7/57). Subjects with *PRKACA* L206R mutant CPAs showed smaller adenoma size (3.24 ± 0.72 vs. 3.87 ± 1.30 cm, $P = 0.044$) and lower DHEA-S level (221 ± 176 vs. 1511 ± 3307 ng/mL, $P = 0.001$) than those with *PRKACA* wild type CPAs. Transcriptome profiling showed that 244 differentially expressed genes between *PRKACA* L206R mutant ($n = 8$) and wild type CPAs ($n = 3$) were identified including 5 up-regulated and 199 down-regulated in *PRKACA* L206R mutant CPAs ($|\text{fold change}| \geq 2$, $P < 0.05$). Using the Ingenuity Pathway Analysis, the top upstream regulator of DEGs was *CTNNB1*. In KEGG pathway, steroid biosynthesis pathway including STAR was up-regulated but Wnt pathway was down-regulated in *PRKACA* L206R mutant CPAs.

Conclusion: *PRKACA* alteration in CPAs causes high hormonal activity with a limited proliferative capacity, which was explained by up-regulation of steroidogenesis-related genes and down-regulation of Wnt pathway through PKA activation.

Partially successful adrenal vein sampling can in some cases reveal the etiology of primary aldosteronism

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Introduction: Adrenal vein sampling (AVS) represents the gold standard in the identification of the source of aldosterone hypersecretion in patients with primary aldosteronism (PA). It is a technically demanding procedure and, in some cases, only one adrenal vein is successfully cannulated. Our study aimed to examine the aldosterone/cortisol ratio between the peripheral and adrenal veins in order to determine peripheral/adrenal vein aldosterone/cortisol ratio cut-off value that differentiates between hyperfunctional and unaffected adrenal gland.

Materials and methods: The study included 31 patients with PA. AVS confirmed unilateral aldosterone secretion in 15 patients who were all surgically treated and achieved biochemical remission of the disease afterwards. In the remaining 16 patients, AVS results were consistent with bilateral adrenal hyperplasia and they were treated conservatively. In all patients aldosterone/cortisol ratio between the peripheral veins and both adrenal veins was analyzed.

Results: Statistical analysis, using ROC curve, showed that peripheral/adrenal vein aldosterone/cortisol ratio ≥ 3 indicates unaffected adrenal gland with the 90% sensitivity and 100% specificity. On the other hand, peripheral/adrenal vein aldosterone/cortisol ratio ≤ 0.6 is 90% sensitive and 100% specific for the affected gland.

Conclusions: Using the diagnostic algorithm based on aldosterone/cortisol ratio between the peripheral and adrenal vein it is possible to determine whether the aldosterone overproduction is caused by the related adrenal gland. Accordingly, this algorithm enables us to accurately detect the source of aldosterone overproduction in the case when only adrenal vein on the unaffected side is cannulated successfully.

Phenotype of patients carrying the c.709(-7-2)del *PRKAR1A* mutation in a large cohort of 40 patients

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Objective: To describe the Carney Complex (CNC) manifestations presented by patients harboring the *PRKAR1A* mutation c.709(-7-2)del (one of the three hotspots) in a large cohort of patients.

Methods: Multicenter retrospective study. Age at the diagnosis or at the screening of the different CNC manifestations is described by mean +/- standard deviation.

Results: Forty patients [12 index cases, 27 females, 46±15 years old (yo)] from 11 families have been included. The *PRKAR1A* mutation had been discovered at 33.3±15.2yo. Twenty-two patients (19 females) were diagnosed in a context of primary pigmented adrenal disease (PPNAD) at 30.0±13.8yo. For the remaining 21 patients, the last overnight dexamethasone cortisol suppression test performed at 44.9±14.7yo was abnormal in 5 patients. Six patients presented with fluctuating anomaly of IGF1 and/or GH after oral glucose tolerance test (last evaluation performed at 42.2±14yo). At the last dermatological examination (40.5±14.6yo), 6 patients presented with lentigines. One patient had a history of thyroid papillary microcarcinoma. At the last thyroid ultrasound (43.6±13.0yo), 2 had bilateral thyroid nodules. At the last cardiac ultrasound, pituitary magnetic resonance imaging (MRI), spine MRI, testicular ultrasound, mammography performed at 40.6±14.9yo, 37.9±14.3yo, 42.9±12yo, 37.0±12.4yo and 46.9±12.3yo, no patient had cardiac myxoma, pituitary adenoma, schwannoma, testicular calcifying tumor or breast myxoma.

Conclusions: The phenotype of this well followed cohort carrying the c.709(-7-2)del *PRKAR1A* mutation is restricted to PPNAD, lentigines, fluctuating somatotroph anomalies and thyroid tumors. Imaging except thyroid ultrasound may not be needed to follow these patients in contrast to other CNC patients.

Urine steroid metabolomics as a novel diagnostic tool for recurrent adrenocortical carcinoma detection

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Objective: Urine steroid metabolomics, combining mass spectrometry-based steroid profiling and machine learning, has been described as a novel diagnostic tool for detection of adrenocortical carcinoma (ACC). This proof-of-concept study evaluated the performance of urine steroid metabolomics as a tool for post-operative recurrence detection after microscopically complete (R0) resection of ACC.

Methods: 135 patients from 14 clinical centers provided post-operative urine samples, which were analyzed by gas chromatography-mass spectrometry. We assessed the utility of these urine steroid profiles in detecting ACC recurrence, either when interpreted by expert clinicians, or when analyzed by Random Forest, a machine learning-based classifier. Radiological recurrence detection served as the reference standard.

Results: Imaging detected recurrent disease in 42 of 135 patients; 32 had provided pre- and post-recurrence urine samples. Conversely, 39 patients remained disease-free for ³3 years. The urine "steroid fingerprint" at recurrence resembled that observed before R0 resection in the

majority of cases. Review of longitudinally collected urine steroid profiles by three blinded experts detected recurrence by the time of radiological diagnosis in 50-72% of cases, improving to 69-92%, if a pre-operative urine steroid result was available. Recurrence detection by steroid profiling preceded detection by imaging by more than 2 months in 22-39% of patients. Specificities varied considerably, ranging from 61 to 96%. The computational classifier detected ACC recurrence with superior accuracy (sensitivity=specificity=81%).

Conclusion: Urine steroid metabolomics is a promising tool for post-operative recurrence detection in ACC; availability of a pre-operative urine considerably improves the ability to detect ACC recurrence.

Anthropometric and hormonal predictors of metabolic obesity phenotypes in menopause

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Objective: Aiming to identify individuals with more benign metabolic profile, we explored the link between anthropometric predictors as well as serum levels of sex hormones and phenotypes of metabolic health in non-obese postmenopausal women.

Methods: A total of 458 non-obese (body mass index, BMI <30kg/m²) postmenopausal women (age 55.2±7.1years, BMI=24.6±2.8kg/m²) were retrieved from the Menopause Clinic of Aretaieio Hospital, National and Kapodistrian University of Athens. The International Diabetes Federation diagnostic criteria for the definition of Metabolic Syndrome were used to classify women into metabolically obese (≥ 3 criteria, MONW) or metabolically healthy (<3 criteria, MHNW).

Results: Prevalence of phenotypes was as follows: MHNW 80.8% (370/458), MONW 19.2% (88/458). Compared to MHNW, MONW was associated with higher age and menopausal age, greater waist circumference & WHR, higher androgenicity (p-value<0.001, all cases); and lower levels of estrogen (p-value=0.047). Waist circumference was superior than WHR in predicting MONW (Waist≥ 86.5cm, sensitivity 72.7%; specificity 69.4%). Waist circumference ≥ 86.5cm predicted the MONW phenotype in a model adjusted for age and menopausal age (OR=4.689, 95% CI: 2.626 to 8.373, p-value<0.001). In models adjusted for age and menopausal age, MONW was predicted by: i) SHBG (OR=0.979, 95% CI: 0.967 to 0.990); ii) FAI (OR=1.339, 95% CI: 1.121 to 1.599, p-value=0.001). The association between FEI/E2 and the MONW phenotype was mediated by age.

Conclusion: Waist circumference greater than 86.5cm or more pronounced androgenicity represent the most significant independent predictors of adverse metabolic health, irrespectively of age and menopausal age, in this sample of non-obese middle-aged women.

SARCOPENIA AND SARCOPENIC OBESITY IN LIVER TRANSPLANTATION POPULATION

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Background: Low muscle mass and obesity in surgical patients are a prevalent phenomenon that is associated with outcomes such as higher surgical and clinical complications and poor. However, the significance of sarcopenia and sarcopenic obesity in the liver transplantation (LT) population remains unclear. The purpose of this study is to investigate the impact of low skeletal muscle mass, muscle quality and sarcopenic obesity on patients awaiting LT.

Methods: We retrospectively analyzed patients who underwent LT at our center, between January 2013 and January 2018. Body composition parameters including skeletal muscle mass index (SMI), intramuscular adipose tissue content (IMAC), visceral fat area (VFA) were evaluated by preoperative plain computed tomography imaging at the level of the third lumbar vertebra (L3) and also clinical and biochemical parameters were taken. This study defined sarcopenia as a low SMI (male $< 52.4 \text{ cm}^2/\text{m}^2$; female $< 38.5 \text{ cm}^2/\text{m}^2$) and obesity a VFA $> 100 \text{ cm}^2$.

Results: The study included 94 patients (76 men) with a mean age of 60,14 (DS 8,57), 72 (76,6%) had sarcopenia and 52 (55,3 %) had sarcopenic obesity. Multivariate analysis identified chronic inflammation ($p 0,04$), sarcopenia ($p 0,048$) and renal function ($p 0,035$) as independent risk factors for death after LT.

Conclusion: Sarcopenia and sarcopenic obesity were highly prevalent in liver transplantation patients and predict worse survival outcomes. That exists a significant correlation between chronic inflammation and sarcopenic obesity. Novel programs focusing on optimizing nutrition and physical activity could be useful in these patients.

Proglucagon peptide family responses after RYGB surgery in obese patients with type 2 diabetes

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Objective: Bariatric surgery is currently the most effective treatment for weight loss and diabetes remission. There are conflicting reports in the literature regarding the glucagon levels after RYGB surgery, likely due to cross-reactivity with oxyntomodulin and glicentin. The aim of this study was to characterize the proglucagon peptide family responses post-RYGB surgery in obese patients with type 2 diabetes using validated assays.

Method: Nineteen obese patients with type 2 diabetes were assessed before and 1, 3 and 12 months post-RYGB surgery. All participants had anthropometric profiling as well as a mixed meal tolerance (MMT) test during each visit. Glucose, insulin, GLP-1, Oxyntomodulin, Glicentin and Glucagon levels were measured at 0, 15, 30, 60, 120 and 180 minutes.

Results: Fasting and post-prandial Glucose levels and fasting Insulin levels decreased significantly whereas post-prandial GLP-1 and Oxyntomodulin levels increased significantly at 1-3 and 12 months post RYGB ($p < 0.0001$). There was a significant decrease in fasting glucagon levels at 3 and 12 months post RYGB as well as a decrease in post-prandial levels during MMT ($p < 0.0001$). These results were measured using an alternative Mercodia protocol and were confirmed against LC/MS-MS.

Conclusions: Fasting and post-prandial glucagon levels decrease post-RYGB in obese patients with type 2 diabetes in parallel with the improvement seen in glucose homeostasis and insulin sensitivity. Mercodia immunoassay is precise in measuring the glucagon levels minimizing the cross-reactivity with glicentin and oxyntomodulin. Analysis with LC/MS-MS corroborated these results.

Evaluation of microRNA in patients with obesity: association with coronary artery disease

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Introduction: Recent studies claim that microRNAs (miRNAs) participate in the pathogenesis of coronary artery disease (CAD).

Objective: To study miRNA expression in patients with obesity, determine their association with CAD.

Methods: MiRNAs were detected in peripheral blood. 66 patients with BMI 30,0-39,9 kg/m² were divided into 3 groups: 1st - with CAD and T2DM, 2nd - with T2DM and excluded CAD, 3rd - with obesity and excluded CAD and T2DM. For miRNA profiling, the RT-qPCR assay was performed.

Results: Expression of miRNA-21 ($p=0.0004$), miRNA-26a ($p=0.003$), miRNA-33a ($p=0.009$) was different in the studied groups, while miRNA-1 ($p=0.065$) didn't show significant difference.

MiRNA-21 correlated with HbA1c ($r = -0.360$; $p=0.001$); cholesterol ($r = -0.222$; $p=0.048$) and with the thickness of interventricular septum ($r = -0.397$; $p=0.0002$) and posterior wall of the left ventricle ($r = -0.382$; $p=0.0005$). In the 2nd group miRNA-21 correlated with cholesterol ($r = -0.425$; $p=0.048$) and HDL ($r = -0.498$; $p=0.018$).

MiRNA-1 correlated with cholesterol ($r=0.255$; $p=0.023$); LDL-cholesterol ($r=0.292$; $p=0.009$); HbA1c ($r=0.297$; $p=0.007$) and with the thickness of interventricular septum ($r=0.338$; $p=0.002$) and posterior wall of the left ventricle ($r=0.409$; $p=0.009$); and ejection fraction ($r = -0.241$; $p=0.032$).

MiRNA-33a correlated with brachiocephalic arteries stenosis ($r=0.453$; $p=0.039$). In the 3rd group, miRNA-33a correlated with cholesterol ($r = -0.419$; $p=0.046$).

In the 1st group miRNA-26a correlated with LDL-cholesterol ($r=0.541$; $p=0.011$) and waist circumference ($r=0.481$; $p=0.027$).

Conclusions: Expression of miRNA-21, miRNA-26a and miRNA-33a differ in patients with obesity. MiRNA-1, miRNA-21 and miRNA-33a were associated with heart remodeling processes and may determine the severity of CAD.

Associations between FSH levels and indices of regional and total obesity in women after menopause

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Objective: Recent evidence reports a controversial extra-gonadal role of follicle stimulating hormone (FSH). Conflicting data support that the association between FSH and obesity might be maintained by a direct or even indirect effect to the adipose tissue. The aim of this study was to evaluate the associations between FSH concentrations and various obesity indices in women after menopause.

Methods: This cross-sectional study included 420 postmenopausal women (age 55.6 ± 6.5 years, 8.01 ± 6.7 years since menopause) with low insulin resistance (inclusion criteria: years since menopause >1 , FSH >25 IU/mL, HOMA-IR <5). We recorded anthropometric parameters. Indices of regional adiposity were sonographically assessed, including subcutaneous fat and preperitoneal fat. Blood samples were obtained for biochemical and hormonal evaluation.

Results: Mean values of BMI were 25.8 ± 4.0 kg/m². Waist circumference and BMI presented a stepwise decrease with increasing quartiles of FSH (Waist, FSH Q1 vs Q2 vs Q3 vs Q4: 93.2 ± 2.4 vs 87.6 ± 4.4 vs 85.4 ± 1.8 vs 80.89 ± 2.8 ; BMI, FSH Q1 vs Q2 vs Q3 vs Q4: 27.6 ± 5.2 vs 26 ± 4.8 vs 25.8 ± 7.1 vs 23.9 ± 2.9 ; ANOVA p-value for linear trend <0.001 , both cases). Similarly, subcutaneous and preperitoneal fat measures decreased linearly with increasing quartiles of FSH (ANOVA p-value for linear trend <0.001). Stepwise linear regression analysis showed that preperitoneal fat is inversely associated with FSH, independently of circulating estrogen (b coefficient $= -0.130$, p-value $= 0.029$) and traditional cardiovascular risk factors. The association between FSH and subcutaneous fat was not evident following adjustment for circulating estrogen, implying a possible mediation effect of the latter on this association.

Conclusions: FSH is inversely associated with indices of total and regional adiposity in women after menopause. The exact mechanism of this interaction remains to be elucidated in future studies.

Subcutaneous white adipocytes histological evaluation in obese bariatric patients: size matters

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Introduction: White adipose tissue cellularity is a highly versatile and precocious marker for metabolic status. Fat morphology can be estimated by comparing body fat mass with average fat cell size. Recent studies have shown that adipocyte hypertrophy is negatively correlated with dyslipidemia and insulin resistance, independent of body composition.

Methods: The study group includes 18 obese patients, with a mean age of 38.76 ± 8.89 years and a mean BMI of 46.06 ± 6.48 kg/m² for which subcutaneous abdominal fat tissue (1–2 g) was harvested during laparoscopic sleeve gastrectomy. Histological sections were analysed using Tissue Gnostic FACS Histo software and Adiposoft for automatic cell size measurement. Metabolic syndrome criteria as established by IDF were evaluated for the patients in the study, leptin, adiponectin, C peptide and HOMA-IR measurements were performed.

Results: Mean subcutaneous adipocyte area was higher in obese patients with associated metabolic syndrome criteria compared with those without metabolic syndrome (3200 vs 1289 μm^2 ; $p=0,001$). For HOMA-IR and C peptide levels a positive correlation ($r= +0,493$; $p=0,017$) respectively ($r= +0,622$; $p=0,002$) was found with mean adipocyte area. Also adipocyte area was correlated with BMI values ($r= + 0,575$; $p=0,004$) and increased Leptin/Adiponectin ratio ($r= +0,602$; $p=0,002$).

Conclusion: Measuring fat cell size might have important implications. Impaired adipogenesis leads to dysfunctional, hypertrophic adipocytes, local inflammation and peripheral insulin resistance. As recently discussed, other parameters are needed to better classify subtypes of obesity that have different impacts on the risk of developing type 2 diabetes and other obesity complications.

Hypoxia modulates effects of fatty acids on human pancreatic β -cells

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Objective: Saturated fatty acids (FAs), e.g. stearic acid (SA), induce apoptosis in pancreatic β -cells while unsaturated FAs, e.g. oleic acid (OA) have nearly no detrimental effect. Moreover, unsaturated FAs are capable of inhibiting the pro-apoptotic effect of saturated FAs. Hypoxia is also known to have deleterious effects on β -cell function and viability. In the present study, we have tested the modulatory effect of hypoxia on the effect of FAs on the growth and viability of human pancreatic β -cells NES2Y.

Methods: We used 4% O₂ concentration to generate moderate hypoxia and 1% O₂ concentration to generate strong hypoxia. 20% O₂ concentration was used as normoxia. In experiments, a defined serum-free medium supplemented with 1 mM SA, a combination of 1 mM SA and 0.2 mM OA, or 0.2 mM OA alone bound to a 2% FA-free bovine serum albumin was used.

Results and Conclusions: We showed that hypoxia increased the pro-apoptotic effect of saturated SA. Endoplasmic reticulum stress signalling seemed to be involved in this effect. Hypoxia also decreased the protective effect of unsaturated OA against the pro-apoptotic effect of SA. Thus, in the presence of hypoxia, OA was unable to save SA-treated β -cells from apoptosis induction. Interestingly, hypoxia itself had only weak detrimental effects on NES2Y cells. Our data suggest that hypoxia could represent an important factor in pancreatic β -cell death induced and regulated by FAs and thus in the development of type 2 diabetes mellitus.

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MTHFR polymorphic variants are associated with the predisposition of weight loss in girls with anorexia nervosa

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Objective: Differences in body weight and clinical features of typical vs atypical anorexia nervosa (A.N) might be explained by the genetic background. We aimed to evaluate the association between the subtypes of A.N. and the genetic polymorphisms of the thrombotic panel or the methyltetrahydrofolate reductase (MTHFR) gene.

Methods: A total of 40 adolescent girls with A.N., aged 13-19 years, were evaluated. We recorded anthropometric parameters, amenorrhoea duration and calculated age-adjusted body mass index (BMI) z-scores. Blood samples were obtained for hormonal assessment and genotyping of: Factor V Leiden, Factor V R2, Factor XIII, Glycoprotein IIb/IIIa, Prothrombin G20210A, MTHFR A1298C or C677T.

Results: Presence of atypical vs typical AN was predicted only by MTHFR mutations (C677T, OR=13.327, 95% CI: 1.384 to 128.3, p-value=0.025; A1298T, OR=0.068, 95% CI: 0.006 to 0.752, p-value=0.028), in models adjusted for age and levels of estrogen. The presence MTHFR1298 but not the MTHFR677 variant differed almost significantly between quartiles of BMI z-scores in AN-girls (Q1 vs Q2 vs Q3 vs Q4: 70% vs 50% vs 25% vs 20%, Chi-square p-value=0.092). The development of atypical vs typical AN is predicted by presence of MTHFR polymorphisms in combination (C677T polymorphism, O.R.=9.133, 95% CI: 1.366-61.074, p-value=0.023; A1298T polymorphism, O.R.=0.055, 95% CI: 0.005 to 0.644, p-value=0.021).

Conclusion: The presence of MTHFR genetic mutations is related with the predisposition of AN-girls to lose weight. Higher prevalence of the C677T mutation seems to be more protective in maintaining body weight compared with the A1298T mutation.

AKR1D1 is a novel regulator of metabolic phenotype in human hepatocytes and is dysregulated in non-alcoholic fatty liver disease

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Objective: Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome. Steroid hormones and bile acids are potent regulators of hepatic carbohydrate and lipid metabolism. Steroid 5 β -reductase (AKR1D1) is highly expressed in human liver where it inactivates steroid hormones and catalyzes a fundamental step in bile acid synthesis.

Methods: Human liver biopsies were obtained from 34 obese patients and AKR1D1 mRNA expression levels were measured using qPCR. Genetic manipulation of AKR1D1 was performed in human HepG2 and Huh7 liver cells. Metabolic assessments were made using transcriptome analysis, western blotting, mass spectrometry, clinical biochemistry, and enzyme immunoassays.

