



Maternal Thyroid and Glucocorticoid Hormone Interactions in Larval Fish Development, and Their Applications in Aquaculture

Christopher L. Brown, Elisabeth Criscuolo Urbinati, Weimin Zhang, Shannon B. Brown & Michelle McComb-Kobza

To cite this article: Christopher L. Brown, Elisabeth Criscuolo Urbinati, Weimin Zhang, Shannon B. Brown & Michelle McComb-Kobza (2014) Maternal Thyroid and Glucocorticoid Hormone Interactions in Larval Fish Development, and Their Applications in Aquaculture, Reviews in Fisheries Science & Aquaculture, 22:3, 207-220, DOI: [10.1080/23308249.2014.918086](https://doi.org/10.1080/23308249.2014.918086)

To link to this article: <http://dx.doi.org/10.1080/23308249.2014.918086>



© 2014 Christopher L. Brown, Elisabeth Criscuolo Urbinati, Weimin Zhang, Shannon B. Brown, and Michelle McComb-Kobza.



Published with license by Taylor & Francis©
Christopher L. Brown, Elisabeth Criscuolo Urbinati, Weimin Zhang, Shannon B. Brown, and Michelle McComb-Kobza



Submit your article to this journal [↗](#)



Article views: 766



View related articles [↗](#)



View Crossmark data [↗](#)

Maternal Thyroid and Glucocorticoid Hormone Interactions in Larval Fish Development, and Their Applications in Aquaculture

CHRISTOPHER L. BROWN,¹ ELISABETH CRISCUOLO URBINATI,² WEIMIN ZHANG,³ SHANNON B. BROWN,⁴ and MICHELLE McCOMB-KOBZA⁵

¹Aquaculture and Enhancement Division, NOAA, NEFSC, Milford, Connecticut, USA

²Centro de Aquicultura, Universidade Estadual Paulista (CAUNESP), Jaboticabal, Sao Paulo, Brazil

³Institute of Aquatic Economic Animals, School of Life Sciences, Sun Yat-Sen University, Guangzhou, PR China

⁴Department of Biological Engineering, University of Florida, Gainesville, Florida, USA

⁵Teens4Oceans, Boulder, Colorado, USA

Thyroid hormones (THs) have long been known to have regulatory roles in the differentiation and maturation of vertebrate embryos, beginning with the knowledge that hormones of maternal origin are essential for human fetal central nervous and respiratory system development. Precise measurements of circulating THs led to insights into their critically important actions throughout vertebrate growth and development, initially with amphibian metamorphosis and including embryogenesis in fishes. Thyroid cues for larval fish differentiation are enhanced by glucocorticoid hormones, which promote deiodinase activity and thereby increase the generation of triiodothyronine (T_3) from the less bioactive thyroxin (T_4). Glucocorticoids also induce the expression of thyroid hormone receptors in some vertebrates. Maternally derived thyroid hormones and cortisol are deposited in fish egg yolk and accelerate larval organ system differentiation until larvae become capable of endogenous endocrine function. Increases in the T_3/T_4 ratio during larval development may reflect the regulatory importance of maternal thyroid hormones. Experimental applications of individual hormones have produced mixed results, but treatments with combinations of thyroid and corticoid hormones consistently promote larval fish development and improve survival rates. The developmental and survival benefits of maternal endocrine provisioning are increased in viviparous fishes, in which maternal/larval chemical contact is prolonged. Treatments with exogenous thyroid and corticoid hormones consistently promote development and reduce mortality rates in larval fishes, with potential hatchery-scale applications in aquaculture.

Keywords thyroid, larvae, embryo, maternal, cortisol

INTRODUCTION

Thyroid hormones (THs) are recognized not only as the main determinant of metabolic rate in homeotherms, but also as primary signals for the regulation of diverse growth and developmental and maturational processes throughout the

vertebrates. Our initial understanding of the actions of THs was based almost entirely on human pathology and physiology, and the familiar and devastating pathological effects of acute thyroid deficiencies in cases of goiter and cretinism. A comparative perspective emerged with the technology for precise quantification of circulating hormones, and critically important morphogenic roles of THs among the vertebrates became apparent. These morphogenic actions evolved in fishes and they are essential to successful embryogenesis.

The first clear link between thyroid function and metamorphosis was reported by Gudernatsch (1912), who described a simple bioassay in which feeding various

© Christopher L. Brown, Elisabeth Criscuolo Urbinati, Weimin Zhang, Shannon B. Brown, and Michelle McComb-Kobza

Address correspondence to Christopher L. Brown, Aquaculture and Enhancement Division, NOAA, NEFSC, 212 Rogers Avenue, Milford, CT 06460, USA. E-mail: Christopher.L.Brown@noaa.gov

mammalian thyroid gland tissues to *Rana* sp. tadpoles produced “extremely small (pigmy-) frogs.” Thyroid-dependent developmental actions extend well beyond the regulation of amphibian metamorphosis and a role in cretinism, and most morphogenic actions of thyroid hormones are far less dramatic than Gudernatch’s (1912) “maturational” effects. Milder transitions, e.g., larval metamorphoses among a majority of fishes, are also controlled by THs (reviewed by Power et al., 2001), as are a range of developmental and growth effects among vertebrates. The maturational actions of THs include the promotion of growth and development by way of hypertrophy and hyperplasia as well as the reorganization of tissues resulting in differentiation. Many of the actions of THs are closely associated with reproduction and embryogenesis.

Serious risks to the offspring of hypothyroid mothers are recognized, and hormone replacement treatment is customary (Lebeau and Mandel, 2006). The human maternal endocrine contribution is viewed as “critical for proper *in utero* brain development” (Howedshell, 2002). Routine screening of pregnant human subjects for adequate thyroid function began in the early 1970s (Dussault, 1999). Maternal thyroid activity is enhanced during human embryogenesis, partly in response to a thyrotropic action of Human Chorionic Gonadotropin (HCG) during pregnancy (Fantz et al., 1999). Human fetal central nervous system (CNS; Haddow et al., 1999) and respiratory tract (e.g., see Rajatapiti et al., 2005) differentiation are among processes in human development that are directly dependent on maternal thyroid contributions. Thyroid hormone receptors (THRs) enable early human embryos to respond to maternal thyroid hormones before fetal thyroid hormone production has begun (Patel et al., 2011). Incidental elevations of circulating maternal THs in pregnant sheep result in changes of the texture and color of wool in the resultant lambs (Kenyon et al., 2004). Elevated maternal circulating levels of thyroxin (T_4) during human pregnancy provide vital support to healthy human embryo differentiation before endogenous fetal hormone production begins, and a suite of placental deiodinases ensures fetal provision of essential THs by even mildly hypothyroidal mothers, as well as protection of the fetus against exposure to excessive quantities (Burrow et al., 1994). The practice of clinical hormone replacement therapy for premature infants also underscores the early developmental importance of maternal endocrine contributions. The effectiveness of treatment of premature infants with T_4 or triiodothyronine (T_3) alone was challenged by various investigators who noted that thyroid hormone applications did not consistently improve survival or correct problems associated with respiratory distress syndrome (see Osborn, 2001; Farwell, 2008). This may have been at least partly a result of the absence of permissive actions imparted by glucocorticoids; the combined effectiveness of thyroid and corticoid hormones administered together is well established (Smith and Sabry, 1983). This combination of treatments is

routinely used to promote lung maturation and surfactant production in preterm babies (see Ballard, 1980).

THYROID HORMONE SYNERGISM WITH CORTISOL IN FISH DEVELOPMENT

A possible significance of THs in early fish growth and development was implied by the acute responsiveness of very young fish to antithyroid drugs and hormone supplementation treatments (reviewed by Youson, 1988; Brown and Bern, 1989; Dickhoff et al., 1990). The sensitivity of newly hatched fish to THs was reported by Lam and others who found that T_4 treatment accelerated development and larval metamorphosis, and increased survival rates (Lam, 1980; Lam, 1985; Lam and Sharma, 1985). Also, in a role similar in many ways to the endocrine regulation of anuran metamorphosis, thyroid signals initiate some developmental changes later than the larval-to-juvenile metamorphosis, such as the transition of upright-swimming larval flatfishes into asymmetrical juveniles beginning after the completion of yolk absorption (Tagawa et al., 1991; Inui et al., 1994). By the time of metamorphosis in flatfishes, maternal hormones stored in yolk have been fully depleted and the larval pituitary/thyroid axis has attained functionality (De Jesus et al., 1991). Metamorphic climax among the flatfishes bears strong similarities to the events seen in amphibian metamorphosis (see Miwa et al., 1988; Tagawa et al., 1991). The regulation of smolting in salmonids is also controlled in part by thyroid system signals (see Robertson, 1949; Miwa and Inui, 1985). Early perceptions of the role of THs in development have been confounded by a history of contradictory reactions to exogenous thyroid compounds; some cases of aberrant development are associated with higher hormone doses (see Table 1) and other negative responses remain unexplained.

Physiological effects of cortisol on thyroid-mediated processes in fishes are more than additive, or synergistic (Ban, 2005). A synergistic action of cortisol and THs has been identified in flatfish metamorphosis (De Jesus et al., 1990; De Jesus et al., 1991), and a close interaction of the two endocrine systems is also seen in the promotion of amphibian metamorphosis (Krug et al., 1983). An emerging view of glucocorticoid signaling is that it not only enables important vertebrate organ systems to respond to THs through synergistic actions, as in amphibians, but that surging glucocorticoid secretions facilitate major transitions within a life cycle, serving a preparatory and synchronizing role in organisms approaching a major change to the next life history stage (Wada, 2008).

In some cases, cortisol treatment results in increases in thyroid hormone activity by increasing the generation of T_3 (Redding et al., 1991). Thyroxin is generally viewed as a thyroid system *prohormone* (Kühn et al., 1994), in which thyroid-mediated endocrine activity is determined largely by the action of peripheral deiodinase enzymes. Peripheral outer ring deiodination converts T_4 into 3,5,3'-triiodothyronine, or T_3 , which

Table 1 Effects of treatment with exogenous thyroid hormones on embryonic/larval fish development

Species	Hormone treatment, dose actions reported	Authors
Chum Salmon (<i>Oncorhynchus keta</i>)	Immersion T ₄ , 0.08–0.4 ppm Accelerated but disproportionate growth and pigmentation	Dales and Hoar, 1954
Chum Salmon (<i>Oncorhynchus keta</i>)	Immersion T ₄ , 1 ppm Reduced weight, physical deformities	Honma and Murakawa, 1955
Chum Salmon (<i>Oncorhynchus keta</i>)	Immersion T ₄ , 0.08 ppm Early hatch	Ali, 1961
Brown trout (<i>Salmo trutta</i>)	Immersion T ₄ , 1.0–10 ppm Rapid differentiation, morphological abnormalities	Woodhead, 1966
Mozambique tilapia (<i>Sarotherodon mossambicus</i>)	Immersion T ₄ , 0.1 ppm Accelerated development and ↑ % survival	Lam, 1980
Mozambique tilapia (<i>Sarotherodon mossambicus</i>)	Immersion T ₄ , 0.1–0.5 ppm Accelerated growth, ↑ % deformities at higher T ₄ doses	Nacario, 1983
Olive flounder (<i>Paralichthys olivaceus</i>)	Immersion T ₄ , 0.01–0.1 ppm Induced metamorphosis	Inui and Miwa, 1985 Miwa and Inui, 1987
Common carp (<i>Cyprinus carpio</i>)	Immersion T ₄ , 0.01, 0.05, 0.1 ppm Improved hatch rate, ↑ % survival	Lam and Sharma, 1985
Milkfish (<i>Chanos chanos</i>)	Immersion T ₄ , 0.5 ppm Accelerated development	Lam et al., 1985
Guppy (<i>Poecilia reticulata</i>)	Immersion T ₄ , 0.5 ppm Shortened brood interval w/intact offspring	Lam and Loy, 1985
Olive flounder (<i>Paralichthys olivaceus</i>)	Immersion T ₄ , 0.01–0.1 ppm Induced metamorphosis	Miwa and Inui, 1987
Striped bass (<i>Morone saxatilis</i>)	Maternal injection T ₃ 20 μg/gbw Improved growth, ↑ % swimbladder inflation, ↑ % survival	Brown et al., 1988a,b
Goldfish (<i>Carassius auratus</i>)	Immersion T ₃ , 0.01–0.02 ppm, T ₄ , 0.01–0.1 ppm Faster fin differentiation, growth and development	Reddy and Lam, 1992a
Mozambique tilapia (<i>Oreochromis mossambicus</i>)	Immersion T ₃ , 0.01 ppm, T ₄ , 0.05 ppm Fin differentiation, deformities at highest dose	Reddy and Lam, 1992b
Rabbitfish (<i>Siganus guttatus</i>)	Maternal T ₄ injection, 1, 10, 100 μg/gbw Improved growth, ↑ % survival	Ayson and Lam, 1993
Brown trout (<i>Salmo trutta</i>)	Maternal T ₃ injection, 20 mg/kg ↑ % skeletal abnormalities	Mylonas et al., 1994
Striped bass (<i>Morone saxatilis</i>)	Immersion T ₃ , 0.05–0.1 ppm At higher dose: ↓ growth, ↓ % survival	Huang et al., 1996
Zebrafish (<i>Danio rerio</i>)	Immersion T ₃ , 5 nM (.003 ppm) T ₄ 30 nM (.02 ppm) Accelerated fin development	Brown, 1997
Amberjack (<i>Seriola lalandi</i>)	Maternal injection T ₃ , 20 mg/kgbw Survival more than doubled	Tachihara et al., 1997
Korean rockfish (<i>Sebastes schlegeli</i>)	Maternal injection T ₃ , 20 mg/kgbw Increased growth, ↑ % survival	Kang and Chang, 2004
Goldfish (<i>Carassius auratus</i>)	Feeding T ₃ , 1.25–6.25 ppm Increased growth, disease resistance	Swain and Sahoo, 2003
Piracanjuba (<i>Brycon orbignyanus</i>)	Immersion T ₃ , 0.01, 0.05, 0.1, 0.5, 1 ppm, ↑ % survival-reduced cannibalism	Landines et al., 2010
Zebrafish (<i>Danio rerio</i>)	Immersion T ₃ , 5 nM = .003 ppm Accelerated pigmentation and ↑ % hatching	Walpita et al., 2007
Matrinxã (<i>Brycon amazonicus</i>)	Maternal injection T ₃ , 10–20 mg/kg Immersion, 0, 0.01, 0.05, 0.1 mg/L Improved growth, ↓ % abnormalities	Urbinati et al., 2008
Nile tilapia (<i>Oreochromis niloticus</i>)	Maternal injection T ₄ , 1 or 10 μg/g Increased growth, rapid development, ↑ % survival	Khalil et al., 2011

is an order of magnitude more biologically potent than T₄ (Orozco and Valverde, 2005). Cortisol promotes the conversion of T₄ into T₃ by activating outer ring deiodinase activity (Vijayan et al., 1988; Arjona et al., 2011), and increasing the T₃/T₄ ratio is one mechanism by which cortisol promotes thyroid-mediated processes. Ontogenetic patterns in developing fishes that reflect this relationship can be seen in the golden

sea bream, *Sparus aurata*; increasing cortisol levels are accompanied by a sharp increase in the ratio of T₃/T₄ late in larval development, resulting in significant physiological and morphological changes (Szisch et al., 2005). Concurrent elevations of T₃, T₄ and cortisol also precede the larval-to-juvenile transition in the silver sea bream, *S. sarba* (Deane and Woo, 2003). Whole body cortisol content increases as

numerous species of larval fishes approach the transition into juvenile forms, possibly to coordinate various events (Wada, 2008), in some cases by synergizing with thyroid hormones (Hwang et al., 1992; Tanaka et al., 1995). Sudden increases in T_3/T_4 ratios coincident with transitions from the larval to juvenile stage have been observed (e.g., see Nayak et al., 2001; McComb et al., 2005), which may or may not reflect glucocorticoid synergism in thyroid-driven developmental actions.

The acute responsiveness of very young larval fishes to THs seemed paradoxical or artifactual for a number of years, since those cases often revealed hormone-sensitivity in animals that had not yet developed functional pituitary/thyroid axes (Mommsen and Walsh, 1988). Hormone radioimmunoassays of yolk extracts revealed the presence of ample amounts of T_4 and T_3 in unfertilized fish eggs (Kobuke et al., 1987; Brown et al., 1987; Tagawa and Hirano, 1987). Maternal deposition of hormones in yolk raises the possibility of maternal/larval endocrine communication in early development in oviparous fishes (Mommsen and Walsh, 1988). Thyroid hormones of maternal origin have been found in unfertilized eggs consistently among oviparous vertebrates, suggesting maternal provisioning and a mechanism of delivering regulatory signals to developing embryos long before the onset of endogenous thyroid competence. Circulating THs in pre-spawning female rabbitfish (*Siganus guttatus*) accumulate in oocytes during vitellogenesis, resulting in improved larval performance and survival (Ayson and Lam, 1993). Developmental research using zebrafish (*Danio rerio*) as a model confirms thyroid stimulation of various processes of fin, scale, and pigment differentiation in this species (Brown, 1997). Goldfish respond in similar ways to exogenous THs, with improvements in fin, skin, and scale development, growth, and resistance to challenges with pathogens (Reddy and Lam, 1992a; Shinobu and Mugiya, 1995; Swain and Sahoo, 2003). Other maternal hormones, especially small steroid molecules such as cortisol are also found in the yolk of unfertilized fish eggs (reviewed by Tagawa, 1996; Brooks et al., 1997) and may be necessary for permissive or other effects. Interactive and sometimes synergistic effects of thyroid and corticoid hormones in larval fish development (Table 2) are consistent with the concept of combinations of maternal signals interacting to coordinate and promote developmental processes in young fishes, increasing the likelihood of larval survival. Maternally derived cortisol and testosterone deposited in yolk interact in the regulation of growth and development in larval damselfishes (McCormick, 1999). Combined treatments with supplemental TH and cortisol consistently accelerate digestive system ontogeny (Kim and Brown, 2000; Nayak et al., 2000a) and swimbladder function, resulting in reduced rates of mortality of larval fishes (Kim and Brown, 1997; Sri Prudi et al., 2002; Nayak et al., 2003).

Extensive evidence implicates THs in the regulation of various aspects of growth (see reviews by Donaldson et al., 1979; Power et al., 2001). A majority of the studies mentioned above indicate that exogenous THs stimulate or accelerate

development and result in enhanced survival in larval fishes. Some species are unresponsive or have very limited responses to alterations of thyroid hormone levels alone (Tagawa and Hirano, 1990; Witt et al., 2009) or show detrimental effects of exogenous THs (see Table 1; Higgs et al., 1982; Huang et al., 1996). Hormone interactions (e.g., low levels of permissive compounds), species differences and dose-dependency may account for some inconsistencies in the responses of larvae to exogenous THs. Among species differences, untoward effects of exogenous THs are often seen in fishes with large eggs, high survival rates, and presumably ample supplies of maternal THs, such as the salmonids (see Mylonas et al., 1994). Overstimulation of skin, bone, and scale development by higher doses of THs in post-larval stages may partially explain their capacity to induce deformities (Karg, 2007). Some deformities may be caused by the promotion by exogenous hormones that regulate developmental processes when the timing of exposure or sensitivity is skewed or when ample amounts of required materials are unavailable (Brown et al., 2010). Similarly, treatment of larval tilapia with cortisol alone promotes growth and development inconsistently and in a dose-related fashion (Mathiyalagan et al., 1996). Under some conditions, treatment with exogenous cortisol alone improves the survival rate of larval Asian seabass, *Latifes calcarifer*, by undetermined mechanisms (Sampath-Kumar et al., 1993).