Results: In human liver biopsies, AKR1D1 expression decreased with advancing steatosis, fibrosis and inflammation. Expression was decreased in patients with type 2 diabetes. In human liver cells, AKR1D1 knockdown decreased bile acid biosynthesis and steroid hormone clearance. RNA sequencing identified disruption of key metabolic pathways, including insulin action and fatty acid metabolism. AKR1D1 knockdown increased hepatocyte triglyceride accumulation, insulin sensitivity, and glycogen synthesis, through increased *de novo* lipogenesis and decreased β -oxidation, fueling hepatocyte inflammation. Pharmacological manipulation of bile acid receptor activation prevented the induction of lipogenic and carbohydrate genes, suggesting that the observed metabolic phenotype is driven through bile acid rather than steroid hormone availability.

Conclusions: Genetic manipulation of AKR1D1 regulates the metabolic phenotype of human liver cells, driving steatosis and inflammation. Taken together, with the observation that AKR1D1 mRNA expression is down-regulated with advancing NAFLD, suggests that it may have a crucial role in the pathogenesis and progression of the disease.

Onset of radiation-induced hypopituitarism in pituitary adenomas

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Objective: Radiotherapy (RT) can achieve tumour control rates of over 90% in pituitary adenomas. The commonest toxicity of irradiation is hypopituitarism. The exact incidence is variable and requires long-term testing for deficiency of all hypothalamic-pituitary axes (HPA). The aim of this study is to determine the time to onset of individual hormonal deficiencies and establish a timeframe for endocrine testing post-RT.

Methods: We retrospectively assessed the late effects of irradiation on pituitary function in patients with pituitary adenomas treated over 2004-2015. Patients with acromegaly or Cushing's disease, those with tumour recurrence undergoing surgery after radiotherapy and patients with incomplete endocrine data were excluded.

Results: 94 patients (59% male; mean age at RT 58.4 ± 12.3 years) were included. Mean duration of endocrine follow-up post-RT was 7.6 ± 3.1 (range: 1.3-14.3) years. Thirty patients (31.9%) had complete loss of anterior pituitary hormone function pre-RT.

Overall prevalence of radiation-induced hypopituitarism was 65.6%. The incidence and mean time to onset of individual hormone deficits post-RT were: GH-57.1% (1.3 ± 0.7 years); LH/FSH-50% (2.0 ± 1.4 years); ACTH-43.3% (3.1 ± 2.2 years, $p=0.04$); TSH-39.6% (2.9 ± 1.7 years, $p=0.01$). Age at RT, gender, RT dose and severity of hypopituitarism pre-RT did not correlate with post-RT hypopituitarism.

By 5 years post-treatment, 100% GH, 75% LH/FSH, 60% ACTH and 75% TSH deficiencies were evident. All HPA dysfunction were detected by 8 years.

Conclusions: GH axis was the most vulnerable and ACTH deficiency was of slowest onset. Regular testing is mandatory for at least 8 years to ensure timely diagnosis and early hormone replacement therapy.

PITUITARY APOPLEXY CLINICAL PRESENTATION AND MANAGEMENT: THE EXPERIENCE OF A SINGLE CENTER

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Purpose: Pituitary apoplexy is a rare endocrine emergency due to abrupt hemorrhage or infarction of a preexisting pituitary tumor. We aimed to present clinical and biochemical characteristics as well as the management of patients presented with pituitary apoplexy at our department.

Methods: Review of the records of all patients presenting with pituitary apoplexy at the Endocrinology department over the last 20 years.

Results: During the period 1998-2018, twenty-one patients (5 women) were hospitalized for pituitary apoplexy. The median age of patients was 56.1 ± 12.5 years. Only one patient had known pituitary adenoma at the diagnosis of pituitary apoplexy. The majority of pituitary adenomas 18/21 (85.7%) were nonfunctioning (NFPAs). Predisposing factors were identified in 15/21 patients (71.4%). Acute and severe headache was the commonest symptom 18/21 (85.7%) followed by visual disturbances 9/21 (42.9%) and ophthalmoplegia 9/21 (42.9%). At presentation, the majority of patients 15/21 (71.4%) had one or more anterior pituitary hormone deficiencies. Twelve of 21 patients (57.1%) underwent within a week transsphenoidal surgery due to visual fields defects, ophthalmoplegia or aggressive tumor. Ophthalmoplegia was corrected in all patients. Four of the 7 patients who underwent surgery had complete visual fields and 3 had improvement postoperatively while 2 of the patients who were treated conservatively, had also improvement of their visual fields. In 11 of 12 patients (91.6%) who had surgery, partial or total anterior pituitary hormone deficiency was remaining, as well as in 8 of 9 patients (88.8%) who had conservative treatment. Low prolactin levels at the onset of pituitary apoplexy did not correlate with anterior pituitary hormone deficiency in the future.

Conclusion: In patients with pituitary apoplexy transsphenoidal surgery is indicated within 7 days when visual fields defects do not improve or worsen.

Bone health and final height in craniopharyngioma patients

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Objective: Craniopharyngioma (CP) is a benign tumor of the sellar/hypothalamic region. It is associated with endocrinopathies, which may potentially impair bone health. Our objective was to determine bone health status in CP patients.

Methods: In this retrospective study, Dutch/Swedish CP patients were included if data was available on fractures, bone mineral density (BMD) (T/Z-score), or final height (age >18 years). Data is presented as mean±standard deviation. Standardized deviation scores (SDS) of final height were calculated based on sex/country of origin. A logistic regression model was developed to evaluate determinants for fractures.

Results: We included 177 patients (48% female, mean age at diagnosis 28±20 years). Fractures occurred in 31 patients (18%). In a multivariable logistic regression model for fractures, significant determinants were female sex (OR 0.3 $P=0.004$), surgery (OR 0.1, $P=0.009$), and use of anti-epileptics (OR 3.0, $P=0.07$). Osteoporosis was not an explanatory variable (OR 2.1, $P=0.21$). Mean BMD T- and Z-scores were normal: Z-scores for total body, femur neck and L2L4 were 0.1±1.5 (range -4.1 – 3.5), -0.1±1.3 (range -2.7 – 4.7) and 0.0±2.0 (range -3.5 – 6.8), respectively. Low BMD occurred in 47 patients (50%). Final height SDS was -0.3±1.2 (no difference between adulthood- or childhood-onset disease ($P=0.67$)).

Conclusions: CP seem to result in a high rate of fractures. Epilepsy treatment was a risk factor and female sex a protective factor for fractures. Mean BMD Z-score was normal, but with a very wide range, resulting in low BMD in 50%. Osteoporosis does not explain fracture risk well. Final height is normal.

Splicing machinery is dysregulated in pituitary neuroendocrine tumors (PitNETs) and associated with aggressiveness features

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Objective and Methods: Recent studies suggest that altered alternative splicing and, consequently, appearance of an abnormal splicing pattern and even of aberrant/oncogenic splicing-variants, represent a common molecular feature of most tumor pathologies, including Pituitary Neuroendocrine Tumors (PitNETs). However, the putative alteration, pathophysiological role and potential therapeutic utility of splicing machinery components [i.e. spliceosome-components (SCs) and splicing-factors (SFs)] remain unknown in PitNETs. Therefore, we aimed to: 1) Analyze the expression levels of selected splicing machinery components, and their association with relevant clinical parameters, in PitNETs [n=261: somatotropinomas (n=138)/ Non-Functioning PitNETs (NFPTs; n=90)/ corticotropinomas (n=24)/ Prolactinomas (n=9)]; and, 2) evaluate the potential antitumor actions (cell-proliferation/viability/hormone-secretion) of a spliceosome-inhibitor (pladienolide-B) in PitNET-cells.

Results: a severe dysregulation of the expression levels of SCs and SFs was found in all the PitNET-subtypes compared to normal-pituitaries, which provided unique molecular fingerprints that accurately discriminate between normal and tumor tissue in each of the PitNET-subtypes analyzed. Results also identified several SCs commonly dysregulated in all PitNET-subtypes. Interestingly, the expression-levels of several SCs and SFs were associated to key clinical features. Notably, pladienolide-B markedly reduced cell-proliferation/viability/hormone secretion in PitNET cell-cultures/cell-lines.

Conclusions: The splicing machinery is severely and distinctly dysregulated in the main PitNET-subtypes which opens a new window to investigate the plausible contribution of splicing dysregulation and its subsequent outcomes to pituitary tumorigenesis, and to assess the potential value of specific splicing machinery components as novel diagnostic/prognostic tools in these pathologies. Furthermore, our study unveils that the spliceosome could be novel actionable therapeutic target to combat PitNETs.

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Somatostatin analogues in the therapy of clinically non-functioning pituitary adenomas- do they decrease the risk of tumour progression?

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Introduction: The management of clinically non-functioning pituitary adenomas (NFPA) remains a debated issue. Surgery, which is indisputably indicated in invasive NFPA, is rarely curative. Moreover, it is not always feasible due to potential complications or contraindications. Expression of somatostatin receptors (SSTR) form the rationale for the use of somatostatin analogues (SSA) in the therapy NFPA. **Aim:** to compare the risk of NFPA progression between patients treated with SSA and patients who did not receive pharmacotherapy.

Material and methods: Fifty seven patients with NFPA (subgroup A-40 after incomplete surgery+subgroup B-17 not operated) were enrolled into the study. SSTR scintigraphy and additionally immunohistochemistry (subgroup A) were performed. The presence of SSTR was confirmed in 25 patients (17 from subgroup A+8 from subgroup B) in whom SSA therapy was started (every 4 weeks: octretide LAR 20 mg intramuscular or lanreotide autogel 120 mg deep subcutaneous injection). The duration of the therapy varied from 16 months to 18 years. Adenoma size was estimated in pituitary magnetic resonance imaging.

Results: Tumour progression rate was twice higher in patients who were not treated with SSA (71,9% vs. 36%). In subgroup A tumour volume increased in 35,3% patients treated with SSA compared to 74% patients without pharmacotherapy. Moreover, in subgroup B tumour progression was noticed in 37,5% SSA treated patients vs. 66,7% not SSA treated patients.

Conclusions: SSA significantly decrease the probability of tumour progression in NFPA, however, further studies should be carried out.

Unusual cause of gigantism - Growth hormone releasing hormone (GHRH)-secreting pancreatic neuroendocrine tumour in a patient with multiple endocrine neoplasia type 1 (MEN1)

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Background: Gigantism is a rare condition with accelerated growth in childhood when the epiphyseal plates are not fused. Most cases are due to growth hormone (GH) secretion from a pituitary adenoma. Rarer causes of GH-related gigantism include somatotroph hyperplasia as part of McCune-Albright syndrome, Carney complex, X-linked acrogigantism or ectopic GHRH production.

Case presentation: An 18-year-old male with c.249_252delGTCT;p.I85Sfs *MEN1* mutation, and history of insulinoma (age 10y) and primary hyperparathyroidism (age 15y) presented with accelerated childhood growth and gigantism. Height: 193.5cm (+2.8SDS).

Biochemistry: IGF1: 970mcg/l (>2x ULN), random GH: 39mcg/l, OGTT (GH nadir): 1.7mcg/l, GHRH: 327ng/l (>5x ULN), calcitonin: 82ng/l (>7x ULN), PRL: 213mU/l (<329), PTH: 8.4pmol/l (0.7-5.6), CgA: 44pmol/l (<60)

Imaging: MRI abdomen: 40mm (head) and 6mm (tail) pancreatic tumours. MRI pituitary: bulky (9.9mm craniocaudally). Review of previous imaging raised possibility of a 3mm lesion in the right inferolateral anterior pituitary.

Treatment: Six-month 120mg/month Lanreotide Autogel treatment reduced GHRH to 180ng/l and IGF-1 to 778mcg/l. Whipple procedure was performed and 4 well-differentiated NETs were identified with the largest showing GHRH and calcitonin immunoreactivity with a ki-67 of 2%. Post-operatively, GHRH was undetectable and IGF-1 returned to normal. The 6mm tail lesion was not resected and patient remains free of diabetes.

Conclusions: Childhood-onset GH excess in MEN1 syndrome patients is mostly due to GHRH-secreting pancreas NETs rather than pituitary adenoma. It is important to diagnose the underlying cause to prevent unnecessary pituitary surgery. Careful discussion between surgeon and patient is important regarding repeated pancreas surgeries in MEN1 syndrome.



Figure 1. MRI abdomen: Circle highlights lesion in the head of the pancreas.

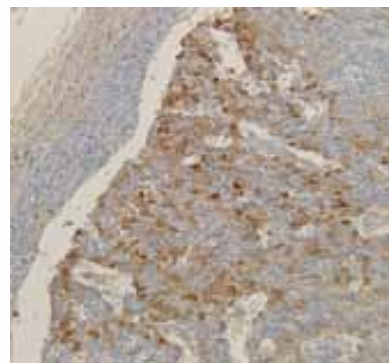


Figure 2. GHRH immunoreactivity in NET cells.

Sparsely and densely granulated growth hormone-secreting pituitary tumours (somatotropinomas): from histopathology to epigenomics

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Objectives: Somatotropinomas form three subgroups with distinct methylation profiles¹, one matching the sparsely granulated (SG) and the other two matching the densely granulated phenotypes (DG-A and DG-B). Publicly accessible raw methylation data¹ and our RNA microarray data were analysed to identify differentially methylated regions (DMRs) and enriched genes between SG, DG-A and DG-B and normal anterior pituitary gland (NP), genes showing differential methylation of promoters with differential expression.

Methods: DMRs were identified using bumpHunter (minimum number of probes/DMRs=7, adjusted $p < 0.05$, false discovery rate (FDR) < 0.05) with gene set enrichment analysis (GSEA) using Fisher's exact test ($p < 0.05$). Interaction hotspots were identified using EpiMod ($p < 0.05$). Differentially expressed genes were identified using Affymetrix data with FDR < 0.05 and fold change of ≥ 2 .

Results: 3 distinct methylation profiles were noted (Figure 1). 3 genes (SG vs NP= 2, DG-B vs NP= 1) showed hyper-methylation of promoter with decreased expression. 21 genes (SG vs NP= 1, DG-A vs NP= 5, DG-B vs NP= 15) showed hypo-methylation of promoter with increased expression. Genes of interest included *IER3* (SG vs NP, methylation value 1.12, log-fold change=-5.28108) and *TET1* (DG-B vs NP, methylation value =-1.13, log-fold change=3.09). One gene set (BRIDEAU_IMPRINTED_GENES) and 6 interaction hotspots (seeds mainly involving inflammatory mediators, Figure 2) were common across all analyses comparing tumour subgroups to normal anterior pituitary gland.

Conclusions: Pathways involving apoptosis (*IER3*), demethylation (*TET1*), inflammation and degradation of extracellular matrix appear central to pituitary tumorigenesis. Further analysis and validation is in progress.

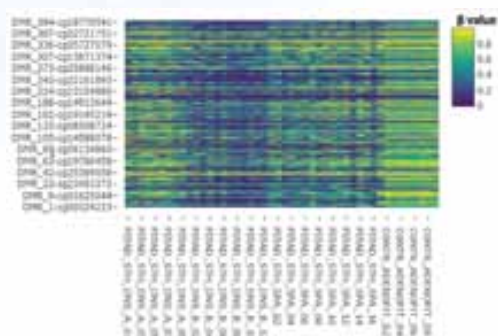


Figure 1. Heatmap of methylation values across tumour subgroups and normal pituitary.

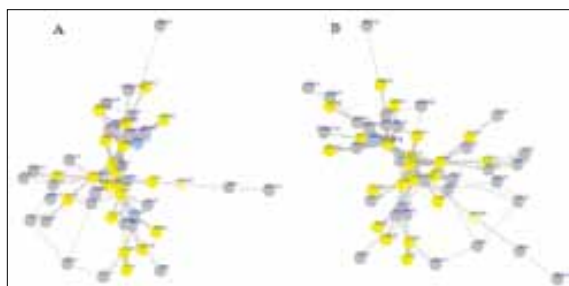


Figure 2. Interaction hotspots with (A) CCL11 and (B) MMP3 as seeds.

Non-functioning pituitary adenomas experience of a reference center

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Objective: Describe clinical, laboratorial, imaging features, therapeutic management and the outcomes of patients with clinically non-functioning pituitary adenomas (NFPAs) presenting at our department.

Methods: Retrospective review of electronic medical records of all patients with NFPAs evaluated at our department between 2010 and 2019.

Results: We evaluated 160 patients, 51.3% female, with a median age of 56.6 years (18–89). Regarding comorbidities, 61.3% had hypertension, 21.3% were diabetic and 51.3% had dyslipidemia. At diagnosis 38.1% had visual field defects (n=61), 31.3% had headache (n=50), 5% apoplexy (n=8) and 25.6% was an incidentaloma (n=41).

Pituitary function assessment showed that 50.6% had hypopituitarism, specifically hypogonadism in 33.1 % (n=53), secondary adrenal insufficiency in 32.5% (n=52) and hypothyroidism in 24.4 % (n=39). The NFPA were mainly macroadenomas (84.3%) with suprasellar extension (53.8%), 7.5% had left cavernous sinus invasion, 10.6% right cavernous sinus invasion, 3.1% bilateral cavernous sinus invasion and 6.9% sphenoidal sinus invasion. Median diameter of the adenoma was 17.5 mm (2.4-45.0). Surgery was performed as primary therapy in 71.9% patients (n=115) and radiotherapy in 0.6% (n=1). Complete removal of the NFPA was achieved with one surgery in 52.2% of patients (n=60). Immunohistochemical analyses showed 57 gonadotrophs, 13 silent corticotroph, 10 plurihormonal adenomas, 5 null-cell and 1 silent thyrotroph. Immunohistochemistry resulted negative in 46.3% of the tested pituitary tissues due to insufficient/ necrotic samples.

Discussion: Our data support the elevated prevalence of mass effect and hypopituitarism in patients with NFPAs. Recurrence due to invasion or incomplete resection of the tumor is quite common.

The role of microRNAs and its targeted genes in development of ACTH-dependent hypercortisolism

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Objective: To analyze the role of miRNAs previously found to be differentially expressed in patients with ACTH-dependent Cushing syndrome (CS).

Materials and methods: We analyzed putative targets of three microRNAs, which were previously found to be differentially expressed in ACTH-dependent CS patients: miR-16-5p, miR-145-5p, miR-7g-5p. We used TargetScan (TS) and DIANA tools (DT) predictions.

Results: We found different plasma expression of miR-16-5p, miR7g-5p and miR-145-5p in CD (n=28) compared to ACTH-ectopic syndrome (n=13). MiR- 16-5p was differently expressed in plasma samples from healthy subjects (n=11) compared to both CD and ACTH-ectopic CS. MiR- 145-5p expression differed between ACTH-ectopic CS vs healthy subjects, but not CD vs healthy subjects; whereas miR- 7g-5p was differently expressed in CD vs healthy control, but did not differ from ACTH-ectopic CS vs healthy subjects.

Using TargetScan (TS) and DIANA tools (DT) we evaluated *HMGA1* and *HMGA2* as possible targets of miR-16-5p and mir-7g-5p, which may explain the rare incidence of malignancy in CD and non-invasive pituitary tumor growth.

miR-16-5p also targets oncogene *SOX5* that is known to stimulate the progression of various cancers. By targeting Sox5 miR-16-5p inhibit pituitary tumor cell proliferation, invasion and migration. Another mir-16-5p target gene is *BCL2* that regulates apoptosis.

miR-145-5p inhibits the mTOR signaling pathway by targeting *AKT3* and can regulate cell proliferation, invasion and apoptosis.

Conclusions: Our findings demonstrate that miR-16-5p, miR-145-5p, miR-7g-5p can be involved in development of ACTH-dependent Cushing syndrome which might be helpful to evaluate malignant potential or therapeutic efficiency in ACTH-dependent Cushing syndrome.

T2-signal intensity, SST receptor expression and first-generation somatostatin analogs efficacy predict hormone and tumor responses to pasireotide in acromegaly

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Objective: MRI T2-signal intensity and somatostatin (SST) receptor expression are recognized predictors of therapy response in acromegaly. We investigate the relationship between these predictors and the hormonal and tumor responses to PAS-LAR therapy, and compare to first-generation somatostatin receptor ligands (SRLs) responsiveness.

Methods: We included 45 acromegalics initially receiving SRLs, followed by a combination therapy including pegvisomant (PEGV), and finally PAS-LAR. Primary endpoints were tumor volume reduction ($\geq 25\%$ from baseline) and IGF-I levels (expressed as upper limit of normal (ULN)) during three months of PAS-LAR. We assessed T2-weighted MRI signal intensity by region of interest (ROI), visual assessment, SST receptor expression and IGF-I reduction (%) after SRLs.

Results: Significant tumor shrinkage was observed in patients with less IGF-I reduction during SRLs (mean 18.6% [SD 24.4] vs 35.1% [23.0], $p=0.036$), higher IGF-I levels during PAS-LAR (mean 1.36 [SD 0.53] vs 0.93 [0.43], $p=0.020$) and adenomas with low SST₂ receptor expression (median 2.0 [IQR 1.0–6.0] vs 12.0 [7.5–12.0], $p=0.040$). Lower IGF-I levels during PAS-LAR were associated with higher T2-signal intensity (β -0.29, 95% CI -0.56–0.01). Patients with PAS-LAR-induced increased T2-signal intensity, achieved lower IGF-I levels (median 0.84 [IQR 0.51–1.28] vs 1.10 [0.82–1.30], $p=0.047$), while harboring relatively larger adenomas during PAS-LAR (median 1719 [IQR 1143–4616] vs 574 [170–2190], $p=0.050$).

Conclusions: Patients unresponsive to SRLs with low SST₂ receptor expression are more prone to achieve tumor shrinkage during PAS-LAR. Surprisingly, tumor shrinkage is not accompanied by achieving lower IGF-I levels, which are associated with higher T2-signal intensity.