THE PITUITARY/THYROID AXIS AND MOLECULAR MECHANISMS IN DEVELOPMENT

The presence of THs and cortisol has been reported in fish at all developmental stages beginning in unfertilized eggs (see Brooks et al., 1997; Szisch et al., 2005), and stimulation by endocrine compounds during embryogenesis and organogenesis appears to be of vital importance. Ontogenetic studies of endocrine functions suggest that the maternal endocrine contributions to offspring sustain fish through the earliest of developmental stages, beginning with fertilization, before developing embryos have acquired endocrine competence. One apparent cascade of actions in oviparous fishes begins with maternal deposition of cortisol and THs in egg yolk, resulting in the promotion of deiodinase activity and THR expression by cortisol, and induction by THs of growth factors in developing embryos leading to accelerated differentiation. The central nervous system, digestive tract, skin, fins, and swimbladder appear to be targets for endocrine stimulation of development. Although some authors conclude that the physiological significance of maternally derived cortisol in fish eggs is uncertain, it appears likely that permissive or synergistic actions of corticoids in thyroid-regulated processes may be of adaptive value (Brooks et al., 1997). Very early contributions of maternal THs to larval differentiation and survival are confirmed by the presence of thyroid hormone receptors (THR) long before endogenous thyroid hormone synthesis begins; several isoforms are expressed from the very first

Table 2 Effects of combined thyroid hormone (T₃ or T₄)/cortisol (F) treatment on larval fish development

Hormones, dose species	Actions reported	Authors
Japanese flounder (<i>Paralichthys olivaceus</i>)	T ₃ or T ₄ 0.001–1.0 + F 0.1 ppm Earlier fin ray resorption	De Jesus et al., 1990
Pacific threadfin, or <i>moi</i> (<i>Polydactylus sexfilis</i>)	T ₃ 2.6 ppm + F 0.1 ppm Earlier initial gut function	Brown and Kim, 1995
Pacific threadfin, or <i>moi</i> (<i>Polydactylus sexfilis</i>)	T ₃ 2.6 ppm + F 0.1 ppm Earlier gut formation, ↑ % survival, ↓ deformities	Kim and Brown, 1997
Pacific threadfin, or <i>moi</i> (<i>Polydactylus sexfilis</i>)	T ₃ 2.6 ppm + F 0.1 ppm Enhanced & earlier digestive enzyme expression	Kim and Brown, 2000
Indian carp (<i>Catla catla</i> Ham.)	T ₄ 2.6 ppm + F 0.1 ppm Earlier yolk absorption, gut & swimbladder formation	Nayak et al., 2000a
Indian catfish (<i>Heteropneustes fossilis</i>)	T ₄ 2.6 ppm + F 0.1 ppm Earlier yolk absorption & gut formation, ↑ % survival	Nayak et al., 2000b
Sand goby (<i>Oxyeleotris marmorata</i> Blkr.)	T ₃ 2 ppm + F 1 ppm Improved swimbladder formation, ↑ % survival	Sri Pudju et al., 2002
Indian catfish (<i>Heteropneustes fossilis</i>)	T ₄ 0.05 ppm + F 0.5 ppm ↑ % hatch, early yolk abs., ↓ deformities, ↑ weight, ↑ % survival	Nayak et al., 2003

stages of development in zebrafish (Darras et al., 2011). Genes encoding the TR α 1 thyroid hormone receptor (TR) begin expression in zebrafish zygotes about 3 hr post-fertilization (Essner et al., 1997), suggesting that hormone responsiveness is an urgent embryonic need. The detection of THR long before the onset of larval thyroid function in zebrafish has led to some doubt of the physiological role of hormone-receptor endocrine signaling in early development (Essner et al., 1997; discussed by Power et al., 2001), but zebrafish embryos have (Walpita et al., 2007) and are capable of responding to THs of maternal origin (Darras et al., 2011).

Unfertilized zebrafish eggs contain maternally derived THR transcripts, followed by early zygotic transcription of TR and TR mRNA (Liu and Chan, 2002; Walpita et al., 2007). Maternal provisioning of egg yolk in the zebrafish also includes cortisol, and experimental interference with the response of zebrafish embryos to glucocorticoids leads to reduced growth, impaired organogenesis, and increases in the rate of mortality (Nesan, 2013). The possible interdependence of cortisol and THs in larval fish development is supported by the maternal provisioning of both groups of hormones in egg yolk and their synergistic actions when applied together experimentally (Table 2). Significant cross-talk between interrenal and thyroid systems may be characteristic of early teleost development, with synergistic promotion by glucocorticoids of the expression of THR and the stimulation of peripheral deiodinases (De Nayer et al., 1987; Terrien and Prunet, 2013). These two mechanisms are at least partly responsible for the synergy of corticosteroids with TH during tadpole metamorphosis (Bonett et al., 2010).

The evolutionary implications of the sensitivity of larval fishes to maternal hormones are profound. Subtle effects of early exposure to maternal hormones on the dynamics of developmental processes include not only improved survival, but also altered trajectories of developmental patterns, with disproportionately large impacts throughout later

developmental stages and substantial evolutionary consequences (Bernardo, 1996). Beneficial effects of maternal investment on development and consequently on larval survival (Brown et al., 1988a,b; Chambers and Leggett, 1996) can have a considerable impact on year-class size through the attainment of reproductive capability (Leggett and Deblois, 1994). Early thyroid-driven events among teleosts led one group of authors to conclude that “even a slight change in activity of the thyroid axis during ontogeny can be the cause of wide morphological variability. . . and may underlie explosive diversification of the species” (Shkil et al., 2010, p. 369).

It is not known whether patterns of maternal signaling may influence behavior in a lasting manner, comparable to the apparent effects on physiology and morphology, although some adaptive behavioral effects of maternal cortisol signals to young fishes and other vertebrates have been described. Female sticklebacks (*Gasterosteus aculeatus*) responded to pre-spawning exposure to simulated threats of predation by producing enlarged eggs with elevated cortisol content (Geising et al., 2010). Enlarged, cortisol-enriched eggs produced fry that showed potentially adaptive physiological and behavioral effects, interpreted by these authors as a maternal signal imparting improved fitness to fry by pre-adapting offspring to a sub-optimal environment (Geising et al., 2010). Exposure of gravid damselfish, *Pomacentrus amboinensis*, to competitors or predators caused elevations in plasma cortisol, with potentially adaptive influences on larval size and quality (McCormick, 1998). Maternal stress in an oviparous lizard, *Lactera vivipara*, increases the corticosteroid content of eggs. Experimental increases of egg content of corticosterone in this species result in altered, apparently adaptive patterns of predator-avoidance behavior in the resultant offspring (Uller and Olsson, 2006).

Insulin-like growth factors 1 and 2 (IGF-1 and IGF-2) are mitogenic factors, which play important roles in growth and development in vertebrates (Jones and Clemmons, 1995)

including teleosts (Wood et al., 2005). The presence of IGFs and their receptors has been demonstrated during early development of fish (Greene and Chen, 1997, 1999). Although lacking direct evidence at present, there exists a possibility that some cortisol and thyroid hormone mediated developmental actions may be transduced by IGF signals, at least partly, to regulate embryogenesis in teleosts.

Both IGF-1 and IGF-2 are expressed in the unfertilized eggs and embryos of gilthead seabream (Funkenstein et al., 1996) and rainbow trout (Greene and Chen, 1997), whereas only IGF-2 mRNA was detected in rabbitfish unfertilized eggs and embryos during the cleavage stage, and IGF-1 mRNA was first detected in the larvae soon after hatching (Ayson et al., 2002). These results suggest that the roles of IGF-2 in fish embryogenesis may be crucial and conserved as in mammals (Dechiara et al., 1990). Cortisol suppression of IGF-1 expression seems to be conserved in teleosts, but in hepatocytes of coho salmon (Pierce et al., 2010) and tilapia (Pierce et al., 2011) cortisol was shown to up-regulate IGF-2 mRNA levels, either directly or via enhanced Growth Hormone (GH) response. In rainbow trout embryos reared from cortisol-enriched oocytes, however, IGF-1 expression was significantly enhanced from the zygote to 21-days post-fertilization (dpf) embryos and IGF-2 was enhanced in the 21-dpf embryos (Li et al., 2010). These results suggest that the regulation of IGF expression by cortisol may be different in fish embryos from that in adults, and cortisol may act via IGF-1 and/or IGF-2 signals to regulate embryogenesis.

Insulin-like growth factors (IGF) expression is promoted by thyroid hormones in fish. Hepatic IGF-1 mRNA expression was stimulated either by T₃ in tilapia (Schmid et al., 2003) and zebrafish (Wang and Zhang, 2011) or by T₄ in sea bream (Leung et al., 2008). Tissue remodeling during metamorphosis in the Atlantic halibut (*Hippoglossus hippoglossus*) is mediated by endocrine changes involving both THs and IGF-1 (Hildahl et al., 2008). However, the basal and GH-stimulated IGF-2 expression was suppressed by T₃ in salmon hepatocytes (Pierce et al., 2010). The above studies in fish adults suggested that hepatic IGF-1 and IGF-2 are inversely and differentially regulated by cortisol and THs. However, in fish embryos, the regulation of IGF-1 and IGF-2 by cortisol and particularly by THs is poorly understood, and worthy of further study.

RELATEDNESS OF THYROID AND REPRODUCTIVE ENDOCRINE SYSTEMS

The connection between thyroid signaling and embryo competence does not appear to be coincidental. It has been suggested that the regulation of reproduction and thyroid function are evolutionarily intertwined (reviewed by Cyr and Eales, 1996). Several lines of evidence point to the interrelatedness of these two endocrine systems, starting with chemical and functional similarities in adenohypophysial compounds in fish. The alpha sub-units of hypophysial glycoproteins

thyrotropin (TSH) and leuteotropic hormone (LH) are identical, with considerable overlap and systemic interaction in their actions (see Norris, 2007); both come from histologically indistinguishable pituitary basophil cells and function by way of cAMP-dependent second messenger systems. Differing functional activities among this related family of glycoprotein hormones are conferred by distinct beta subunits, encoded by different genes than the shared alpha subunits (Szkudlinski et al., 2002). Prevailing opinions are that these regulatory hormones arose from a series of gene duplications, with considerable conservation of structural and biochemical characteristics (Wallis, 2010). The elaboration of hypophysial glycoproteins (TSH, LH, FSH) appears to have begun with an ancestral hormone in the cyclostomes, probably with gonadotropic function (Kawauchi and Sower, 2006).

A consistent functional link has persisted between cyclic changes in thyroid and gonadal activities in modern fishes. Although fishes exhibit innumerable reproductive strategies, a pattern of increased thyroid hormone activity during early to peak oogenesis is consistently seen among diverse female fishes (Cyr and Eales, 1996).

Transfer of maternally derived corticoid hormones to fish eggs reportedly has a mix of beneficial and harmful effects on embryogenesis. It is possible that adaptive acceleration of organogenesis contingent on transient endocrine effects including thyroid/corticoid synergism may give way to damaging effects of relatively higher or more prolonged, dose-dependent maternal signals during longer-term stress. Prolonged elevations of cortisol in rainbow trout (*Oncorhynchus mykiss*) under chronic stress resulted in compromised larval fitness (Campbell et al., 1992, 1994).

MATERNAL HORMONES IN ELASMOBRANCH REPRODUCTION, AND THE EVOLUTION OF VIVIPARITY

The reproductive strategies of elasmobranchs (sharks, skates, and rays) are subject to tremendous diversity, with oviparity being the most ancestral mode and the one found in all skates and a minority of sharks. Viviparity is the predominant mode; live birth is found in 55% of chondrichthyan fishes and in 70% of shark species (245–270 species). There are 270 viviparous ray species, which include stingrays, guitarfish, electric rays, and the sawfish. In contrast, only 2–3% of bony fish are viviparous. Viviparity has evolved from oviparity on as many as 18 separate occasions (Wourms and Lombardi, 1992).