Clinical features of primary hyperparathyroidism in women of different age groups according to the Russian Online Register database

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Objective: The aim of the study was to compare the clinical features in three age-groups of women with primary hyperparathyroidism.

Methods: the data about biochemical profile and disease complications in women with active stage of disease (n=645) was collected from the Russian Primary Hyperparathyroidism Registry. Group 1 included women 20-49 years old (n=215) unless the patients with suspected or confirmed multiple endocrine neoplasia syndrome, group 2 - women 50-69 years old (n=215), group 3 - women over 70 years old (n=215). Data analysis was performed using Statistica v. 13.3 (TIBCO Software Inc., USA). Three groups were compared using the Kruskal-Wallis test.

Results: There was no statistically significant difference between the three groups with respect to parathyroid hormone, total and ionized serum calcium levels ($p > 0.05$); however the daily urinary calcium excretion increased ($p < 0.001$) and glomerular filtration rate decreased ($p < 0.001$) with age. Using X-ray densitometry in group 1 osteoporosis occurred in 21.9%, in group 2 - 50.2%, in group 3 - 69.8% ($p < 0.001$) and low-energy fractures were presented in 10.7%, 17.2% and 36.7% respectively ($p < 0.001$). Kidneys ultrasound examination showed that younger patients had nephrolithiasis less often: group 1 - 2.79%, group 2 - 5.58% and group 3 - 9.30% ($p = 0.016$). Also the frequency of hypertension was age-dependent (17.2%, 36.7% and 52.6% of cases respectively) ($p < 0.001$).

Conclusion: According to our study the frequency of classical and non-classical primary hyperparathyroidism complications increases with age probably because of comorbid status that must be considered in management strategies.

Osteoprotegerin and receptor activator of nuclear factor kappa-B ligand levels and their association with BMD in acromegaly

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Objective: The purpose of the study was to investigate osteoprotegerin (OPG) and receptor activator of nuclear factor kappa-B ligand (RANK-L) levels in acromegaly patients with regard to the disease activity. The associations between OPG, RANK-L and random growth hormone (GH), insulin-like growth factor 1 (IGF-1), lumbar spine (LS) bone mineral density (BMD), femoral neck (FN) BMD were also evaluated.

Methods: A study group included 72 patients with acromegaly, and was divided into three subgroups: 9 active acromegaly (AA), 24 controlled acromegaly (CTA) and 39 cured acromegaly (CA). 54 age- and sex-matched healthy individuals were recruited to the control group (CG). Serum concentrations of OPG, RANK-L, GH and IGF-1 were measured. Dual-energy x-ray absorptiometry was performed at two sites: LS and hip.

Results: The patients with acromegaly had significantly higher OPG levels than CG (AA+CTA+CA vs CG; $p < 0,0001$). There were no significant differences in RANK-L levels among the subgroups of patients, despite of subject classification. OPG correlated negatively with IGF-1, FN T-score, FN BMD in the groups AA+CTA+CA, CTA+CA and CTA ($p < 0.05$). Positive correlations between RANK-L and IGF-1 were observed in the following groups: AA+CTA+CA, CTA+CA, AA and CA ($p < 0,05$). There were also positive correlations between RANK-L and FN T-score, FN Z-score, FN BMD, LS BMD in the groups AA+CTA+CA and CTA+CA and between RANK-L and FN T-score, FN Z-score, FN BMD in the CTA and CA groups ($p < 0.05$).

Conclusions: OPG/RANK-L system might play a role in bone remodeling in acromegaly.

Vitamin D deficiency in pregnant women in Russia Federation

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Pregnant women are at risk of developing diseases associated with deficiency of essential micronutrients.

Objective: To assess the prevalence of vitamin D deficiency among pregnant women and its dependence on the trimester of pregnancy.

Methods: we examined 476 pregnant women at different gestational periods from three regions of Russia (Moscow, Ivanovo, Smolensk). Concentration of 25(OH)vitamin D (ng/ml) was estimated by immunometric method. We collect information about intake of vitamin supplements.

Results: median of vit.D in Moscow was 14.9 ng/ml, in Ivanovo - 17.3 ng/ml, in Smolensk - 15.8 ng/ml. In Moscow only 5.6% of all women have level above 30 ng/ml, 76% have vitamin D deficiency (below 20 ng/ml). 17% of patients have insufficiency of this element (20-30 ng/ml).

In Ivanovo: 6% - optimal level, 66% - deficiency, 28% - insufficiency. In Smolensk: 4.7% - optimal level, 76% - deficiency, 19% - insufficiency. Women who have optimal level of vit.D was on therapy with native vit.D. When assessed dependence of concentration of vit.D on the trimester of pregnancy, a significant decrease was found with an increase in gestational age.

Conclusions: we revealed the presence of vit.D deficiency in pregnant women in Russia. It was also found that vit.D deficiency increases with increasing gestational age. Now there are no long-term data on the safe dosage of vitamin D preparations during pregnancy, so further research is needed on this topic. These results must be considered for adjusting vitamin-containing supplements prescribed to pregnant women.

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Quality of Life in Chronic Hypoparathyroidism

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Introduction: reduced health-related quality of life (HRQoL) is common in patients with chronic hypoparathyroidism treated conventionally with active vitamin D and calcium supplements.

Aim: to determine the HRQoL of patients with hypoparathyroidism with disease persisting for more than 1 year.

Methods: We identified 32 patients (women/men - 31/1, median (Me) age 48 years [38; 59.5]). The average duration of the disease was 4 years [2; 8]. All participants completed the 36-Item Short-Form Health Survey (SF-36) and multidimensional fatigue inventory (MFI-20). Descriptive statistics were expressed as Me and values of the 1st and 3rd quartiles [Q1; Q3]. The statistical significance level was set at $P < 0.03$ after the Bonferroni correction.

Results: all patients were treated conventionally, but most of them did not reach the target calcium level. Hypoparathyroidism patients had significantly lower SF-36 scores, especially – role limitations due to physical problems (25.0 [0; 100]), vitality (40 [30; 65]), physical (39.5 [34.5; 43.5]) and mental health (MH) (37.5 [30; 49]). The participants demonstrated increased MFI-20 subscales (more than 12), especially in general (16 [13; 18]) and physical fatigue (14 [11; 16]) and activity (14 [9; 16]). We didn't find any correlation between SF-36 and MFI-20, neither with the duration of the disease, nor with therapy received or calcium and magnesium parameters. However, there was a weak negative correlation between role limitations due to emotional problems and MH and serum magnesium (Spearman's ρ , -0.5; $P = 0.001$ and -0.4; $P = 0.008$ respectively).

Conclusion: Patients with chronic hypoparathyroidism are experiencing diminished HRQOL.

Antiosteoporotic drugs effectiveness and Ca/Vit D supplementations intake in elder patients with osteoporosis

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Objective: to investigate osteoporosis features in elder patients in Moscow population

Materials and Methods: It was a retrospective study, during which we analyzed the data of 192 outpatients admitted to our Centre. In the focus of our attention was patients' past medical history and T-criteria values assessed by DEXA-scan. The statistical analysis was performed using Prism 8 Version 8.0.1 (145). Statistically significant were differences with $p < 0,05$.

Results: Median age of the patients was 77 [73;87] years. The number of patients with 3 and more fractures was quite high and was 89. The most frequent localization of fracture was lumbar vertebrae (53%). The values of T-criteria for hip and spine according to DEXA-scans showed significantly lower T-criteria ($p=0,04$) for lumbar vertebrae vs hip: Me -3.1 [-2.6;-3.6]. 50% of the patients did not receive any antiosteoporotic treatment; treated patients received bisphosphonates in most cases (63%, $n=59$), followed then by denosumab (18%, $n=17$) and teriparatide (9%, $n=8$). The adverse effects were much higher in BF group (90% of all cases). Patients receiving only Ca supplementation had approximately the same prevalence of fractures compared to patients with no Ca/Vit D supplementation, meanwhile patients receiving only vitamin D had significantly lower prevalence of fractures [$p=0,045$], and patients receiving Ca+VitD did not differ from only Vit D-group.

Conclusion: Vitamin D and combined supplementation is extremely important in prevention of fractures, meanwhile Ca alone does not have any protective effect. In severe osteoporosis the preference should be given to anabolic treatment for better results.

Effect of treatment with Cinacalcet on TBS and BMD in patients with chronic renal failure with secondary hyperparathyroidism in hemodialysis

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Background: Fractures are frequent in patients with chronic renal failure (CRF) with secondary hyperparathyroidism (SHPT) undergoing hemodialysis. Cinacalcet (CT) is a drug used in the reduction of hypercalcemia in these patients that acts through the intestinal calcium sensor in the parathyroid gland. Recently, it has been pointed out that CT can reduce fractures in these patients by unknown mechanisms (EVOLVE Trials 2015).

Objectives: To evaluate the effect of CT on Trabecular Bone Score (TBS) and Bone Mineral Density BMD in patients with CRF and SHPT.

Methods: Cross-sectional study with two groups: patient in treatment with CT and patients without treatment with CT (control group). Dimensional measurement by DXA Hologic 4500 QDR and TBS with MediMaps software.

Results: 14 patients with CT and 24 patients in the control group. Mean age was 56.2 ± 11.6 vs. 62.5 ± 14.9 ($p = 0.39$) years, sex M / W 6/8 vs. 15/8. Body mass index (BMI): 22.6 ± 2.5 vs. 23.6 ± 3.5 , $p = 0.33$, in the group with CT and control respectively. TBS 1.234 ± 0.106 vs. 1.373 ± 0.154 , $p = 0.05$; BMD (lumbar) 0.778 ± 0.163 vs. 0.832 ± 0.143 $p = 0.48$; BMD (femoral neck) 0.640 ± 0.090 vs. 0.709 ± 0.16 , $p = 0.15$; BMD (total hip) 0.540 ± 0.072 vs. 0.615 ± 0.172 , $p = 0.12$; BMD (wrist) 0.507 ± 0.078 vs. 0.617 ± 0.151 , $p = 0.01$, respectively in the group with CT and control. T-score (lumbar): -2.566 ± 1.373 vs. -1.723 ± 1.666 , $p = 0.26$; T-score (femoral neck): -2.807 ± 0.671 vs. -2.255 ± 1.381 , $p = 0.21$; T-score (total hip): -2.500 ± 0.749 vs. -1.895 ± 1.361 , $p = 0.02$; T-score (wrist): -3.992 ± 1.182 vs. -2.250 ± 2.641 $p = 0.02$.

Conclusions: TBS values in patients undergoing treatment with CT were lower than those in the control group, in the presence of similar BMD values in both groups. Further studies are needed to confirm that CT has positive effects on bone quality as measured by TBS.

Efficacy of sex hormone replacement and growth hormone therapy on bone mineral density in patients with Turner syndrome

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Objective: Growth hormone (GH) and sex hormone replacement therapy (SHRT) are standard treatment for patients with Turner syndrome (TS) that enhances bone mineral density (BMD), puberty, and quality of life. We aimed to evaluate the efficacy of SHRT and GH on BMD in TS patients.

Methods: Cross-sectional study was performed in LUHS Kauno Klinikos in 2014-2018. 27 females with TS were enrolled. BMD and Z score of the lumbar vertebrae and femur were measured by dual - energy X-ray absorptiometry (DEXA) and compared between these groups: users and non-users of SHRT; natural estrogen (NE) users vs. combined oral contraceptive pills (COC's) users; initiated with SHRT <15 years vs. >15 years; patients who received treatment with GH vs. not treated; patients who had and did not have spontaneous puberty.

Results: BMD and Z score of femur was higher in patients who did not use SHRT (BMD 0,9 (0,81 – 1,12) vs. 0,81 (0,58 – 1,04), $p=0,049$; Z score -0,2 (-0,9 – 2,3) vs. -1 (-2,9 – 0,8), $p=0,049$). No significant differences in BMD and Z score depending on SHRT initiation (<15; >15 years), between NE and COC's users ($p>0,05$) were found. Femur BMD and Z score were higher in patients who underwent spontaneous puberty (BMD 0,91 (0,73 – 1,2) vs. 0,81 (0,58 – 1,04), $p=0,038$, Z score -0,15 (-1,7 – 2,3) vs. -1 (-2,9 – 0,8) $p=0,036$). No significant differences were found between users and non-users of GH ($p>0,05$).

Conclusions: SHRT and GH did not influence BMD in females with TS. Spontaneous puberty had positive effect on BMD.

Real-world management of male idiopathic infertility in indication for FSH treatment: a multicenter, longitudinal, observational cohort study (open registry)

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Objective: The management of male idiopathic infertility is challenging. The Italian Medicines Agency (AIFA) note 74 regulates the empirical administration of follicle-stimulating hormone (FSH), although its application in clinical practice remain conflicting. The aim was to explore the management of male idiopathic infertility and to assess the actual use of FSH.

Methods: A multicenter longitudinal prospective observational study (open-registry), involving 10 Italian Andrological and Gynecological Centers was carried out. Adult men with idiopathic infertility and serum FSH levels <8 IU/L were considered. Semen and hormonal parameters were recorded at baseline and after treatment.

Results: 718 patients were enrolled (age 37.6±6.5 years). FSH treatment was prescribed in 55.3% of patients, with a significant difference between Andrological (61.3%) and Gynecological (30.3%) Centers (p<0.001). Recombinant-FSH was chosen in 64.5% and the urinary form in 35.5%. When prescribed, the adherence to regimen suggested by AIFA note (FSH at the dosage of 150 IU every other day) was almost complete (>90%). Concomitant hormonal treatment was prescribed to 23 patients (3.2%), nutraceuticals alone to 109 patients (15.2%), and nutraceuticals plus FSH for 42 patients (5.9%). Sperm concentration significantly increase compared to baseline (p=0.016) in patients treated with FSH.

Conclusions: Only half of infertile patients are treated with FSH, although the note 74 guarantees this therapeutic approach. FSH treatment is more frequently prescribed by Andrological Centers, confirming the heterogeneous management of male infertility. This real-life analysis confirms the beneficial effect of FSH in male idiopathic infertility, although future properly-designed studies are needed to confirm this improvement.

Genetic background predicts the presence of oligo- or amenorrhea in girls with anorexia nervosa

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Objective: To evaluate the association between genetic background and the presence of oligo- or amenorrhea in a sample of adolescent girls diagnosed with anorexia nervosa compared with controls.

Methods: A total of 40 adolescent girls diagnosed with anorexia nervosa aged 14-17 years, as well as 10 age-matched girls, were included in the study. We recorded anthropometric parameters and calculated body mass index (BMI) z-scores adjusted for age, as well as duration of amenorrhea. Blood samples were obtained for genotyping and hormonal assessment. Genetic polymorphisms of MTHFR (methylenetetrahydrofolate reductase C677T and A1298T) GpIIb/IIIa (glycoprotein IIb/IIIa) and prothrombin were investigated.

Results: Presence of the GpIIIa Leu33/Pro was evident almost solely in the subgroup of anorexic girls (cases vs controls, 27.6% vs 5.9%, p-value=0.073). Anorexic girls had higher odds than controls to carry: i) the GpIIa leu33/pro or G20210A mutation (34.5% vs 5.9%, p-value=0.028); ii) the GpIIIa Leu33/Pro mutation or the MTHFR A1298C (62.1% vs 29.4%, p-value=0.032). Furthermore, girls with oligo- or amenorrhoea compared with girls presenting with normal menses had significantly higher prevalence of: i) the GpIIIa Leu33/Pro mutation (30.3% vs 5.9%, p-value=0.048); ii) GpIIIa Leu33/Pro or the G20210A mutation (36.4% vs 5.9%, p-value=0.020); iii) any mutation from the panel, consisting of the GpIIIa Leu33/Pro or MTHFR A1298C (60.6% vs 29.4%, p-value=0.037). Logistic regression analysis proved that the presence of any mutation from the panel, consisting of G20210A or the GpIIIa Leu33/Pro mutation, as well as levels of estrogen, predict the development of amenorrhoea (OR 15.618, p-value=0.043), in a model adjusted for age, BMI z-score and diagnosis of anorexia nervosa.

Conclusions: Genetic background can predict the presence of oligo- or amenorrhea in girls diagnosed with anorexia nervosa.

Polycystic ovary syndrome: inositol vs. Metformin vs. Oral contraceptives – a prospective study

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Introduction: Polycystic ovary syndrome (PCOS) is a hyperandrogenic endocrine disorder associated with chronic oligo-amenorrhea, hirsutism, polycystic ovary morphology (PCOM) and often with insulin resistance. Due to its heterogenic etiology, there is no general treatment, but rather an individual approach, according to patient's symptoms, needs and wishes.

The aim of this study is to detect possible variations in clinical and biochemical outcome in PCOS cases, after treatment with either combined oral contraceptive pills (COCP), metformin or inositols.

Methods: This prospective study presents 56 patients in fertile age (18 – 36 years), diagnosed with PCOS, that received treatment with either COCP (30mg Etinylestradiol+Dienogest), Metformin (2x500mg) or inositols (2g Myoinositol). Patients were evaluated clinically and biochemically at baseline, 3 and 6 months.

Results: In patients treated with COCP, LH levels decreased by 77,71% after 3 months, and LH:FSH ratio with 54.01% ($p=0.0005$) after 6 months. There was a 52% improvement in PCOM at ultrasound examination from 3 months treatment on ($p<0.0001$), but no significant decrease in menstrual cycle length. Metformin proved superior in decreasing abdominal circumference and HbA1c. The inositol group had the most significant improvement after 3 months, all parameters being significantly improved apart from FG score; menstrual cycle pattern improved significantly after 3 months of treatment (54.7%, $p=0.0008$).

In conclusion, there are significant differences in clinical and biochemical parameters outcome between the different treatments, yet none of them turned out superior in all main symptoms, (hyperadrogenism, ovarian dysfunction and PCOM). Treatment in PCOS patients should be adapted to patient's symptoms and needs.

The influence of sex on the evolution of mesenteric metastasis in small intestinal neuroendocrine tumours

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Objective: A mesenteric mass with surrounding mesenteric fibrosis (MF) is a hallmark of small intestinal neuroendocrine tumours (SI-NETs) and known to induce abdominal complications. However, little is known on the evolution over time and the pathways involved in progression. Our aim was to assess the development of the metastatic mesenteric mass over time and find predictors for progression.

Methods: Retrospectively, 530 patients with proven SI-NET and ≥ 2 available CT-scans were included for analysis. The presence and growth of a mesenteric mass was assessed according to RECIST 1.1 on every CT-scan. Based on these results, expression of estrogen receptor alpha (ESR1) and androgen receptor (AR) were assessed by RT-qPCR.

Results: Mesenteric metastasis was present in 64.2% of the patients and males had a significant increased risk (OR 1.88, $P = 0.001$). Growth was observed in 9.2% of the patients with a median time to growth of 39.4 months. Independent predictors of growth were having a mesenteric mass at baseline (OR 7.99, $P = 0.001$) and male gender (OR 2.02, $P = 0.03$). Analysis of 20 primary SI-NETs and paired normal intestine showed significantly increased *ESR1* and *AR* expression in tumours and significantly increased *ESR1* expression in tumours of patients with severe MF.

Conclusion: We found that the SI-NET-associated mesenteric mass has an indolent growth pattern. Also, our results suggest that sex steroids might be involved in the pathobiology of mesenteric metastases as we found an increased risk for mesenteric mass growth in males and increased expression of *ESR1* in patients with MF. Further research is ongoing to determine *ESR1* and *AR* expression in the mesenteric mass and distribution within the tumour.

Defining molecular mechanisms regulating SIRT1 expression and its roles in human granulosa-lutein cells

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Objective: Sirtuin1 (SIRT1), an NAD⁺-dependent enzyme, affects diverse cellular processes. Yet the reproductive functions of SIRT1 remain unclear. The aim of the study was to reveal the regulation of SIRT1 expression and its roles in human granulosa-lutein cells (hGLCs).

Methods: hGLCs were retrieved from women undergoing IVF during oocytes retrieval. SV40-transfected, immortalized hGLCs (t-hGLCs) were used as a model for hGLCs. Cells were treated with SIRT1 activators (resveratrol/SRT2104/metformin), cAMP-elevating agents (hCG/forskolin) or their combination. The roles of SIRT1 were examined using exogenous SIRT1 activators, and silencing endogenous SIRT1 with specific siRNA. To identify the cAMP effector proteins regulating SIRT1, t-hGLCs were cultured with PKA inhibitor or EPAC1 activator. Cells were collected for qPCR and Western blot analyses.

Results: SIRT1 activators and cAMP elevating agents effectively upregulated SIRT1 expression. Combining resveratrol with hCG had additive stimulatory effects on SIRT1, suggesting convergent pathways induced by these compounds, possibly on cAMP levels and other cellular events. Moreover, SIRT1 activation augmented VEGFA, while inhibiting endothelin-2 (EDN2) transcripts. In agreement, SIRT1-silenced cells expressed reduced VEGFA and elevated EDN2. Surprisingly, cAMP effector proteins oppositely affected SIRT1; EPAC1 activator significantly increased, while inhibition of PKA enhanced basal and SRT2104 activated SIRT1 levels.

Conclusions: SIRT1 is dynamically regulated in hGLCs, where a positive feedback loop appears to exist between SIRT1 activity and expression. These findings also ascribe a distinct roles for EPAC1 vs. PKA in the cAMP-dependent SIRT1 activation. Moreover, since SIRT1 activators modulate VEGFA and EDN2 expression, SIRT1 may be implicated in the ovulatory process.

Seasonal changes of serum gonadotropins and testosterone in men: a reappraisal from a large data set of real-world observations over eight years

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Objective: Environmental rhythmicity seems able to affect the hypothalamic-pituitary-gonadal axis in animals, but the extent of its influence in humans is still controversial. This study was designed to evaluate seasonal fluctuations of the main hormones involved in the hypothalamic-pituitary-gonadal axis in men, using a big data approach.

Methods: An observational, retrospective, big data trial was carried out, including all testosterone, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) measurements performed in a single laboratory between January 2010 and January 2019. Subjects presenting any factor interfering with the hypothalamic-pituitary-gonadal axis were excluded. The trend and seasonal distributions were analysed using autoregressive integrated moving average models.

Results: A total of 12,033 data were included, accounting for 7,491 men (mean age 47.46 ± 13.51 years, range 18-91 years). Mean testosterone serum levels (5.34 ± 2.06 ng/dL, range 1.70-15.80 ng/dL) showed a seasonal distribution with higher levels in summer ($p=0.008$) and a direct relationship with environmental temperatures and daylight duration. LH (mean 4.64 ± 2.54 IU/L, range 1.00-15.00 IU/L) presented 2 peaks of secretion in autumn and spring ($p=0.001$), independently from temperatures and daylight duration. FSH levels did not show any seasonal distribution.

Conclusions: A clear seasonal fluctuation of both LH and testosterone was demonstrated in a large cohort of adult men, although a circannual seasonality of hypothalamic-pituitary-gonadal hormones in humans could be not strictly evolutionarily required. Testosterone seasonality seems independent from LH fluctuations, which could be regulated by cyclic central genes expression, and more sensible to environmental temperatures and daylight duration.

Sarcopenia is associated with poor glycemic control and peripheral neuropathy in elderly women with type 2 diabetes mellitus

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Objective: investigate the association between presence of sarcopenia and type 2 diabetes mellitus (T2DM).

Methods: the study included 138 women over 60 years old (Me 72[67;78] years) (76 patients with T2DM). Patients were examined with evaluation of muscle mass, muscle strength and muscle function. Muscle strength was measured with carpal dynamometry, muscle function was evaluated with short physical performance battery tests. Skeletal muscle mass index (SMMI) was evaluated with bioimpedance testing. Sarcopenia was defined as a SMMI $\leq 6,75$ kg/m². Peripheral neuropathy was studied with calculation of NIS-LL scale (max points=96). Patients with T2DM were divided into 2 groups: with sarcopenia (S+, n=29) and without sarcopenia (S-, n=47). We did not find any significant difference between age and diabetes duration in S+ and S- groups. Multivariable logistic regression model were adjusted for age.

Results: Sarcopenia was observed in 29 patients (38%). The frequency of HbA1c level more than 8% were 72% in S+ group and 49% in group S- (p=0,041). Glomerular filtration rate was lower in S+ group than S- group (60[49;71,5] vs 67[59,5;75,5]ml/min, p=0,043). S+ group less frequently received metformin (p=0,011) and insulin (p=0,044). Diabetic neuropathy was more severe in S+ group than in S- group (NIS-LL: 12[7;17] vs 6 [4,8], p<0,001). Frequency of falls and fractures was noted more often in S+ group than in S- group (66% vs 36%, p=0,013, 36% vs 13%, p=0,003). The univariate logistic regression analysis revealed the associations of presence of sarcopenia in T2DM patients with HbA1c over 8% (OR-2,74; 95%CI[1,01-7,4], p=0,047), history of falls ≥ 2 (OR-3,35; 95%CI[1,27-8,84], p=0,014) and NISLL more than 11 points (OR-23,89; 95%CI[6,56-86,94], p<0,001). The multivariable logistic regression analysis revealed the associations of presence of sarcopenia in T2DM patients with NISLL more than 11 points (OR-22,14; 95%CI[3,68-133,30], p=0,001).

Conclusions: Sarcopenia evaluated with bioimpedance technique with calculation SMI $\leq 6,75$ kg/m² and with or without decrease of muscle function or strength associated with presence of peripheral sensorimotor neuropathy, poor glycemic control, lack of treatment with metformin.

Glucocorticoid treatment is associated with dose-dependent insulin resistance in healthy male volunteers

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Objective: Currently, 2-3% of the population of the UK and US receive glucocorticoid (GC) therapy. Significant adverse effects are not confined to chronic use; recurrent short-course administration is associated with increased morbidity and mortality. The efficacy of GC therapy is not in doubt but data about the cumulative dose responsible for adverse effects during GC treatment are still lacking. The aim of this study was to test the impact of 7 days of 10 or 15mg of Prednisolone on glucose metabolism in healthy male volunteers.

Methods: 16 healthy male volunteers were recruited from the Oxford Bio Bank and divided into 2 groups as following: 6 volunteers received 10 mg of Prednisolone and 10 volunteers received 15 mg of Prednisolone for 7 days. All participant underwent low dose hyperinsulinaemic euglycaemic clamp (HEC), before(pre) and after (post) treatment. The main outcome measure was the M-value gathered from the HEC.

Results: Age, BMI and fasting blood glucose were not different between the two groups at baseline. After one week of prednisolone 10 or 15 mg, no differences were found in delta (Δ =post-pre) fasting glucose (FG) (median Δ FG_{15mg} 0.15 ± 0.36 nmol/L vs Δ FG_{10mg} 0.15 ± 0.36 nmol/L, $p=0.635$). However, M-value was significantly reduced in patients taking 15 mg of prednisolone (median Δ M_{15mg} -2.5 ± 2.0 mg/Kg/min vs Δ M_{10mg} -0.4 ± 1.3 mg/Kg/min, $p=0.016$).

Conclusions: In this small cohort of healthy male volunteers, we demonstrated that GC treatment is associated with a worsening of insulin sensitivity through a dose-dependent effect. Further studies are needed to confirm our findings in larger cohort of patients.

Effects of novel antidiabetic agents on the arterial wall elastic properties as a marker of vascular function in patients with type 2 diabetes mellitus

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Background: Arterial stiffness is a well-established surrogate marker of vascular properties and arterial dysfunction in patients with type 2 diabetes mellitus (DM2). We aimed to investigate whether optimization of DM2 therapy with, additional to metformin, novel antglycemic agents may improve arterial wall properties and achieve better glycemic control.

Methods: We enrolled 99 consecutive patients (male gender=63.3%) receiving metformin for DM2 who did not achieve therapeutic targets under current treatment. Subjects were assigned to age and sex matched equal groups (n=33 per group) of an additional antiglycemic agent; either dipeptidyl peptidase-4 inhibitor (DPP-4), sodium/glucose co-transporter-2 inhibitors (SGLT2) (n=28) or glucagon like peptide-1 (GLP-1) liraglutide. Applanation tonometry was used to assess non-invasively augmentation index (AIx) and aortic pulse wave velocity (PWV) as a measure of arterial stiffness at baseline and at 3-month follow-up. Among other demographics data, hemoglobin A1c (HbA1c) was measured.

Results: There was no difference for male gender (p=0.10) or age (64.92 ± 8.30 years, p=0.27) between the 3 study groups. Interestingly, baseline values improved significantly after SGLT2 and DPP4 administration both for PWV (11.46 ± 2.77 vs. 9.83 ± 2.19 m/s and 10.89 ± 2.35 vs. 9.68 ± 1.77 m/s respectively, p=0.01 for both) and AIx (28.81 ± 8.55 vs. 25.82 ± 7.40 and 27.91 ± 13.05 vs. 24.91 ± 12.70 respectively, p=0.01 for both), when compared to those at follow-up time. In contrast, GLP-1 administration decreased PWV (12.82 ± 3.00 m/s at baseline vs. 11.67 ± 2.77 m/s during follow-up, p<0.001) but not AIx (31.64 ± 6.21 vs. 30.18 ± 6.03 , p= 0.18). HbA1c at baseline was uniformly decreased in all study groups when compared to follow-up (7.52% vs. 6.72% for SGLT2, 7.76% vs. 6.92% for DPP4 and 8.19% vs. 6.85% for GLP1, p<0.001 for all).

Conclusion: The optimization of DM2 treatment with SGLT-2, DPP4 or GLP1, added to metformin, not only helps to achieve better glycemic control but significantly ameliorates arterial stiffness indices and achieves therapeutic targets in patients with DM2.

β-hydroxybutyrate and risk for incident type 2 diabetes: results from the prevend prospective cohort study

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Objective: A potential role for the ketone body beta-hydroxybutyrate (β-OHB) has received increasing interest in the study of metabolic disease, but the association of β-OHB with Type 2 Diabetes (T2D) risk remains unclear. The present study aimed to explore the association of β-OHB with incident T2D in a prospective population-based cohort.

Methods: We measured plasma concentrations of β-OHB using nuclear magnetic resonance spectroscopy in 6095 participants followed for a median of 8.1 years. We estimated the risk of incident T2D using multivariable-adjusted Cox regression models.

Results: Cox regression analyses revealed a significant association between β-OHB and incident T2D. The hazard ratio (HR) per one standard deviation of β-OHB was 1.17 (95% confidence interval (CI): 1.08-1.26, $P < 0.001$) after adjustment for age, sex, BMI, family history of T2D, smoking and alcohol consumption, systolic blood pressure, fasting plasma glucose, insulin, total cholesterol/HDL cholesterol ratio, triglycerides, eGFR and urinary albumin excretion. Likewise, the association remained significant after full adjustment when β-OHB was evaluated by quartiles (HR for the highest vs. lowest quartile = 2.63, 95% CI: 1.67-4.14, $P < 0.001$). Furthermore, the Net Reclassification Improvement index was enhanced after addition of β-OHB to a traditional risk model ($P < 0.01$), improving the reclassification of 20% of participants.

Conclusions: This prospective study revealed that high plasma concentrations of β-OHB are prospectively associated with an increased risk of T2D. The association remained independent after adjusting for several traditional risk factors. Our results shows that plasma β-OHB is a strong biomarker for developing T2D and improves the risk classification for T2D.

Arterial stiffness is an independent predictor for risk of mortality in patients with type 2 diabetes mellitus: the REBOUND study

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Objective: Brachial-ankle pulse wave velocity (baPWV) was used as a noninvasive marker of arterial stiffness. The aim of this study was to assess the association between arterial stiffness and cause specific mortality in patients with type 2 diabetes mellitus (T2DM).

Methods: This multicenter prospective observational study analyzed 2,320 patients with T2DM. The patients were divided into two groups according to baPWV (cutoff baPWV of 1,750 cm/s). Causes of death were obtained from death certificates, and cause-specific mortality rates were compared with four groups according to their baPWV. Cox regression models were used to estimate hazard ratios (HRs).

Results: There were 205 deaths (8.8%) in the study population during the 8.6 years of study. A univariate analysis revealed that the high-baPWV group predicted a greater risk of all-cause mortality (HR = 4.41, $P < 0.001$), cancer mortality (HR = 3.85, $P < 0.001$), and cardiovascular mortality (HR = 3.33, $P < 0.001$) than the low-baPWV group. A multivariate analysis adjusted for clinical variables including age and sex showed that the high-baPWV group remained predicted a greater risk of all-cause mortality (HR = 2.57, $P < 0.001$), cancer mortality (HR = 2.19, $P = 0.010$), and cardiovascular mortality (HR = 1.74, $P = 0.061$) than the low-baPWV group.

Conclusions: The high-baPWV group predicted the risk of mortality in T2DM, supporting the prognostic utility of baPWV.

Reduced insulin clearance relates to increased liver fat content in recent-onset type 2 diabetes and to impaired glucose control in recent-onset type 1 diabetes

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Objective: Insulin clearance can be lower in longstanding insulin-resistant states, whereas hepatic insulin kinetics are not yet clear in newly diagnosed diabetes mellitus.

Methods: Volunteers with type 1 (T1D; n=276, 66% male) or type 2 diabetes (T2D; n=451, 69%) and glucose-tolerant humans (CON; n=143, 65%) underwent hyperinsulinemic-euglycemic clamps to assess whole-body insulin sensitivity (M-value) and whole-body insulin clearance (IC_{WBIC} , $ml \cdot kg^{-1} \cdot min^{-1}$). Hepatic insulin clearance was calculated from the areas under the curve of plasma C-peptide and insulin during intravenous glucose tolerance (IC_{IVGTT} , 0-60 min) and mixed-meal tolerance tests (IC_{MMT} , 0-180 min). Hepatocellular lipid content (HCL) was measured by 1H-magnetic resonance spectroscopy. Analyses were adjusted for age, sex and BMI.

Results: Compared to T2D and CON, T1D had a lower IC_{IVGTT} ($7,9 \pm 5,4$ vs. $10,6 \pm 3,6$ and $10,7 \pm 3,1$, all $p < 0,05$) as well as IC_{MMT} ($5,9 \pm 2,8$ vs. $9,9 \pm 3,4$ and $8,6 \pm 2,3$, all $p < 0,05$), which in turn correlated negatively with HbA1c ($r = -0,234$ and $r = -0,029$, both $p < 0,05$). In T2D, IC_{IVGTT} was positively correlated with M-value ($r = 0,379$, $p < 0,05$). T2D patients with hepatic steatosis (n=76) had 8% and 7% lower IC_{WBIC} and IC_{IVGTT} (both $p < 0,05$) compared to T2D without (n=56). CON with steatosis (n=21) showed a trend towards impaired IC_{WBIC} ($p = 0,059$) than those without (n=94). IC_{MMT} positively correlated with M-value ($r = 0,289$ and $r = 0,272$, both $p < 0,05$) in T1D and T2D, but not in CON.

Conclusion: Glycemic control impairs insulin clearance in T1D patients, whereas steatosis reduces clearance in T2D suggesting different compensatory mechanisms of insulin kinetics.

Increased risk of site-specific cancer in people with type 2 diabetes: a national cohort study

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Objective: To evaluate cancer risk among people with type 2 diabetes mellitus (T2DM) in Lithuania.

Methods: A retrospective cohort design was used. The cohort was established by identifying all patients with the first diagnosis of T2DM in the National Health Insurance Fund database during 2000–2012. Cancer cases were identified by record linkage with the Lithuanian Cancer Registry. Standardized incidence ratios (SIRs) were calculated.

Results: 127 290 people were included and 5959 cases of cancer in men and 6661 cancer cases in women with T2DM were observed. Statistically significant increase in risk for all cancer sites was observed in women, SIR 1.16 (95% CI 1.14–1.19), but not in men, SIR 1.00 (95% CI 0.98–1.03). Among males, significant increase of liver (SIR 2.11, 95% CI 1.79–2.49), pancreas (SIR 1.77, 95% CI 1.57–1.99), kidney (SIR 1.46 95% CI 1.31–1.62), thyroid (SIR 1.83, 95% CI 1.32–2.54), colorectal (SIR 1.23, 95% CI 1.14–1.31), skin melanoma (SIR 1.40, 95% CI 1.11–1.76) and non-melanoma skin (SIR 1.14, 95% CI 1.05–1.23) cancer was observed. For females with T2DM, significant increase in risk of cancer of the liver (SIR 1.45, 95% CI 1.17–1.79), pancreas (SIR 1.74, 95% CI 1.56–1.93), kidney (SIR=1.43, 95% CI 1.28–1.60), thyroid (SIR=1.40, 95% CI 1.22–1.62), breast (SIR=1.24, 95% CI 1.17–1.31) and corpus uteri (SIR 2.07, 95% CI 1.93–2.21) was observed.

Conclusion: People with T2DM in Lithuania have an increased risk of site-specific cancer.

Relationship between hematological and glycemc parameters and degenerative complications in type 2 diabetes mellitus in a prospective study

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Objective: Diabetes mellitus is the global epidemic of the 21st century, and it leads to the development of microvascular and macrovascular complications. Elevated blood glucose level in T2DM causes disturbances of blood cells and its parameters. The aim of the research is to determine changes in the complete blood count (CBC) depending on glycemc control, the disease duration and their association with degenerative complications.

Methods: The study was prospective from 2016 to 2017. It included a total of 137 subjects, 90 with T2DM and 47 healthy. The subjects were divided into several ways, with and without T2DM, with HbA1c \leq 7% and with HbA1c $>$ 7%, and groups with and without complications. We analyzed CBC parameters, parameters of glycoregulation, lipid status and performed anthropometric measurements.

Results: There were statistical difference between group with T2DM and healthy subjects for WBC, eosinophils, Hgb, MCH, MCHC, ESR in 2016. and neutrophils, monocytes, RDW, PDW, ESR in 2017. In the group of T2DM patients with duration of disease longer than 6 years we found elevated value of MCHC, PDW. In relationship to glycoregulation, significant differences in PMDW, large platelets and RDW were found in the group HbA1c $>$ 7%. According to degenerative complications significant differences were revealed in lymphocytes, neutrophils in the group with microvascular complication, and PDW in the group with macrovascular complications.

Conclusion: Based on the results of our research, it can be concluded that there is an association between particular hematological parameters and glycoregulation, diabetes mellitus, as well as relationship with degenerative complications in patients with T2DM.

Serum metabolomic fingerprinting of diabetes reveals persistent changes 3 days after the episode

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Objectives: Broad insight into metabolic disturbances caused by diabetes ketoacidosis (DKA) and persist after pH normalization.

Methods: Three groups of children with type 1 diabetes were recruited: after an episode of DKA (DKA, n=20), with established diabetes (EDM, n=10) and with new onset diabetes without DKA (NDM, n=10). EDM and NDM groups were matched to the DKA one for sex and age. Serum samples were collected at three time points: 0-24h-72h since the admission for DKA and NDM groups and once for EDM patients. Metabolic fingerprinting was performed with LC-QTOF-MS (Agilent 6550 iFunnel).

Results and Conclusions: After technical filtering 248 metabolomic features out of 712 (in positive ionization) and 295 out of 652 (in negative ionization) were suitable for between-group comparisons. Statistical analysis selected 22 metabolic features as putative biomarkers of episodes of DKA occurrence in nearest 72h. From those features 4 metabolites were successfully identified - 3 with higher after DKA episode versus comparative groups: lysophosphatidylcholine (LPC) (18:1), sphingomyeline (SM) (34:0), SM (d18:0/15:0) and one with lower level - LPC (18:0). Measurement of LPC (18:1) and LPC (18:0) were proposed as diagnostic test of past DKA episode with area under curve (AUC) equaling 0.88 (95%CI 0.81-0.95), sensitivity 79.1% (95% CI 63.5-89.4%) and specificity 85.0% (95%CI 69.5-93.8%). Metabolic disturbances caused by diabetes ketoacidosis episode may last up to 72 hours and may further distress organisms of children with type 1 diabetes.

The study was financially supported by a Scientific Grant from Diabetes Poland.

Flash Glucose Monitoring technology in the management of children and adolescents with type 1 Diabetes leads to improved glycemic control

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Objective: Flash Glucose Monitoring (FGM) is becoming increasingly popular among children with Type 1 diabetes. Our aim was to evaluate real-life data from children using FGM followed in our center.

Methods: We studied 37 patients (51.4% males), with a mean \pm SD age of 10.1 \pm 3.9 years at FGM start for a period of 10.1 \pm 6.5 months. HbA1c, BMI z-score, number of self-reported and severe hypoglycemia, total insulin daily dose/kg (TDD/kg), as well as the number of blood glucose self-measurements (SMBGs) by fingerprick were collected and compared with paired analysis before and after introducing FGM.

Results: Mean HbA1c was reduced significantly (7.82% \pm 1.78 vs 7.19% \pm 0.69, $p=0.04$) after FGM introduction. The number of hypoglycemia/month (6.3 \pm 7 vs 4.6 \pm 5.3, $p=0.31$), the BMI z-score (0.68 \pm 0.99 vs 0.76 \pm 0.8 kg/m², $p=0.473$) and the insulin TDD/kg (0.58 \pm 0.3 vs 0.68 \pm 0.24 IU/kg/day, $p=0.061$) did not change. No severe hypoglycemia were recorded before or after FGM. As expected, there was a significant reduction in the number of SMBGs /day (7.05 \pm 2.7 vs 2.45 \pm 2.38, $p<0.001$). All families report a high level of satisfaction by the combined use of SMBG and FGM despite frequent discrepancies between them, especially at low glucose levels. All patients use FGM continuously, except from two adolescents who use it intermittently, especially on holidays. The main complaint is sensor detachment especially during summer. The families rarely download the sensor at home.

Conclusions: Short-term follow-up of children using FGM has shown a beneficial effect on HbA1c, with no increase in hypoglycemia. Long-term studies will provide additional information on the impact of FGM on diabetes management.

Conservative management of diabetic foot ulceration complicated by underlying osteomyelitis

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Objective: To describe the clinical presentation of forefoot and midfoot diabetic foot ulcers (DFUs) complicated by osteomyelitis and their outcomes with conservative management in a multi-disciplinary care environment and determine predictors of ulcer healing.

Methods: This is a retrospective study of all consecutive cases of DFUs complicated by osteomyelitis presenting to our multi-disciplinary diabetes foot clinic between 1st January and 30th June 2016. Data was collected on patient demographics, clinical presentation, diabetes related laboratory values, radiology, ulcer treatments, diabetes complications and co-morbidities. Outcome measures included ulcer healing, amputation, death with an ulcer and re-ulceration.

Results: 41 ulcer episodes in 38 patients were identified (mean age 66 +/-8 years, 79% male, mean duration of diabetes 17 +/-2 years, median HbA1c 59.5mmol/mol (47.5-78.5), 95% type 2 diabetes, 20% end stage renal failure, 34% established cardiovascular disease), mean number of non-diabetes co-morbidities 3 +/-0.2). Successful healing was achieved in 66%. Median time to healing was 98 days (56-156). 12% re-ulcerated. Patients that failed conservative management were more likely to be over 70 years ($p=0.04$), be immunosuppressed ($p=0.04$), and have diabetes for more than 20 years ($p=0.01$), peripheral vascular disease ($p=0.03$), end stage renal failure ($p=0.048$) and Charcot arthropathy ($p=0.02$). 24% DFU episodes resulted in amputation (80% minor). 5% patients died with their wound. No significant predictors of ulcer healing were detected on contingency analysis.