The evolution of viviparity in elasmobranchs has resulted in lecithotrophic and matrotrophic modes. Yolksac viviparity involves retention of eggs inside the female until fully developed with no maternal chemical contribution beyond yolk. This is the most widespread mode in elasmobranchs and confers adaptive advantages over the vulnerabilities inherent in egg deposition. There are matrotrophic modes including histotrophy, in which yolk stores are supplemented with maternal

proteins and lipid-rich histotroph secreted directly from the uterus, and oophagy in which embryos continually ingest unfertilized eggs. The most highly derived form of matrotrophic viviparity is the placental association in which embryonic yolk sacs eventually become depleted and differentiate into the fetal portion of placentas, providing direct humoral exchange with the maternal circulation (Wourms and Demski, 1993). Prolonged exposure to yolk followed by direct humoral exchange via placentae enables plasticity in maternal contributions of development-promoting hormones (Hamlett, 1993).

Progesterone has been identified as a potential driver as it inhibits myomertrial contractions preventing egg laying while also inhibiting vitellogenin synthesis necessary for yolk production driving placental evolution (Callard et al., 1992). Thyroid hormone roles in elasmobranch reproduction and early development have been studied in a limited number of sharks and rays. Thyroxin levels have been correlated with reproductive status in the Atlantic stingray, *Dasyatis sabina* and the placental viviparous bonnethead shark, *Sphyrna tiburo* (Volkoff et al., 1999; Gash, 2000). Levels of T_4 and T_3 follow a pattern of variation in the maternal serum and yolk of *S. tiburo* during pre-ovulatory, ovulatory, and early gestation stages, with highest TH levels in serum and yolk occurring concurrently during the gravid state nearing implantation. Embryonic *S. tiburo* show indications of endogenous TH synthesis later, as yolk stores approach depletion (McComb et al., 2005). Significant increases were seen in T_3/T_4 ratios later in pregnancy. It is possible that early endogenous TH synthesis could be supplemented by absorption of maternal TH diffusing into the yolk as a later component of maternal endocrine provisioning. Levels of corticosterone were determined in the freshwater stingray, *Potamotrygon cf. hystrix* (Brinn et al., 2012) and in a separate study levels of T_4 , T_3 , and corticosterone were determined in the serum and yolk of several freshwater ray species. A nearly nine-fold increase was found in the glucocorticoid concentration of uterine fluids that bathed the developing embryos as compared to yolk and maternal serum levels, suggesting that these maternal fluids provide a means of continuous and modulated transfer of development promoting hormones. These fluids also contained T_3 and T_4 presumably of maternal origin (M. McComb-Kobza, Teens4Oceans, unpublished data).

Continuous access to maternal endocrine signals imparts profound developmental and survival advantages. This, together with prolonged nourishment and physical protection appears to be a strong suite of drivers behind the repeated evolution of viviparity as a reproductive strategy.

AQUACULTURE APPLICATIONS OF THYROID AND CORTICOID HORMONES

Increasing recognition of the importance of hormones for growth and differentiation of embryos was identified as a central theme of “the new endocrinology” (Bern, 1990, 1992).

Overlapping roles of hormones and growth factors are critically important in early embryogenesis, especially with the knowledge that maternally derived regulatory compounds are transferred to and stored in yolk and active from the earliest stages of development (de Pablo and Roth, 1990). Maternal compounds are supplemented by *de novo* embryonic mRNAs beginning in extremely early developmental stages, possibly directing tissue remodeling and differentiation processes as paracrine/autocrine factors (Sanders and Harvey, 2008).

Aquaculture management is an effort to optimize aquatic animal development, growth, survival, and reproduction under artificial conditions. Aquaculture as a production system has inherent biological advantages and disadvantages in comparison with wild fisheries; hatchery production often imposes artificially high densities and simplified nutrition parameters to which some species respond more favorably than others. The agrarian approach to fish relies on enhanced survival and accelerated growth, as compared with the survival of an orders-of-magnitude smaller percentage of wild fishes to reproductive age. Nutrition can be controlled and predation and environmental contamination can be regulated or eliminated in aquaculture settings. The reproductive strategy of the culture subject is a major source of variation in the selection and development of culture methods. Freshwater fishes generally produce larger eggs with a higher probability of hatching and survival (by about tenfold; Rao, 2003). Among marine species that produce large numbers of tiny pelagic eggs, with smaller yolk reserves and less maternal investment per individual egg (often described as *r-selected*) the larvae are consequently small and fragile and rearing them in the hatchery is technically challenging. Most of the species exhibiting increased survival in response to exogenous hormones fit in this category and could be characterized as pelagic spawners that produce large numbers of small, delicate larvae that would normally be subject to high rates of mortality. It is noteworthy that early feeding is among the most problematic of larval rearing issues among these fishes, and that the GI tract, fins, and swimbladder are repeatedly observed to be among targets of exogenous TH (see Tables 1 and 2). Demersal spawning involves a smaller number of larger eggs, and with a higher probability of survival—a reproductive strategy that has been viewed as a preliminary form of parental care (Duarte and Alcaraz, 1989).

The substitution of formulated feeds for natural diets can have endocrine consequences; e.g., Atlantic halibut (*Hippoglossus hippoglossus*) larvae fed *Artemia* have a hypothyroid status compared with larvae that eat wild zooplankton; *Artemia* has relatively poorer iodine content, resulting in elevated frequencies of incomplete and problematic halibut metamorphoses (Solbakken et al., 2002). *Artemia* enriched with iodine impart thyroid-mediated advantages to developing fish (Hawkyard et al., 2011). Further complicating the endocrine implications of aquaculture feeds is the confirmation that *Artemia* synthesize and store both T_4 and T_3 (see Hawkyard et al., 2011). Fishmeal-based aquaculture diets also contain T_4 ,

among other hormones (Feist and Schreck, 1990). Dietary ingestion of T_4 —including the consumption of *Artemia*—can induce negative feedback, leading to reduced TSH secretion, resulting in both reduced thyroid hormone production and decreased deiodination of T_4 into T_3 (Conti et al., 1978).

The use of thyroid and glucocorticoid hormones to promote survival in larval fishes for food production is subject to stringent and somewhat complicated regulation in the USA; both Food and Drug Administration (FDA) approval and Environmental Protection Agency (EPA) compliance are required (Johnson and Bosworth, 2012). Hormone use in food production arouses popular concerns, in part because hormone applications are popularly associated with patterns of misuse and with anabolic and secondary sex disfigurement. Public perceptions of hormone use in the food industry are often poorly distinguished from heavy and at times abusive antibiotic and steroid use in the meat industries, or with the production of genetically modified organisms. Because consumer-oriented publications strongly encourage the public to avoid meat products of animals exposed to antibiotics, negative associations with hormone use have accelerated (e.g., see Bohne and Halloran, 2012). The Food and Agriculture Organization of the United Nations concludes that the general public's acceptance of aquaculture products is affected by perceptions of chemical hazards that can be far out of proportion to real health or environmental risks (FAO, 1997).

In addition to a resistance by popular opinion, chemical use by aquaculture farms is also under stringent governmental regulation because, relative to meat industries, it is a relatively new practice and the potential for contamination of surrounding bodies of water is more significant (FAO, 1997). Producers must closely monitor hormone levels in fish and the surrounding environment in order to comply with United States regulations, but this can be particularly challenging for imported aquaculture products, or for domestic producers that lack the means to do the requisite testing (FAO, 1997).

A typical approach of fish culturists wishing to use endocrine methods to reduce mortality in larviculture in the USA is to seek a limited-term exception, an Investigational New Animal Drug or INAD exemption. Direct applications of hormones in food production are prohibited, even though the chance of residual thyroid hormones from larval treatments is negligible. Thyroid hormones deposited in egg yolk disappear as yolk is consumed, and before endogenous production begins (e.g., see Greenblatt et al., 1989). Exogenously applied THs are metabolized shortly after hatching (e.g., see Tachihara et al., 1997). Material Safety Data Sheet (MSDS) hazard ratings are lower for Thyroxin, rated at zero for each of the four hazard categories, than those published for Vitamin C, for which two numerically-ranked categories of hazards are listed.

Some aquaculture-related efforts have been made to enhance maternal hormone synthesis and transfer of development-promoting hormones by environmental and dietary manipulations to promote endogenous production, with encouraging results (see Witt, 2008; Witt et al., 2009). A more

direct approach is the maternal injection of exogenous hormones; a cost-effective method that is favored where it can be used because a single, simple procedure can improve the egg quality of an entire cohort (Tagawa, 1996). For practical reasons, many advances involving applications of TH in larval fish culture have occurred in countries other than the United States. In Japan, maternal T_3 injections increased the survival of larval amberjack, *Seriola ialandi*, by four-fold, with production-scale application in an aquaculture center (Tachihara et al., 1997). Maternal T_3 injections of the viviparous Korean rockfish *Sebastes schlegeli*, improved growth and survival sufficiently to provide “a distinct advantage on the enhancement of seedling productivity...” (Kang and Chang, 2004, p. 652). The larval development of numerous cultured fish species has been accelerated or improved by thyroid hormone supplementation (reviewed by Tagawa, 1996; see Table 1), and many of the beneficial effects can be seen in desirable but difficult-to-culture marine species that produce small eggs and altricial larvae.

The larvae of several freshwater fishes of South America with strong aquaculture potential have also responded favorably to experimental thyroid supplementation, including the pintado, *Pseudoplatystoma coruscans* and the dourado *Salminus maxillosus* (Landines Parra, 2003), the matrinxã, *Brycon amazonicus* (Urbinati et al., 2008; Leonardo et al., 2013), and the piracanjuba, *Brycon orbignyanus* (Landines et al., 2010).