Conclusion: High rates of healing and low rates of amputation were achieved despite the changing demographics of diabetic foot disease to include more disease burden and multiple co-morbidities.

Endothelial function and arterial stiffness indices remain unchanged following intensification of glycemic control in poorly controlled patients with long-standing type 2 diabetes mellitus

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Objective: Clinical trials aiming at strict glycemic control in high-risk patients with type 2 diabetes (T2DM) failed to show reduction in the incidence of cardiovascular events. The exact mechanisms remain unclear. We aimed to investigate the effect of intensive antidiabetic therapy on vascular indices of T2DM patients.

Methods: We studied 62 T2DM patients [mean age 64 years, 52% males, mean T2DM duration 14 years) with poor glycemic control (HbA1c $\geq 7.5\%$), at baseline and a median of 9 months after intensive treatment to achieve optimal glycemic control according to current guidelines. Brachial artery flow-mediated dilation (FMD), pulse wave velocity (cfPWV), augmentation index (Aix), large (C1) and small artery elasticity (C2), carotid intima-media thickness (cIMT) and ankle-brachial index (ABI), were assessed.

Results: Improvement of HbA1c $>0.5\%$ was achieved in 81% of patients, while mean HbA1c decreased from 9.4 (1.8)% to 7.3 (1.1)%, $p < 0.001$. Triglycerides decreased from 169 (132) to 135(70) mg/dl and cIMT increased (from 0.97 (0.25) to 1.03 (0.27) mm (both $p < 0.05$). No other significant changes were found. Interestingly, cIMT remained unchanged in those with <5 years duration, while it was increased among patients with longer disease duration ($p < 0.05$).

Conclusions: In T2DM, aggressive glycemic control (mostly achieved with insulin treatment) was not associated with improvement in vascular indices at follow-up. Attenuation of cIMT was observed for those with short disease duration. The effect of optimal glycemic control on vascular indices at an earlier disease stage, with newer antidiabetic agents and/or over a more prolonged time period, requires further study.

Influence of empagliflozin on serum calcium and phosphorus concentrations in patients with type 2 diabetes

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Background and aims: Recent studies show that SGLT-2 inhibitors affect phosphorus and calcium homeostasis in healthy individuals, but their effects in patients with type 2 diabetes are still unclear. The aim of this study was to evaluate effects of empagliflozin on parameters of calcium and phosphorus metabolism in patients with type 2 diabetes mellitus (T2DM) and preserved kidney function.

Materials and methods: The subjects were 30 patients with T2DM, who had inadequate glycemic control despite their therapy. Patients were between 45 and 65 year old and had eGFR > 60 ml/min per 1.73 m², and glycated hemoglobin > 7.5% to 9.0%. Patients were administered empagliflozin at a dose of 10 mg every day for 12 weeks. We measured circulating phosphorus (P), calcium (Ca) and fibroblast growth factor 23 (FGF23) levels at baseline and after 12 weeks of treatment.

Results: Mean serum Ca was 1.19 ± 0.13 mmol/l and serum P was 1.02 ± 0.24 mmol/l. Median FGF23 before treatment was 1.87 pmol/l (1.13 - 2.65). Compared with baseline, no statistically significant differences were obtained in Ca concentrations after 12 weeks of treatment (0.6%; 95% CI -0.5% to 1.8%; $p = 0.32$). Empagliflozin increased serum P by 13% (95% confidence interval, 8% to 19%; $p = 0.0034$), FGF23 by 17% (9% to 25%; $p = 0.002$) at the end of treatment. No correlation was found between the change in FGF23 and the change in serum P ($r = 0.1$, $p = 0.31$).

Conclusion: Empagliflozin increases serum P and FGF23 after 12 weeks of treatment in patients with T2DM. The lack of a significant correlation between the concentration of FGF23 and P may be due to differences in the availability of vitamin D, glycemia and body weight of patients.

Treatment intensification with novel antidiabetic agents alters platelet function parameters in patients with type 2 diabetes

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Background: Patients with type 2 diabetes (T2D) are at higher risk for thrombotic events and as a result cardiovascular disease. Platelet function may be used to assess prothrombotic state in patients with cardiovascular disease.

Purpose: We aimed to investigate whether the administration of novel antidiabetic agents influence platelet function in T2DM patients.

Patients and Methods: We 60 enrolled consecutive patients with T2DM, on stable anti-diabetic therapy, who did not achieve therapeutic targets. Subjects were assessed to receive an additional anti-diabetic agent; dipeptidyl peptidase-4 inhibitor (DPP4i, n=14), glucagon like peptide-1 receptor agonist (GLP1RA, n=24), sodium/glucose cotransporter-2 inhibitor (SGLT2i, n=22). Platelet reactivity was measured with PFA-200 collagen/epinephrine (c-EPI) and PFA-200 collagen/ADP (c-ADP) closure time. Glycosylated hemoglobin (HbA1c), c-EPI and c-ADP were assessed at baseline and 3 months after treatment intensification.

Results: There was no difference between the study groups regarding gender, age, hypertension, dyslipidemia, smoking, HbA1c and CADP or CEPI (p=NS for all) at baseline. All groups achieved better glycemic control in terms of HbA1c values between baseline and follow-up (for DPP4i: 7.4±0.2% vs 6.7±0.2%, for GLP1RA: 8.3±0.2% vs 6.9±0.1%, for SGLT2i: 7.5±0.1% vs 6.7±0.1% and for insulin 9.8±0.5% vs 7.7±0.4%, p<0.001 for all). After a 3 month-period, treatment intensification with these novel agents did not influence c-EPI and c-ADP values [155.4±6.64 sec vs 152.9±8.28 sec (p=0.678) and 106.6±4.30 sec vs 106.8±3.93 sec (p=0.955) respectively] in whole population. In subgroup analysis, for patients off antiplatelet treatment (n=31), c-EPI was significantly decreased from 148.4±8.5 to 129.8±13.9 sec (p=0.036), but not c-ADP (from 1054±5.3 to 99.3±4.9 sec, p=0.094). In patients who did receive antiplatelets (n=37), c-EPI and c-ADP were not significantly changed (c-EPI 163.1±10.9 to 179.6±13.9 sec p=0.201, c-ADP and from 106.6±8.2 sec to 114.6±7.3 sec, p=0.318) respectively.

Conclusion: Antiplatelet treatment prevents thrombotic risk in T2DM patients receiving novel antidiabetics. Effects of novel antidiabetics on platelet reactivity -as well as any distinct class properties- merits further investigation.

GP 1

Papillary thyroid carcinoma and Graves disease: a case report

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Background: Papillary thyroid cancer (PTC) is the most common type of thyroid carcinoma, but it rarely presents as an intrathoracic mass with concurrent hyperthyroidism due to Graves disease.

Case presentation: A 73-year-old man presented with weight loss. Imaging by computed tomography (CT) documented a large mediastinal mass in the infrathyroidal space separate from the thyroid gland and pulmonary lesions suggestive of metastases. Neck ultrasound showed two spongiform nodules in the right lobe of the thyroid gland, with a benign and non-diagnostic cytology. A few months later, the patient refers significant weight loss, palpitations and hand tremors. Blood tests identified overt hyperthyroidism (TSH <0.02 µUI/mL, T4L 3.86 ng/dL, T3L 9.2 pg/mL). He was then referred to our center for diagnostic evaluation. Endobronchial ultrasound-guided needle biopsy of the mediastinal mass was compatible with metastasis from PTC with thyroglobulin in the washout of the needle above 30.000ng/mL. 99m Pertechnetate scintigraphy showed increased diffuse uptake in the thyroid parenchyma and absence of uptake in the paratracheal mass and in the lung nodules. Further study of the hyperthyroidism revealed a Graves disease (TRAB 21.9 UI/L). At this time CT was repeated, showing significant growth of the mediastinal mass with tracheal invasion and mediastinal vessels infiltration. For this reason, the patient was not considered for surgical intervention and is waiting for palliative radiotherapy.

Conclusions: The association between PTC and Graves disease is infrequent. Furthermore, this case highlights the importance of obtaining a histological examination of an intrathoracic mass, in order to ensure an early diagnosis and treatment.

Coexistence of papillary thyroid cancer and sarcoidosis - how many associated complications?

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Background: Papillary thyroid cancer (PTC) incidence has increased substantially over the last decades. Although 4% of thyroid cancers may induce a sarcoid reaction in the thyroid gland, sarcoidosis (SA) as a disease may exist with PTC, although causality remains uncertain and their coexistence is rarely reported in the literature. They occurs in both genres, between 30-40 years, but females are more predisposed.

Case presentation: A 65-year-old man, known with pulmonary SA came to our clinic 4 years ago with the suspicion of PTC lymphnode metastasis (he underwent a mediastinoscopy for SA). Thyroid ultrasound pointed to multinodular goiter with a suspect right lobe nodule. He underwent surgery. The histopathological exam confirmed PTC-T3N1b. He received two radioactive iodine cures (total amount-300mCi). Immediately after administration, he developed transient hypercalcemia with low parathormone, 25 HO-vitamin D and high normal 1,25-HO vitamin D levels, probably sarcoidosis induced. His persistent respiratory symptoms imposed glucocorticoid therapy over the past year. At this admission, he accused moderate dyspnea. Biochemical and hormonal tests revealed diabetes secondary to corticosteroid therapy (HbA1C=6,9%), secondary hyperparathyroidism (parathormone=104.6 pg/ml, 25 HO-vitamin D=11.1 pg/ml), normal crosslaps and low-osteocalcin (3.30 ng/ml), possibly corticoid induced. Cardiology exam diagnosed pulmonary hypertension due to sarcoidosis, ischemic heart disease, atrial fibrillation.

Conclusions: The association of SA and PTC may be a challenge for clinicians in the differential diagnosis of cervical lymphadenopathies. It requires a multidisciplinary approach and the association has a worsen prognosis. Complications occur and are determined by glucocorticoids, late age onset, gender, persistence of symptoms and organ damage.

GP 3

Medullary Thyroid Carcinoma (MTC); unusual metastatic sites.

Two case reports

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Background: MTC tends to metastasize early in the course of the disease affecting usually regional lymph nodes; in 7-23% of patients distant metastases may be present at diagnosis (common metastatic sites: liver, lungs, bone). We present two MTC cases with unusual metastases to the breast, pancreas and mandible.

Case presentation: Patient No 1: a 48-year-old female was diagnosed with MTC in 1990. Total thyroidectomy was performed followed by neck dissection. Ten years later, cervical and mediastinum lymph node dissection took place. In 2009, disease progression was confirmed by elevated Calcitonin and CEA levels along with a positive uptake (Octreoscan) in mediastinum and liver. A bone scan revealed additional metastases in the thoracic spine and external bone radiotherapy and liver chemoembolisation were performed. In 2013, mediastinum MRI revealed a lesion in the right breast confirmed by mammography. Histology of breast tumor-ectomy confirmed MTC metastasis and treatment with vandetanib was initiated. Patient No 2: a 55-year-old female was diagnosed with MTC in 2003. Total thyroidectomy with neck dissection was performed. Due to cervical nodal metastases, she underwent modified radical neck dissections. In 2014, recurrent metastatic disease in the right shoulder was confirmed by MRI and external radiotherapy was performed. Furthermore, an abdominal MRI revealed a head pancreatic tumor. MTC metastasis was confirmed by biopsy and treatment with vandetanib was initiated. Additionally, the histology of a resected painful mass in the right mandible revealed a well differentiated MTC.

Conclusions: These two MTC cases, although apparently rare, highlight the need for watchful care and prompt recognition of unexpected metastases in MTC patients.

GP 4

A case of a MEN2A syndrome with relapsed medullary thyroid carcinoma and primary hyperparathyroidism but no pheochromocytoma

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Background: 55 year-old male is admitted in 2019 to the hospital for relapsed MEN syndrome. Case report: The patient first presented to the hospital in march 2012 acusing dysphonia. He was diagnosed with vocal cord paralysis due to locoregional extension of MTC, based on the ultrasound aspect, calcitonin >2000 pg/mL, chromogranin= 123 ng/mL and also with primary hyperparathyroidism due to right lower parathyroid adenoma (hypercalcemia=12,8 mg/dL, PTH= 214 pg/mL) confirmed with scintigraphy, followed by genetic testing presenting a MEN 2A syndrome with RET proto-oncogene 634 mutation of exon 11. Investigations for pheochromocytoma were negative. 3 months after the patient was submitted to surgery calcitonin was over 300 pg/mL, CEA=15,6 ng/mL (N<3,4), cervical CT revealed a nodule in the right thyroid lodge 1,2/1,2 cm and paratracheal iodophilic tissue 0,5/0,7 cm but cerebral CT, neck ultrasound, liver and adrena l MRI showed no secondary lesions. 15 months after surgery cervico-mediastinal CT revealed laterocervical and bilateral paratracheal nodules, with calcitonin levels doubled so that 26 months after the first thyroidectomy another surgical intervention was performed, with neck dissection and excision of 32 lymph nodes. In 2019 whole body CT suggests suspicious local lesions with no clear distant metastasis despite high calcitonin levels.

Conclusions: Patient with MEN 2A who underwent two surgical procedures has some particularities: despite high residual calcitonin levels, we could not find any distant metastasis and despite genetic mutation specific for pheochromocytoma, the patient relapsed for primary hyperparathyroidism which is not specific and does not present with pheochromocytoma, a more frequent association.

GP 5

Vandetanib in medullary thyroid cancer-related Cushing syndrome: a case report

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Background: Medullary thyroid cancer is a rare neuroendocrine neoplasm that can secrete variety of hormones, including ACTH. Cushing syndrome due to ectopic ACTH secretion is a rare complication of medullary thyroid cancer, usually associated with metastatic disease. Around 50 percent of patients with medullary thyroid carcinoma and ectopic Cushing syndrome die due to complications of hypercortisolism. Based on the aforementioned, efficient management of hypercortisolism is crucial.

Case presentation: A 44-year old female with history of metastatic medullary thyroid cancer presented with malaise, generalized oedema, hypertension, hirsutism, fragile skin and finger ulceration. Laboratory results showed marked hypokaliemia and hyperglycaemia. The diagnosis of Cushing syndrome due to ectopic ACTH secretion was made. The patient was initially treated with ketoconazole, followed by metyrapone and vandetanib. After introduction of metyrapone and vandetanib, a rapid decrease in serum cortisol and improvement of clinical symptoms were observed as well as the reduction of tumor metastases. As an adverse effect to vandetanib, the patient developed palmar-plantar erythrodysesthesia. The rash resolved after topical corticosteroid treatment.

Conclusion: Management of Cushing syndrome in medullary thyroid carcinoma is challenging. Use of drugs, such as steroid inhibitors, is often unsuccessful and bilateral adrenalectomy is sometimes required. In recent years, the use of tyrosine kinase inhibitors, especially vandetanib, has been shown to successfully control hypercortisolism. Despite adverse effects, some of which are potentially serious, vandetanib is an important and efficient drug in the achievement of eucortisolism in patients with medullary thyroid cancer-related Cushing syndrome as well as in inducing tumor control.

GP 6

A Review of Myxedema Madness: Case Reports of acute hypothyroidism presenting as psychosis

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Background: Hypothyroidism is a common disorder presenting with both somatic and psychiatric symptoms. Two cases of late onset psychosis are presented as an initial manifestation of myxedema.

Case presentation: 1. An 80-year old woman who had no past medical history presented with auditory and persecutory hallucinations. During her hospital stay she was found to have a decreased level of consciousness (GCS:4), and a blood investigation showed the presence of severe hypothyroidism. Following thyroid replacement therapy, the patient's consciousness improved and she recovered from her psychosis.

2. A 38-year old woman with a known history of Hashimoto thyroiditis had stopped her treatment one year earlier presented disoriented with persecutory hallucinations. A blood analysis revealed severe hypothyroidism and was immediately treated accordingly. The patient showed immediate response and became cooperative and mentally stable.

Conclusions: Myxedema madness should be considered particularly in acute and late-onset psychosis as a possibly reversible condition with no need of long-term antipsychotics administration.

GP 7

Graves' Disease and Thymic Hyperplasia

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Background: The association between Graves' disease and thymic hyperplasia is well documented in the literature. Despite that it remains largely unrecognized in routine clinical practice. The lack of familiarity of usually benign nature of thymic hyperplasia associated with Graves' disease may result in an aggressive management course, along with associated risks.

Case presentation: A previously healthy 32-year-old female was admitted to hospital with palpitations, intensive sweating, tremor and progressive weight loss in the proceeding two weeks. Laboratory test values were the following: TSH <0.01 mIU/L (reference range 0.55 – 4.78), FT4 – 80.9 pmol/L (reference range 11.5 – 22.7) and FT3 – 24.5 pmol/L (reference range 3.5 – 6.5). A thyroid ultrasound was performed and a diffuse thyroid disease was verified. In addition, a sharply bordered mass, which corresponds to the thymus, was determined under the thyroid gland.

A CT scan of the chest was conducted and it revealed a solid triangular shape thymic mass in the anterior part of the mediastinum with the largest diameter of 4.6 cm laterolateral, 1.7 cm anteroposterior and 10.7 cm craniocaudal. The volume was calculated to be 43.79 cm³.

Four months after initial presentation, the patient was biochemically and clinically euthyroid. A repeated CT scan of the chest revealed that the volume of the hyperplastic thymus had reduced to 19.98 cm³.

Conclusions: Raising awareness of usually benign thymic hyperplasia associated with Graves' hyperthyroidism and its resolution with the treatment of the hyperthyroid state should prevent unnecessary thymic evaluation, biopsy and surgery with its corresponding risks and costs.

Coexistence of metastatic osteosarcoma and multifocal papillary carcinoma in thyroid gland

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Background: The presence of secondary tumors to the thyroid is well known, although a rare entity (0,5-1,2%). The simultaneous appearance of papillary carcinoma and metastasis from hip osteosarcoma has never been reported.

Case presentation: The patient is a 60year old female who presented with a suspicious left thyroid nodule and a long history of osteosarcoma. The preoperative FNA of the left thyroid nodule was consistent with papillary malignancy (Bethesda classification VI). In January 2019 she had a total thyroidectomy for a multifocal papillary carcinoma with 2 positive lymph nodes from a total of 3 pretracheal (delphian) nodes excised and a 6,2cm metastatic osteosarcoma of the left thyroid lobe with extensive necrosis and mixed cartilaginous and osteoid production, infiltrating the strap muscles. Postoperatively she was treated with Iodine ablation. Thyroiditis Hashimoto was also present.

In January of 2018 she had a tumor excised from the base of her tongue. The histologic examination showed a malignant neoplasm from peripheral nerve sheaths.

In July 2017 the FDG PET-CT showed a left upper lung lobe metastatic nodule and a hypodense left thyroid nodule. She had a left upper lobectomy for a metastatic osteosarcoma of 4,3cm size. Postoperatively she was treated with pazopanib 800mg/day, (a tyrosine kinase inhibitor also used successfully in treating thyroid carcinoma).

In 2012, she was diagnosed with a sacral bone chondroblastic osteosarcoma which was completely excised.

Conclusions: Secondary tumors of the thyroid together with papillary carcinoma may rarely happen and is a diagnostic problem. Its presence often indicates a poor prognosis.

GP 9

Papillary thyroid carcinoma and Hodgkin Lymphoma in young patients – case report

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Introduction: Differentiated thyroid cancer is one of the most common endocrine malignancies. The most common thyroid cancer in adolescence is PTC. It presents with a high rate of loco regional ganglionic metastasis. Hodgkin lymphoma (HL) is a heterogeneous group of neoplasms with an incidence, in Europe, estimated around 2.2-2.7 per 100 000 cases per year. In front of each adolescent case, with concomitant thyroid and lymph nodes, the main question that arises is the presence of intrathyroid lymphoma, PTC with ganglionic determination or the concomitance of two neoplastic tumors. The specialty literature recommends lymphoma approach with identification by biopsy of the cancer with the most malignant potential. In case of concomitance of lymphoma and thyroid cancer, thyroid treatment will be performed only after hematological stabilization.

Case presentation: Our paper presents the case of two adolescents with high risk on ultrasound thyroid lesions and concomitant lymph nodes. One patient has a history of treated Hodgkin Lymphoma and PTC after one year after lymphoma treatment, the other presents massive invasive lymphadenopathies from PTC.

Conclusion: Concomitant thyroid cancer and lymphoma is rare. The minimum time, in literature, between exposure to regional radiation and the occurrence of thyroid cancer, as the second cancer, is minimum 3 years, mean time 5-10 years. Whenever the concomitance of two cancers is probable, excluding lymphoma is the first necessary diagnostic and prognostic step, the oncologic benefit surpassing the surgical radicality.

Advanced metastatic sporadic medullary thyroid carcinoma: a case of thirty-year survival with progressive disease

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Background: Medullary thyroid carcinoma (MTC) is a rare thyroid neoplasm with a high degree of malignancy derived from the parafollicular calcitonin-secreting cells. This carcinoma may occur sporadically in about 80% of cases or it may be part of the autosomal dominant multiple endocrine neoplasia (MEN) type 2. While the 10-year survival rate is around 40-75%, for metastatic disease, it's just below 20%.