The matrinxã, *Brycon amazonicus*, and the piracanjuba, *Brycon orbignyanus*, are omnivorous fishes that present low survival rates and intense cannibalism during the earlier stages of development in captivity (Senhorini et al., 1998). Supplementation of T_3 was tested in both species either by maternal injection or egg immersion. A study comparing the larval performance of matrinxã after maternal T_3 injection or egg immersion of T_3 showed that both routes of T_3 administration stimulated the early growth of larvae of this species, but earlier effects were documented when broodstock females were injected. Larvae from T_3 -injected females had increased length after hatching and higher weight from 24 h after hatching, while the length of larvae produced from T_3 -immersed eggs exceeded the control values from 6 days and weight from 8 days (Urbinati et al., 2008). More recently, Leonardo et al. (2013) demonstrated that newly-hatched larvae were significantly heavier when eggs were immersed in T_3 and this effect persisted until 12 days post-hatch when larvae were transferred to earthen tanks in the routine of the farming of this fish. Larval survival increased following the hormone treatments, from 26.5% in the control group to approximately 40% in groups treated with T_3 . Cannibalism was not affected by the treatments. The higher weight of T_3 -supplemented larvae at hatching may have contributed to the improvement in the survival rate. Previously, Urbinati et al. (2003) showed that maternally administered T_3 significantly improved the survival of matrinxã, probably as a result of reduced cannibalism. Treated larvae grew more than control specimens up to 6 days post-hatch and had similar weight at 9 days but at 12–18 days

the control group showed higher growth compared to the treated group. Heterogeneous growth in control larvae may have resulted in an increase in the rate of cannibalism, which accelerates growth and could account for the lower survival rate (21.8%) compared with the hormone-treated group (61.6%).

Triiodothyronine (T_3) has also been demonstrated to promote organogenesis in developing matrinxã as seen in accelerated muscle hypertrophy in larvae developing from eggs exposed to the hormone. Those larvae presented larger transverse section area of the muscle fibers than untreated control larvae at 54 hr after hatching (Vasques, 2003). Moreover, T_3 also promoted the development of components of the larval digestive system. Larvae from T_3 -treated groups showed the digestive lumen partially at 18 hr after hatching and, at 30 hr, it was observed that the mucus layers of the stomachs of treated larvae were more highly organized than those of control larvae. At 54 hr, in treated larvae the number of vilosities in the mucus layer was higher than those of the control larvae, and they also presented vacuolus cells among those forming the stomach mucus layer. Only liver tissue of larvae from the T_3 treatments had cells organized in parallel strings.

The supplementation of the matrinxã larvae diet with tyrosine, precursor for the biosynthesis of THs, also showed positive results in the early larval development of this species (Hoshihira, 2007). Dietary tyrosine enrichment (5.39 g/100 g diet—2.4 times the amount of the commercial diet) promoted higher growth in terms of both weight and length, reduced cannibalism and enhanced larval survival.

In the piracanjuba, which has recently been listed as an endangered species (Fundação Biodiversitas, 2003), T_3 increased the survival to 15 days (Landines et al., 2010), without affecting growth rate. In another study (Dr. Leonardo and E. Urbinati, Universidade Estadual Paulista, personal communication), T_3 immersion quadrupled the hatch rate compared with controls (to 858,890 from 204,020 respectively) and hormone-supplementation also produced significant increases in larval length and weight.

Thirty six hours after hatching larvae were transferred to aquaria and monitored up to the 9th day of rearing. The weight and length difference remained along the rearing period and survival was similar among larvae from all treatments. Two carnivorous fish species were also investigated in the same laboratory, the dourado, *Salminus maxillosus*, and the pintado, *Pseudoplatystoma coruscans* (Landines Parra, 2003). In both species, fertilized eggs immersed in T_3 solutions did not show significant changes in larval growth, but had dramatic improvements in rates of survival (21% for dourado and 23% for pintado).

CONCLUDING REMARKS

Maternal TH supplementation alone or in combination with cortisol can confer distinct developmental advantages to

larvae, and has the potential to dramatically enhance fingerling survival and hatchery production rates (Tables 1 and 2). This appears to reflect an evolutionary mechanism in which maternally derived endocrine signals stimulate embryogenesis and thereby convey survival value through the critical time of first-feeding, and it has potential applicability as a means of improving production in the mass culture of fishes with large numbers of small, delicate larvae. Perceived and perhaps legitimate hazards of thyroid and glucocorticoid hormone applications in aquaculture are the subject of legal and public opinion based concerns.

ACKNOWLEDGMENTS

Sincere thanks are expressed to Dr. Masatomo Tagawa at Kyoto University and to Emeritus Professor Lam at the National University of Singapore for their thoughtful and constructive reviews of this manuscript.

FUNDING

This work was partly supported by the Special Fund for Agro-scientific Research in the Public Interest (201403008) of the People's Republic of China.

REFERENCES

- Ali, M. A. Effect of thyroxine plus thiourea on the early development of the chum salmon (*Oncorhynchus keta*). *Nature* **191**: 1214–1215 (1961).
- Arjona, F. J., L. Vargas-Chacoff, M. P. Martin del Rio, G. Flik, and J. M. Mancera. Effects of cortisol and thyroid hormone on peripheral outer ring deiodination and osmoregulatory parameters in the Senegalese sole (*Solea senegalensis*). *J. Endocrinol.*, **208**: 323–330 (2011).
- Ayson, F. G., E. G. de Jesus, S. Moriyama, S. Hyodo, B. Funkenstein, A. Gertler, and H. Kawauchi. Differential expression of insulin-like growth factor I and II mRNAs during embryogenesis and early larval development in rabbitfish, *Siganus guttatus*. *Gen. Comp. Endocrinol.*, **126**(2): 165–174 (2002).
- Ayson, F. D., and T. J. Lam. Thyroxine injection of female rabbitfish *Siganus guttatus* broodstock: Changes in thyroid hormone levels in plasma, eggs, and yolk-sac larvae, and its effect on larval growth and survival. *Aquaculture*, **109**: 83–93 (1993).
- Ballard, P. L. Hormonal influences during fetal lung development. *Ciba Found Symp.*, **78**: 251–274 (1980).
- Ban, M. Synergistic effects of thyroxine and cortisol on the seawater tolerance of sockeye salmon (*Oncorhynchus nerka*). research note. *Bull. Natl. Salmon Resour. Cent.*, **7**: 117–121 (2005).
- Bern, H. A. The “new” endocrinology: Its scope and its impact. *Am. Zool.*, **30**: 877–885 (1990).
- Bern H. A. The development of the role of hormones in development—A double remembrance. *Endocrinology*, **131**: 2037–2038 (1992).
- Bernardo, J. Maternal effects in animal ecology. *Am. Zool.*, **36**(2): 83–105 (1996).

- Bohne, M. and J. Halloran. *Consumer Reports: Meat on Drugs*. June 2012. MeatWithoutDrugs.org, Yonkers, NY (2012).
- Bonett, R. M., E. D. Hoopfer, and R. J. Denver. Molecular mechanisms of corticosteroid synergy with thyroid hormone during tadpole metamorphosis. *Gen. Comp. Endocrinol.*, **168**(2): 209–219 (2010).
- Brinn, R. P., J. L. Marcon, D. M. McComb, L. C. Gomes, J. S. Abreu, and B. Baldisseroto. Stress responses of the endemic freshwater cururu stingray (*Potamotrygon cf. hystrix*) during transportation in the Amazon region of the Rio Negro. *Comp. Biochem. Physiol. A*: **162**(2): 139–145 (2012).
- Brooks, S., C. R. Tyler, and J. P. Sumpter. Egg quality in fish: what makes a good egg? *Rev. Fish. Biol. Fisher.*, **7**: 387–416 (1997).
- Brown, D. D. The role of thyroid hormone in zebrafish and axolotl development. *Proc. Natl. Acad. Sci. USA*, **94**: 13011–13016 (1997).
- Brown, C. L., and H. A. Bern. Hormones in early development, with special reference to teleost fishes, pp. 289–306. In: *Hormones in Development, Maturation, and Senescence of Neuroendocrine Systems. A Comparative Approach*. (Schreibman, M. P. and C. G. Scanes, Eds.). NY: Academic Press (1989).
- Brown, C. L., M. Cochran, S. Doroshov, and H. A. Bern. Enhanced survival in striped bass fingerlings after maternal triiodothyronine treatment. *Fish Physiol. Biochem.*, **7**(1–6): 295–299 (1988a).
- Brown, C. L., S. Doroshov, J. Núñez, C. Hadley, R. S. Nishioka, and H. A. Bern. Maternal triiodothyronine injections cause increases in swimbladder inflation and survival rates in larval striped bass, *Morone saxatilis*. *J. Exp. Zool.*, **248**: 168–176 (1988b).
- Brown, C. L., and B. G. Kim. Combined application of cortisol and triiodothyronine in the culture of larval marine finfish. *Aquaculture*, **135**: 79–86 (1995).
- Brown, C. L., D. M. Power, and J. M. Núñez. Disorders of Development in Fish, pp. 166–182. In: *Fish Disease and Disorders, Volume 2. Non-Infectious Disorders, Second Edition*. (Leatherland, J. K. and P. T. K. Woo, Eds.). Wallingford, UK: CAB International Press (2010).
- Burrow, G. N., D. Fisher, and P. R. Larsen. Maternal and fetal thyroid function. *N. Engl. J. Med.*, **331**: 1072 (1994).
- Callard, I. P., L. A. Fileti, L. E. Perez, L. A. Sorbera, G. Giannoukous, L. L. Klosterman, T. Paul, and J. A. McCracken. Role of the Corpus luteum and progesterone in the evolution of vertebrate viviparity. *Am. Zool.*, **32**(2): 264–275 (1992).
- Campbell, P. M., T. G. Pottinger, and J. P. Sumpter. Stress reduces the quality of gametes produced by rainbow trout. *Biol. Reprod.*, **47**: 1140–1150 (1992).
- Campbell, P. M., T. G. Pottinger, and J. P. Sumpter. Preliminary evidence that chronic confinement stress reduces the quality of gametes produced by brown and rainbow trout. *Aquaculture*, **120**: 151–169 (1994).
- Chambers, R. C., and W. C. Leggett. Maternal influences on variation in egg sizes in temperate marine fishes. *Am. Zool.*, **36**: 180–196 (1996).
- Conti, A., H. Studer, F. Kneubuehl, and H. Kohler. Regulation of thyroidal deiodinase activity. *Endocrinology*, **102**(1): 321–329 (1978).
- Cyr, D. G., and J. G. Eales. Interrelationships between thyroidal and reproductive endocrine systems in fish. *Rev. Fish Biol. Fisher.*, **6**: 165–200 (1996).
- Dales, S., and W. S. Hoar. Effects of thyroxine and thiourea on the early development of chum salmon (*Onchorhynchus keta*). *Can. J. Zool.*, **32**: 244–251 (1954).
- Darras, V. M., S. L. J. Van Herck, M. Heijlen, and B. DeGroef. Thyroid hormone receptors in two model species for vertebrate embryonic development: chicken and zebrafish. *J. Thyroid Res.*, Article ID 402320, **2011**(402320): 1–8 (2011).
- De Jesus, E. G., T. Hirano, and Y. Inui. Changes in cortisol and thyroid hormone concentrations during early development and metamorphosis in the Japanese flounder, *Paralichthys olivaceus*. *Gen. Comp. Endocrinol.*, **82**(3): 369–376 (1991).
- De Jesus, E. G., Y. Inui, and T. Hirano. Cortisol enhances the stimulating action of thyroid hormones on dorsal fin-ray resorption of flounder larvae in vitro. *Gen. Comp. Endocrinol.*, **79**: 167–173 (1990).
- De Nayer, P., B. Dozin, Y. Vandeput, F. C. Bottazzo, and J. Crabbe. Altered interaction between triiodothyronine and its nuclear receptors in absence of cortisol: a proposed mechanism for increased thyrotropin secretion in corticosteroid deficiency states. *Eur. J. Clin. Invest.*, **17**(2): 106–110 (1987).
- De Pablo, F., and J. Roth. Endocrinization of the early embryo: an emerging role for hormones and hormone-like factors. *Trends Biochem. Sci.*, **15**(9): 339–342 (1990).
- Deane, E. E., and N. Y. S. Woo. Ontogeny of thyroid hormones, cortisol, hsp70 and hsp90 during silver sea bream larval development. *Life Sciences*, **72**(7): 805–818 (2003).
- Dechiara, T. M., A. Efstratiadis, and E. J. Robertson. A growth-deficiency phenotype in heterozygous mice carrying an insulin-like growth factor II gene disrupted by targeting. *Nature*, **345**: 78–80 (1990).
- Dickhoff, W. W., C. L. Brown, C. V. Sullivan, and H. A. Bern. Fish and amphibian models for developmental endocrinology. *J. Exp. Zool.*, **4**: 90–97 (1990).
- Donaldson, E., U. H. M. Fagerlund, D. A. Higgs, and J. R. McBride. Hormonal enhancement of growth, pp. 455–597. In: *Fish Physiology, Volume VIII Bioenergetics and Growth*. (Hoar, W. S., D. J. Randall, and J. R. Brett, Eds.). San Diego: Academic Press (1979).
- Duarte, C. M., and M. Alcaraz. To produce many small or few large eggs: a size-independent reproductive tactic of fish. *Oecologia*, **80**: 401–404 (1989).
- Dussault, J. H. The anecdotal history of screening for congenital hypothyroidism. *J. Clin. Endocrinol. Metab.*, **84**(12): 4332–4334 (1999).
- Essner, J. J., J. J. Breuer, R. D. Essner, S. C. Fahrenkrug, and P. B. Hackett. The zebrafish thyroid hormone receptor alpha 1 is expressed during early embryogenesis and can function in transcriptional repression. *Differentiation*, **62**(3): 107–117 (1997).
- Fantz, C. R., S. Dagogo-Jack, J. H. Ladenson, and A. M. Gronowski. Thyroid function during pregnancy. *Clin. Chem.*, **45**(12): 2250–2258 (1999).
- FAO. Towards safe and effective use of chemicals in coastal aquaculture. Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection, GESAMP Reports and Studies No. 65, Rome: FAO. Available from http://www.jodc.go.jp/info/ioc_doc/GESAMP/r65e.pdf (1997).
- Farwell, A. P. Thyroid hormone therapy is not indicated in the majority of patients with the sick euthyroid syndrome. *Endocr. Pract.*, **14**(9): 1180–1187 (2008).
- Feist, G., and C. B. Schreck. Hormonal content of commercial fish diets and of young coho salmon (*Oncorhynchus kisutch*) fed these diets. *Aquaculture*, **86**(1): 63–75 (1990).
- Fundação Biodiversitas. Lista oficial da brasileira ameaçada de extinção. (2003) <http://www.biodiversitas2003.org.br>.

- Funkenstein, B., R. Shemer, R. Amuly, and I. Cohen. Nucleotide sequence of the promoter region of *Sparus aurata* insulin like growth factor I gene and expression of IGF-I in eggs and embryos. *Mol. Mar. Biol. Biotechnol.*, **5**:43–51 (1996).
- Gash, T. A. Seasonal thyroid activity in the bonnethead shark, *Sphyrna tiburo*. M.s. Thesis, Texas A. & M. University, College Station, Texas 77843 (2000).
- Geising, E. R., C. D. Suski, R. E. Warner, and A. M. Bell. Female sticklebacks transfer information via eggs: effects of maternal experience with predators on offspring. *Proc. Royal Soc. B: Biol. Sci.*, **278**(1712): 1753–1759 (2010).
- Greenblatt, M., C. L. Brown, M. Lee, S. Dauder, and H. A. Bern. Changes in thyroid hormone levels in eggs and larvae and in iodide uptake by eggs of coho and chinook salmon, *Oncorhynchus kisutch* and *O. tshawytscha*. *Fish Physiol. Biochem.*, **6**(5): 261–278 (1989).
- Greene, M. W., and T. T. Chen. Temporal expression pattern of insulin-like growth factor mRNA during embryonic development in a teleost, rainbow trout (*Oncorhynchus mykiss*). *Mol. Mar. Biol. Biotechnol.*, **6**: 144–151 (1997).
- Greene, M. W., and T. T. Chen. Quantitation of IGF-I, IGF-II, and multiple insulin receptor family member messenger RNAs during embryonic development in rainbow trout. *Mol. Reprod. Dev.*, **54**: 348–361 (1999).
- Gudernatsch, J. F. Feeding experiments on tadpoles. I. The influence of specific organs given as food on growth and differentiation. A contribution to the knowledge of organs with internal secretion. *Ach. Entwicklungsmech., Org.*, **35**: 457–481 (1912).
- Haddow, J. E., G. E. Palomaki, W. C. Allan, J. R. Williams, G. J. Knight, and J. Gagnon. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N. Engl. J. Med.*, **341**: 549–555 (1999).
- Hamlett, W. C. Ontogeny of the umbilical cord and placenta in the Atlantic sharpnose shark, *Rhizoprionodon terraenovae*. *Environ. Biol. Fishes*, **38**(1–3): 253–267 (1993).
- Hawkyard, M., Ø. Sæle, A. Nordgreen, C. Langdon, and K. Hamre. Effect of iodine enrichment of *Artemia* sp. on their nutritional value for larval zebrafish (*Danio rerio*). *Aquaculture*, **316**(1–4): 37–43 (2011).
- Higgs, D. A., U. H. M. Fagerlund, J. G. Eales, and J. R. McBride. Application of thyroid and steroid hormones as anabolic agents in fish culture. *Comp. Biochem. Physiol.*, **73B**: 143–176 (1982).
- Hildahl, J., D. M. Power, B. T. Björnsson, and I. E. Einarsdóttir. Involvement of growth hormone-insulin-like growth factor I system in cranial remodeling during halibut metamorphosis as indicated by tissue- and stage-specific receptor gene expression and the presence of growth hormone receptor protein. *Cell Tissue Res.*, **332**: 221–225 (2008).
- Honma, Y., and S. Murakawa. Effects of thyroxine and thiourea on the development of chum salmon larvae (*Oncorhynchus keta*). *Japan. J. Ichthyol.*, **4**: 83–93 (1955).
- Hoshihara, M. A. Enriquecimento da alimentação das larvas de matrinxã (*Brycon amazonicus*) com aminoácidos. Influência no crescimento inicial e sobrevivência das larvas. 102 p. Dissertação (Mestrado). Faculdade de Ciências Agrárias e Veterinárias, UNESP, Jaboticabal, São Paulo (2007).
- Howdshell, K. L. A model of the development of the brain as a construct of the thyroid system. *Environ. Health Perspect.*, **110**(Supplement 3): 337–348 (2002).
- Huang, L., J. L. Specker, and D. A. Bengtson. Effect of triiodothyronine on the growth and survival of larval striped bass (*Morone saxatilis*). *Fish Physiol. Biochem.*, **15**(1): 57–64 (1996).
- Hwang, P.-P., S.-W. Wu, J.-H. Lin, and L.-S. Wu. Cortisol content of eggs and larvae of teleosts. *Gen. Comp. Endocrinol.*, **86**: 189–196 (1992).
- Inui, Y., and S. Miwa. Thyroid hormone induces metamorphosis of flounder larvae. *Gen. Comp. Endocrinol.*, **60**(3): 450–454 (1985).
- Inui, Y., S. Miwa, K. Yamano, and T. Hirano. Hormonal control of flounder metamorphosis, pp. 408–411. In: *Perspectives in Comparative Endocrinology* (Davey, K. G., R. E. Peter, and S. S. Tobe, Eds.). Ottawa: National Research Council of Canada (1994).
- Johnson, B., and B. Bosworth. Investigational New Animal Drug (INAD) exemptions and the national INAD program (NIP). Southern Regional Aquaculture Program publication no. 4709. Available from: <https://srac.tamu.edu/index.cfm/event/getFactSheet/whichfactsheet/242/> (2012).
- Jones, J. L., and D. R. Clemmons. Insulin-like growth factors and their binding proteins: biological actions. *Endocr. Rev.*, **16**: 3–34 (1995).
- Kang, D.-Y., and Y. J. Chang. Effects of maternal injection of 3,5,3'-triiodo-L-thyronine (T₃) on growth of newborn offspring of rockfish, *Sebastes Schlegeli*. *Aquacul.*, **234**: 641–655 (2004).
- Karg, S. K. Effect of oral administration of L-thyroxine (T₄) on growth performance, digestibility, and nutrient retention in *Channa punctatus* (Bloch) and *Heteropneustes fossilis* (Bloch). *Fish Physiol. Biochem.*, **33**: 347–358 (2007).
- Kawauchi, H., and S. A. Sower. The dawn and evolution of hormones in the adenohypophysis. *Gen. Comp. Endocrinol.*, **148**(1): 3–14 (2006).
- Kenyon, P. R., R. G. Sherlock, and S. T. Morris. Are elevated maternal thyroid hormone concentrations after-mid-pregnancy shearing responsible for changes in lamb fleece characteristics? *Proc. N. Z. Soc. Animal. Prod.*, **64**: 272–276 (2004).
- Khalil, N., H. Allah, and M. Mousa. The effect of maternal thyroxine injection on growth, survival and development of the digestive system of Nile tilapia, *Oreochromis niloticus*, larvae. *Adv. Biosci. Biotechnol.*, **2**: 320–329 (2011).
- Kim, B. G., and C. L. Brown. Interaction of cortisol and thyroid hormone in the larval development of the Pacific threadfin. *Am. Zool.*, **37**: 468–479 (1997).
- Kim, B. G., and C. L. Brown. Hormonal manipulation of digestive enzyme ontogeny in marine larval fishes—Effects on digestive enzymes. Spawning and maturation of aquaculture species. US-Japan Natural Resources Panel, University of Hawaii Sea Grant Technical report # 28, pp. 47–55 (2000).
- Kobuke, L., J. L. Specker, and H. A. Bern. Thyroxine content of eggs and larvae of coho salmon. *Oncorhynchus kisutch*. *J. Exp. Zool.*, **242**: 89–94 (1987).
- Krug, E. C., K. V. Honn, J. Battista, and C. S. Nicoll. Corticosteroids in serum of *Rana catesbeiana* during development and metamorphosis. *Gen. Comp. Endocrinol.*, **52**(2): 232–241 (1983).
- Kühn, E. R., K. Mol, and V. M. Darras. Peripheral deiodination of thyroid hormones: Biological significance. *Neth. J. Zool.*, **45**(1–2): 135–139 (1994).
- Lam, T. J. Thyroxine induces larval development and survival in *Sarotherodon (Tilapia) mossambicus* Ruppel. *Aquaculture*, **21**: 287–291 (1980).