Case presentation: We report the case of a 60-year-old female patient diagnosed with sporadic MTC with a somatic RET mutation Cys608Arg at the age of 27. After diagnosis, she underwent multiple surgical interventions, from total thyroidectomy to radical neck dissection and re-interventions for loco-regional metastasis excision. In the evolution of the disease, bone, kidney, liver and ganglia metastasis appeared. Zoledronic acid was administered in high doses with the intention to contain the bone metastasis but maxillary osteomyelitis developed, with severe pain that seriously affected her quality of life. Her current calcitonin levels have been stationary through the 6 years in which she has been under our care, at about 20 000 pg/ml. She has been under treatment with somatostatin analogues, with Octreotide LAR 40 mg/28 days for about 8 years with the slow progression of the metastatic disease over time. Her current quality of life is satisfactory, with no subjective complaints.

Conclusions: We described the case of a 60-year-old female with advanced metastatic medullary thyroid carcinoma with a survival of over 30 years, with a good subjective quality of life.

GP 11

Cushing's Syndrome presenting in patient with well differentiated pancreatic neuroendocrine tumor

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Background: Hormonal disturbances may be encountered in the context of paraneoplastic syndromes. Neuroendocrine tumors (NETs) represent a rare group of cancers, derived from the group of chromaffin cells, thus their paraneoplastic potentials remain relatively unexplored.

Case presentation: Middle-aged female presented to the local A&E with psychosis, hyperglycemia, mild hypokalemia. Background includes resected ovarian cancer and chemotherapy before 30 years, as well as a recent diagnosis of metastatic well-differentiated pancreatic NET, originally treated with distal pancreatectomy and splenectomy, under surveillance monitoring. Blood tests indicated ACTH 445ng/L; cortisol 5,500nmol/L, suppressed remaining pituitary hormones and slightly elevated amylase. Clinical evaluation identified only mild epigastric tenderness. MRI of the pituitary showed no abnormality. A CT colon showed a 3cm solid mass in the body of pancreas. The Gallium-68 PET scan showed avid abdominal and left supraclavicular lymph node metastases and small volume liver metastases. The FDG PET scan could not identify avid malignancy. These results were compatible with ectopic ACTH syndrome of rapid onset, hence no cushingoid signs were clinically evident. Treatment involved etomidate infusion to regulate levels of cortisol, bilateral adrenalectomy and replacement with exogenous hydrocortisone and fludrocortisone. Subsequently, 5FCarboStrep chemotherapy was initiated for tumor control. Twenty months later the lady exhibits good partial response of her liver metastases and has no evidence of disease progression in the chest.

Conclusion: Pancreatic NETs represent a source of possible ectopic ACTH production, which may result to the full clinical picture of Cushing's syndrome in some cases. Treatment consists mainly of bilateral adrenalectomy and hormone replacement.

GP 12

Long term evolution of a patient with metastatic neuroendocrine carcinoma of unknown primary site: A clinical puzzle for the endocrinologist

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Background: Carcinoid tumors are rare and slow growing malignancies derived from enterochromaffin cells. Two-thirds of carcinoid tumors arise in the gastrointestinal tract, and in 3% of these cases the primary site cannot be determined. Presenting symptoms depend on the location of the primary tumor may be nonspecific and in 13% of patients distant metastases are discovered on diagnosis.

Case presentation: A 64 years old woman was admitted for diffuse abdominal pain, especially in the epigastric, upper right quadrant and unintentional weight loss (10 kg in the last 5 months), being known with 19 years evolution of well differentiated neuroendocrine carcinoma (Ki 67=1%), with no identifiable primary and metastases since 2000: mesenteric, peritoneal, bladder, ovary treated by surgical removal (70 cm of intestinal resection and total hysterectomy with bilateral anexectomy) followed up by chemotherapy. Current therapy: Sandostatin LAR 40 mg/28 days (since 2012). Paraclinic evaluation: high serum serotonin values (3xULN), IRM scan showed multiple different nodular hepatic images (maximum 5 cm) followed by the GI endoscopy with gastric tumor findings.

Conclusions: This is a case of a patient who developed invasive gastric tumor after long term evolution of a multiple metastatic neuroendocrine carcinoma of unknown primary site. Despite symptomatic treatment, pointing to a reserved prognosis, the patient has had a long stable evolution of the disease.

GP 13

Multiple bilateral lipid-rich adrenal adenomas- how challenging can be a diagnostic process?

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Background: ACTH-Independent Macronodular Adrenal Hyperplasia (AIMAH) is usually manifested as both-sided adrenal incidentalomas with subclinical overproduction of cortisol (<2% of Cushing's syndrome). The pathogenesis involves genetic factors, expression of adrenal aberrant hormone receptors and paracrine adrenal corticotropin (ACTH) secretion. Treatment is usually bilateral adrenalectomy, but in some cases also unilateral adrenalectomy or pharmacologic therapy can be considered.

Case Presentation: Here, we present two cases of AIMAH. 48 year old male suffering from resistant hypertension and 69 year old asymptomatic female with adrenal incidentalomas. Both patients manifested lack of diurnal cortisol rhythm, inhibited ACTH level and no cortisol suppression in 1 and 8 mg dexamethasone test, although 24-h urinary free cortisol was normal. CT revealed 8 lipid-rich bilateral adenomas in man and 3 lipid-rich adenomas in woman. In dynamic tests- upright posture test was positive in two cases, cortisol rise in metoclopramide test and oral glucose tolerance test were detected individually. Whole body octreotide scintigraphy was performed. Unilateral uptake in patient's adrenals in ¹³¹I-norcholesterol scintigraphy (INCS) resulted in one-sided adrenalectomy. Histopathological evaluation of resected adrenal gland in man confirmed AIMAH and his blood pressure dropped after surgery.

Conclusions: AIMAH may be manifested as adrenal incidentalomas with lack of Cushing's syndrome symptoms. Non-standardized hormonal tests facilitate pharmacotherapy in AIMAH patients. Determination of hyperactive adrenal gland by INCS in case of bilateral adrenal tumors enable to preserve contralateral adrenal gland and avoid permanent adrenal insufficiency. To obtain a wide spectrum of therapeutic possibilities a diagnostic process should cross beyond a routine management.

Takotsubo Cardiomyopathy: Always Exclude Pheochromocytoma

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Background: Pheochromocytomas are catecholamine-producing neuroendocrine tumors, arising from the adrenal medulla or from paraganglionic chromaffin tissue. Their clinical presentation, mainly attributable to the increased catecholamine production and it is highly variable. We herein present a case of a 42-year-old female patient with recurrent episodes of Takotsubo cardiomyopathy due to a pheochromocytoma.

Case presentation: The patient presented two years earlier to local hospital's emergency department with chest pain and vomiting. The ECG showed sinus tachycardia, mild ST-segment elevation in leads I and aVL, and ST depression in leads II, III, aVF and V4-V6. An echocardiogram revealed marked hypokinesia of the midsegment and apical segment of the left (LV) ventricle with severely depressed LV function (LVEF): $\leq 30\%$. The patient underwent coronary angiography, which excluded the presence of significant coronary artery disease. Cardiac magnetic resonance (CMR) imaging, revealed myocardial edema with no late gadolinium enhancement. The patient was discharged on ramipril and carvedilol with a diagnosis of Takotsubo cardiomyopathy. A follow-up CMR study revealed normal LV systolic function with complete resolution of the myocardial edema and no late gadolinium enhancement. Medical treatment was stopped 6 months later and the patient remained asymptomatic.

Two years later, the patient was admitted with acute heart failure following an episode of increased hypertension and was transferred to our hospital for further treatment. Her echocardiogram revealed severe LV dysfunction (LVEF: 20%) with global, severe hypokinesia. After receiving medical supportive treatment, the patient exhibited a marked recovery of the LV function. During further evaluation, the patient underwent abdominal MRI, which revealed a solid, nodular lesion of 63mm × 55mm × 56mm at the right adrenal gland. Metanephrine, normetanephrine, and vanillylmandelic acid levels in 24-h urine were elevated (9696mcg/24h, 683mcg/24h, and 40mg/24h, respectively) and consistent with pheochromocytoma. The patient was transferred to the Endocrinology Unit and was started on phenoxybenzamine, and 30 days later she underwent a laparoscopic right adrenalectomy. Pathological examination confirmed the diagnosis of pheochromocytoma. Patient re-evaluation during follow-up with scintigraphy and metanephrine measurement did not reveal any abnormal findings.

Conclusion: Patients with a clinical picture of acute myocardial infarction with Nonobstructive Coronary Arteries should always be investigated for pheochromocytoma / paraganglioma.

GP 15

Challenges in the management of severe constipation due to metastatic paraganglioma

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Background: Pheochromocytoma and paragangliomas (PPGLs) are rare disorders with a rate of malignancy of 10-20%. The control of the hormonal symptoms caused by the catecholaminergic burden in the metastatic disease is a challenging task. Hypertension is the most recognized feature, but gastrointestinal manifestations can be hard to manage and life-threatening.

Cases Presentation: We present three cases of metastatic PPGLs who developed intestinal pseudo-obstruction. The first case refers to a 39-year-old man, *SDHC*-positive, with a plurimetastatic PPGL that progressed after different lines of therapy, who had several hospital admissions due to intestinal pseudo-obstruction. Laxative therapy, with osmotic agents, lubricants, emollients and gastrointestinal stimulants were ineffective; a trial with neostigmine and erythromycin was also unsuccessful. He was submitted to ileostomy that also failed to resolve the severe constipation. In the second case, a 34-year-old man, *SDHB*-positive, was admitted to ICU because of congestive heart failure due to catecholamine-induced myocardial injury. After 2 months in the ICU, with slight improvement of the heart condition, intestinal pseudo-obstruction was similarly difficult to manage, with partial response to repeated enemas and optimized oral therapy. The last case was the easiest to manage: a 70-year-old woman, with negative genetic screening, presented with acute severe pseudo-obstruction that was managed by aggressive medical therapy.

Conclusions: Management of intestinal pseudo-obstruction in PPGLs is challenging because it is usually refractory to medical therapy in the advanced cases, being poorly defined in the literature with very few cases reported. Occasionally it can lead to megacolon, perforation and sepsis portending high morbidity and mortality.

GP 16

Association of adrenal cortisol-producing adenoma and invasive papillary thyroid carcinoma in an older patient: coincidence or multiple endocrine neoplasia (MEN)?

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Background: Association of differentiated thyroid carcinoma (DTC) and cortisol-producing adrenal adenoma is not part of the classical MEN syndromes. We present a clinical case raising the question of a common etiology for these tumours.

Case Presentation: A 58-year-old female presented in 2010 for the investigation of a 6 cm left adrenal tumour incidentally discovered by abdominal CT. Medical history included smoking, obesity, myocardial infarction, hypertension, cardiac insufficiency, coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease. Family history was negative for endocrine disease, including tumours. On physical examination the patient appeared Cushingoid. LDDST revealed unsuppressed cortisolemia=8.74ug/dL (N<1.8). Thyroid clinical examination revealed a right thyroid nodule, subsequent ultrasonography demonstrating a 2.4/1.2 cm hypoechoic nodule with multiple calcifications. The patient repeatedly refused FNAB. She underwent laparoscopic left adrenalectomy in 2012 and subsequent cortisolemia was suppressible by dexamethasone. 5 yrs later, FNAB of the right thyroid nodule revealed a follicular lesion (Bethesda IV). Total thyroidectomy was performed with selective lymphadenectomy. Pathological examination revealed stage IVA (pT3N1bM0) PTC. She received 100 mCi of radioiodine for remnant ablation and subsequent administration of 100 mCi. She currently presents with incomplete biochemical (unstimulated Tg=6.41 ng/mL) and structural therapeutic response (two right jugular tumoral lymph nodes). Surgery is not an option, due to severe cardiovascular disease.

Conclusion: Our case highlights apparent MEN combining adrenal Cushing's and DTC, the underlying genetic cause being as yet unidentified. Long-term follow-up is required and patient compliance can lead to delayed therapy, as illustrated by our case.

GP 17

Etomidate as a treatment option in severe ACTH-dependent (ectopic) Cushing syndrome

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Background: Etomidate is mainly used in general anesthesia. In some rare cases it can also be helpful in treating life-threatening severe hypercortisolaemia (in much lower doses) in patients who are not able to take oral medications or when oral drugs are not available.

Case Presentation: 57-year-old woman with symptoms of virilization, hypokalemia and muscle weakness for 6 months was admitted to Department of Endocrinology. On admission cortisol concentration was extremely high (64 ug/dl) with ACTH level 662 pg/ml. Androstendione and testosterone concentrations were 4-fold above upper limit of normal. Test using Corticotropin-releasing hormone indicated on an ectopic source of ACTH. Repeated twice whole body CT, MRI of hypophysis and somatostatin receptor scintigraphy did not reveal any tumors. Meantime, due to the lack of ketoconazol and metopirone, etomidate intravenously was administered in the initial dose of 2.5mg in bolus, and infusion was continued at 0.5-1 mg/h, adjusted to the cortisol levels. Decrease in cortisol levels was observed and the concentration was maintained at about 10-12 ug/dl. Simultaneously with etomidate administration the patient developed *S. aureus* (MSSA) sepsis of unknown origin. Eventually she was treated with several antibiotics, also due to hospital-acquired urinary tract infections. After three months of treatment with antibiotics and etomidate, when patient condition was improved, bilateral adrenalectomy was performed as no source of ACTH excess was found.

Conclusions: Etomidate is useful and valuable hypocortisolaemic agent in case of severe Cushing syndrome. Its action is potent, immediate and well-tolerated, thus should be considered in selected cases.

Clinical case of adrenocortical carcinoma: rapid metastatic progression after mitotane discontinuation

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Background: Adrenocortical carcinoma (ACC) is a rare malignant tumor with a poor prognosis. The only curative therapy is complete surgery (R0). A 5-year local recurrence and distant metastasis rate after R0 is 80-85%. Mitotane is widely used as an adjuvant treatment in patients with a high risk of recurrence. According to the most studies, it can delay and possibly prevent a recurrence of the disease in 35-50%. However, its efficacy is controversial, as well as the optimal duration of the treatment

Case Presentation: A 31-year-old white male patient with adrenocortical tumor (8 cm, 35-42 HU, non-contrast CT) underwent radical surgery in September, 2017. Microscopy and immuno-histochemistry showed a poorly differentiated ACC with ki-67 from 10% to 45%. An adjuvant treatment with mitotane was initiated immediately (plasma level range, 13.4 – 16.7 µg/ml, 2 months after initiation and later). A follow-up included computed tomography (CT) of the abdomen, pelvis and chest, as well as hormonal and biochemical tests every 3 months. The patient had no clinical, laboratory and imaging findings of tumor recurrence or metastatic spread. Between March and June this year, the patient have not been taking mitotane for financial reasons. In June this year, CT revealed lung (S5) and multiple para-aortic lymph node metastasis (see Fig. 1).

Conclusions: Adjuvant mitotane may be highly effective in patients with a poor prognosis. In addition, to determine an optimal duration of the treatment is essential. Some experts recommend to continue treatment for 3 to 5 years, while others discontinue after 2 to 3 years. It should last at least 2 years, anyway.

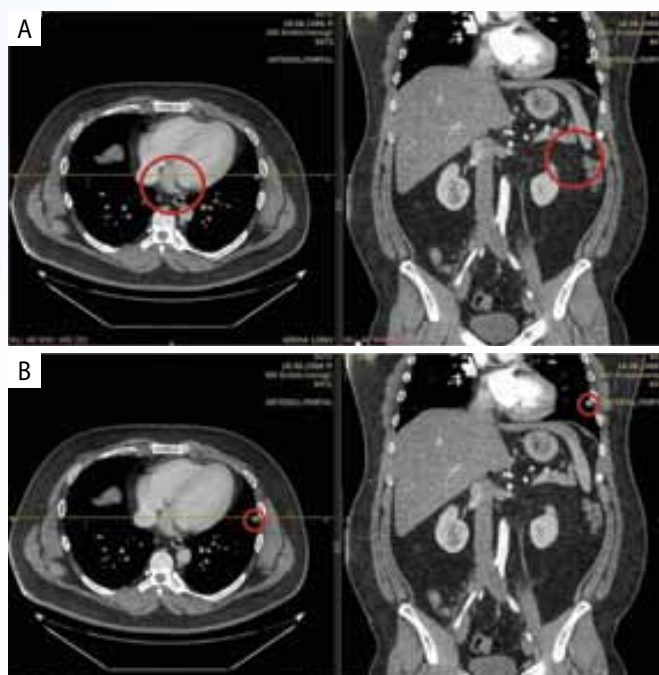


Figure 1. CT of the Abdomen, Pelvis and Chest. CT images show lung (Pannel B) and multiple para-aortic lymph node (Pannel A) metastasis.

GP 19

The trap of endometriosis treatment in the diagnosis of Cushing's syndrome. Paradoxical response to Dexamethasone or not?

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Background: Cushing's syndrome is the most common cause of endogenous hypercortisolism that results from the excessive exposure to glucocorticoids. Even though this syndrome is represented by a constellation of clinical signs and symptoms, the most common next features are the truncal obesity and the moon facies, making it hard not to be recognized. It is more common in women (F/M=5-8:1) with an average age of 20 to 40 years.

Case Presentation: A 37 years old woman, allergic to fluoroquinolones, was admitted for muscle weakness, hypertension and increased cortisol levels with suppressed ACTH and paradoxical response to 1 mg overnight and 2x2 mg dexamethasone suppression tests. She was known with endometriosis (immunohistochemically diagnosed) after a partial cystectomy for a bladder tumor, currently receiving treatment with oral contraceptives. Clinical evaluation revealed truncal obesity, moon facies, buffalo bump. Paraclinical evaluation showed high levels of late night salivary cortisol (0.379 ug/dL), urinary free cortisol at the upper limit (100 ug/24h), the overnight 1 mg dexamethasone test and 2x2 mg dexamethasone test revealed unsuppressed levels of cortisol (>1.8 ug/dl), even higher than baseline, 25.22 ug/dl, respectively 21.26 ug/dl. Abdominal CT and MRI with contrast substance indicated a left adrenocortical tumor (2.11 cm/1.90 cm). Hormonal treatment with oral contraceptives, specifically estrogen, is increasing CBP levels leading to a paradoxical response to dexamethasone.

Conclusions: The particularity of the case is based on the endometriosis treatment and allergy treated with glucocorticoids making Cushing's syndrome harder to diagnose and postponing it.

Pheochromocytoma, unmasking the chameleon

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Background: Pheochromocytoma is a rare catecholamine secreting tumor originating usually from adrenal medulla and representing approximately 5% of adrenal incidentalomas. Currently 10% of all pheochromocytomas are discovered incidentally during imaging studies for unrelated disorders.

Case presentation: A thirty five year old woman with no relevant medical history presented at the emergency department with symptoms of left flank pain and vomiting. Abdominal ultrasonography revealed renal microlithiasis and a right adrenal mass. The abdominal computed tomography confirmed a heterogeneous right adrenal mass with 118 x 105 mm with cystic and hemorrhagic component consistent with right adrenal pheochromocytoma. The hypertension was controlled with verapamil 40 mg twice daily.

Biochemistry tests revealed markedly raised plasma normetanephrines (12746 µg/24h, reference range 162-527), slightly increased metanephrines (518 µg/24h, reference range 64-302), elevated chromogranin A (31 nm/L reference range <3) and 3-methoxytyramine (2227 µg/24h, reference range 103-434). The metaiodobenzylguanidine (MIBG) scintigraphy only identified hyperfixation in the right adrenal gland.

After alpha and beta blockade patient underwent laparoscopic right adrenalectomy, and the histopathologic features were consistent with pheochromocytoma. Following surgery her hypertension has resolved and the value of metanephrines and normetanephrines four weeks after the surgery was normal. The result of genetic testing (VHL, MAX, SDHB, SDHC, SDHD) was negative.

Conclusions: Pheochromocytoma is a rare catecholamine-producing tumor requiring a high index of suspicion for early diagnosis. Our case report highlights the importance of considering pheochromocytoma in the workup of patients with adrenal incidentalomas, whose incidence is increasing due to the better availability and accessibility of imaging procedures.

GP 21

Myocardial Infarction with non-obstructed coronary Arteries (MINOCA) – An uncommon presentation of pheochromocytoma

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Background: Although pheochromocytoma classically presents with headaches, palpitations and paroxysmal hypertension, uncommon presentations such as cardiomyopathy, stroke and subarachnoid haemorrhage have been documented. We present one such infrequent presentation of myocardial infarction with normal coronary arteries (MINOCA).

Case presentation: A 79-year Caucasian female presented with central crushing chest pain radiating to left arm associated with headache, palpitations, sweating and difficulty in breathing. For two years, she experienced brief episodes of headache, tinnitus, dizziness, palpitations, and sweating that spontaneously resolved.

Clinical examination was unremarkable except for high blood pressure (210/105 mmHg). Her electrocardiogram showed T wave inversions from V1-V6 and serum troponins were high (774 ng/l at baseline and 932 ng/l three hours from baseline). Following evaluation, patient was diagnosed with acute coronary syndrome. Coronary angiography showed normal coronary arteries. She was treated as MINOCA.

During the in-patient hospital stay, patient continued to experience episodic headaches, palpitations, dizziness and erratic blood pressures. Further investigations revealed raised urine nor-adrenaline (4724 nmol/24hr, reference <554 nmol/24hr), urine adrenaline (92863 nmol/24hr, reference <77nmol/24hr). Computerised tomography scan showed well-defined rounded mass in right adrenal gland, measuring 5cm x 3.7cm x 5 cm. Patient was diagnosed with pheochromocytoma and medically stabilized with alpha- and beta-adrenergic receptor blocker (doxazosin and bisoprolol). She was then referred to tertiary care hospital for tumour removal.

Conclusion: Through this case, we highlight the importance of thorough investigation for the underlying cause for MINOCA. In patients with unexplained erratic blood pressure control, pheochromocytoma should be considered as a differential diagnosis.