- Lam, T. J. Role of thyroid hormone on larval growth and development in fish, pp. 481–485. In: *Current Trends in Comparative Endocrinology* (Lofts, B. and W. N. Holmes, Eds.). Hong Kong: Hong Kong University Press (1985).
- Lam, T. J., J. V. Juario, and J. E. Banno. Effect of thyroxine on growth and development in post-yolk-sac larvae of milkfish, *Chanos chanos*. *Aquaculture*, **46**(3): 179–184 (1985).
- Lam, T. J., and G. L. Loy. Effect of l-thyroxine on ovarian development and gestation in the viviparous guppy, *Poecilia reticulata*. *Gen. Comp. Endocrinol.*, **60**(2): 324–330 (1985).
- Lam, T. J., and R. Sharma. Effects of salinity and thyroxine on larval survival, growth and development in the carp, *Cyprinus carpio*. *Aquaculture*, **44**: 201–212 (1985).
- Landines Parra, M. A. Efeito da triiodotironina (T₃) no desenvolvimento embrionário e no desempenho das larvas de pintado (*Pseudoplatystoma fasciatum*), piracanjuba (*Brycon orbignyanus*) e dourado (*Salminus maxilloso*). 146 p. Tese (Doutorado) - Centro de Aqüicultura da UNESP, Jaboticabal, São Paulo, Brasil (2003).
- Landines, M. A., A. I. Sanabria, J. A. Senhorini, and E. C. Urbinati. The influence of triiodothyronine (T₃) on the early development of the piracanjuba (*Brycon orbignyanus*). *Fish Physiol. Biochem.*, **36**: 1292–1296 (2010).
- Lebeau, S. O., and S. J. Mandel. Thyroid disorders during pregnancy. *Endocrinol. Metab. Clin. North Am.*, **35**(1): 117–136 (2006).
- Leggett, W. C., and E. Deblois. Recruitment in marine fishes—Is it regulated by starvation and predation in the egg and larval stages. *Neth. J. Sea Res.*, 119–134 (1994).
- Leonardo, A. F. G., M. A. Márcio Aquio Hoshiba, E. C. Urbinati, and J. A. José Augusto Senhorini. Improvement of matrinxã, *Brycon amazonicus*, larviculture by exposing eggs to triiodothyronine. *J. World Aquacult. Soc.*, **44**(1): 141–147 (2013).
- Leung, L. Y., A. K. Kwong, A. K. Man, and N. Y. Woo. Direct actions of cortisol, thyroxine and growth hormone on IGF-I mRNA expression in sea bream hepatocytes. *Comp. Biochem. Physiol. A Mol. Integr. Physiol.*, **151**: 705–710 (2008).
- Li, M., D. Bureau, W. A. King, and J. F. Leatherland. The actions of *in ovo* cortisol on egg fertility, embryo development and the expression of growth related genes in rainbow trout embryos, and the growth performance of juveniles. *Mol. Reprod. Dev.* **77**: 922–931 (2010).
- Liu, Y. W., and W. K. Chan. Thyroid hormones are important for embryonic to larval transitory phase in zebrafish. *Differentiation*, **70**(1): 36–45 (2002).
- Mathiyalagan, A., P. K. Reddy, and T. J. Lam. Effects of cortisol on growth and development in tilapia larvae, *Oreochromis mossambicus*. *Fish Physiol. Biochem.*, **15**(6): 453–458 (1996).
- McComb, D. M., J. Gelsleicher, C. A. Manire, R. Brinn, and C. L. Brown. Comparative thyroid hormone concentration in maternal serum and yolk of the bonnethead shark (*Sphyrna tiburo*) from two sites along the coast of Florida. *Gen. Comp. Endocrinol.*, **144**: 167–173 (2005).
- McCormick, M. I. Behaviorally induced maternal stress in a fish influences progeny quality by a hormonal mechanism. *Ecology*, **79**(6): 1783–1883 (1998).
- McCormick, M. I. Experimental test of the effect of maternal hormones on larval quality of a coral reef fish. *Oecologia*, **118**: 412–422 (1999).
- Miwa, S., and Y. Inui. Effects of L-thyroxine and ovine growth hormone on smoltification of amago salmon (*Oncorhynchus rhodurus*). *Gen. Comp. Endocrinol.*, **58**(3): 436–442 (1985).
- Miwa S., and Y. Inui. Effects of various doses of thyroxine and triiodothyronine on the metamorphosis of flounder (*Paralichthys olivaceus*). *Gen. Comp. Endocrinol.*, **167**(3): 356–363 (1987).
- Miwa, S., M. Tagawa, Y. Inui, and T. Hirano. Thyroxine surge in metamorphosing flounder larvae. *Gen. Comp. Endocrinol.*, **70**: 158–163 (1988).
- Mommsen, T. P. and P. J. Walsh. Vitellogenesis and oocyte assembly, pp. 347–406. In: *The Physiology of Developing Fish: Eggs and Larvae* (Hoar, W. S. and D. J. Randall, Eds.). NY: Academic Press (1988).
- Mylonas, C. C., C. V. Sullivan, and J. M. Hinshaw. Thyroid hormones in brown trout (*Salmo trutta*) reproduction and early development. *Fish Physiol. Biochem.*, **13**: 485–493 (1994).
- Nacario, J. F. The effect of thyroxine on the larvae and fry of *Sarotherodon niloticus* L. *Tilapia nilotica*. *Aquaculture*, **34**: 73–83 (1983).
- Nayak, P. K., C. T. Mahapatra, J. Mishra, and T. K. Mishra. Effect of treatment of eggs with thyroxin and cortisol on larval morphometry and survival in the freshwater carp, *Catla catla* (Ham.). *Indian J. Fish.*, **47**(4): 337–342 (2000a).
- Nayak, P. K., T. K. Mishra, and J. Mishra. Combined application of cortisol and thyroxin in the culture of larvae of freshwater catfish, *Heteropneustes fossilis*. *J. Aquacult. Trop.*, **15**(4): 323–328 (2000b).
- Nayak, P. K., T. K. Mishra, and S. Ayyappan. Effect of thyroxin and cortisol on the hatching of eggs, larval morphometry and survival of *Heteropneustes fossilis* (Bloch) larvae. *Indian J. Fish.*, **50**(2): 223–230 (2003).
- Nayak, P. K., B. B. Satpathy, T. K. Mishra, and S. Ayyappan. Thyroid hormone dynamics during early development in freshwater catfish, *Heteropneustes fossilis* (Bloch). *Indian J. Fish.*, **48**(4): 403–408 (2001).
- Nesan, D. *The Role of Glucocorticoid Receptor Signaling in Zebrafish Development*. PhD Dissertation, University of Waterloo, Ontario, Canada. 314 pp. (2013).
- Norris, D. O. *Vertebrate Endocrinology. Fourth Edition*, 550 pp., Amsterdam: Academic Press (Elsevier) (2007).
- Orozco, A., and R. C. Valverde. Thyroid hormone deiodination in fish—A review. *Thyroid*, **15**(8): 799–813 (2005).
- Osborn, D. A. Thyroid hormones for preventing neurodevelopmental impairment in preterm infants. *Cochrane Database Syst. Rev.*, **4**: CD001070 (2001).
- Patel, J., K. Landers, H. Li, R. H. Mortimer, and K. Richard. Thyroid hormones and fetal neurological development. *J. Endocrinol.*, **209**: 1–8 (2011).
- Pierce, A. L., J. P. Breves, S. Moriyama, T. Hirano, and E. G. Grau. Differential regulation of Igf1 and Igf2 mRNA levels in tilapia hepatocytes: effects of insulin and cortisol on GH sensitivity. *J. Endocrinol.*, **211**(2): 201–210 (2011).
- Pierce, A. L., J. T. Dickey, L. Felli, P. Swanson, and W. W. Dickhoff. Metabolic hormones regulate basal and growth hormone-dependent IGF2 mRNA level in primary cultured coho salmon hepatocytes: effects of insulin, glucagon, dexamethasone, and triiodothyronine. *J. Endocrinol.*, **204**(3): 331–339 (2010).