Atypical manifestation of pheochromocytoma

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Background: Tako-tsubo cardiomyopathy (TTC) is a non-ischemic condition manifested with a temporary weakening of the myocardium after an acute stress. The association between pheochromocytoma (PHEO) and TTC is rare and is attributed to catecholamine excess. We present a case of a young women with an atypical manifestation of PHEO.

Clinical case: Patient, F, aged 37, known with multinodular goiter with hypothyroidism for several years, having paroxysmal hypertension from the age of 35 years (max. 220/170 mmHg) accompanied by frontal-parietal headache, sweating, hands pallor, inferior limb paresthesia, is referred to surgery for thyroidectomy. Immediately after anesthesia induction, the patient presented ventricular fibrillation with cardio-respiratory arrest. She is resuscitated and converted to sinus rhythm. ECG shows sinus rhythm, VA: 80 bpm, negative T wave in DI, DII, aVL, aVF, V3-V6. Echocardiography: dilated left ventricle, apical-septal and 1/3 apical-anterior dyskinesia, EF=30%; she had normal epicardial coronary arteries at coronarography. Few days later, EF=44%, apical akinesia, hemodynamic stable and was diagnosed with TTC. Subsequent endocrine evaluation reveals plasma free normetanephrines 557 pg/ml (20-200), urinary normetanephrines 842 ug/24 h (100-600), Chromogranin A 660 ng/ml (20-100), normal plasma free metanephrines and cortisol secretion. CT scan showed right adrenal mass of 1.95/2.31 cm. Negative RET mutation. After adequate preoperative treatment, she underwent an uneventful laparoscopic adrenal surgery, with pathological confirmation of a PHEO. One year later, the patient underwent thyroidectomy without any incidents.

Conclusion: The particularity of our case is the association between a stressful condition and a PHEO crisis which triggered Takotsubo cardiomyopathy. Although rare, PHEO should be considered in the differential diagnosis of TTC especially in younger patients.

GP 23

A rare case of adrenal incidentaloma- pheochromocytoma presenting with anemia, thrombocytosis, and proteinuria. A case report and review of the literature

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Introduction: Pheochromocytoma (PHEO) is a rare neuroendocrine tumor, which presents with various clinical phenotypes, depending on the size of the tumor, the secreting activity, and the secreting product. Large PHEOS exhibit symptoms related to mass effects and malignant PHEOS symptoms related to metastases. Some PHEOS present as adrenal incidentalomas (AI) or with an unusual clinical phenotype.

Case report: A 54-year-old Russian female presented with severe anemia and thrombocytosis in addition to nonspecific symptoms, for 6 months (weakness, fatigue, anorexia, weight loss). Clinical examination revealed skin and conjunctival paleness, sinus tachycardia and mild edema of the lower extremities. Laboratory testing revealed anemia, thrombocytosis, increased inflammation markers, severe hypoalbuminemia, and albuminuria. The abdominal CT scan revealed a right AI, sized 9x7x8cm, with heterogeneous uptake, possible liver infiltration and thrombosis of the inferior vena cava. The hormonal evaluation showed increased levels of 24hr-urine metanephrines. She underwent right adrenalectomy, nephrectomy, and splenectomy. Histopathology confirmed the diagnosis of a pheochromocytoma. The patient showed full recovery at the 3-month follow-up.

Conclusion: This case concerns a PHEO presented as AI with anemia, thrombocytosis, and proteinuria, namely an atypical clinical phenotype. The early recognition and diagnosis contribute to the safe treatment and better course of the disease and its comorbidities.

GP 24

Acute severe hyponatremia in patient on terlipressin for recurrent variceal bleeding

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Background: Terlipressin is a vasopressin agonist used in acute variceal bleeding due to its effect on vasopressin V1 receptors, causing splanchnic vasoconstriction. Although it has good safety profile, it has been shown to act as partial agonist of V2 receptors but its effects on serum sodium concentration can be variable.

Case Presentation: 58 year old lady was admitted after banding for variceal bleed found at routine screening. She was started on terlipressin, antibiotics and admitted for monitoring. Hemoglobin continued to dropped and she was scoped again and found a bleeding varix and was banded. On day 3, her sodium level started dropping, coming down to 128 mmol/L from 140 mmol/L at admission. Over next 48 hours, it further dropped to 116mmol/L despite halving the dose of terlipressin. She was euvolemic on examination with a urinary sodium of 209, urinary osmolality 598 and serum osmolality 252. She became symptomatic, was given hypertonic saline, and started on fluid restriction. Terlipressin was withdrawn with sodium level returning back to 135 mmol/L over next 48 hours. She was observed as an inpatient for sodium level and further bleeding for 2 days and then discharged after remaining stable during the observation period.

Conclusions: Acute hyponatremia can develop during treatment with terlipressin for portal-hypertensive bleeding, can develop rapidly and usually reversible with cessation of therapy.

GP 25

Atypical presentation of an acromegalic patient

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Background: Acromegaly is a rare disorder, with a prevalence of 6 cases of 100000 and an annual incidence of 3-4 new cases of one million. It is almost always the consequence of GH secreting pituitary adenomas and, rarely, caused by nontumoral somatotrophic hyperplasia.

Case presentation: 54 years old patient, heavy smoker, hypertensive, dyslipidemic, obese, presents in June 2019 with unspecific symptoms: physical asthenia, hypersomnia (falls asleep during interview), dyspnea, disorientation and visual and auditive hallucinations, that aggravated progressively during the last 3 months. Clinically, the patient has a discrete acromegalic phenotype and hyperpigmentation of the skin. A cerebral IRM was performed that revealed a 2 cm pituitary macroadenoma. Laboratory findings show normal cortisol levels and adequate suppression after dexamethasone, normal prolactin and thyroid hormone levels, but an increased IGF1 and elevated levels of GH after standard testing of GH in OGTT. Also, the patient had severe respiratory insufficiency, for which was evaluated in a pneumonology department, taking into consideration the possibility of sleep apnea. After the correction of the respiratory failure, the patient's hallucinations stopped and the breathing improved significantly.

Conclusions: The particularity of the case is that, based on the progressive hyperpigmentation of the skin, the metabolic and psychiatric disorders, the initial suspicion was of a Cushing's disease, but that was not confirmed by laboratory investigation. More so, the psychiatric manifestations were related to the respiratory failure, and not to the disease itself.

Multiple endocrine neoplasia type 1 presented with gastric neuroendocrine tumor: a case report

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Background: Multiple endocrine neoplasia type 1 (MEN1) is an inherited syndrome, characterized by primary MEN1 tumors: parathyroid, pancreatic and pituitary. We describe the case of a patient with MEN1 syndrome, initially presented with a gastric neuroendocrine tumor (NET).

Case presentation: A 33-year-old male patient, initially treated for perforated gastric ulcer, presented 7 years later with dyspepsia, diarrhea and weight loss. Abdominal CT scan revealed marked thickening of the whole gastric wall and several enlarged lymph nodes. The patient underwent total gastrectomy without lymph nodes resection.

Histopathological examination and immunochemistry showed well differentiated G2 NET, with Ki-67 of 3.8%, positive for chromogranin A, synaptophysin and somatostatin receptor type 2. The serum gastrin and chromogranin A levels were elevated, thereby treatment with lanreotide was initiated.

Furthermore, the patient presented elevated serum calcium and PTH levels. Sestamibi scintigraphy identified a right parathyroid adenoma and subtotal parathyroidectomy was performed. Following a pituitary CT, a double non-functioning pituitary adenoma was found. The genetic test confirmed the MEN1 diagnosis.

The ⁶⁸Gallium-DOTATATE PET/CT scan showed high uptake in several abdominal lymph nodes, and also in the pancreatic head. The patient was treated with 4 cures of peptide radio receptor therapy (PRRT) with lymph node shrinkage. Further assessment of the possibility of pancreatic tumor resection is considered.

Conclusions: Up to 30–50% of patients with MEN1 will develop gastric NETs. We presented a case of a patient with confirmed MEN1 syndrome with hyperparathyroidism, pituitary adenoma and a pancreatic tumor, who also associated a gastric NET with metastatic lymphadenopathies.

GP 27

Rare case of hypopituitarism

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Background: Hypopituitarism can be expressed throughout many symptoms and can stay unrecognized for a long time. Xanthogranulomas are extremely rare in sellar region, with prevalence of ~0.6% in reported pituitary tumours and are presented with visual disturbance, hyperprolactinemia, diabetes insipidus and/or hypopituitarism. Its ethiopathogenesis is still not certain, but it can be of primary or systemic cause. It's almost always diagnosed postoperatively and has good outcome with adequate hormonal substitution.

Case Presentation: A 34-year old man was referred to our Clinic due to a 3-year-history of polymorphic symptoms: weight loss, headaches, fatigue, mood changes, loss of libido...After endocrinology evaluation, diagnosis of partial hypopituitarism was established and hydrocortisone, levotyroxine and testosterone substitution was ordained in corresponding doses. Congenital cause was clinically excluded. NMR detected: non-homogenic intra-, supra- and para-sellar mass sized 14x15x8mm, without damage of optic-hyasm and cavernous sinuses, with coincidental finding of pineal gland cyst. After transsphenoidal extirpation, patohistological diagnosis was sellar xanthogranuloma, CD3+, CD20+, IgG4- i CD1a-. Screening on systemic causes was negative. One year after (on therapy) findings of thyroxine and total testosterone were normal, cortisol levels were low normal and control NMR detected possible sellar rest sized 4x8x4mm.

Conclusions: Xanthogranuloma-causing hypopituitarism is not easy to diagnose preoperatively based on NMR appearance. However, since it is known that these lesions occur more frequently in young population, it should be suspected when discovered in young patients presenting with cystic pituitary lesions. These tumours have favorable endocrine outcomes based on its rare post-operative recurrence rate.

Case Report: Cushing disease developed from a nonfunctioning pituitary adenoma

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Background: Only a few cases of pituitary tumor swift from non-functioning to Cushing disease (CD) have been previously presented in the literature. The exact mechanism is still unknown.

We present a case of a patient with a non-functioning pituitary adenoma, who developed CD from the residual tumor, 13 years after the initial diagnosis and following 2 surgical interventions and radiation therapy.

Case presentation: A 51-year-old woman initially presented with amenorrhea and galactorrhea. The clinical examination showed bitemporal hemianopsia. Laboratory tests: PRL=49.52 ng/ml; FSH=0.76 U/l; LH=0.17 U/l. The CT scan showed a large 2.68 cm (tr) x 3.98 cm (cc) pituitary mass, extending towards the suprasellar compartment, with compression of the optic chiasm.

The patient underwent 2 surgical interventions: transfrontal (2005) and transsphenoidal (2006). 4 years later she received radiation therapy (50 Gy).

Almost 13 years later (2018), the patient developed mild cushingoid features and the residual pituitary mass developed into an ACTH-secreting adenoma: elevated ACTH level (79.63 pg/ml), loss of circadian rhythm of plasma cortisol with negative result to 1 mg overnight dexamethasone suppression test (9.06 mcg/dl).

The patient underwent a third transsphenoidal surgery. At the one month follow-up she had normal values of ACTH and plasma cortisol, positive results to 2x2 mg dexamethasone suppression test and a small tumor remnant of 1.3 cm (post-surgical MRI scan).

Conclusions: This case report emphasizes the importance of long term follow-up of each patient for tumor regrowth but also from the hormonal point of view - for pituitary deficiency but mainly cortisol level.

GP 29

Relapsed acromegaly after 3 years of remission following pituitary apoplexy

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Background: Pituitary apoplexy is a rare clinical syndrome manifested by rapid enlargement of a pituitary mass. When apoplexy occurs in functioning adenomas, it may result in spontaneous remission with or without associated hypopituitarism. Cases of recurrence in such patients are reported in literature.

Case description: We present a case of a 44 years old male, overweight and dyslipidemic that presented to our clinic in 2016 and was diagnosed with acromegaly after finding an insulin-like growth factor 1 (IGF-1) of 1116.3 ng/ml, a nadir growth hormone (GH) after oral glucose tolerance test (OGTT) of 16.2 ng/ml, with no other hormonal abnormalities and a pituitary adenoma of 1.6 cm. Two days before transfenoidal adenomectomy, he complained of intense headache associated with dyspeptic symptoms and after further evaluation, the diagnosis of pituitary apoplexy is made. Following the episode of apoplexy and surgical intervention, his clinical labs revealed normal IGF-1 with normal GH after OGTT and no hypopituitarism. The adenoma decreased to 0.8 cm cranio-caudal/0.46 cm - transverse. After 3 years of clinical and biochemical remission of the acromegaly, repeated IGF-1 showed mild elevation of 260 ng/ml (N<227 ng/ml) with suppressed GH after OGTT with a two fold increase in the transvers diameter of the tumor at the computed tomography scan.

Conclusion: We presented a case of relapsed acromegaly after 3 years of remission following pituitary apoplexy, suggesting that such patients require long-term follow-up for the possibility of recurrence of active hormonal hypersecretion.

A rare case of spontaneously cured acromegaly by the apoplexy of the pituitary adenoma

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Background: Acromegaly is a rare disease characterised by an excessive production of growth hormone (GH), from a pituitary adenoma. It is a curable disease, either by surgery or by medical treatment, but very rare it can spontaneously cure by the apoplexy of the pituitary adenoma.

Case presentation: We present the case of a 58-year-old female who was suspected of acromegaly due to her physical appearance: soft tissue swelling and enlargement of the extremities, increase in shoe size, coarsening of facial features, prognathism, macroglossia, frontal bossing and cutis verticis gyrata. The patient complained of visual field defects and headaches, but she never claimed a clinical episode suggestive of pituitary apoplexy. She also presented some of the most frequent complications of acromegaly: high blood pressure, type 2 diabetes mellitus, sleep apnoea syndrome and benign colon polyps.

The hormonal dosing revealed a normal insulin like growth factor 1 (IGF1) value of 72.08 ng/ml (normal range: 46-238), with a mean GH/24 hours of 0.2 ng/ml. Hormone studies on thyrotrophyc, corticotrophyc, gonadotrophyc and lactotrophyc lines were normal.

Magnetic resonance imaging revealed the pituitary gland reduced in dimensions, plated by the sellar floor, with a pseudo-empty sella aspect, without the traction of the optic chiasm. Visual field examination revealed bilateral concentric shrinking. Lateral radiograph of the skull revealed thickened skull vault, pneumosinus dilation and prognathism, and AP radiograph of the hand showed ungal tufting.

Conclusions: In summary, we report a very rare case of acromegaly, which cured spontaneously by the apoplexy of the pituitary tumor.

GP 31

Partial recovery of hypopituitarism and spontaneous pregnancy in a patient with Sheehan's syndrome

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Background: Sheehan's syndrome occurs after a delivery complicated with hemorrhage causing ischemic pituitary necrosis and panhypopituitarism. It is rare for a patient with Sheehan's syndrome to obtain recovery of the pituitary function. We report the case of a patient with Sheehan's syndrome who obtained a spontaneous pregnancy 2 years after the initial diagnosis.

Case Presentation: A 23-year-old-woman, without a significant personal medical history, gave birth, uneventfully, to a healthy boy in 2015. After delivery, she failed to lactate and remained amenorrheic. Seven months later, she consulted in another endocrinology service for persistent amenorrhea, weight gain, extreme fatigue and sleepiness. The hormonal dosages revealed panhypopituitarism and the magnetic resonance imaging (MRI) detected a pituitary hypotrophy, all consistent with Sheehan syndrome. A substitutive treatment was prescribed with Prednisone 2,5 mg/day, Thyroxin 50 µg/day and oral cyclic estrogen/progesterone combination (COC). After two years, by her own initiative, the patient stopped taking COC, became pregnant spontaneously and gave birth uneventfully to a healthy girl. Post-partum, she still failed to lactate but menstrual cycles restored. In 2019, hormonal dosages showed recovery of the thyrotropic, somatotropic and gonadotropic functions, but persistence of the corticotroph and lactotroph failure and persistent pituitary atrophy in MRI. The replacement therapy with Prednisone 5 mg/day was continued.

Conclusions: This case illustrates the possible occurrence of Sheehan syndrome even in women with **normal delivery** and, in time, the possible **partial recovery** of the pituitary function, pointing out the necessity of long-time monitoring of these patients.

Metabolic differences between women with various phenotypes of polycystic ovary syndrome (PCOS)

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Objective: To compare metabolic characteristics of women with different phenotype of polycystic ovary syndrome (PCOS) based on Rotterdam criteria.

Materials and methods: One thousand one hundred women with PCOS, aged 17 to 40, were recruited. The patients were divided into four subgroups according to the phenotype of PCOS defined by Rotterdam criteria: (A): oligo- and/or anovulation (Oligo), hyperandrogenism (HA), polycystic ovaries (PCO); (B): oligo+ HA; (C): HA+ PCO, (D): oligo+ PCO. Anthropometric measures and metabolic parameters were assessed in subjects from each group. Blood samples were collected for the quantification of biochemical parameters using the electrochemiluminescence immunoassay (ECLIA) methods or colorimetry.

Results: In groups with HA worse metabolic profile was observed compared to group without HA. Compared lipid profile, statistically significant differences in total cholesterol and LDL cholesterol concentration were observed between group A and D; patients without HA were characterized by the lowest triglycerides concentration. There were statistically significant differences in glucose levels and insulin resistance parameters between groups with HA compared to group D. Groups with HA were characterized by significantly higher body mass index (BMI). No statistically significant differences in fibrinogen level between groups were observed.

Conclusions: Women with PCOS and HA have unfavorable metabolic profile compared to women without HA. Metabolic parameters of phenotypes A, B and C are similar. HA is accompanied by higher BMI, worse lipid profile, higher glucose levels and insulin resistance parameters and therefore associated with higher risk of future metabolic disorders.

GP 33

Features of pituitary-ovarian axis functioning in woman of reproductive age with acromegaly and Cushing's disease

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Context: The prevalence of reproductive dysfunction among patients with acromegaly (ACRO) and Cushing's disease (CD) is high enough, and menstrual disturbances are often the first clinical symptoms of the disease. Objective. The purpose of this study was to assess the functioning of the pituitary-ovarian axis by examination of key hormones.

Methods and patients: The study included 58 patients of reproductive age, 21 with ACRO, the average age was 36.6 ± 4.9 years and 37 patients with CD, the average age was 30.0 ± 5.9 years.

Results: All patients with ACRO had macroadenoma, the GH median was 15.95 [9.4, 38.5], IGF-1 703.45 [560.8, 869.4]. Amenorrhea was observed in 12 patients (42.9%), 2 presented oligomenorrhea (9.5%) and 10 had normal menstrual cycle (47.6%). Mild hyperprolactinemia was noted in 11 patients (52.4%). Median FSH was 4.0 [2.7, 4.8], LH - 2.8 [1.5, 3.8], E2 - 112.1 [87.1, 153.9], inhibin B - 54, 2 [25.0, 86.2], PRL - 387.5 [109.0, 557.0]. The presence of a negative correlation between E2 and IGF-1 ($r = 0.36$, $p < 0.05$) was noted. Among patients with CD, microadenoma was confirmed in 22 patients (59.5%), 7 had macroadenomas (19%), adenoma was not visualized by MRI in 8 (21.6%). Median evening level of ACTH was 47.1 [35.4, 74.7], evening cortisol - 592.0 [445.0, 847.6]. Amenorrhea was observed in 15 patients (40.5%), oligomenorrhea in 10 (27.0%), normal menstrual cycle in 11 (29.7%), menometrorrhagia in 1 patient (2.7%). Hyperprolactinemia was registered only in 9 patients (24.3%). Median FSH was 4.7 [3.3, 5.6], LH - 3.9 [2.7, 6.0], E2 - 116.4 [90.2, 182.3], inhibin B - 53.4 [73.3], PRL - 351.7 [260.2, 536.1]. It is an interesting fact that the level FSH had inverse relationship with cortisol and also some direct correlation between LH and inhibin B ($r = 0.40$, $p < 0.05$) was signed. Despite the lower values of FSH and LH medians in the group of patients with CD compared to ACRO, the difference did not reach statistical significance ($p = 0.09$ and $p = 0.08$, respectively).

Conclusions: Thus, the prevalence of menstrual dysfunction in patients with ACRO and CD is very high and reaches 52.4% and 24.3% respectively. Measurement of gonadotropins in the patients does not reveal pathological mechanisms of menstrual abnormalities. The frequency of concomitant hyperprolactinemia is higher in patients with ACRO than CD (52.4% vs. 24.3%). The depression of FSH secretion in women with CD is inversely correlated with the level of cortisol.

GP 34

Spontaneous pregnancy outcomes in a patient with Turner syndrome

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Background: Turner syndrome (TS) occurs in approximately 1 in 2500 live female births. The frequency of pregnancies in TS patients is 2-5%. However, these pregnancies are at high risk of recurrent miscarriage, malformations in the children and poor cardiovascular outcomes in pregnant TS females.

Case Presentation: A 34 year-old woman was diagnosed with TS (46XX/46Xr) at age 9. From 16 to 20 years old she was treated with sex hormone replacement therapy and had regular menstrual cycles (MC 28/5). Physical examination at age 18 showed: weight 50 kg, final height 151,7 cm, BMI 21,92 kg/m², pubertal stage P5, B5. Patient did not have any cardiovascular or other organ pathologies neither before nor after pregnancies. After withdrawal of hormonal therapy she continued to have regular menstrual cycles (MC 30/5). Woman conceived naturally at 22, 24 and 28 years. All three newborns were born at full-term by cesarean section due to fetopelvic disproportion.

1st child, a girl, was born healthy, weighing 3460 g. Subsequent growth and development were normal.

2nd child, a boy, was born healthy, with 3660 g. He was diagnosed with growth retardation at age 3 but did not require treatment with growth hormone.