- Power, D. M., L. Llewellyn, M. Faustino, M. A. Nowell, B. T. Björnsson, I. E. Einarsdottir, A. V. M. Canario, and G. E. Swee-ney. Thyroid hormones in growth and development of fish. *Comp. Biochem. Physiol. C Toxicol Pharmacol.* **130**(4): 447–459 (2001).
- Rajatapiti, P., M. K. Kester, R. R. de Krijger, R. Rottier, T. J. Visser, and D. Tibboel. Expression of glucocorticoid, retinoid, and thyroid hormone receptors during human lung development. *J. Clinical Endocrinol. Metabol.*, **90**(7): 4309–4314 (2005).
- Rao, T. R. Ecological and ethological perspectives in larval fish feeding, pp. 145–178. **In:** *Sustainable Aquaculture: Global Perspectives* (Jana, B. B. and C. D. Webster, Eds.). Binghamton, IL: Food Products Press (2003).
- Redding, J. M., R. Patiño, and C. B. Schreck. Cortisol effects on plasma electrolytes and thyroid hormones during smoltification in Coho salmon (*Oncorhynchus kisutch*). *Gen. Comp. Endocrinol.*, **81**: 373–382 (1991).
- Reddy, P. K., and T. J. Lam. Effect of thyroid hormones on the morphogenesis and growth of larvae and fry of telescopic-eye black goldfish, *Carassius auratus*. *Aquaculture*, **107**: 383–394 (1992a).
- Reddy, P. K., and T. J. Lam. Role of thyroid hormones in tilapia larvae (*Oreochromis mossambicus*): I. Effects of the hormones and an antithyroid drug on yolk absorption, growth and development. *Fish Physiol. Biochem.*, **9**(5–6): 473–485 (1992b).
- Robertson, O. H. Production of the silvery smolt stage in rainbow trout by intramuscular injection of mammalian thyroid extract and thyrotropic hormone. *J. Exp. Zool.*, **110**(3): 337–355 (1949).
- Sampath-Kumar, R., A. D. Munro, J. Lee, and T. J. Lam. Exogenous cortisol promotes survival of Asian seabass (*Lates calcarifer*) hatchlings exposed to hypersalinity but not hyposalinity shock. *Aquaculture*, **11b**(2–3): 247–255 (1993).
- Sanders, E. J., and S. Harvey. Peptide hormones as developmental growth and differentiation factors. *Dev. Dyn.*, **237**(6): 1537–1552 (2008).
- Schmid, A. C., I. Lutz, W. Kloas, and M. Reinecke. Thyroid hormone stimulates hepatic IGF-I mRNA expression in a bony fish, the tilapia *Oreochromis mossambicus*, *in vitro* and *in vivo*. *Gen. Comp. Endocrinol.*, **130**: 129–134 (2003).
- Senhorini, J. A., F. L. M. Mantelatto, and S. M. C. Casanova. Growth and survival of larvae of Amazon species “matrinxã,” *Brycon cephalus* (Pisces, Characidae), in larviculture ponds. *Boletim Técnico CEPTA*, **11**: 13–28 (1998).
- Shinobu, N., and Y. Mugiya. Effects of ovine prolactin, bovine growth hormone and triiodothyronine on the calcification of otoliths and scales in the hypophysectomized goldfish *Carassius auratus*. *Fish. Sci.*, **61**: 960–963 (1995).
- Shkil, F. N., V. B. Borisov, B. Abdissa, and S. V. Smirnov. Role of thyroid hormone in the ontogeny and morphological diversification of *Barbus intermedius sensu* Banister, 1973 of Lake Tana in Ehtio- pia. *Russ. J. Dev. Biol.*, **41**(6): 369–380 (2010).
- Smith, B. T., and K. Sabry. Glucocorticoid-thyroid synergism in lung maturation: A mechanism involving epithelial-mesenchymal interaction. *Proc. Natl. Acad. Sci. U. S. A.* **80**: 1951–1954 (1983).
- Solbakken, J. S., M. H. G. Berntessen, B. Norberg, K. Pittman, and K. Hamre. Different iodine and thyroid hormone levels between Atlantic halibut larvae fed wild zooplankton or *Artemia* from first exogenous feeding until post metamorphosis. *J. Fish. Biol.*, **61**: 1345–1362 (2002).
- Sri Pudju, R. R., S. Dewi, and M. Zairin. Effect of triiodothyronine and cortisol on development, growth and survival rate of sand goby (*Oxyeleotris marmorata* Blkr.) larvae. *Jurnal Akuakultur Indonesia*, **1**(1): 15–20 (2002).
- Swain, S. K., and P. K. Sahoo. Effects of feeding triiodothyronine on growth, food conversion and disease resistance of goldfish, *Carassius auratus* (Linn.). *Asian Fisheries Science*, **16**: 291–298 (2003).
- Szisch, V., N. Papandroulakis, E. Fanouraki, and M. Pavlidis. Ontogeny of the thyroid hormones and cortisol in the gilthead sea bream, *Sparus aurata*. *Gen. Comp. Endocrinol.*, **142**: 186–192 (2005).
- Szkudlinski, M. W., W. Mariusz, V. Fremont, C. Ronin, and B. D. Weintraub. Thyroid-stimulating hormone and thyroid-stimulating hormone receptor structure-function relationships. *Physiol. Rev.*, **82**(2): 473–502 (2002).
- Tachihara, K., M. K. Zibdeh, A. Ishimatsu, and M. Tagawa. Improved seed production of goldstriped amberjack *Seriola lalandi* under hatchery conditions by injection of triiodothyronine (T_3) to broodstock fish. *J. World Aquacult. Soc.*, **28**(1): 34–44 (1997).
- Tagawa, M. Current understanding of the presence of hormones in fish eggs, pp. 27–38. **In:** *Survival Strategies in Early Life Stages of Marine Resources* (Watanabe, Y., Y. Yamashita, and Y. Oozeki, Eds.). Rotterdam: A. Balkema (1996).
- Tagawa, M., and T. Hirano. Presence of thyroxine in eggs and changes in its content during early development of chum salmon, *Onchorhynchus keta*. *Gen. Comp. Endocrinol.*, **68**: 129–135 (1987).
- Tagawa, M., and T. Hirano. Effects of thyroid-hormone deficiency in eggs on early development of the medaka, *Oryzias latipes*. *J. Exp. Zool.*, **257**: 360–366 (1990).
- Tagawa, M., S. Miwa, Y. Inui, E. G. de Jesus, and T. Hirano. Changes in thyroid hormone concentrations during early development and metamorphosis of the flounder, *Paralichthys olivaceus*. *Zool. Sci.*, **7**: 93–96 (1991).
- Tanaka, M., J. B. Tanangonana, E. G. de Jesus, M. Tagawa, H. Nishida, R. Isaka, R. Kimura, and T. Hirano. Development of the pituitary, thyroid and interrenal glands and applications of endocrinology to the improved rearing of marine fish larvae. *Aquaculture*, **135**(1–3): 111–126 (1995).
- Terrien, X., and P. Prunet. *Crossregulation of the Thyroid Hormone and Corticosteroids in Amphibians and Fish: The Effects of Endocrine Disruption, Insights from Veterinary Medicine* (Dr. Rita Payan Carreira, Ed.). ISBN: 978-953-51-1005-7, InTech, (2013) DOI: 10.5772/54314. Available from <http://www.intechopen.com/books/insights-from-veterinary-medicine/crossregulation-of-the-thyroid-hormone-and-corticosteroids-in-amphibians-and-fish-the-effects-of-end>
- Uller, T., and M. Olsson. Direct exposure to corticosterone during embryonic development influences behavior in an ovoviparous lizard. *Ethology*, **112**: 390–397 (2006).
- Urbinati, E. C., M. C. F. Soares, and J. A. Senhorini. Preliminary study of the effect of maternal triiodothyronine on early development of matrinxã *Brycon cephalus* (Characidae). *J. Aquacult. Trop.*, **18**: 217–224 (2003).
- Urbinati, E. C., L. H. Vasques, J. A. Senhorini, V. L. Souza, and F. D. Gonçalves. Larval performance of matrinxã, *Brycon amazonicus* (Spix & Agawssiz 1829), after maternal triiodothyronine injection or egg immersion. *Aquacult. Res.*, **39**: 1355–1359 (2008).

- Vasques, L. H. Participação do hormônio triiodotironina (T_3) no desenvolvimento inicial do matrinxã *Brycon cephalus*. 146 p. Tese (Doutorado)—Centro de Aquicultura da UNESP, Jaboticabal, São Paulo, Brasil (2003).
- Vijayan, M. M., P. A. Flett, and J. F. Leatherland. Effect of cortisol on the *in vitro* hepatic conversion of thyroxine to triiodothyronine in brook charr (*Salvelinus fontinalis* Mitchell). *Gen. Comp. Endocrinol.*, **70**(2): 312–318 (1988).
- Volkoff, H., J. P. Wourms, E. Amesbury, and F. Snelson. Structure of the thyroid gland, serum thyroid hormones, and the reproductive cycle of the Atlantic stingray, *Dysatus sabina*. *J. Exp. Zool.* **284**: 505–516 (1999).
- Wada, H. Glucocorticoids: mediators of vertebrate ontogenetic transitions. *Gen. Comp. Endocrinol.*, **156**: 441–453 (2008).
- Wallis, M. Molecular evolution of the thyrotrophin-releasing hormone precursor in vertebrates: insights from comparative genomics. *J. Neuroendocrinol.*, **22**(6): 608–619 (2010).
- Walpita, C. N., S. Van der Geyten, E. Rurangwa, and V. M. Darras. The effect of 3,5,3'-triiodothyronine supplementation on zebrafish (*Danio rerio*) embryonic development and expression of iodothyronine deiodinases and thyroid hormone receptors. *Gen. Comp. Endocrinol.*, **152**(2–3): 206–214 (2007).
- Wang, Y., and S. Zhang. Expression and regulation by thyroid hormone (TH) of zebrafish IGF-I gene and amphioxus IGF-I gene with implication of the origin of TH/IGF signaling pathway. *Comp. Biochem. Physiol. A Mol. Integr. Physiol.*, **160**: 474–479 (2011).
- Witt, E. M. Effects of broodstock diet and environmental iodide concentrations on larval growth, survival, egg and whole body concentration of thyroid hormones and cortisol in Pacific threadfin, *Polydactylus sexfilis*. M.S. Thesis, University of Hawaii, 83 pp. (2008).
- Witt, E. M., C. W. Laidley, K. M. Liu, T. Hirano, and E. G. Grau. Correlation between environmental iodide concentrations and larval growth, survival, and whole body concentrations of thyroid hormones and cortisol in Pacific threadfin (*Polydactylus sexfilis*). *Aquaculture*, **289**: 357–364 (2009).
- Wood, A. W., C. Duan, and H. A. Bern. Insulin-like growth factor signaling in fish. Review. *Int. Rev. Cytol.*, **243**: 215–285 (2005).
- Woodhead, A. D. Effects of thyroid drugs on the larvae of the brown trout, *Salmo trutta*. *J. Zool. (Lond.)*, **149**: 394–413 (1966).
- Wourms, J. P., and L. S. Demski. The reproduction and development of sharks, skates, rays, and ratfishes: introduction, history, overview, and future prospects, pp. 7–21. In: *The Reproduction and Development of Sharks, Skates, Rays, and Ratfishes* (Demski, L. S. and Wourms, J. P. Eds.). Dordrecht, The Netherlands: Kluwer Academic Publishers (1993).
- Wourms, J. P., and J. Lombardi. Reflections on the evolution of piscine viviparity. *Am. Zool.* **32**: 276–293 (1992).
- Youson, J. H. First metamorphosis, pp 135–196. In: *The Physiology of Developing Fish: B. Viviparity and Posthatching Juvenile* (Hoar, W. S. and D. J. Randall, Eds.). NY: Academic Press (1988).