3rd child, a boy, was born weighing 4160 g. He was diagnosed with cleft lip and cleft palate at birth. These malformations were repaired by surgery. No maternal or pregnancy complications were detected.

Conclusions: Pregnancy and child bearing in TS can be particularly challenging due to maternal and neonatal complications. All TS pregnancies should be under multidisciplinary supervision during pregnancy and after delivery.

Energy deficiency, menstrual disorders and low bone mineral density in female athletes: a systematic review

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Background and Aim: Low energy availability (LEA) may lead to menstrual disorders and low bone mineral density, predisposing to the female athlete triad (FAT) syndrome. The primary aim of this review was to systematically investigate the impact of sports on the energy status of professional female athletes compared to sedentary, recreationally active controls, with regard to their menstrual status and bone mineral density (BMD). A secondary aim was the estimation of the combined prevalence of the components of FAT in athletes as compared with non-athletes.

Materials and methods: A systematic review was conducted from 2007 to February 2018. Inclusion and exclusion criteria of studies were established in advance of the literature search, according to the clinical inquiry and the study design.

Results: Four studies were included in this systematic review. The FAT syndrome was more prevalent in professional athletes compared with non-athletes. The same results occurred for both LEA and menstrual disorders. However, BMD and Z-scores showed high heterogeneity among the studies.

Conclusions: Both professional athletes and sedentary women are prone to LEA and subsequent menstrual disorders and low BMD or osteoporosis. Future studies are needed to examine the energy availability in elite female athletes, as well as in non-athletes.

Effective combined treatment of secondary hyperparathyroidism in patient on hemodialysis with ectopied parathyroid gland

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Background: Secondary hyperparathyroidism (SHPT) is severe complication of chronic kidney disease, characterized by high serum parathyroid hormone (PTH), parathyroid gland hyperplasia, and disturbances in mineral metabolism. Effective management of SHPT includes measures to prevent hyperphosphataemia and excess PTH, to maintain serum calcium within the normal range. In dialysis patients with severe SHPT, medical treatment may fail and parathyroidectomy (PTX) is indicated for definitive treatment. However, PTX does not always lead to disease compensation. In this case only a combined surgical and medical approach could help to control SHPT.

Case Presentation: We presented the clinical case of patient with an 8-year history of renal insufficiency secondary to chronic glomerulonephritis. Long-term disease decompensation (PTH level of 2500 pg/ml, severe hypercalcemia 2,8 mmol/l and hyperphosphatemia 2,03 mmol/l) led to multiple fractures in the spine, ribs and sternum handle, extraskeletal calcification. The ultrasound and SPECT/CT with MIBI revealed hyperplasia of four parathyroid glands in a typical place and the fifth parathyroid gland, ectopied in the mediastinum. Despite the surgical removal of four parathyroid glands, PTH and calcium levels remained high. The surgical resection of ectopic parathyroid tissue is not feasible due to anatomical difficulties. In the postoperative period, we prescribed combination therapy with Paricalcitol, calcium supplements and Denosumab with positive effect - the compensation of phosphorus-calcium metabolism parameters, bone pain reduction, an increase in motor activity and overall well-being.

Conclusions: Dialysis patients with severe SHPT need the timely initiated treatment, to control the disease and its complications and improve the quality of life.

Calcium infusion test in primary hyperparathyroidism- sensitivity of calcium sensing receptor, possible new theories?

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Objective: Ionized calcium via calcium sensing receptors (CaSR) mediates feedback inhibition of parat hormone (PTH) secretion. The aim of this study is to evaluate the difference in PTH response during calcium infusion test (CIT), between patients with primary hyperparathyroidism (PHPT) and healthy control (HC).

Methods: Study consisted of 15 patients with confirmed PHPT and parathyroid adenoma (57.20 ± 11.38 yrs) and 15 healthy subjects-HC (57.20 ± 11.41 yrs) matched for age and gender. In all subjects, basal levels serum calcium, ionized calcium and PTH levels were measured before, during and after CIT (–30, 0, 1, 2, 3, 5, 8, 10 min). Statistical analysis included Spearman correlation, Student T test.

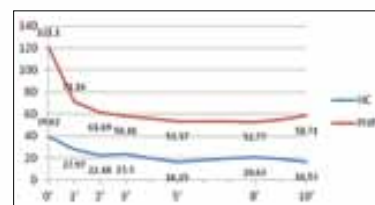
Results: Before CIT, basal PTH levels were 121.1 ± 92.06 ng/l (PHPT) and 39.62 ± 12.73 ng/l (HC) ($p < 0.01$). During CIT, PTH level is suppressed to a minimum mean value 52.77 ± 42.04 ng/l (56.4%) in PHPT and 16.25 ± 4.72 ng/l (58.9%) in HC group. Reduction of PTH levels is more pronounced in the PHPT group in the first minute of the test compared to the HC group (42% vs. 30%), in order to get closer in 5. minute of CIT. Average PTH nadir was measured in PHPT group in 8. minute, while in HC group was measured in 5. minute of CIT.

Conclusion: In parathyroid adenomas, chief cells retain the similar ability to suppress secretion of PTH during increase of Ca^{2+} , as well as healthy, without differences in suppression levels. The main components of this process are related to the function of CaSR and the influence of vitamin D on the PTH- Ca^{2+} set-point.

Table 1. Mean values of PTH during CIT in PHPT and HC groups and suppression in percentages compared with basal values of PTH before CIT

PHT(-30min)	PHPT	121.1±92.06	$p < 0.01$	PTH suppression percentage (%) compared with basal values of PTH before CIT
	HC	39.62±12.73		
PHT(0min)	PHPT	115.18±94.64	$p < 0.01$	
	HC	37.76±17.91		
PHT(1min)	PHPT	71.16±52.09	$p < 0.01$	42%
	HC	27.97±13.58		30%
PHT(2min)	PHPT	61.69±51.84	$p < 0.01$	49%
	HC	22.48±9.68		43%
PHT(3min)	PHPT	58.41±23.30	$p < 0.01$	52%
	HC	23.30±17.09		42%
PHT(5min)	PHPT	53.37±43.17	$p < 0.01$	56%
	HC	16.25±4.72		59%
PHT(8min)	PHPT	52.77±42.04	$p < 0.01$	57%
	HC	20.63±11.63		48%
PHT(10min)	PHPT	58.71±55.06	$p < 0.01$	52%
	HC	16.53±8.84		59%

Chart 1. PTH response (mean PTH values, ng/l) during CIT (minutes) in PHPT and HC groups.



Charts 2. (left) i 3(right). PTH suppression- apsolute PTH values (left) and percentage of suppression (%) (right) during CIT

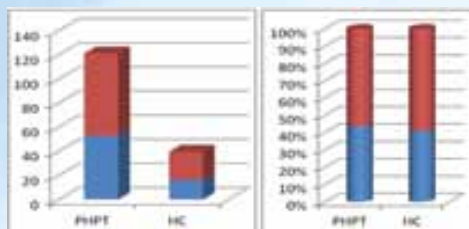
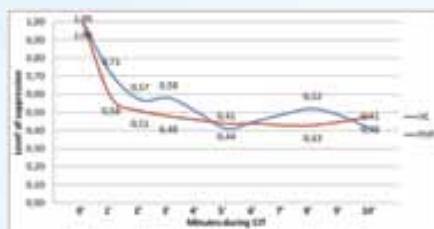


Chart 4. Suppression of PTH during CIT in PHPT and HC groups



GP 38

Management of (severe) primary hyperparathyroidism in pregnancy

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Primary hyperparathyroidism (PHPT) is a common endocrine condition but is relatively rare in very young people and during pregnancy. The diagnosis in pregnancy poses a unique challenge and is often missed as the symptoms of hypercalcemia mimic those in pregnancy.

We present the case of a 20-year old woman who was found to have severe hypercalcemia after she had persistent vomiting in early pregnancy. Biochemistry revealed adjusted calcium of 5.34mmol/L, parathormone of 103.9pmol/L and normal Vitamin D. Further investigations revealed hypercalciuria, renal impairment and renal medullary calcification. She was fluid resuscitated aggressively. She decided to undergo medical termination of this unplanned unwanted pregnancy at nine weeks gestation. She was commenced on cinacalcet but hypercalcaemia remained refractory. She had no family history of hypercalcemia or multiple endocrine neoplasias. Neck ultrasound and sesta-MIBI failed to localize a parathyroid lesion. Subsequent 4-D CT and methionine PET revealed a large mediastinal ectopic parathyroid lesion. She had parathyroidectomy at thoracic surgery centre and calcium normalized after surgery.

This case highlights the challenges in diagnosis, investigation and management of PHPT in pregnancy. The diagnosis needs a high index of suspicion. In our case, detailed probing revealed an 18-month history of weakness, polyuria, nocturia, vomiting, and memory impairment. Localization of abnormal parathyroid glands is difficult as ultrasound is the only safe imaging. Most calcium-lowering drugs are contraindicated, with rehydration being the mainstay of treatment. If parathyroidectomy is indicated, it is best performed in second trimester when organogenesis is complete and the risk of preterm delivery relatively low.

Chronic hypophosphatemia in a child: case report

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Background: Chronic hypophosphatemia in children mimics diverse conditions and may be underpinned by genetic disorders (e.g. X-linked hypophosphatemia), primary hyperthyroidism, tubular disorders (Fanconi syndrome) and neoplasia. Severe sequelae like rickety deformities of the skeleton, mental and physical retardation, osteoporosis and osteomalacia, etc require prompt diagnosis and treatment. Here we present a case report of untreated chronic hypophosphatemia mimicking ketoacidosis on the admission.

Case presentation: A male patient of 3 years old presented with vomiting, shortness of breath and altered mental status. He had history of poor weight gain since 2 months old, bone deformities and loss of unassisted walking since 1.4 y.o. Family history was remarkable for bowing of lower extremities in his aunt. Taking into account clinical presentation and ketonuria, the differential diagnosis with diabetic ketoacidosis was conducted. On examination: physical and mental retardation, stigma of disembryogenesis, rickety deformities of the trunk and extremities. Height - 77 cm; weight - 7.9 kg, respectively. Laboratory findings included hypochromic anemia (I degree), normal glycemia, hypophosphatemia, normal serum Ca, elevated alkaline phosphatase, high parathyroid hormone level, secondary hypothyroidism. On the X-ray: osteoporosis. In view of the abovementioned data a provisional diagnosis "chronic hypophosphatemia" was established. As other causes were ruled out, a hereditary form of hypophosphatemia was suspected. To specify the diagnosis the patient was referred to a genetic counseling.

Conclusions: Physicians should be suspicious of hereditary forms of hypophosphatemia when a patient has abovementioned clinical presentation, as prompt diagnosis and treatment may compensate for physical and mental developmental delay, and prevent surgery.

Congenital hyperinsulinism due to a novel activating glucokinase mutation: a case report and literature review

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Background: Congenital Hyperinsulinism (CH) or, as previously named, Hyperinsulinemic Hypoglycemia (HH), constitutes a major cause of persistent and recurrent hypoglycemia, especially in the neonatal period, showing notable phenotypical heterogeneity among affected subjects. Mutations in genes implicated in insulin release, represent the majority of the cases of CH. Activating mutations of the Glucokinase gene (*GCK*) are responsible for mild forms of hypoglycemia usually easily medically managed.

Case presentation: We present a patient with neonatal hypoglycaemia, due to hyperinsulinism. Genetic study was performed for the investigation of mutations associated with hyperinsulinemic hypoglycemia. Analysis revealed that both the mother and the child were heterozygotes for the activating novel mutation p. Val71 Ala in exon 3 of the *GCK* gene.

Conclusions: *GCK* gene mutations result in varying phenotypic characteristics and responsiveness to diazoxide depending on the type of activating mutation.

Budd-Chiari syndrome in a young patient with type 1 Diabetes Mellitus: a case report

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Background: Budd-Chiari syndrome, characterized by abdominal pain, ascites and hepatomegaly, is a rare condition, caused by thrombotic hepatic venous outflow obstruction. Diabetes mellitus is associated with impairment of the coagulation and fibrinolysis pathway, suggesting its involvement in the pathogenesis of venous thromboembolism. There are few cases of patients with Budd-Chiari syndrome and Diabetes Mellitus, reported in the literature.

Case presentation: A 30-year-old woman presented in the Emergency Department because of nausea and abdominal discomfort developed the last 25 days. She used tobacco, was not pregnant, did not use oral contraceptives, without family history of thrombotic episodes. She had type 1 Diabetes mellitus since the age of ten, treated with insulin degludec and insulin aspart. Routine laboratory tests showed mild elevation of liver enzymes and poor glycemic control (HbA1c 8%). Abdominal ultrasonography revealed moderate ascites. Computed tomography and Magnetic Resonance Angiography showed ascitic fluid, hepatomegaly, heterogeneity of liver parenchyma, enlarged caudate lobe and absence of blood flow in hepatic veins, indicating the presence of acute-subacute Budd-Chiari syndrome. The patient was heterozygous for MTHFR mutations and had positive anti-β2 glycoprotein-I IgM antibodies in two consecutive tests, but not in the third, without other pathological findings.

Conclusions: During the diagnostic approach, not any known cause of Budd-Chiari syndrome was identified. Neither hyperhomocysteinemia nor antiphospholipid syndrome was overt in this patient. We conclude that there is a potential association between the hypercoagulable state of Diabetes mellitus and hepatic vein thrombosis, which should be further investigated.

GP 42

Paraneoplastic hypoglycemia in a patient with recurrent pleural tumor

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Background: Solitary fibrous tumor of pleura represents a prototypical mesenchymal neoplasm that induces non-islet cell tumor hypoglycemia due to overproduction of insulin-like growth factor 2, named Dodge Potter syndrome.

Case Presentation: An 86-year-old man, non-diabetic, was admitted to hospital with a few months history of repetitive hypoglycemic symptoms and documented low blood glucose of 1.9 and 1.2 mmol/L on two occasions when he lost consciousness. His medical history was notable for primary pleural fibroma which was resected twenty years previously and for tumorous mass of right pulmonal lobe 103mm described on CT chest scan for respiratory infection six months prior to hospitalization. During hospitalization hypocorticism and hypopituitarism were ruled out. He spontaneously developed mild neuroglycopenic episodes, when we confirmed hypoinsulinemic hypoglycemia accompanied with suppressed levels of growth hormone and IGF1, and IGF2:IGF1 ratio of 7, which was all suggestive of paraneoplastic etiology. The response of glucose in Glucagon test was adequate. Beta-hydroxybutyrate was not done due to technical limitations. Abdominal MRI showed a few well-circumscribed cysts in the liver and hemangioma. Octreoscan revealed zone of diffuse increased uptake in right hemithorax. Subsequently, he was started on prednisolon for COPD exacerbation with which his hypoglycemic episodes subsided. Patient declined surgery and he was released with glucocorticoid therapy.

Conclusions: We report a rare case of hypoinsulinemic hypoglycemia in a patient with suppressed levels of hGH and IGF1 and higher-than-normal IGF2:IGF1 ratio, along with recurrent pleural tumor which is somatostatine-receptor positive.

Wolfram (didmoad) syndrome: a case of two sisters

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Background: Wolfram syndrome is an autosomal recessive neurodegenerative disorder characterised by Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also referred to as DIDMOAD). An estimated prevalence is 1 in 770,000 and an estimated carrier frequency is 1 in 354. Herein, we describe the course of wolfram syndrome in two female siblings.

Case presentations: The first patient is a 30-year old female, who, was diagnosed with type 1 diabetes mellitus at the age of 3. Blood glucose is well-controlled on insulin analogues. At the age of 13 she was diagnosed with optic atrophy with a total vision loss by the age of 28. One year later an audiologic examination revealed sensorineural deafness, for which she is using a hearing aid. Diabetes insipidus was diagnosed at the age of 25, and is well-controlled on desmopressin 15 mcg daily.

The first patient has a 21-year old sister, who was diagnosis with type 1 diabetes mellitus at the age of 7, but has had a more rapid progression of the disease. Two years later, optic atrophy and diabetes insipidus were diagnosed. Her blood glucose is adequately controlled with insulin analogues and she is on 15 mcg desmopressin. Since the age of 17, She has had voiding difficulty due to atonic bladder and is using self intermittent catheterisation two to three times a day.

Conclusion: Cases having early onset insulin-dependent diabetes mellitus and optic atrophy need to be evaluated with respect to Wolfram. The use of careful clinical monitoring and supportive care can help relieve the suffering of patients and improve their quality of life.

GP 44

A rare cause of artifactual hypoglycemia

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Background: Glycemia point-of-care testing (POCT) is performed with fingerstick capillary whole-blood glucose measurement. These values correlate well with plasma glucose values. Hypoglycemia can be observed with POCT but should always be confirmed on plasma. True hypoglycemia must meet Whipple's triad: signs/symptoms of hypoglycemia; low plasma glucose; improvement after glucose administration. Artifactual hypoglycemia is a discrepancy between POCT and plasma glucose and occurs in cases of decreased capillary flow.

Case Presentation: A 86-year-old woman was admitted because she fell in her nursing home. Primary assessment POCT measured a glucose of 20mg/dl. There were no signs of hypoglycemia. Plasma glucose was 91mg/dl. She had no history of diabetes mellitus. HbA1c measured 42mmol/mol. C-peptide was never elevated. POCT was compared multiple times with plasma glucose and showed regular discrepancy. POCT using blood from the ear lobe however correlated strongly with plasma glucose. Clinical examination revealed sclerodactyly and Raynaud's phenomenon. She had complaints of dysphagia and had facial telangiectasia. She had positive ANF-antibodies and anti-centromere antibodies. The patient was therefore diagnosed with CREST syndrome, the limited cutaneous variant of systemic sclerosis. Due to the sclerodactyly, capillary blood flow is decreased, therefore the rate of tissue glucose withdrawal is increased.

Conclusions: POCT is useful to check glucose values. However, artifactual hypoglycemia can occur in decreased capillary flow or increased glycolysis. Patients presenting with measured hypoglycemia but without symptoms of hypoglycemia do not fulfill Whipple's triad and should raise suspicion for other etiologies. Connective tissue diseases such as systemic sclerosis can falsify capillary glucose.

Incidental finding on Retinal screening-seeing is not always believing

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Case Presentation: 37-year-old woman of South Asian origin was referred from retinopathy screening to our diabetes clinic for evaluation of an unusual finding during her retinal screen. Her retinal blood vessels appeared white in contrast to normal pink to red colour. She was recently diagnosed with type 2 diabetes and with type 1 hyperlipidaemia (T1 HPLA) confirmed by genotype for more than 10 years for which she had suboptimal control with multiple hospitalisations with recurrent pancreatitis.

On examination, she had multiple naevi on her skin; rest of the examination was unremarkable. Patient did not report of any visual disturbance and had intact visual acuity. Investigations showed raised total cholesterol (12.5 mmol/l) and triglycerides (57.7 mmol/l). Following evaluation, patient was diagnosed with lipemia retinalis secondary to T1 HPLA.

Patient was managed conservatively to reduce cholesterol and triglyceride burden. However, therapies with Orlistat, statin, fibrates and colestyramine failed. Only total dietary prudence and use of MCT oil with glycaemic control optimised with insulin showed some improvements in her lipid profile. Unfortunately, this had led her to become fat soluble vitamin deficient and she was hence treated with appropriate supplementation. Following significant changes, her lipid parameters improved and lipemia retinalis resolved.

Conclusions: Lipemia retinalis is an uncommon incidental finding of T1 HPLA that does not affect vision and acute intervention is not indicated. The management of associated dyslipidemia is challenging with minimal response to conventional treatment. Increased awareness of the condition and specialist management is needed for regular patient monitoring and personalised management.

GP 46

Prevention of hypertriglyceridemia-induced recurrent pancreatitis during pregnancy: The role of regular plasmapheresis

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Background: Familial hypertriglyceridemia may lead to acute pancreatitis also during pregnancy in some cases. We present two cases with hypertriglyceridemia-induced pancreatitis that recurred despite diet and medical therapy during pregnancy.

Case presentation: Twenty-eight-year-old woman presented with hypertriglyceridemia-induced pancreatitis (serum triglyceride: 8502mg/dL) that was complicated with respiratory distress at 25 weeks of gestation. Following plasmapheresis serum triglyceride level was 613mg/dL but her pregnancy was terminated due to intrauterine fetal demise. She was started on fenofibrate therapy but was lost to follow-up. One year later, she presented with acute pancreatitis (serum triglyceride: 2425mg/dL) again during pregnancy at 23rd week. She improved after plasmapheresis but refused gemfibrozil therapy. Four weeks later pancreatitis recurred (serum triglyceride: 4382mg/dL), she was put on gemfibrozil and regular plasmapheresis was planned to prevent recurrences. Plasmapheresis was performed 8 times between 28th and 35th weeks with intervals based on triglyceride levels. The mean decrease in triglyceride was 62%. She gave birth to a healthy female infant at 35th+3/7 week (Apgar 1.min: 8, 5.min:10; weight: 2470gr).

Second patient was a 24-year-old woman with untreated hypertriglyceridemia who presented with acute pancreatitis (serum triglyceride: 1268mg/dL) at 23rd gestational week. The pancreatitis resolved without complications following plasmapheresis. Gemfibrozil therapy (1200mg/day) and fish oil were started and serum triglyceride levels remained around 1054-1381mg/dL. Five weeks later, pancreatitis recurred (serum triglyceride:3069mg/dL) and plasmapheresis on a 2-week-basis was applied until delivery. She did not experience pancreatitis thereafter and gave birth to a healthy female infant at 39th+4/7 week (Apgar 1.min:8, 5.min: 10; weight: 3230gr).

Conclusion: Regular plasmapheresis may be an option for unique cases such as pregnant patients with familial hypertriglyceridemia to prevent recurrent pancreatitis.

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